Quality of life after oral and maxillofacial surgery procedures

Tuk, J.G.C.

Publication date
2023
Document Version
Final published version

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Printing: Proefschriftenprinten.nl, Print Service Ede

De omslag is door M.A.C. Tuk-Otten vervaardigd en beschikbaar gesteld

Financial support for printing and distibution of this thesis was kindly provided by:
ACTA
KNMT
NVMKA

ISBN/EAN: 978-90-833601-5-7

Quality of life after Oral and Maxillofacial Surgery procedures

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. ir. P.P.C.C. Verbeek
ten overstaan van een door het College voor Promoties ingestelde commissie,
in het openbaar te verdedigen in de Aula der Universiteit
op woensdag 6 september 2023, te 14.00 uur

door Jacques Gooyert Cornel Tuk
geboren te Hilversum

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Chapter 1

General introduction and outline of this thesis

General introduction and outline of this thesis

Within the Oral and Maxillofacial Surgery residency program, much emphasis is placed on the development of proficient surgical performance. A resident's skills are expected to meet the level and standard of an average surgeon, and procedural success is primarily measured based on technical outcomes. Many published studies investigate the biomedical outcomes of performed surgeries; however, increasing numbers of studies now report patients' quality of life (QoL) as a result measurement.[1] QoL is defined as a patient's perception of the impact of their disease or treatment, or both, on their daily life and their physical, psychological, and emotional well-being.[2] The measurement of postoperative QoL determines the impact of surgical procedures on the patient's change in everyday functioning activity, and degree of postoperative pain and discomfort.[3]

Dentoalveolar surgical procedures can result in inflammatory complications—such as pain, swelling, trismus, and infection—and many patients report negative impacts on lifestyle and oral function.[3] Therefore, in contemporary oral and maxillofacial surgery, main goals include the reduction of preoperative anxiety, pain-free surgical procedures, proper postoperative care, reduction of postoperative pain, and monitoring of any changes in quality of life.

As the majority of dentoalveolar procedures are performed with local anesthesia, dental injections are necessary to perform these surgical procedures. Mandibular block anesthesia is frequently used to achieve a pain-free procedure. In the Netherlands, many patients experience injection-related anxiety (16.1%), and a small proportion suffer from dental phobia (1%).[4, 5] These patients most likely fear the pain of the injection and the bodily injury.[6] Mandibular block injections are considered mildly painful, and the pain lasts only a few seconds for the majority of people. However, around 8% of patients experience the mandibular block injection as being very painful, rating it with a score of 7 or higher on the 11-point visual analog scale (VAS).[7] As such, many researchers have tested different techniques to reduce the pain and anxiety provoked by dental local anesthesia. Reported options include the preinjection use of local topical creams or sprays [8], or ice to dull the pain.[9]

Low-level laser/light therapy (LLLT), also known as photobiomodulation therapy [10], can be used to prevent postoperative pain, and improves local circulation and increases vasodilatation. LLLT may be beneficial for reducing pain during the administration of local anesthesia. With LLLT, patients receive a dose of low-laser light beams on the injections site, varying from 632 to 904 nm, prior to administration of local anesthesia. The precise mechanism underlying the effects of LLLT is not fully known, but the positive reported benefits include photobiomodulation of cellular proliferation, reduced oxidant radical formation, and improved tissue metabolism.[11] It is assumed that LLLT interrupts the pain-associated neurosensory pathway.[12] Moreover, it has been hypothesized that patients who receive a dental injection—e.g. local anesthesia or mandibular block anesthesia—would suffer less pain and anxiety following preinjectional treatment with LLLT.

The removal of third molars can have a great impact on patients, potentially leading to temporary pain, swelling of the cheek, trismus, feeding problems, and reduced activities of daily life. A large prospective study conducted in the United States of America assessed complications following the removal of 8,748 third molars. The reported complications included alveolar osteitis (7.4%), inferior alveolar nerve injury (1.6%), trismus (1.2%), and postoperative infection (1.1%) of the extraction site.[13]

Overall, the surgical removal of third molars will lead to a significant decrease in the oral health-related quality of life (OHRQoL), especially during the first 5 postoperative days.[14] Postoperative interventions to reduce inflammatory complications after third mandibular molar surgery include analgesics, antibiotics, corticosteroids, mouthwashes, topical gels, cryotherapy, and ozone therapy.[15] One well-known therapy to decrease postoperative sequelae after third molar removal is the application of a iodine tampon in the extraction site for a short postoperative period.[16] This drainage of the extraction site can lead to reduced pain, swelling of the cheek, trismus, and infections.[17] Another method for reducing postoperative surgical complications is the use of a Monoject syringe filled with tap water to irrigate the extraction wound after third molar removal, which results in significantly reduced postoperative alveolar osteitis and pain.[18]

In the current literature, there is an increased interest in reducing the risk of inferior alveolar nerve (IAN) damage, which can occur in about 1–3.6% of cases following surgical removal of the mandibular third molar. This damage can be permanent, resulting in persistent sensory loss of the lower lip and chin. Because the IAN runs deeply in the mandible, mostly apical on the lingual or buccal site, coronectomy has been described as an alternative treatment. In coronectomy, the crown of the wisdom tooth is removed and the non-mobile roots are left in place, thus avoiding any manipulation of or interaction with the IAN.[19-21] The main goal of this procedure is to prevent damage to the IAN when removing the wisdom tooth, located near the IAN. To date, studies of coronectomy have mainly focused on the technical procedure, postoperative root migration, and registration of any damage of the IAN. No studies have been performed to assess how coronectomy impacts postoperative OHRQoL in the first week after coronectomy, when it is expected that patients will experience the most discomfort.

Another frequent outpatient oral and maxillofacial procedure is periapical surgery, which is performed when endodontic orthograde retreatment fails to successfully eliminate a periapical infection.[22] The procedure causes swelling, discomfort, and pain, and will negatively influence the patient's OHRQoL especially in the first 48 hour.[23] To date, little information is available about patients' well-being after periapical surgery, but the number of studies is increasing. Additional measures might ameliorate the effects of periapical surgery, in terms of postoperative pain and OHRQoL, including the postoperative use of corticosteroids, or the use of platelet concentrates during surgery, but conflicting outcomes have been reported.[24, 25]

Dentofacial deformities are characterized by disharmony among the face and skeletal structures, and may have negative impacts on facial aesthetics and the stomatognathic system balance. Skeletal deformities can be associated with malocclusion and neuromuscular system imbalance, potentially leading to impairments of respiration, mastication, and phonation. Orthognathic surgery under general anesthesia is performed to correct facial asymmetries, including undergrowth or overgrowth of the jaws or chin. In the field of orthognathic surgery, many research studies have investigated quality of life, mostly using the OHIP-14 questionnaire.[26-33] However, there are no published data regarding the development of OHIP-14 scores during the first postoperative week.

Aims and outline of this thesis

The aim of this thesis was to obtain more information regarding anxiety, pain, and quality of life in relation to some oral and maxillofacial procedures. We initially performed two clinical studies on local dental injections.

In **Chapter 2**, to obtain further insight regarding the mechanism underlying this physiological response, we assessed patients' primary physiological processes (e.g. anxiety and previous experiences with mandibular block injections) and biological differences (greater sensitivity to pain resulting in a higher physiological response). We hypothesized that patients with a higher pain score (VAS > 7) had a greater physiologic response than patients with a lower pain score (VAS < 7).

In **Chapter 3**, we performed a double-blinded randomized controlled trial, in which we tested pre-injection low-level laser/light therapy (LLLT) prior to administering mandibular block or infiltration anesthesia for the removal of an upper or lower wisdom tooth. We hypothesized that patients undergoing local anesthesia or mandibular block procedures would benefit from LLLT performed prior to injection, in terms of reduced pain and anxiety. Subsequently, we investigated the experienced pain and the quality of life after the most common oral and maxillofacial surgical procedures.

In **Chapters 4–6**, we evaluated patients' oral health-related quality of life (OHRQoL) after mandibular third molar surgery. In **Chapter 4**, a prospective crossover randomized controlled study was performed to assess the efficacy of applying an iodine tampon after mandibular third molar surgery, in terms of OHRQoL, use of painkillers, postoperative sequela, and self-care behaviors during the first postoperative week. Patients with bilateral symmetrically horizontally impacted mandibular third molars were treated, and each surgical site was randomly allocated to receive either a iodine tampon at the surgical site or postoperative rinsing with a disposable syringe (Monoject®). In **Chapter 5**, patients with impacted mandibular third molars were randomly assigned to two groups: one group receiving an alveolar iodine-containing tampon in the extraction socket, and the other group using postoperative rinsing with a Monoject®. In **Chapter 6**, a prospective study was carried out

to assess OHRQoL in patients who underwent coronectomy for an impacted mandibular third molar.

Next, in **Chapter 7**, we investigated the effects of periapical surgery on pain and OHRQoL during the first post-operative week. Finally, we carried out a longitudinal study, over at least one year post-operatively, to investigate the quality of life of patients who underwent orthognathic surgery **(Chapter 8)**.

All of our findings are summarized in the general discussion in **Chapter 9**, where we also provide some guidance for future studies. **Chapter 10 and 11** presents the general summary of this thesis, in both English and Dutch.

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Chapter 2

Anxiety and pain related to mandibular block injections: Comparison of self-reported measures and physiological response

This chapter is based on the publication:
Anxiety and pain related to mandibular block injections: Comparison of self-reported measures and physiological response

J.G.C. Tuk, J.A.H. Lindeboom, L. Hoogendoorn, B.W. Taylor, A.J. van Wijk

Published: Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 2017

Abstract

Objective: The aim of this study was to determine whether patients with a pain score ≥7 (high pain group) after a mandibular block injection had a higher physiological response than patients with scores <7 (low pain group).

Study design: Prior to oral surgery, patients (n = 66) filled out questionnaires to measure anxiety and expected pain. Questionnaires also assessed the patients' experiences with dental injections and dental anxiety, as well as their emotional state and intensity of anxiety. Before, during, and after the injection, physiological responses were measured using the Nexus-10. Patients were then asked about the pain and anxiety they experienced.

Results: The mean score for pain experienced was 3.45 (SD 2.17) on an 11-point rating scale. Eight patients (12.1%) experienced high injection pain. There was a significant increase in mean sweat secretion and a significant decrease in mean respiration between the relaxing and injection phases. There was a significant positive relationship between experienced anxiety and mean heart rate during the injection phase. No significant difference was found in physiological response between patients who experienced high vs. low pain.

Conclusion: Reported pain was not associated with the physiological response of patients receiving mandibular block injections.

Introduction

Effective pain control is an important aspect of dental care and can be achieved with oral local anesthetic injections; however, the injections are not pain free and some patients are afraid of receiving local anesthesia.[1] In the Netherlands, an estimated 16.1% of patients report anxiety about injections and approximately 1% of the population suffers from injection phobia.[2] The two most common dimensions of oral injection fear are the pain of injection and bodily injury.[3] There are a number of factors associated with the pain caused by oral injections, such as gender, type of anesthetic fluid, amount of injection fluid, injection pressure[4], expertise of the operator, the location of the injection, and the methods of injection.[5] Other variables that are possibly related to pain as a result of oral injections are differences in needle gauge, temperature of the injection fluids, and mandibular block injection techniques. However, one study found that needle gauge is not related to the pain from oral injections.[6] In addition, results from another study[7] showed that differences in mandibular block injection techniques did not influence pain. Psychological factors, in particular anxiety, appear to play an important role in the perception of pain. It is well known that anxious people tend to feel more pain.[8] It is obvious that the relationship between anxiety and pain can also be found in dentistry.[9] According to earlier research[10,11], anxious people with negative experiences with oral injections appear to feel more pain during an oral injection.

Based on an earlier report[11], mandibular block injections can be considered mildly painful, with pain lasting only a few seconds for the majority of patients. A mean score of 2.4 was given for pain on an 11-point numerical rating scale (NRS). About 8% of patients experienced the mandibular block injection as very painful, with a score ≥7. It would be interesting to see whether this difference in perception is the result of primarily psychological processes (such as anxiety and previous experiences with dental injections) or can be accounted for by biological differences (more sensitivity to pain leading to a stronger physiological response).

Therefore, in the present study, pain from mandibular block injections was studied using psychological questionnaires and physiological responses (heart rate [HR], galvanic skin response [GSR], respiration [RSP], and blood oxygen

saturation [SpO_2]). The aim of this study was to determine whether a patient with an experienced pain score ≥7 (high pain group) on a NRS also experienced a higher physiological response compared with a patient with an experienced pain score <7 (low pain group).

Material and methods

Participants

Patients cared for at the Department of Oral and Maxillofacial Surgery of Amstelland Hospital (Amstelveen, The Netherlands) who required a mandibular block injection before treatment were eligible to participate in this study. Inclusion criteria were a minimum age of 15 years and a maximum age of 65 years; the ability to read, understand, and fill out questionnaires; and willingness to participate. Data collection took place from October 19, 2012 to December 12, 2012. The study was performed with the understanding and written consent of each subject and according to the ethical principles described in the Declaration of Helsinki. The research protocol was reviewed and approved by the medical ethical committee of the Free University of Amsterdam, The Netherlands (2012/336).

Expected and experienced pain and anxiety

Prior to the injection, patients were asked what level of anxiety they felt and what level of pain they expected. After the injection, patients were asked what level of anxiety and pain they experienced during the injection. Answers were given on an 11-point NRS. The scale for expected pain and experienced pain ranged from 0 (no pain) to 10 (worst possible pain), as did the scale for pre-operative anxiety and experienced anxiety (0 = not anxious, 10 = extremely anxious).

Experience with dental injections

To assess patients' previous experiences with oral injections, patients were asked to answers five different questions from the Dental Needle Experience questionnaire (DNE).[12] Answers were given on a 5-point answer scale.

Dental Anxiety Inventory

The S-DAI, which has been shown reliable and valid[13], was used to measure dental anxiety. The S-DAI is the short version of the Dental Anxiety Inventory and consists of nine questions, answered on a 5-point rating scale, ranging from 1 (not at all) to 5 (very well).

Profile of Mood States

The mood state of the patients was measured using the Profile of Mood States (POMS). The original POMS consisted of 65 items, which indicate six different types of changeable mood states: five negative mood states (tension, depression, anger, fatigue, and confusion) and one positive mood state (vigor).[14] Later, this was converted into five mood states.[15] The POMS short-form is a 32-item Dutch shortened version of the original POMS.[16] For each item, patients were asked to indicate to what extent the description fits with their feeling the moment before the oral injection. The different items were answered on a 5-point rating scale.

State-Trait Anxiety Inventory

The intensity of feelings of anxiety were measured using the State-Trait Anxiety Inventory (STAI) short-form.[17] This form has two subscales, one to measure the state of anxiety and one to measure the anxiety trait. For the STAI-state subscale, patients were asked to answer 20 statements about their emotional state at the moment before they were given an oral injection. These statements were rated on a 4-point rating scale ranging from 1 (not at all) to 4 (very much).

Physiological response

To measure the physiological response, the Nexus-10 was used. The Nexus-10 is a multi-channel physiological monitoring and feedback platform. The Nexus allows the simultaneous measurement of multiple physiological variables such as HR, RSP, temperature, GSR, oximetry, electromyography, electroencephalography, electrocardiography, and electrooculography, depending on which of the 10 sensor channels are used. The accompanying software, called Biotrace+, can be used for physiological monitoring, data analysis, signal processing, and clinical biofeedback-neurofeedback (Mind Media BV). In this study, the Nexus-10 was connected via Bluetooth to a laptop. The data were transmitted real-time to the program Biotrace+. The HR, GSR,

and RSP were registered. The SpO_2 was also registered with a pulse oxygen meter (CSI Criticare, model 506 DXN/SPO 2/Comfort Cuff, Firma Medicare).

Dental injection

All patients received a standardized mandibular block injection. The location, the temperature, the amount of anesthetic fluid (articaine/hydrochloride 40 mg with epinephrine 0.01 mg, 1.7-mL syringe Ultracain D-S forte, Sanofi-Aventis Netherlands BV, Gouda, The Netherlands) and type of needle (27 gauge/0.40 x 35 mm) were all standardized. One highly experienced oral and maxillofacial surgeon gave all the mandibular block injections.

Procedure

In the waiting room, eligible patients were informed about the present study and asked to participate. Participation was on a voluntary basis. On agreement, an informed consent form was signed. The patients were informed that the study consisted of two parts. The first part consisted of filling out questionnaires in the waiting room. Patients were told that during the second part they would be connected to sensors that registered physiological responses before, during, and after the injection. After being seated in the surgery room, patients were connected to the sensors of Nexus-10 and instructed to relax. At the moment of injection, a marker was placed in the Biotrace+ software. After the injection, the oral and maxillofacial surgeon left the room and the patients were asked to relax again for 30 s. After these 30 s, patients were asked what level of pain and anxiety they experienced during the injection (NRS).

Statistical analysis

The distribution of categorical variables was analyzed with the χ^2 test. Independent mean scores were compared with the independent-sample *t*-test and one-way ANOVA for more than two groups. The paired-samples t-test was used to compare dependent mean scores. Pearson's correlation coefficient was used as a measure of linear association. The level of significance was set at an alpha of 0.05.

Results

In total, 72 patients were eligible to participate. One patient opted out because she did not want to be disturbed. Three patients did not have sufficient understanding of the Dutch language and were, therefore, excluded. One patient did not receive an oral injection and one patient received a different local anesthetic. These patients were also excluded from analyses. A total of 66 patients were included in the study. Of the participants, 34 were male and 32 were female. The male and female participants were approximately the same mean age (mean 30.70 years SD 12.63), $t(64)=0.41$; $p=0.68$. Thirteen female patients reported when their last menstruation period started. The independent-samples t-test was used to determine if there was a difference in the mean experienced pain scores between the two female patients in the luteal phase and six female patients in the follicular phase, and a significant difference was found (luteal phase: mean 8.00 SD 0.00 vs. follicular phase: mean 3.67 SD 2.16), $t(6)=2.69$; $p=0.036$.

Pain and anxiety as a result of injection

The mean scores of pre-operative injection anxiety, expected injection pain, experienced anxiety, and experienced pain are presented in Table I. The mean score for experienced pain was 3.45 SD 2.17 on an 11-point NRS. The paired-samples t-test was used to determine the difference between expected and experienced injection pain. The mean expected pain was significantly higher than the experienced pain, $t(65)=5.22$; $p<0.01$. The independent-samples t-test showed no significant difference between the experienced pain mean scores from males (mean 2.97 SD 1.83) and females (mean 3.97 SD 2.40), $t(64)=-1.90$; $p=0.06$. Nineteen patients (28.8%) expected low injection pain. Only eight patients (12.1%) actually reported high injection pain. Two were males and six were females. Males and females were equally distributed across the low and high pain groups, $X^2(1)=2.56$; $p=0.11$.

A paired-samples t-test showed no significant difference between the pre-operative anxiety and experienced anxiety, $t(65)=1.69$; $p=0.10$. The independent-samples t-test showed a significant difference between the mean pre-operative anxiety scores of males (mean 3.76 SD 2.69) and females (mean 5.44 SD 2.70), $t(64)=-2.52$; $p=0.01$. Twenty-one (31.8%) patients had

pre-operative anxiety scores in the range of 7-10; yet, only 15 (22.7%) patients experienced anxiety in a range of 7-10. There was no significant relationship between gender and pre-operative anxiety scores between 7-10 or below, $X^2(1)=2.22$; p=0.14.

Table 1: Mean scores, standard deviation, and score distribution for anxiety and pain intensity.

	Mean	SD	NRS 0-6	NRS 7-10
Pre-operative anxiety	4.58	2.80	68.2%	31.8%
Expected injection pain	4.73	2.44	71.2%	28.8%
Experienced anxiety	4.02	2.93	77.3%	22.7%
Experienced injection pain	3.45	2.17	87.9%	12.1%

NRS, Numerical rating scale; SD, standard deviation.

Physiological response

The GSR data for two patients were discarded from analyses because the scores were more than 3 times SD above the mean score. To be able to analyze the results of the physiological response, four phases and two markers were distinguished (Figure I). Phase 1 was the relax-phase without the oral and maxillofacial surgeon present in the operation room. Phase 2 was the relax-phase while the oral and maxillofacial surgeon was in the operation room. Between phase 1 and phase 2, a marker (oral and maxillofacial surgeon) was placed when the oral and maxillofacial surgeon entered the room. Phase 3 started when the operation chair went down until the moment of injection. This moment was marked with "injection" and phase 4 consisted of the oral injection. Mean scores from the physiological response are presented in Table II. Pearson's correlation coefficient was used to determine the associations between pre-operative anxiety, expected injection pain, experienced anxiety, and experienced injection pain and the physiological response for phases 2 and 4 (Table 3). There was a significant positive relationship between experienced anxiety and the HR in phase 4, r = 0.30 (n=66); P= 0.01.

Table 2: Mean scores physiological response.

	GSR			RSP			HR		
Phase	Mean	SD	N	Mean	SD	N	Mean	SD	N
1	10.32	4.98	30	21.40	6.95	31	86.81	13.69	31
2	10.98	6.58	64	22.35	6.22	66	85.64	14.60	66
3	12.06	8.40	64	22.61	7.34	66	88.98	14.37	66
4	16.15	11.67	64	20.14	5.47	66	83.35	15.85	66

GRS, galvanic skin response; RSP, respiration; HR, heart rate; SD, standard deviation.

Table 3: Pearson's correlation coefficients between pain, anxiety, and physiological responses for phase 2 and 4.

		1	2	3	4	5	6	7
1	Experienced pain							
2	Experienced anxiety	0.54**						
3	GSR phase 2	-0.19	-0.08					
4	RSP phase 2	-0.21	-0.14	0.04				
5	HR phase 2	0.07	0.20	0.08	0.16			
6	GSR phase 4	-0.07	0.01	0.85**	-0.09	0.13		
7	RSP phase 4	-0.22	-0.20	0.01	0.18	-0.06	0.01	
8	HR phase 4	0.07	0.30*	0.01	-0.05	0.78**	0.21	-0.08

**= $p<0.01$

* = $p<0.05$

GSR, galvanic skin response; HR, heart rate; RSP, respiration.

Experienced pain and physiological response

A significant increase in mean sweat secretion values (mean difference 5.17 SD 7.01, $t(63)=5.90$; $p<0.01$) and a significant decrease in mean RSP values (mean difference -2.28 SD 7.52, $t(65)=-2.40$; $p=0.02$) were found between the relax-phase and the oral injection. There was no significant difference in mean HR values ($t(65)=-1.84$; $p=0.07$). The independent-samples t-test was used to determine if there was a difference in physiological response (phase 2 and phase 4) between patients who had a low pain response score and those with a high pain response score. Mean scores of the physiological response are presented in Table III. There was no significant difference between the two pain groups for the physiological response.

For 35 patients, the oral and maxillofacial surgeon was already present in the operation room. For the other 31 patients, the oral and maxillofacial surgeon entered the operation room when the patient had already been seated in the operation chair. This allowed analysis of whether or not the presence of the oral and maxillofacial surgeon had any effect or influence on the physiological arousal of patients. A paired-samples t-test was used to determine an increase or decrease in physiological response between phase 1 and 2. There was a significant increase in the mean sweat secretion values between phase 1 and phase 2 (mean difference 1.65 SD 2.31, $t(29)=3.92$; $p<0.01$), but no significant differences in mean RSP values ($t(30)=0.59$; $p=0.56$) or mean HR values ($t(30)=1.84$; $p=0.08$). The independent-samples t-test was used to determine if there was a difference in phase 2 between the 31 patients whose oral and

maxillofacial surgeon entered the operation room at a later stage and the 35 patients whose oral and maxillofacial surgeon was already present in the operation room. The mean HR in phase 2 was significantly higher when the oral and maxillofacial surgeon entered the room at a later stage (mean 90.37 SD 13.60) compared with when the oral and maxillofacial surgeon was already present in the operation room (mean 81.46 SD 14.36), t(64)=2.58; p=0.01.

Table 4: Mean scores physiological response from the two groups of the experienced injection pain.

	Experienced injection pain					
	<7			7-10		
	Mean	SD	N	Mean	SD	N
GSR phase 2	11.27	6.90	56	8.97	3.14	8
GSR phase 4	16.47	12.36	56	13.89	4.40	8
Δ GSR	5.20	7.44	56	4.92	2.65	8
RSP phase 2	22.57	6.36	58	20.75	5.15	8
RSP phase 4	20.30	5.32	58	18.97	6.74	8
ΔRSP	-2.28	7.76	58	-1.78	5.84	8
HR phase 2	85.62	14.74	58	85.83	14.54	8
HR phase 4	83.04	15.80	58	85.56	17.12	8
ΔHR	-2.58	10.30	58	-0.27	9.07	8

GSR, galvanic skin response; HR, heart rate; RSP, respiration; SD, standard deviation

Pain, anxiety, and mood states

Pearson's correlation coefficient was used to determine the association between pre-operative anxiety, expected injection pain, experienced anxiety, experienced injection pain, POMS, S-DAI, and the STAI. Results are presented in Table V. There was a significant positive correlation between pre-operative anxiety and experienced injection pain (r=0.51 [n=66]; p<0.01). Anxious people appeared to sense more pain during the oral injection. The highest correlation was between the POMS subscale tension and the experienced anxiety (r=0.73 [n=65]; p<0.01). Factors that influenced the pain experience were the POMS subscale tension (r=0.43 [n=65]; p<0.01), depression (r=0.28 [n=65]; p=0.03), fatigue (r=0.26 [n=65]; p=0.04), the S-DAI (r=0.28 [n=66]; p=0.02), and STAI-state (r=0.49 [n=64]; p<0.01). The experienced injection pain most strongly correlated with expected injection pain (r=0.64 [n=66]; p<0.01), which was also the strongest predictor.

Table 5: Pearson's correlation coefficients between all pain and anxiety measures.

		1	2	3	4	5	6	7	8	9	10	11
1	Pre-operative anxiety											
2	Expected pain	0.69**										
3	Experienced anxiety	0.56**	0.56**									
4	Experienced pain	0.51**	0.64**	0.54**								
5	POMS tension	0.54**	0.48**	0.73**	0.43**							
6	POMS depression	0.10	0.27*	0.26*	0.28*	0.42**						
7	POMS anger	0.10	0.27*	0.23	0.12	0.37**	0.72**					
8	POMS vigor	0.05	-0.03	-0.09	-0.03	-0.03	-0.18	-0.28*				
9	POMS fatigue	0.08	0.28*	0.27*	0.26*	0.26*	0.57**	0.51**	-0.28*			
10	S-DAI	0.37**	0.31*	0.55**	0.28*	0.71**	0.38**	0.34**	-0,03	0.17		
11	STAI-state	0.52**	0.50**	0.62**	0.49**	0.82**	0.48**	0.50**	-0,27	0.26*	0.67**	
12	STAI-trait	-0.03	0.11	0.09	0.01	0.17	0.27*	0.51**	-0.29*	0.27*	0.12	0.29*

*= p<0.05

**= p<0.01.

POMS, Profile of Mood States; S-DAI, short version of Dental Anxiety Inventory; STAI, State-Trait Anxiety Inventory.

Experience with dental injections

All patients were asked about their experiences with oral injections (Table VI). Fourteen patients (21.2%) had never experienced an oral injection before. Patients with different dental needle experiences were compared regarding pre-operative anxiety, expected injection pain, experienced injection anxiety, and experienced injection pain using one-way ANOVA. Patients who reported no memory of the experience before were excluded from this analysis. There was no significant difference in experienced pain between the groups that differed on the effectiveness of a previous oral injection (DNE-2), $F(3,48)=0.28$; $p=0.84$. There was a significant difference in experienced pain between the groups that differed on the amount of pain the previous oral injection had caused (DNE-3), $F(3,46)=7.53$; $p<0.01$. Post hoc analysis showed the more pain one felt during the last injection, the more pain one felt during this injection. There was a significant difference in experienced pain between the groups that differed on the amount of anxiety felt during a previous oral injection (DNE-4), $F(4,46)=5.60$; $p<0.01$. Post hoc analysis showed that the more anxiety someone felt during a previous oral injection, the more pain someone felt during this oral injection.

Table 6: Scores for preoperative anxiety, expected pain, experienced pain according to experience with injections.

		Pre-operative anxiety		Expected injection pain		Experienced anxiety		Experienced injection pain		
Question	Answer	Mean	SD	Mean	SD	Mean	SD	M	SD	n
DNE-2*	Always	4.24	3.11	4.43	2.82	3.19	2.42	4.19	3.37	21
	Usually	4.43	2.21	4.78	1.98	3.22	1.86	3.70	2.84	23
	Reasonably	6.67	2.66	4.33	3.50	4.00	3.10	4.67	3.72	6
	Little bit	4.50	3.54	4.00	4.20	4.00	1.41	5.00	2.83	2
	Total	4.62	2.72	4.56	2.53	3.33	2.20	4.06	3.10	52
DNE-3*	Severe	6.29	3.15	7.00	2.83	6.71	3.15	6.29	2.63	7
	Average	5.00	3.02	5.67	2.15	3.67	3.42	3.25	2.01	12
	Mild	3.88	2.15	3.79	1.79	3.79	2.78	2.96	1.68	24
	No pain	3.86	2.91	3.00	2.83	2.86	1.77	2.00	1.00	7
	Total	4.48	2.69	4.58	2.51	4.04	3.02	3.36	2.18	50
DNE-4*	Very relaxed	1.00	1.41	3.50	3.54	0.50	0.71	3.50	0.71	2
	Relaxed	2.46	2.18	2.54	1.66	2.38	2.33	1.85	1.07	13
	Neutral	4.24	2.05	4.19	2.11	3.29	2.26	3.00	2.05	21
	Quite anxious	6.77	0.83	6.23	1.54	6.54	2.82	4.85	2.30	13
	Very anxious	10.0	0.00	9.50	0.71	10.0	0.00	6.50	2.12	2
	Total	4.53	2.68	4.47	2.48	4.04	3.12	3.33	2.22	51

*P < 0.05 (analysis of variance).

DNE-2 = "How well does an oral injection usually work for you?"

DNE-3 = "Thinking about your last oral injection, how much pain did you feel?"

DNE-4 = 'Thinking about your last oral injection, how anxious were you?"

DNE, Dental needle experience.

Discussion

This study examined the physiological responses, such as sweat secretion, RSP, and HR, of 66 patients after receiving local anesthetics as well as the pre-operative anxiety, expected injection pain, experienced anxiety, and experienced injection pain related to a mandibular block injection. In earlier studies by our research group, subjects were instructed to raise their hand when feeling pain from the injection for as long as they felt pain, and to lower their hand as soon as the pain was gone.[11,18] Time or duration of pain was measured using a stopwatch. It was expected that adding physiologic measures, such as HR, GSR, and RSP, to the different questionnaires would make it possible to assess to what extent the subjective outcomes corresponded with the physiologic response of patients experiencing the injection as painful.

The aim of this study was to determine if there was a difference in the physiological responses between patients with low pain scores (<7 NRS) and patients with high pain scores (7-10 NRS). There was a significant increase in sweat secretion and a significant decrease in RSP between the relax-phase and the oral injection. There was also a significant positive relationship between experienced anxiety and HR in phase 4. Patients with higher scores for experienced anxiety had a higher HR during the injection. However, there was no significant difference in the physiological response between patients who had scores <7 and ≥7 for experienced pain. This could possibly be explained by the small group of patients in the higher pain group. There were only eight patients with scores ≥7 for experienced pain.

One could postulate that physiologic responses are mainly caused by the vasoconstrictor in the local anesthetic. Vasoconstrictors, principally adrenalin, contribute to successful local anesthetic by increasing the depth and duration of analgesia and providing hemostasis. Furthermore, by concentrating the local anesthetic agent at the infiltration site, the vasoconstrictor decreases the risk for systemic side effects of the local anesthetic. The hemodynamics during local anesthesia are greatly affected by pain and anxiety and slightly by the vasoconstrictor.[19] The hemodynamic effects of epinephrine-containing local anesthetics are considered small. Several authors found only a small increase in HR and a small reduction in mean arterial blood pressure after a single local anesthetic injection containing epinephrine.[20-22] Several studies demonstrated that the cardiovascular effect of administration of dental anesthetic is mainly influenced by anxiety and is most significantly manifested by an increase in HR.[19,24,25] Larger amounts of epinephrine-containing local anesthetics, however, result in an increased HR, stroke volume, and cardiac index in a dose-dependent fashion with no significant changes in blood pressure.[26]

In the present study, the mean expected pain score was significantly higher than the experienced pain score. This was also found in an earlier study by our research group where the experienced mean pain intensity as a result of a mandibular injection was 2.4, which is slightly lower than the pain intensity of 3.4 found in the present study.[11] The relationship between the intensity of dental anxiety and the treatment experience is controversial. Dental anxiety is greatest among people who had never visited a dentist and lowest among

those who routinely visit them for preventive care.[27] Students who had never received dental injections had higher anxiety scores for these injections than students who had previously experienced them.[28] Also, the type of anesthetic injection is related to more anxiety. In a recent review article, the specific type of anesthetic injection affected patient anxiety, with patients who required specific block type local anesthesia reporting significantly higher anxiety immediately after the procedure than those who had infiltration anesthesia.[29] In our study, higher anxiety scores were associated with more pain during the local anesthesia and high pain during a previous injection was also associated with more pain during the injection. We also found this in our earlier study, more negative experiences with injections were related to more anticipated and experienced anxiety and pain.

In our study, pre-operative anxiety was more severe in women than in men. Similarly, Yusa et al. found higher STAI-state scores on day 2 in women than in men.[30] There was no significant difference in the anxiety scores of subjects who had impacted vs non-impacted tooth removal, suggesting that the extraction itself caused anxiety for the patients, irrespective of the condition of the removed tooth and extraction procedure. Women generally have higher anxiety about dental treatment than men.[19] Other studies performed in different countries have shown that women, in general, report higher anxiety than men.[27,31] There was no significant difference between the experienced pain mean scores from males vs. females in the present study. This is in contrast with most studies that reported women and men report different amounts of pain in the orofacial region. Women responded to a pulp tester at a lower level than men, suggesting a lower pain threshold.[32] The luteinizing hormone may desensitize the opioid receptor, increasing pain sensitivity in women during ovulatory and luteal phases.[33,34] However, although women showed a lower pain threshold, the phases of the menstrual cycle and the use of oral contraceptives did not affect injection discomfort or local anesthetic efficacy and duration.[32] Hapidou & de Catanzaro found there is a significantly higher pain threshold during the follicular phase (days 8-14) compared with the luteal phase (day 15-21).[35] In the present study, the same outcome was found, but data from only eight female patients were used in this analysis. Thus, the limited number of patients and the lack of information about the use of

oral contraceptives or regularity of menstruation make it impossible to draw definite conclusions for the data in our study.

In the present study, a significant increase in sweat secretion occurred when the oral and maxillofacial surgeon entered the room. There was also a significant difference in the mean HR values in phase 2 when comparing patients whose oral and maxillofacial surgeon entered the operation room later and patients whose oral and maxillofacial surgeon was already present in the operation room. When the oral and maxillofacial surgeon entered the room at a later stage, the HR in phase 2 was significantly higher. To keep patients as relaxed as possible in the relax-phase, it is advisable that the oral and maxillofacial surgeon is already present in the operation room. The increase in mean HR may be a result of many factors not related to the local anesthesia, such as patient arousal due to people, especially the oral and maxillofacial surgeon, entering the room. Other factors, such as the handling or arranging of instruments prior to surgery, adjustment of the operation chair, or the draping of the patient might cause anxiety. A significant and sudden increase in HR occurred when patients sat down in the dental chair and when surgical drapes were put on.[25]

A limitation of the study was that we encountered some problems in the precise measurement of the SpO2. We used a pulse oxygen meter with a two digit display. Therefore, the device was capable of displaying a SpO2 of 0-99%, but a displayed value of 99% was actually a value of 98.5-100%. The device was also not equipped with the option to view the gradient graph. Therefore, it was too difficult to distinguish the SpO2 between the four phases. Using a modified device with the option to view the gradient graph should solve this problem for future studies.

After the patients filled out the questionnaires, they often commented on the amount of questions. Thus, it is possible that the patients lost interest, which may have resulted in participants rushing to complete the questionnaire. This could have resulted in poorly justified answers by the participants on the STAI-trait questionnaires; therefore, bias is possible. The predicting factors that influenced the experienced pain were the POMS subscale tension, depression, fatigue, the ATB, and STAI-state. The experienced injection pain most strongly correlated with expected injection pain. A mean score of 3.45 SD

2.17 was given for experienced injection pain on an 11-point rating scale. Eight patients (12.1%) had experienced pain scores in the range of 7-10, but their physiological response did not significantly differ from that of patients who had experienced pain scores <7.

Conclusion

As in earlier studies, the mean score of experienced pain was lower than expected pain. We found a significant increase in mean sweat secretion and a significant decrease in mean RSP between the relax-phase and the injection phase, but no significant difference in the physiological response between patients who experienced high or low pain.

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Chapter 3

Analgesic effects of preinjection low-level laser/light therapy (LLLT) before third molar surgery: a double-blind randomized controlled trial

This chapter is based on the publication:
Analgesic effects of preinjection low-level laser/light therapy (LLLT) before third molar surgery: a double-blind randomized controlled trial

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Published: Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 2017

Abstract

Objective. The aim of this study was to evaluate the analgesic effects of low-level laser therapy (LLLT) on pre-injection sites in patients scheduled for third molar removal.

Study Design. This double-blind randomized controlled trial included 163 healthy patients undergoing third molar extractions who were randomly divided into a LLLT and placebo group. Objective and subjective datasets were obtained from physiological feedback (heart rate, and sweat response) and a questionnaire, respectively. In the LLLT group each targeted injection site was irradiated twice with 198 mW continuous wave for 30 s with a 0.088 cm2 focal spot at an applied energy of 5.94 J and fluence of 67.50 J/cm2. Measurements were recorded from four time-points during data acquisition.

Results. The LLLT and placebo groups did not significantly differ in pain experience scores associated with the injected sites for maxillary or mandibular third molar extractions. Mean heart rates before and during injection were lower in the LLLT group than in the placebo group for both maxillary and mandibular regions. No statistically significant differences were observed for any remaining parameters.

Conclusions. The present data indicated that pre-injection LLLT did not effectively decrease the pain felt during local anesthetic injections prior to third molar surgery.

Introduction

Successful oral surgery requires the use of local anesthesia, such as mandibular block or local infiltration anesthesia.[1–3] However, these procedures have the drawback of inducing pain upon injection. In particular, patients who fear dental treatment commonly perceive the insertion of the needle as a painful experience, and the fear of dentistry-associated pain is closely associated with the intraoral administration of local anesthetics.[4] Numerous factors reportedly influence the pain of injection, including injection speed, needle size, needle insertion, needle placement, type of anesthetic fluid, volume of injected anesthetic fluid, injection pressure, the experience of the performer (dentist), and individual patient characteristics.[5]

During a dental injection, highly anxious patients experience greater pain and for a longer duration.[6] Clinical studies demonstrate that anxiety regarding dental injections and pain can be intense enough to necessitate alternative techniques or pretreatment strategies.[7] Several methods have been tested to reduce pain during injection of local anesthetics, including topical anesthetic creams or sprays.[8] One study reports that local application of ice to dull the pain of needle insertion into mucosa provided effective pain reduction, and took less time and was easier to apply when compared to a eutectic mixture of local anesthetic creams.[9]

Low-level laser/light therapy (LLLT), also referred to as photobiomodulation therapy, could be another potentially useful approach to improve the overall experience for patients undergoing dental injections. Following oral surgery, successful analgesia can reportedly be achieved using LLLT with all main wavelengths from 632-904 nm.[10] LLLT involves the projection of low-power laser light (i.e., not a heat-based ablating laser) into the designated target of interest, producing an analgesic effect.[11] Several beneficial biological effects of LLLT have been reported, including photobiomodulation of cellular proliferation, improved tissue metabolism, and reduced oxidant radical formation.[12–15]

Pain responses occur due to nociceptor membrane depolarization, upon which the ascending sensory nerve transfers information to the spinal column and

the medulla. The postsynaptic neuron brings the stimulus to the thalamus. At the synapse, approaching neural signals are transferred to the cerebral cortex, where they are analyzed and converted into an emotional response, causing both pain and protective reflexes.[16,17] LLLT is thought to interrupt this pain-associated neurosensory pathway; however, the exact mechanism remains elusive. LLLT may enhance the release of endorphins, which bind to the opiate receptors of the nociceptors and, thereby, block the receptors and the pain stimulus pathway.[16] Another hypothesis is that LLLT increases the activity of acetylcholine esterase (an enzyme that breaks down the neurotransmitter acetylcholine at the synaptic cleft), and the increased acetylcholine neutralization blocks the pain stimulus.[16] Data also indicate that promoting collagen formation and tensile strength has positive effects on postoperative pain control and enhancement of tissue repair.[17,18] A prospective single-blind clinical trial recently demonstrated that a gallium-aluminum-arsenide laser did not decrease pain perception due to needle insertion into the maxillary buccal mucosa.[19]

We hypothesized that patients undergoing local anesthesia or mandibular block procedures would benefit from LLLT performed prior to injection, with regards to reduced pain and anxiety. To test this hypothesis, we conducted a single-center double-blind randomized controlled trial (RCT) in a cohort of healthy patients undergoing either maxillary or mandibular third molar extractions. To objectively evaluate the results, we collected data using both physiological and questionnaire-based sources.

Materials and methods

This study was performed in accordance with the principles established in the Declaration of Helsinki (Fortaleza, October 2013). The guidelines and procedures for this investigation were reviewed and approved by the Medical Ethical Committee of the Academic Medical Center of the University of Amsterdam (Reg. Nr. NL46371.018.14). Each participant received a detailed explanation of the study procedures and gave their signed informed consent.

Study participants

Between March and June of 2015 a single-center double-blind randomized controlled trial (RCT) was conducted. Male and female patients who were referred for maxillary or mandibular third molar extractions at the Department of Oral and Maxillofacial Surgery of the Amstelland Hospital in Amstelveen, The Netherlands were eligible for participation. Patients were approached for enrollment during the preoperative consultation, 45 min before their scheduled wisdom tooth removal. Informed consent was obtained during this consultation by two dental students (IM and ZK). Inclusion criteria were as follows: referral to a maxillofacial surgeon for surgical removal of third molars, ASA≤2 (excluding pregnancy), and age of ≥18 years. The exclusion criteria were previous history of oral disease, refusal to give signed informed consent, and allergy to articaine/hydrochloride.

Study procedure

Local anesthesia or mandibular block anesthesia was performed by an oral and maxillofacial surgeon (OMFS) following a standardized protocol. Two experienced surgeons performed the third molar extractions in this study. All included patients received local anesthesia with articaine/hydrochloride 40 mg with epinephrine 0.01 mg (1.7-mL syringe Ultracain D-S forte, Sanofi-Aventis Netherlands BV, Gouda, The Netherlands), using a 27-G needle (Terumo® 27×13/8, Somerset, NJ, USA).

Anxiety and pain measurement instruments

Each patient was asked to complete a questionnaire to measure their expected pain and pre-injection anxiety. This questionnaire comprised three different parts. The first two parts included questions about the patient's expectations and previous experience with dental injections of local anesthesia, and were completed before the injection. The third part was completed immediately after local anesthetic injections, and focused on the patient's experience after the injections. The first part (expectations) included two questions about expected pain and pre-injection anxiety, which were answered on an 11-point numerical rating scale (NRS), with 0 indicating no pain/anxiety and 10 severe pain/anxiety. The second part (previous experience with dental injections of local anesthesia) began with one question about the patient's previous experience with local anesthesia injections (Have you previously had a dental

local injection?), which was answered as yes or no. Patients who answered "yes" were directed to answer three subsequent questions using a 5-point NRS. These three questions asked about how well the previous injection had worked for the patient (0, did not work at all; 5, worked well), the intensity of pain that the patient had felt during their prior injection (0 no pain at all; 5, extremely painful), and how the patient had felt about the previous injections (0, very relaxed; 5, extremely anxious). The last question of the second part of the questionnaire was used to obtain information about anxiety regarding future injections was also answered using a 5-point NRS, with 0 indicating very relaxed and 5 indicating extremely anxious. The third and final part of the questionnaire was completed after the injection, and was focused on evaluating the patient's experience after the injection. It comprised two questions about the pain and anxiety experience during the injection, which were answered using an 11-point NRS.

To obtain additional measurements of the pain and anxiety experienced during the injections, each patient was connected to two finger cuff-based sensors: a blood volume pulse (BVP) sensor and a sweat conductance or galvanic skin response (SC/GSR) sensor. The BVP sensor was connected to the index finger of the left hand, and measured heart rate (HR) and relative blood flow (rBF) based on arterial expansion in the finger, with a registration range of 40-240 beats/minute. This sensor can detect a nociceptive response starting before and during the injection procedure, which can be interpreted a measurement of pain and anxiety. The SC/GSR sensor was attached to both the middle finger and the ring finger of the left hand. This sensor uses two electrodes that both measure relative changes in skin conductance, relaying information regarding sweat gland activity. The registration range of the SC/GSR sensor is 0.1-1000 microsiemens. These sensors were coupled to the NeXus-10, a multi-channel real-time physiological monitoring and biofeedback system (Mind Media BV, Herten, The Netherlands). The sensors' signals were recorded online in real-time using the Biotrace+ software (Mind Media BV) on a computer connected through a wireless Bluetooth interface. The Biotrace+ software registered physiological measurements before and during the injections.

Low-level light/laser therapy (LLLT)

LLLT was performed using a commercially available LX2 Control Unit with a single-laser dental probe (810 nm, 200 mW; THOR Photomedicine Ltd., Chesham, UK). LLLT instruments typically use lasers that emit wavelengths ranging from 600 nm (red) to 1000 nm (near-infrared; NIR). LLLT power densities range from 5 mW/cm^2 to 5 W/cm^2 as the instruments can deliver as little as 1 mW and up to 10 W. Treatment time is generally in the range of 30-60 s per target point. LLLT produces no heat and does not damage any tissue. The delivered light energy is believed to provoke a reaction mechanism comparable to photosynthesis. All intraoral preinjection sites were irradiated twice, with 30 s intervals, for 30 s with 198 mW continuous wave with a 0.088 cm^2 focal spot at an applied energy of 5.94 J and a fluence of 67.50 J/cm^2.

Experimental procedures

All third molar surgeries were performed by two experienced OMFS (JT and JL). Before the initiation of experimental procedures, all patients completed the first two parts of the questionnaire in the waiting room. The three fingers required for sensor attachment were cleaned and disinfected with 70% alcohol and dried. Then, the BVP and SC/GSR sensors were connected for data acquisition. After the patients were coupled to the NeXus-10, the OMFS pointed to the precise points of needle insertion. A surgical marker was used to make a mark just lateral to the injection insertion sites, such that the purple ink would not affect the LLLT path of irradiation. One study investigator (always the same person, ZK) observed the surgeon as he pointed out the injection insertion sites. After indicating the injection insertion points, the OMFS left the treatment room, such that the surgeon was blinded to the LLLT randomization of each patient. A computer model randomly assigned patients to receive LLLT or placebo (no LLLT). A second investigator (again, always the same person, IM) administered LLLT pretreatment to the patients in the LLLT group.

To ensure that patients were blinded to their LLLT group assignment, all patients were fitted with protective eyewear. For each maxillary or mandibular region targeted by LLLT, two sites were irradiated. For maxillary third molar extractions, the first irradiated site targeted the posterior superior alveolar nerve, treating the first injection insertion site on the mucosa, at the mucobuccal fold just superior to the maxillary second molar. The second irradiated site targeted the

branches of the greater palatine nerve, treating the second injection insertion point of the palatal mucosa, just posterior to the second maxillary molar. For mandibular third molar extractions, the first irradiated site targeted the buccal nerve, treating the first injection insertion site at the buccal mucosa. The second irradiated site targeted the inferior alveolar nerve, treating the second needle insertion site on the mucosa, between the deepest part of the coronoid notch just lateral to the pterygomandibular raphe. In both the maxillary and mandibular LLLT irradiation protocols, the two target sites were continuously irradiated for 30 s each, and each target site was irradiated twice in sequence, for a total irradiation time of 2 min (30 s interval between site irradiations); a total of 135 J/cm^2 or 11.88 J was delivered to each preinjection site. Directly following LLLT irradiation, the Nexus-10 was activated to initiate data acquisition.

After pretreatment with the LLLT the OMFS was signaled to enter the room to perform the injections. During data acquisition, a digital marker was dropped to identify at least four observed time-points: the surgeon's entry into the treatment room, the start of the injections, the end of the injections, and when the surgeon exited the treatment room. After the surgeon left the room, the patients were asked to complete the third part of the questionnaire. All data acquisition and analysis was performed by two investigators (IM and ZK).

Statistical analysis

Power analysis, using an independent-samples, alpha 5%, power 80%, two-tailed testing and a medium effect size (0.5), resulted in a total required sample size of 128.

We used the Mann-Whitney U test to compare ordinal data from the two groups. Independent samples t-tests were used to analyze quantitative numerical variables. The Pearson correlation was used as a measure of linear association. The level of significance was set at alpha 0.05.

Results

Descriptive analysis

Our study included 163 patients who were scheduled for third molar extraction: 122 for mandibular third molar extraction and 41 for maxillary third molars extraction. Patient ages ranged from 18 to 75 years old, 81 were male (mean age, 31±14 years) and 82 were female (mean age, 30±12 years). A total of 18 patients were excluded for the following reasons: they were too anxious (n=2), treatment was deferred (n=1), the NeXus-10 did not properly record the data (n=3), or they were <18 years old (n=12). The computer model randomly assigned 82 patients to receive LLLT (44 female, 39 male), and 81 patients to the placebo group, which didn't receive LLLT (38 female, 42 male). Two OMFS (OMFS1 and OMFS2) participated in this study. Only one OMFS was present at a time, and the included patients were approximately equally distributed between the two surgeons, with 90 patients treated by OMFS1 and 73 by OMFS2. Table I presents the results of these descriptive analyses.

Table I: Descriptive data and comparison between the placebo and LLLT groups

		PL (n=80)	LLLT (n=83)	p-value
Gender	Male	42	39	0.48
	Female	38	44	
Extraction	Mandibular	64	58	0.14
	Maxillar	16	25	
Age	Mean (SD)	29.1 (11.6)	31.5 (13.8)	0.23
	Max	71	75	
	Min	18	18	
OMFS	1	42	48	0.49
	2	38	55	
Anxiety	Mean (SD)	4.3 (2.9)	4.5 (3.1)	0.68
Pain		4.8 (2.2)	5.2 (2.4)	0.21
Experience*	Exp1	68.8	86.3	0.93
	Exp2	77.1	59.5	0.01
	Exp3	61.2	71.9	0.09
	Exp4	81.4	82.6	0.87

*: Mean rank numbers from Mann-Whitney U test, LLLT: low-level laser therapy; Exp1: How well does a dental injection usually work for you?; Exp2: How much pain did you experience the last time you had a dental injection?; Exp3: How did you feel the last time you had a dental injection?; Exp4: If you went to the dentist tomorrow for a dental injection, how would you feel about that?

Randomization assessment

We used the Mann-Whitney U test to evaluate the distribution of patients with different experiences across the two groups. Successful randomization would lead to near-equal distribution of patients with more and less experience with dental local injections between the placebo and LLLT groups. Table I presents the results of this Mann-Whitney U test, indicating adequate randomization of the population. Except for question 2 (Exp2), all of the scores were equally distributed.

LLLT versus no LLLT (placebo)

Table II presents the data acquired by the NeXus-10 from the mandibular region, and Table III presents the data from the maxillary region. The data from mandible extractions show small differences in the mean physiological response scores between the placebo and LLLT groups. Mean HRs during phase 1 and phase 2 were a bit higher in the placebo group (ph1: 89.0, ph2: 80.1) compared to the LLLT group (ph1: 86.5, ph2: 79.9). In contrast to the expected results, mean sweat production during phase 1 and phase 2 was slightly higher in the LLLT group (ph1: 5.1, ph2: 6.7) compared to the placebo group (ph1: 4.1, ph2: 5.3). The subjective measurements obtained from the questionnaires also showed small differences related to the above parameters. The pain experienced during injection was slightly higher in the placebo group (m: 4.2) than in the LLLT group (m: 4.1). Only the difference in sweat production between the LLLT and placebo group was significant ($P<0.05$).

Data from the maxillary region also revealed several small differences in mean HRs in both phase 1 and phase 2 (Table III). During phase 1, the mean HR was lower in the placebo group (ph1: 83.1) than in the LLLT group (ph1: 84.1). On the other hand, during phase 2, the mean HR was higher in the placebo group (ph2: 76.8) compared to the LLLT group (ph2: 69.5). Questionnaire data revealed that the mean score for pain experience was lower in the LLLT group (m: 3.64) than in the placebo group (m: 3.81). Notably, the anxiety experienced during the injection was slightly higher in the LLLT group (m: 4.0) compared to the placebo group (m: 3.7). None of these differences between the placebo and LLLT groups or between the two dental arch regions were found to be significant.

Table II: Physiological and subjective results for the lower jaw obtained by the independent samples t-test

	Placebo		*LLLT*		n	*P*
	M	SD	M	SD		
Expected injection pain	4.9	2.1	5.2	2.4	122	0.46
Pre-injection anxiety	4.5	2.9	4.4	3.1	122	0.95
Experienced injection pain	4.2	2.3	4.1	2.4	122	0.70
Experienced injection anxiety	4.1	2.7	4.0	2.9	122	0.96
HR ph1	89.0	14.6	86.5	14.3	122	0.34
GSR ph1	4.1	2.3	5.1	2.7	122	0.02
HR ph2	80.1	18.7	79,9	13.7	122	0.94
GSR ph2	5.3	2.7	6.7	3.6	122	0.02

LLLT, low-level laser therapy; M, mean; SD, standard deviation; HR, heart rate; ph1, phase 1; GSR, galvanic skin response; ph2, phase 2.

Table III: Physiological and subjective results for the upper jaw obtained by the independent samples t-test

	Placebo		*LLLT*		n	*P*
	M	SD	M	SD		
Expected injection pain	4.1	2.3	5.2	2.5	41	0.17
Pre-injection anxiety	3.6	3.1	4.6	3.1	41	0.31
Experienced injection pain	3.8	2.7	3.6	2.0	41	0.82
Experienced injection anxiety	3.7	2.8	4.0	2.9	41	0.74
HR ph1	83.1	14.5	84.1	15.6	41	0.83
GSR ph1	5.6	7.6	4.1	2.1	41	0.35
HR ph2	76.8	16.8	69.5	18.5	41	0.21
GSR ph2	7.3	10.7	8.0	14.5	41	0.87

LLLT, low-level laser therapy; M, mean; SD, standard deviation; HR, heart rate; ph1, phase 1; GSR, galvanic skin response; ph2, phase 2.

Assessment of gender differences

Table IV presents the comparison of variables between male and female patients. Relative to male patients, female patients scored significantly higher on the NRS for questionnaire items regarding expected pain, pre-injection anxiety, experienced pain, and experienced injection anxiety. These data indicated that females experienced more fear of dental injections than males. Physiological data further showed that women had higher mean scores for HR and sweat production during both phase 1 and phase 2. The differences in sweat production were statistically significant ($P<0.05$).

We further performed separate comparisons among male and female patients in the LLLT versus placebo groups for the mandibular region (Table V) and

for the maxillary region (Table VI). Male participants showed lower HR in the LLLT group than in the placebo group, but this difference was not significant. Unexpectedly, almost all of the mean scores of the measured variables were higher in the LLLT group than in the placebo group. The experienced injection pain and sweat production during phase 1 and phase 2 were lower in the placebo group than in the LLLT group, but these differences were very small and not statistically significant. Overall, the differences between the placebo and LLLT groups in the mandibular region were not statistically significant among males or females, with the exceptions that female patients showed a significant difference in the expected injection pain between the LLLT and placebo groups ($P<0.05$), and a significant difference in sweat production during phase 1 ($P<0.05$).

Table IV: Independent samples t-test results for differences in subjective and physiological responses between male and female participants

	Male		*Female*			
	M	SD	M	SD	n	*P*
Expected injection pain	4.6	2.2	5.4	2.4	163	0.03
Pre-injection anxiety	3.2	2.7	5.6	2.9	163	0.00
Experienced injection pain	3.6	2.4	4.5	2.2	163	0.01
Experienced injection anxiety	2.9	2.4	5.1	2.8	163	0.00
HR f1	83.8	14.2	89.8	14.5	163	0.01
GSR f1	4.5	2.5	4.7	4.0	163	0.74
HR f2	74.9	14.4	81.2	19.0	163	0.02
GSR f2	5.6	3.2	7.2	9.5	163	0.15

M, mean; SD, standard deviation; HR, heart rate; f1, phase 1; GSR, galvanic skin response; f2, phase 2.

Table V: Independent samples t-test results for the lower jaw in male and female patients

	Male						*Female*					
	Placebo		*LLLT*				*Placebo*		*LLLT*			
	M	SD	M	SD	n	*P*	M	SD	M	SD	n	*P*
Expected injection pain	4.5	1.8	5.3	2.6	60	0.19	5.5	2.4	5.2	2.3	62	0.60
Pre-injection anxiety	3.5	2.8	3.4	2.8	60	0.88	5.8	2.3	5.2	3.1	62	0.39
Experienced injection pain	3.6	2.1	3.8	2.6	60	0.76	5.1	2.3	4.3	2.2	62	0.19
Experienced injection anxiety	3.1	2.4	3.1	2.6	60	0.96	5.3	2.7	4.8	*2.9*	62	0.44
HR ph1	87.0	14.4	84.5	14.2	60	0,51	91.6	14.6	88.1	*14.3*	62	*0.35*
GSR ph1	4.2	2.2	5.0	3.1	60	0.24	3.9	2.5	5.2	2.5	62	0.04
HR ph2	77.7	14.8	76.1	13.0	60	0.65	82.9	22.5	82.7	13.7	62	0.97
GSR ph2	5.4	2.8	6.2	3.7	60	0.32	5.3	2.7	7.1	3.5	62	0.03

LLLT, low-level laser therapy; M, mean; SD, standard deviation; HR, heart rate; ph1, phase 1; GSR, galvanic skin response; ph2, phase 2.

Table VI: Independent samples t-test results for the upper jaw in male and female patients

	Male						Female					
	Placebo		*LLLT*				*Placebo*		*LLLT*			
	M	**SD**	**M**	**SD**	**n**	*P*	**M**	**SD**	**M**	**SD**	**n**	*P*
Expected injection pain	3.6	1.7	4.1	2.3	21	0.62	4.6	2.7	6.6	1.8	20	0.06
Pre-injection anxiety	1.6	1.9	2.9	2.4	21	0.23	5.1	3.1	6.8	2.8	20	0.21
Experienced injection pain	3.9	3.3	3.1	2.1	21	0.55	3.8	2.4	4.3	2.0	20	0.62
Experienced injection anxiety	2.6	1.9	2.4	2.4	21	0.89	4.6	3.2	6.0	2.3	20	0.26
HR ph1	78.3	14.2	77.4	11.9	21	0.87	86.7	14.5	92.7	15.9	20	0.39
GSR ph1	4.4	2.0	4.3	2.6	21	0.94	6.6	10.1	3.9	1.2	20	0.38
HR ph2	72.2	17.2	67.4	12.9	21	0.49	80.5	16.6	72.3	24.3	20	0.41
GSR ph2	5.4	2.7	5.3	3.3	21	0.91	8.7	14.3	11.4	21.6	20	0.75

LLLT, low-level laser therapy; M, mean; SD, standard deviation; HR, heart rate; ph1, phase 1; GSR, galvanic skin response; ph2, phase 2.

Pre-injection anxiety, expected pain, and experienced pain

Patients were asked how afraid they were of dental injections, how much pain they expected from the injection, how afraid they were during the injections, and how much pain they experienced during the injections. Table VII shows the assessed correlations between these variables. Experienced injection pain was most strongly correlated with anxiety during the injections (r=0.61), and was to a lesser extent correlated to the experienced injection pain (r=52). Pre-injection anxiety was correlated to the expectation of injection pain (r=0.63) and to the anxiety experienced during the injection (r=0.75), and was less strongly correlated with the pain experienced during the injection (r=0.44). Pearson's correlations showed no strong correlations between the physiological measurements and the subjective measurements determined by questionnaire. Interestingly, the strongest correlation found was between pre-injection anxiety and HR during injections in phase 2 (r=0.29).

Table VII: Pearson's correlations between expected pain and anxiety and experienced pain and anxiety

	1	2	3	4	5	6	7
1 HR ph1							
2 GSR ph1	0.19*						
3 HR ph2	0.67*	0.23*					
4 GSR ph2	0.16*	0.56*	−0.13				
5 Experienced injection anxiety	0.33*	0.03	0.27*	0.13			
6 Pre-injection anxiety	0.43*	0.09	0.29*	0.14	0.75*		
7 Expected injection pain	0.20*	0.08	0.12	0.11	0.58*	0.63*	
8 Experienced injection pain	0.20*	0.03	0.16*	0.08	0.61*	0.44*	0.52*

*$P<0.05$

HR, heart rate; ph1, phase 1; GSR, galvanic skin response; ph2, phase 2.

Discussion

In the present study we examined 163 patients who required third molar extractions. These patients were asked about their expectations regarding anxiety and pain before the injection, and about their experienced anxiety and pain during the injection. We further obtained complementary physiological measurements during the injections. Less than one-third of participants (n=50) rated their experienced pain as 6 or higher on the NRS. Of these 50 patients, 25 were in the placebo group and 25 in the LLLT group. Furthermore, both maxillary and mandibular region data revealed lower mean scores for experienced pain and heart rate (in both phase 1 and phase 2) in the LLLT group compared to the placebo group, although these differences were not statistically significant. The placebo and LLLT groups did not significantly differ with regards to either the subjective or physiological variables in either dental arch region.

An earlier study of 66 volunteers recruited among dental students also demonstrated no positive effect of laser pretreatment with regards to reducing pain perception during needle insertion.[19] Their data showed that laser pretreatment did not decrease pain perception, but actually increased it. However, the results were skewed and pain perception was much higher in the laser group among female participants. Sattayut[20] compared LLLT,

20% benzocaine topical anesthesia, pressure, and light touch as a control in palatal injections. They found no statistically significant difference in pain score among the groups; however, the median pain score in the LLLT group was clearly reduced compared to in the other groups. The inconsistent results associated with LLLT from our study and others may be perhaps explained by different irradiation parameters and application technique.

Gender comparisons in prior studies suggest that women experience a higher pain expectation and higher anxiety rate. Compared to men, women had higher mean scores on the fear of dental pain (FDP) and the short version of the Dental Anxiety Inventory (S-DAI).[5] In the data from our population women showed higher mean scores in pain and anxiety expectations and experiences, this is similar to previous findings.[4,5,19] Women also showed higher physiological measurements, including higher mean scores for HR and sweat production, although only the difference in sweat production was found to be significant.

There are several points that should be considered regarding the present study. Pain experience is partly influenced by previous experiences, this is difficult to account for in an investigation and reduces the reliability of the results acquired from questionnaires. Moreover, data for both mandibular block and palatal injection procedures were included. Data from a previous study suggest that the pain experience varies among different injection locations, with palatal injections found to be the most painful.[6] Unfortunately, in our study, only 41 participants underwent maxillary third molar extractions compared to 122 participants undergoing procedures in the mandibular region. Thus, the major limitation of our study was that the number of participants with palatal injections was insufficient to draw reliable conclusions regarding the clinical application of LLLT specifically for palatal injections (Power 80%: n=122).

The NeXus-10 was used to detect physiological changes that could indicate pain experience during local injections. In addition to pain, anxiety can also enhance epinephrine release. In general, elevated epinephrine levels can cause increases in HR and sweat production, so it is possible that higher physiological responses were influenced by both the pain during the injection and the anxiety regarding the needle itself.[6,7] This physiological reasoning supports the reliability of data obtained from the NeXus-10.

Overall, the results in this report suggest that preinjection LLLT - at least administered according to the parameters depicted by in this study - did not effectively reduce the pain sensation associated with local anesthetic injection among patients undergoing third molar extractions. Further studies are warranted to provide definitive conclusions regarding the utility of LLLT for acute pain sensory modulation in routine dental scenarios.

Conclusions

LLLT did not effectively decrease the pain felt during local anesthetic injections prior to third molar surgery. The presently analyzed datasets showed no indication that LLLT had analgesic effects that blunted pain sensation.

Acknowledgements

We express our gratitude to all participating patients and to the staff of the Amstelland Hospital for their continued patience and support of this project. The authors wish to express their appreciation to Dr. J.E. Raber-Durlacher and J.D. Carroll for their kind assistance.

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Chapter 4

Alveolar iodine tampon packing reduces postoperative morbidity after third molar surgery

This chapter is based on the publication:
Alveolar iodine tampon packing reduces postoperative morbidity after third molar surgery

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Published: Journal of Oral and Maxillofacial Surgery, 2019

Abstract

Purpose: The aim of this study was to assess the efficacy of an iodine tampon after mandibular third molar surgery on oral health related quality of life (OHRQoL) use of painkillers, postoperative sequela and self-care behaviors in the first postoperative week.

Study design: This prospective cross-over, randomized controlled study included patients undergoing surgical removal of bilateral symmetrically, horizontally impacted mandibular third molars. The surgical site was randomly allocated to receive an iodine tampon after surgery or wound closure and rinsing with a Monoject® syringe. Primary outcomes measured each day during the first postoperative week were the Oral Health Impact Profile (OHIP)-14 score and postoperative sequela, including pain, swelling, limited mouth opening, pain, postoperative infection, and alveolar osteitis. Secondary outcome measures were several self-care behaviors. Data were analyzed using repeated measures ANOVA and paired-samples t-tests.

Results: A total of 54 patients (25 men and 29 women; mean age 25.1 years) were enrolled with a total of 108 surgically removed impacted mandibular third molars. The use of an iodine tampon resulted in a significantly lower impact on oral health-related quality of life (m=21.5, sd=9.6 vs m=26.5, sd=10.6) on the first postoperative day, which was observable until the 7th postoperative day. In addition, following removal the impacted third molar, patients in the iodine tampon condition reported less pain (m=5.2, sd=1.9 vs m=6.1, sd=2.1 on day one, lasting throughout the week), less use of painkillers, less limited mouth opening, fewer problems chewing, less swelling, and earlier recovery.

Conclusion: The use of a postoperative iodine packing after the removal of impacted mandibular third molars significantly reduces OHRQoL and postoperative sequela.

Introduction

As in any surgery, the surgical removal of a mandibular third molar causes tissue damage and impacts quality of life (QOL). Pain, swelling, and trismus are known sequelae of third molar surgery that can significantly affect an individual's QOL.[1-3] Surgical removal of a mandibular third molar leads to significant deterioration of oral health related quality of life (OHRQoL), particularly during the first 5 days.[1] The number of studies evaluating the influence of third molar surgery on QOL is growing.[1-11] An earlier study by our research group demonstrated that the short-term consequences of third molar surgery have a strong effect on patients' QOL.[10] After third molar surgery, patients feel that the procedure exerts its impact on their QOL primarily by reducing their ability to eat and interfering with daily life.[6]

In one of the largest prospective studies (the age-related American Association of Oral and Maxillofacial Surgery age-related third molar study), postoperative complication rates were 16.3%.[12] Among 8748 removed third molars, the most common complications were alveolar osteitis (AO, 7.4%), inferior alveolar injury (1.6%), unexpected trismus (1.2%), and postoperative infection (1.1%). Even though the overall incidence of postoperative complications in mandibular third molar surgery remains relatively low, it is clinically important because a large volume of cases result in significant numbers of complications.[12,13] Experiencing postoperative complications substantially amplifies this effect.[6]

A variety of medications, such as antibiotic prophylaxis,[14-18] corticosteroids,[19-21] chlorhexidine (CHX) mouth rinses,[22-24] platelet-rich fibrin,[25,26] hyaluronic acid spray,[27] and bromelain therapy [28] have been used to reduce postoperative inflammatory reactions. Different studies have reported a beneficial effect of a locally applied gauze drain in mandibular third molar surgery on AO[29] and pain, trismus, and swelling.[30-32] A recent review reported an obvious positive effect on postoperative sequela after mandibular third molar removal.[33] In the meta-analysis, patients who had received surgical drainage, such as a tube drain, rubber drain, or gauze drain, had significantly less facial swelling, a better mouth opening, and less pain after surgery.

The aim of this study was to assess the efficacy of an iodine tampon in the extraction socket after mandibular third molar surgery regarding OHRQoL in the first postoperative week. We also assessed the effect of alveolar tampon packing on postoperative pain, AO, and pain medication and infection in the week following third molar surgery.

Material and methods

Study design and patient selection

This article is reported according to the CONSORT (Consolidation Standards of Reporting Trials) statement for providing the quality of reports of randomized trials (http://www.consort-statement.org/).[61] The study was designed as a prospective randomized crossover study in patients who were referred to the Department of Oral and Maxillofacial Surgery of Amstelland Hospital (Amstelveen, the Netherlands) for surgical removal of two impacted mandibular third molars.

Only native Dutch speakers with bilateral horizontally impacted mandibular third molars, with a Gregory-Pell 3B grade impaction,[35] who were planning to undergo bilateral mandibular third molar surgery were included in the study. Other inclusion criteria were age ≥18 years; American Society of Anesthesiology (ASA) 1, patients with no systemic diseases or medical conditions; no discernible active pathology associated with the third molars, and no acute pericoronitis; and the patient was free of periodontal disease.

Exclusion criteria were smoking, allergy to ibuprofen, presence of systemic disease, history of recent and/or symptomatic peptic ulcer, anti-platelet or anticoagulant therapy, pregnancy or lactating, recent local infection prior to surgery (<15 days), previous radiation therapy to the maxillofacial region, local pathology (e.g., cysts or tumor) associated with the third molars, or lack of consent to the procedure or the study.

Data collection occurred from January 1, 2016, to July 31, 2017. The study was performed with the understanding and written consent of each subject and according to the ethical principles described in the Declaration of Helsinki. The research protocol was reviewed and approved by the medical ethical committee

of the Academic Medical Center, University of Amsterdam, the Netherlands (METC NL52968.018.15 2015_126). All patients were informed about the procedures, postoperative recovery times, and possible complications and signed a detailed consent form. Treatment was started after a full medical and dental history and orthopantomogram, as well as a 3D CT scan if indicated.

Surgical procedure

All patients underwent surgical removal of impacted mandibular third molars under local anesthesia. All surgeries were performed by one surgeon in a standardized fashion using a similar technique. The patients underwent surgery on only one side at a given appointment, with the second side being operated on after a period of 8 weeks. All patients received a standardized mandibular block injection with additional infiltration of the buccal nerve. The location, temperature, amount of anesthetic fluid (articaine/hydrochloride 40 mg with epinephrine .01 mg, 1.7-mL syringe Ultracain D-S forte; Sanofi-Aventis, Netherlands BV, Gouda, the Netherlands), and type of needle (27 gauge/.40 × 35 mm) were all standardized according to our hospital's protocol. A triangular flap was used in all patients; an incision was made from the distobuccal edge of the second molar dropping at a slight oblique angle, curving forward into the mandibular vestibule. The second part of the incision was made from the mandibular ramus to the distobuccal aspect of the second molar. Any bone overlying the crown of the impacted third molar was removed with a round surgical bur. A fissure bur was used to section the tooth. Copious irrigation with sterile saline was performed through rotary instrumentation. Following delivery of the tooth, any dental follicular soft tissue was removed, and the socket thoroughly irrigated with saline. [62] In the experimental condition, a 1 x 2 cm iodine tampon (Opraclean; Lohmann & Rauscher International GmbH &Co. KG, Rengsdorf, Germany) was placed in the surgical site for the intervention. In the control condition, no dressing was placed. The surgical site was closed using Undyed Vicryl Rapide (Ethicon, Somerville, MA, USA). None of the surgical sites were primarily closed. In the control condition, a disposable syringe, the Monoject® Curved 412 Tip Syringe (Tyco/healthcare-Kendall, Mansfield, MA, USA), was used to rinse the wound with a saline solution four times daily. Immediately after surgery, the details of the procedure were recorded, including the duration of surgery in minutes from the time of incision to the insertion of the last suture.

Study tampons and procedures.
Given the crossover design, eligible patients were randomly assigned to the use of an iodine tampon or the Monoject® syringe. Patients were scheduled for surgery (tampon or no tampon) in two separate clinical sessions (one side at a time) at least 2 months apart.

Randomization and the concealment of allocation
This study consisted of two trial conditions; first third molar removal with a tampon (tampon condition) followed by surgical removal without a tampon (Monoject® condition) or first third molar removal without a tampon (Monoject® condition) followed by surgical removal with a tampon (tampon condition). Prior to the first surgery, a surgical assistant allocated the patient to either trial condition using a computer random generator. After the allocation to a trial condition another surgical assistant assigned a side to either the experimental treatment or the control treatment side using again a computer random generator. The concealment of allocation was guaranteed through a sealed envelope. The operator received the envelope after the arrival of the patient in the surgery room and the envelope was opened by a surgical assistant after completion of the surgery.

For the Monoject® condition (control condition), after surgery, the patients were provided a curved Monoject® syringe and oral and written instructions regarding the use of the syringe. They were instructed to start irrigating the wound 48 hours after surgery. They had to bring the tip to the distal side of the second molar in the wound and irrigate four times a day with a saline solution.

For the tampon condition, a loosely administered 2 cm iodine tampon (Opraclean; Lohmann & Rauscher International GmbH &Co. KG, Rengsdorf, Germany) was placed in the socket for 1 week after removal of the impacted third mandibular molar. At the 1-week control visit, the tampon was removed.

Postoperative instructions
All patients were instructed to bite on gauze for 30 minutes. They were also instructed not to rinse or spit during the first 24 postoperative hours. Tooth brushing could be started the day after surgery. Ibuprofen 600 mg (Brufen, Abbot BV, Hoofddorp, the Netherlands) three times a day was prescribed

postoperatively. No postoperative antibiotics were given. The day after surgery, patients began using a .12% aqueous CHX mouth rinse twice a day for 1 minute for 7 days. Patients were given verbal and written postoperative instructions and were recalled for review after 1 week.

Parameters for outcome assessment

The primary outcome measures consisted of an OHRQoL measure, the short version of the Oral Health Impact Profile (OHIP)-14,[35,36] and questions about possible postoperative sequela (e.g., pain, swelling, limited mouth opening) and self-care (e.g., use of pain medication, cooling with ice), VAS pain scores, and inflammatory complications (e.g., wound infection and AO).

Questionnaires

Quality of life

To measure oral health related quality of life the OHIP-14 was used. [62] Participants rate on a 5-point scale (0 = never – 4 = very often) the experience of their dental problems. The total score ranges from 0 – 56. Examples of items are "Have you had trouble pronouncing any words because of problems with your teeth or mouth"; Have you found it uncomfortable to eat any foods because of problems with your teeth or mouth;.

The OHIP-14 was filled out each consecutive evening in the first post-operative week. Pain was measured using an 11-point numerical rating scale (NRS) and measured each postoperative day for one week.[10,11] Only one extra item (number of hours cooling with an ice pack) was added to the first day questionnaire.

Assessment of wound infection and alveolar osteitis

One independent assessor evaluated the presence of wound infection or AO. Infection was defined by any of the following:[37] the presence of purulent discharge in the extraction socket and/or excessive swelling with fluctuation, with or without pain; presence of a local abscess; or onset of facial or cervical cellulitis plus other signs suggesting infection, such as pain, increased heat, erythema, and/or fever. In patients diagnosed with infection, wound care

(drainage) was followed by a 5-day oral course of 500 mg amoxicillin three times a day. The number of postoperative visits, type and amount of analgesic, type and amount of antibiotics, and operative intervention were documented.

A diagnosis of AO was established if there was new onset or increasing pain more than 36 hours after removal of the mandibular third molar in combination with an absence of the hematic clot in the socket, resulting in exposed bone. A putrid smell may be present in combination with intense neuralgic type pain. Gentle probing or irrigation of the wound aggravated the pain. All elements needed to be present for the diagnosis of AO.

If AO was diagnosed, it was managed by wound care (gentle saline irrigation), an iodine tampon dressing, and oral analgesics. The patient returned for follow-up daily until the symptoms were adequately controlled. The number of postoperative visits and type and amount of analgesic prescribed were documented. The outcome variable was characterized as a binary outcome, as the presence or absence of complications.

Data management

Data were collected and imported into a database. The demographic variables were age and gender (male/female). Age was computed in years as the difference between the date of operation and the subject's date of birth. The Gregory and Pell classification of M3 position was used to describe the degree and type of mandibular third molar impaction.[34]

Sample size calculation

A power calculation was performed using G*Power 3.1.9.2.[38] Using a paired-samples t-test, an alpha of 5%, a power of 90%, two-tailed testing and an effect size of 0.5 (a moderate effect size was used since the effect should be clinically relevant) results in a total sample size of 44 patients. Given possible drop-outs (related to the longitudinal character of the study) a sample size of at least 50 patients was aimed for.

Statistical analysis

Conventional descriptive statistics were used to characterize the sample. The chi^2 test was used to examine associations between categorical variables. Mean

scores from multiple measurements in the same subjects were compared using ANOVA for repeated measures. Mean scores of two repeated measurements were compared using the paired samples t-test. For skewed data (i.e., number of painkillers), analyses were repeated using the Friedman test and Wilcoxon signed-rank test. For the level of significance, an alpha of 5% was used.

Results

Data from 54 patients (29 females and 25 males) were available for analysis, with a mean age of 25.1 years (SD 3.9). A total of 25 patients started with surgical removal of the mandibular third molar using the iodine tampon (12 males, 13 females), and the other 29 patients started with surgical removal without the use of a tampon (13 males, 16 females). The chi^2 test revealed no significant association between gender and condition (X^2 (1) = .05, p = .82), indicating an approximately equal distribution of gender across conditions. Concerning the OHIP-14-data, only 3 values were missing. These missing values were replaced by the mean item score on the respective day of measurement.

Using independent-samples t-tests, the two conditions were compared regarding the mean OHIP-14 total scores to test for an order effect. No significant differences were found. Therefore, data were pooled for surgical extraction with and without the iodine tampon.

Impact of surgical third molar removal

In order to evaluate the impact of the third molar extraction on OHRQoL and the level of pain felt, several repeated measures ANOVA were carried out comparing the mean scores on each postoperative day, separately for the experimental and control extractions (Table 1). For extraction using the iodine tampon, a significant difference was found between the multiple measurements for the mean OHIP-14 total score (F (6, 318) = 140.04, p < .001) and mean pain intensity scores (F (6, 318) = 105.02, p < .001). Pairwise comparisons showed that all dependent measurements differed significantly from each other (all p<.001) for both outcome measures. For extraction without the use of a tampon, identical results were found, i.e., a significant difference between the multiple measurements for the mean OHIP-14 total score (F (6, 318) = 134.24,

p < .001) and mean pain intensity scores (F (6, 318) = 82.19, p < .001). Pairwise comparison showed that all dependent measurements differed significantly from each other (all p<.001) for both outcome measures.

Effect of the iodine tampon on OHRQoL and pain

To determine the effect of the iodine tampon, the mean OHIP-14 total score on each postoperative day following extraction using the iodine tampon was compared to the mean score on the same postoperative day following extraction using wound closure and Monoject® syringe use by the paired samples t-test. An identical analysis was performed on the mean pain intensity scores. Significant differences were found for each comparison for both scores, in favor of extraction using the iodine tampon (Table 1).

Table 1: Mean OHIP-14 total scores and pain scores on postoperative day (POD) 1-7

	OHIP-14 total scores					Pain intensity scores				
POD	Iodine tampon		Monoject®			Iodine tampon		Monoject®		
	Mean	SD	Mean	SD	ES[a]	Mean	SD	Mean	SD	ES[a]
1	21.5	9.6	26.2	10.6	-.60	5.18	1.89	6.09	2.11	-.45
2	14.1	9.4	20.6	11.6	-.64	3.86	2.19	5.41	2.29	-.61
3	10.5	9.3	18.0	12.1	-.79	3.18	2.22	5.13	2.42	-.78
4	7.4	8.6	13.2	10.7	-.74	2.12	1.96	4.07	2.34	-.85
5	5.5	7.7	10.9	10.3	-.71	1.68	1.95	3.42	2.42	-.84
6	3.7	6.8	7.5	9.1	-.60	1.10	1.58	2.67	2.22	-.77
7	2.3	5.1	5.2	7.6	-.52	.76	1.41	2.06	2.11	-.66

Note: Repeated-measures analysis of variance showed that all repeated mean scores differed significantly from each other (P < 0.001).

Abbreviations: ES, effect size (d_s); OHIP-14, Oral Health Impact Profile 14; POD, postoperative day; SD, standard deviation.

ANOVA measures demonstrated that all repeated mean scores differed significantly from each other (p < .001).

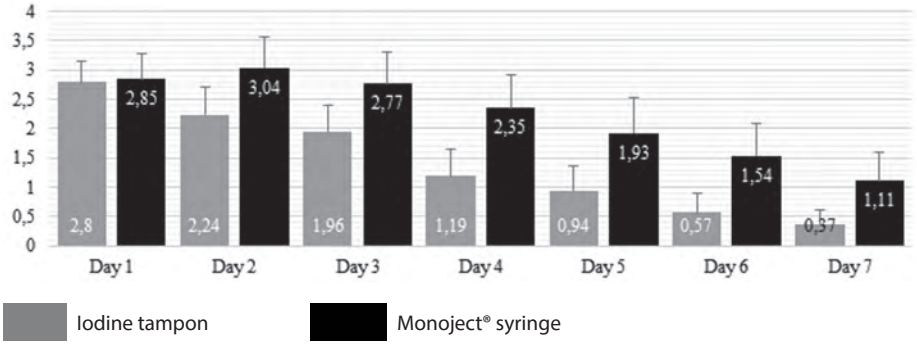
[a] All paired-samples t-tests resulted in P < .001.

Use of painkillers

The mean number of prescribed painkillers used the first seven postoperative days following intervention or control extractions is shown in Figure 1. Paired samples t-tests showed that, on the first postoperative day, there was no significant difference in the mean number of painkillers taken between the two conditions. On day 2 through 7, however, significantly fewer painkillers were taken in the intervention condition (all p<.010). Given the skewed distribution

of these data, the analysis was repeated using the Wilcoxon signed-rank test, which resulted in identical conclusions.

Figure 1: Mean number of prescribed analgesics used on postoperative days 1-7.



Significantly fewer analgesics were used after the iodine tampon intervention compared to the Monoject®-syringe (all $p < .01$). Data are presented as mean + 1.96 SE (=95% confidence interval). Identical conclusions were found when the analysis was repeated using the Wilcoxon signed-rank test, given the skewed distribution of the data.

Effect of the alveolar iodine tampon on the first postoperative week

Table 2 provides information on a number of variables. The first postoperative week was superior in all aspects for extraction using the iodine tampon relative to extraction without the tampon. Generally, one can compare two dependent proportions using the McNemar test. However, given the eight different aspects in Table 2, 7 days would require 56 McNemar tests. Rather than knowing whether a particular aspect differs statistically on a particular day, the clinical relevance is more important and seems quite high which can be illustrated by a couple of examples. For example, on day 7 after extraction using the iodine tampon, 33 patients (61.1%) reported no problems at all versus 15 patients (27.8%) following extraction using wound closure and Monoject® syringe use. On day 4 after extraction using the iodine tampon, 25 patients (46.3%) used the prescribed pain medication versus 39 patients (72.2%) following extraction using wound closure and Monoject® rinsing. Similar results were found for limited mouth opening on day 4 (27 versus 45), limited chewing ability on day 4 (28 versus 41), and pain on day 6 (10 versus 37).

For the first postoperative days, patients were asked to report the number of hours they spent using an ice pack. The paired samples t-test showed no significant difference between the intervention and control extraction ($t(53) = 1.31$, $p = .19$; mean 5.5 h, range 0-15 h).

Duration of surgery

The duration of surgery (mean ±standard deviation) was 11.2 min (SD 1.27) in the iodine tampon condition and 11.48 min (SD 1.41) in the control condition. Operation time did not significantly differ between the two conditions.

Table 2: Frequency of patients who answered yes on each of the self-care and perceived inconvenience items (N=54)

		Postoperative day						
Question		**1**	**2**	**3**	**4**	**5**	**6**	**7**
Did you use the prescribed pain medication? (yes)	T	49	38	37	25	18	10	9
	C	49	45	44	39	28	21	13
Did you use additional medication? (yes)	T	13	11	9	4	1	3	2
	C	11	14	14	9	13	15	12
Did you experience limited mouth opening? (yes)	T	51	50	42	27	21	15	9
	C	52	53	39	45	36	32	22
Did you experience reduced chewing ability? (yes)	T	52	48	40	28	23	14	10
	C	51	50	48	41	36	26	20
Did you experience a swollen cheek? (yes)	T	45	48	48	33	22	6	5
	C	46	50	49	41	32	21	12
Did you experience pain as a result of surgery? (yes)	T	48	36	40	28	24	10	8
	C	47	46	44	43	37	37	26
Did you experience no problems at all? (yes)	T	1	1	2	7	16	24	33
	C	0	0	0	2	2	4	15

Abbreviations: C, Monoject syringe; POD, postoperative day; T, iodine tampon.

Postoperative complications

No cases of postoperative AO were observed after 1 week. One postoperative infection occurred in the control condition during the first postoperative week. The patient presented after 4 days with increasing swelling and pus formation at the surgical site. The abscess was drained with a subsequent 5-day oral course of 500 mg amoxicillin 3 times a day. No sensory disturbances of the inferior alveolar nerve were scored after surgical removal of the mandibular third molars.

Discussion

Pain, swelling, and trismus can cause great distress after mandibular third molar surgery, and anything that compromises QOL, even for a short period of a few days, is unacceptable to the highly cognizant and extremely busy generation of today. The purpose of this study was to assess the efficacy of the application of an iodine tampon in the extraction socket after mandibular third molar surgery regarding postoperative QOL. The results showed a significant reduction in postoperative morbidity in patients after the application of a post-operative iodine tampon dressing.

As in earlier studies, a crossover clinical trial design was used, with tampon or no tampon (the Monoject® control condition) treatments used in the same patient in the present study.[29,39,40] The crossover design eliminates confounding by anatomical surgical factors that could have affected QOL after the surgical procedure, such as position with respect to the occlusal plane, grade of impaction, and surgical difficulty. In addition, patient-related factors, such as age, gender, habits, and the use of oral contraceptive, are eliminated from influencing the results. The severity of postoperative pain and discomfort can vary from patient to patient, and using the patient as his/her own control could eliminate the patient as a variable. The grade of impaction was similar in both conditions, just as the mean operation time and operation technique (ostectomy and sectioning the tooth). The results also demonstrated no difference if the tampon was used in the first or second surgery, as one could postulate that the experience of the first surgery may have influenced the outcome or the patient's perception of the second surgery. The uniformity of included patients with bilateral impacted third molars was established by including only patients with bilateral horizontally impacted (grade 3B Gregory-Pell) mandibular third molars to eliminate the effect of surgical difficulty and the grade of impaction on postoperative outcome. The bilateral impacted mandibular third molars were judged by preoperative clinical and radiological examination with regard to the depth of impaction and position in the mandible and were considered equally difficult to remove.

The OHIP questionnaire is a valid, reliable, and sensitive method to assess QOL.[10,11] The OHIP-14 can be considered internally responsive to changes in

the impact of oral conditions as a result of surgical third molar removal and is able to differentiate the effect of several clinical variables. In the present study, the mean total OHIP-14 scores were lower (which means less impact of surgery on OHRQoL) after tampon use, throughout the first postoperative week, relative to the control condition. The intensity of postoperative pain was also reduced significantly in the tampon condition. For all interventions, pain was worst on the first day and slowly decreased during the week. Studies have found that pain reaches its maximum intensity during the first 8 hours after surgery, attributable to increased production of pain mediators and the declining effect of the local anesthetic.[41,42] It is to be assumed that none of the patients will be without postoperative pain, and surgery does significantly affect the patient's QOL, particularly during the first 3 days.[9,43,44] Fifty percent of the patients continue with their work activity the day after surgery, and most of the patients (90%) can return to work by day 3.[5] After mandibular third molar surgery, a decrease in food enjoyment has been reported with an average number of 3.9 days of eating difficulties.[9] In a study by Conrad, 63.5% of patients reported their worst pain as severe (5 to 7 out of 7) on the first postoperative day. By postoperative day 7, only 15% of patients reported their worst pain as severe.[45]

In the present study, the consumption of painkillers was higher in the Monoject® condition. Patients used 600 mg of ibuprofen three times a day and if necessary were instructed to combine the 600 mg of ibuprofen with 1,000 mg of paracetamol in case of high pain intensity. The combination of paracetamol and ibuprofen works effectively compared to taking ibuprofen alone.[46] In the current study, the effect of a tampon in the extraction socket was also obvious in terms of the intake of the prescribed analgesic and additional medications. It can be assumed that the iodine tampon dressing reduced the degree of inflammation and, consequently, the intake of the prescribed and other over-the-counter (OTC) pain relief medications. The significant difference ($p < .01$) in analgesic intake appeared on the second postoperative day and continued until the seventh postoperative day. Furthermore, less OTC pain relief medication was taken in the tampon condition (4%) compared to the Monoject® condition (22%). These different patterns regarding the intake of analgesics coincide with the significant difference in the postoperative daily mean pain score

The use of a tampon in the extraction socket is a form of surgical drainage. Other types of surgical drainage in third molar surgery are the use of a tube and a rubber drain. A recent meta-analysis of 10 randomized clinical trials found that surgical drainage after impacted mandibular third molar surgery results in less facial swelling and a better mouth opening during both the early stage (2-3 postoperative days) and late stage (5-7 postoperative days).[33] Postoperative pain was significantly less in the drainage group during the early stage, but there were no significant differences in the late stage. In the review, the tube drain had better results in terms of facial swelling and trismus compared to the rubber or gauze drain. However, the rubber drain was more effective regarding pain than the tube and gauze drains.[33] The advantage of the gauze drain compared to the rubber or tube drain is that its removal is easy, and no sutures are needed to fix the drain. Also, the medication impregnated in the gauze can have a positive effect on the postoperative sequela. Our results are in agreement with the different impregnated gauze studies, in which reduced pain, swelling, and trismus was seen after the use of a tampon at the surgical extraction site.[30,31,47] Assessing the effect of chlortetracycline ointment gauze, Akota et al. found a reduction in postoperative AO but failed to find beneficial effects on pain, swelling, and trismus.[29] Pain was less in the no-drain group on the day of surgery and first 2 postoperative days, but the mean pain intensity was not significantly different compared to the control group, which is in contrast with the findings of the present study. However, from the third day onwards, the pain was less in the drain group. Egbor and Saheeb evaluated the effect of whitehead varnish dressing in the extraction socket on postoperative pain, swelling, and trismus.[32] They found reduced swelling and trismus in the dressing group but no significant postoperative pain reduction. Although the difference in mean pain score was not significant between the study groups, the mean pain score was consistently lower in the dressing group. However, in that study, patients also received oral doses of 500 mg amoxicillin and 200 mg metronidazole every 8 h for 5 days. Therefore, it is unclear if the reduction in postoperative sequela was not influenced by the antibiotic administration.

Cerqueira et al. found that a drain helped control swelling, but found no effect on pain or trismus.[40] The pain was more severe in the non-drain group at 72 h and 7 days postoperatively, but at 24 h the pain was more severe in the drain group. The Cerqueira study could not be compared with the present study

because all patients received antibiotic prophylaxis. In addition, the pain was most severe when the mandibular third molar was in the distoangular position, and in the present study we only evaluated third molars in a symmetrical horizontal position.

The Rakprasitkul study had a comparable design to our study and no antibiotics were prescribed, but surgical times of 21.9 minutes in the drain group and 19.9 minutes in the non-drain group were significantly longer than in our study.[39] Surgical drainage had a positive effect on facial swelling and trismus but not on postoperative pain. In the present study, the surgical times for both procedures were similar, which eliminated surgical duration as a variable for postoperative pain, swelling, and infection. Surgical duration significantly correlates with trismus, pain, and total analgesics.[37,43]

In deeply impacted lower third molars, the mean duration of surgery can exceed 30 minutes. In one study, the mean duration of the difficulty classes was 36.8±22.8 minutes.[43] However, all the surgeries in that study were carried out by postgraduate students, which explains the difference in surgical time between most studies. Conrad found that prolonged surgery time, third molars below the occlusal plane, and female gender predicted longer recovery times.[45] Bui et al. reported that mesioangular impactions are associated with a higher risk of postoperative complications.[13] Deep impacted molars and insufficient space available in relation to the ramus are risk factors for severe postoperative discomfort.[3,20]

Infection rates were very low in the present study, with one case and no cases of AO observed. The incidence of AO in the literature varies, with rates ranging from 1% to 37%.[48] As in our study, zero incidence of AO was reported by Koray et al.[27] Special care was given to create bleeding or a blood clot in the alveolus during surgery and to instruct the patients not to rinse in order to not disrupt the blood clot formation in the socket.

Of course, the fact that no AO cases were observed in the present study is very positive, and may be attributed to the fact that no smokers were included in the study. In addition, the postoperative use of a CHX mouth rinse and the strict Monoject® rinse instructions may have contributed to the low infectious

complication rate. CHX is effective against both aerobic and anaerobic, and both Gram-positive and Gram-negative microorganisms and yeasts, and oral rinsing with CHX has been shown to reduce the quantity of oral microbial populations and may be effective in reducing the incidence of AO.[23,49] However, there is still considerable controversy regarding the effect of CHX on the incidence of AO. Some studies have found no beneficial effect of postoperative irrigation with saline compared to CHX, whereas other studies have reported a reduction in AO when using CHX.[23,49, 50]

In the present study, the extraction wound was not primarily closed. The secondary closure technique allows for drainage of wound fluid and involves healing by secondary intention. Complete closure has the advantage of better control of bleeding during the postoperative period, but could lead to a greater infection rate, as a valve effect that allows food debris to enter the socket without being able to escape.[51] In an earlier study, Lyall found that surgical wounds at third molar sockets were best kept open with a dressing, and that primary closure is not desirable.[47] Patients were instructed to rinse the extraction socket that did not receive a tampon with a Monoject® syringe and a saline solution, starting 48 h after surgery. The patients mixed a cup of water with a teaspoon of salt and rinsed four times a day, preferably after every meal and in the evening before going to bed. In a recent randomized study, irrigation of the surgical site with tap water using a curved syringe following extraction of the third molar was demonstrated to be effective in reducing the risk of inflammatory complications.[52]

The disadvantage of using a tampon after mandibular third molar surgery is that patients with the iodine dressing must return to the clinic for removal of the tampon. An extra visit is necessary, but many patients do appreciate the extra checkup, and the clinical benefits of the iodine tampon were obviously demonstrated in the present study. Although allergic reactions to iodine have been reported in the literature, no allergic side effects were seen in our study.

Another disadvantage is that the use of the iodine tampon may delay socket healing, as packing dressings into extraction sockets may delay healing and invoke foreign body reactions.[53] In the present study, the socket was only partially filled with the 2 cm tampon, which may not have had the same

impact regarding wound healing delay. An animal study however, showed that gelfoam packing impregnated with medication enhanced early socket healing.[53]

The use of antibiotics to prevent AO and postoperative infection is still controversial, but recent studies and systematic reviews have demonstrated that systematic antibiotics significantly reduce the risk of dry socket and infection in third molar surgery.[17,18,54] In a recent meta-analysis combining the results from 21 trials, the use of antibiotics reduced the risk of infection by 57% (RR=.43; 95% CI .33-.56). The efficacy of penicillin's was slightly greater than the efficacy of nitroimidazoles.[17] In a study of 1877 patients having 5631 third molars removed, the overall complication frequency in the group receiving postoperative antibiotics was 4.3% versus 7.5% in the group not receiving antibiotics.[18]

However, the use of antibiotics puts patients at risk of adverse reactions, such as allergies or diarrhea, and contributes to the development of antibiotic resistance.[55] Sekhar et al estimated that 6-7% of patients receiving antibiotics have adverse reactions.[56] In the present study, no infections were found in the tampon sites. Therefore, the use of a tampon may be a good alternative for antibiotic prophylaxis in mandibular third molar surgery requiring bone removal.

In the present study, all patients received an ice pack immediately after surgery. They were instructed to use the packs with a 10-min interval during the day of surgery until bedtime. However, Van der Westhuijzen et al. did not find any significant difference in postoperative swelling between the postoperative application of an ice pack and no ice application.[57] The difference with the present study was that patients in the previous study received continuous ice packs for up to 21 h. The patient's perception was that the control of postoperative pain and discomfort over the first 24 h was better with the ice packs.[57]

Despite the strength of the methodology chosen for this study, there are still some limitations that must be considered when interpreting the results. The data acquired from the patients were all self-reported. The disadvantage of using subjective data is that it cannot be controlled and, therefore, involves a risk

of bias. The only follow-up with the patients occurred 1 week postoperatively; thus, long-term complications could not be assessed. All the patients reported pain, swelling, problems with opening their mouth, mastication problems, and self-care interventions, such as taking the prescribed analgesics and applying cold packs. Pain, swelling, and functionality problems are the most important parameters of inflammation. Because of the lack of recall on days 3 or 4, the severity of the inflammation in these cases could not be determined. Another follow-up on the third or fourth postoperative day would be advantageous, as the problems peak at that time. In the present study, the changes in OHRQoL were assessed during the first 7 days after third molar surgery. Delayed onset infections are a rare complication that usually occur approximately 1 month after extraction.[58] Possible long-term complications could not be evaluated because late infections can occur after surgery. Patients were instructed to call or visit the outpatient clinic in case of any late adverse events, such as swelling and pain. Only three patients returned after the 1-week visit; one patient after 2 weeks for reassurance that everything was uneventful and two other patients (one after surgical mandibular third molar extraction with an iodine tampon and one after surgical removal without a tampon) returned after 3 weeks with some pain, which resolved after rinsing out the healing socket.

Blinding the patients for the intervention was not possible because the patients were able to taste the presence of the iodine-containing dressing in the extraction socket. The patients may have considered the placement of a dressing or the iodine-containing dressing to be a necessary part of any wound closure procedure; therefore, the patients' perception of the therapeutic superiority of the iodine-containing dressing could have been affected by placebo effect bias.

Another limitation is that we did not have information on how well or how often patients were able to use the Monoject® syringe. At the control visit, we reviewed the rinsing method but, as an earlier study demonstrated, a significant number of patients fail to use the syringe according to the instructions regardless of the education level of the patient.[52] Placing a tampon avoids the need for local irrigation, and the alveolar packing reduces exposure of the postoperative bone, which may result in a reduction in pain and food impaction.

Facial swelling and limited mouth opening occur as a response to surgical trauma after third molar surgery.[59] The onset of swelling is gradual, with peak swelling occurring 48 h after surgery, but the swelling increases the third day after surgery and lasts until the seventh day. Another limitation of the present study was that facial swelling was not measured, but reported on the OHIP-14 questionnaire. Previous studies have evaluated postoperative swelling by measuring three linear facial distances,[20,21] a tape measure method,[27] or 3D face scanning.[28] A limitation of the present study is that we used the OHIP-14 scores to subjectively assess postoperative swelling. However, all of the different methods for assessing the degree of postoperative swelling may not be more accurate than the estimations made by patients themselves.[4] As stated by Happonen et al., there is no objective way to assess the degree of intraoral swelling, which is experienced by the patients as being at least as unpleasant as extraoral swelling.[60]

However, the greatest limitation of the study is the number of participants which limits the number of subsequent complications after surgery. The study also is not applicable across broad populations due to the number of participants and the recruiting restrictions in the design. Although a sample size calculation showed that the number of patients included in the study was sufficient for a reasonable power, further research is necessary to assess the usefulness of the iodine tampon for broad populations

Conclusion

Within the limitations of this study, we conclude that the administration of an iodine-containing tampon positively improves the OHRQoL. Therefore, clinicians should take this intervention into consideration in order to reduce the postoperative inconveniences perceived by patients following the surgical removal of impacted mandibular third molars.

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Chapter 5

Alveolar iodine tampon packing after impacted third molar surgery improves oral health-related quality of life and postoperative sequela: a randomized study

This chapter is based on the publication:
Alveolar iodine tampon packing after impacted third molar surgery improves oral health-related quality of life and postoperative sequela: a randomized study

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Published: Oral and Maxillofacial Surgery, 2021

Abstract

Objective The aim of this study was to evaluate the effect of an iodine tampon on postoperative discomfort after surgical removal of a mandibular third molar.

Material and methods Patients were randomly assigned to two groups: one group received an alveolar iodine-containing tampon in the extraction socket (N = 44), and the other group used a disposable syringe (MonojectÒ) to rinse the wound (N = 43). Postoperative discomfort was assessed with the Oral Health Impact Profile-14 (OHIP-14) questionnaire, Pain Intensity Numerical Rating Scale (PI-NRS), and questions about self-care and discomfort.

Results This study included 87 patients (52 women and 35 men) with an average age of 26.47 years (SD, 6.36). The mean OHIP-14 sum scores were significantly lower in the iodine tampon group compared with the Monoject® syringe group. Mean PI-NRS scores significantly differed between the iodine tampon group (3.33; SE, 0.27) and Monoject® syringe group (4.46; SE, 0.27) ($F(1, 85) = 8.16$, $p < 0.01$), with no interaction effect between time and PI-NRS ($F(6, 510) = 1.26$, $p = 0.28$). Patients in the iodine tampon group reported less postoperative discomfort.

Conclusions Insertion of an iodine-containing tampon in the post-operative socket reduced the pain and impact on oral health related quality of life during the first postoperative week, and positively influenced post-operative sequelae.

Introduction

Surgical removal of an impacted lower third molar violates the integrity of soft tissues and bone, resulting in postoperative pain, swelling, and trismus and thus negatively impacts quality of life (QoL) [1–5]. A significant reduced QoL as a result of pain has been reported with patients experiencing their greatest pain on the first postoperative day slowly decreasing during the week [3-4, 6-8]. Postoperative complications like alveolitis and surgical site infection are associated with more and longer lasting postoperative pain [3].

Many efforts have been studied to prevent or reduce complications after third molar surgery. Antibiotic prophylaxis, chlorhexidine (CHX) mouth rinses, and local corticosteroids have been used to avoid infectious complications and ameliorate pain after mandibular third molar surgery [9-13].

Different studies have reported a beneficial effect of a locally applied gauze drain after the surgical removal of a mandibular third molar on alveolar osteitis, pain and swelling [14-17]. In a recent cross-over design study of our research group we found that insertion of an iodine-containing tampon into the extraction alveolus had a positive effect on oral health-related quality of life (OHRQoL), pain, trismus, and several self-care behaviors during the first postoperative week after surgical removal of a mandibular third molar [8].

Recently, a multicenter randomized controlled trial analyzing 333 surgically removed mandibular third molars in 280 patients demonstrated that rinsing out the surgical wound with a Monoject® syringe significantly reduced alveolar osteitis and pain [18].

In the present randomized design, we hypothesized that we would find the same positive effects in patients who received an iodine-containing alveolar tampon on the oral health-related quality of life and pain scores, as well as improved postoperative self-care and discomfort, compared with patients who rinsed the extraction alveolus with a disposable syringe (Monoject®) after wisdom tooth removal as was propagated in the Ghaeminia study [18].

Materials and methods

Study design

This prospective randomized controlled trial (RCT) was conducted between April and October of 2018. It was reviewed and approved by the Institutional Ethics Committee (METC) of the Academic Medical Centre of Amsterdam in the Netherlands.

Study population

Our study included patients who were referred by their dentist for surgical removal of an impacted mandibular third molar at the department of Oral and Maxillofacial Surgery of the Amstelland Hospital, Amstelveen, the Netherlands. After clinical examination, a panoramic radiograph was taken of each patient. Then an independent oral and maxillofacial surgeon decided whether the patient met the inclusion criteria. If the patient met the criteria and gave their signed informed consent to participate, the patient was given the Oral Health Impact Profile-14 (OHIP-14) questionnaire with instructions.

Inclusion and exclusion criteria

This study included only native Dutch speakers who were referred for surgical removal of one impacted mandibular third molar. Other inclusion criteria were age of ≥18 years, American Society of Anesthesiology (ASA) score of 1 (i.e., no systemic diseases or medical conditions), no discernible active pathology associated with the third molars, no acute pericoronitis, and no periodontal disease. Exclusion criteria were allergy to ibuprofen or iodine, smoking habit, presence of systemic disease, history of recent and/or symptomatic peptic ulcer, anti-platelet or anticoagulant therapy, pregnancy or lactating, recent local infection within 15 days prior to surgery, previous radiation therapy to the maxillofacial region, local pathology (e.g., cysts or tumor) associated with the third molars, and lack of consent to the procedure or the study.

Sample Size

For sample size calculations, we performed an a priori power analysis using G*Power 3.1.9.4 [19]. Using an independent-samples *t*-test, an alpha of 5%, a beta of 15%, one-tailed testing, and an effect size of 0.6, we determined that we needed a sample size of 41 patients per group.

Randomization and concealment of allocation

This prospective randomized controlled trial (RCT) comprised two groups: an intervention group, which received a postoperative iodine-containing tampon, and a control group, which was instructed to clean their wound with a Monoject® syringe. Following patient inclusion, participants were randomly assigned to a treatment group using a computer randomization generator. The data from the OHIP-14 questionnaire were collected by a student during the follow-up. The questionnaire results were disclosed to the surgeon after statistical analysis of the data.

Procedures

All surgical procedures were performed by one oral and maxillofacial surgeon. All patients received local anesthesia (articaine hydrochloride 40 mg with 0.01 mg epinephrine, 1.7 mL Ultracain D-S forte; Sanofi-Aventis, Gouda, the Netherlands) to block the inferior alveolar nerve, following the hospital's protocol. Additionally, infiltration anesthesia was administered in the buccal fold and distal of the incision in the mandibular ramus region.

A triangular incision flap technique was used for all patients [8, 20]. The first incision started from the distobuccal edge of the adjacent second molar, dropping down at a 45° angle with the gingival margin, into the mandibular vestibule. The second incision started laterally in the mandibular ramus, and extended to the middle the second molar, connecting to the distobuccal edge. The mandibular bone surface was exposed, and bone overlying the crown of the wisdom tooth was removed using a surgical bur. The crown was then split using a high-speed turbine handpiece. The bone removal and tooth splitting were accompanied by copious irrigation using sterile saline (0.9% NaCl). Following full removal of the tooth, the alveolus was inspected, and follicular tissue was removed. The socket was rinsed with 10 mL sterile saline (0.9% NaCl).

In the experimental group, an iodine-soaked tampon of 1 × 2 cm (Opraclean; Lohmann & Rauscher BV, Almere, The Netherlands) was placed into the surgical site. The Opraclean tampon is a 100% cotton gauze impregnated with an iodine ointment. The Opraclean dressing supports wound cleaning by absorbing exudate, cell debris and bacteria and has an antimicrobial effect. In the control group, nothing was placed into the surgical site. In both groups,

the surgical wound was sutured using Vicryl Rapide 3/0 (Undyed Vicryl Rapide; Johnson & Johnson, New Brunswick, NJ). The post-extraction socket was not primarily closed in either group.

Postoperative instructions

Immediately after surgery patients were given verbal and written postoperative instructions. Patients in both groups were provided with an ice pack for postoperative cooling. Patients in the control group were given additional instructions about how to use the disposable syringe (Monoject®) to rinse the wound 3–4 times daily with tap water for the next week, starting 48 hours after surgery. Patients in the tampon group did not receive a disposable syringe. All patients were instructed to bite on a gauze for 30 minutes. They were also instructed not to rinse or spit during the first 24 postoperative hours. Ibuprofen (Brufen; Abbot BV, Hoofddorp, The Netherlands), 600 mg 3 times a day, was prescribed. No postoperative antibiotics were given. The day after surgery, patients began using 0.12% aqueous chlorhexidine mouth rinse twice a day for 1 minute for 7 days. Patients were instructed to complete the daily OHIP-14 questionnaire at the end of the day (before bedtime) and they were recalled for review after 1 week.

Follow-up

One week after surgery, patients were seen by another surgeon to assess the wound healing of the surgical site, and check for alveolitis and wound infection. The patient's experience of sensory disorders was assessed using a 2-point discrimination test and static light touch detection test. At this time, the completed OHIP-14 questionnaires were collected.

Outcome measurements

The primary outcome measurements were OHRQoL measured using the OHIP-14, the presence of pain and the pain intensity, and the presence of postoperative sequelae, such as, trismus, swelling, and chewing problems. The secondary outcome measurements were self-care activities, surgical and anatomical variables, and presence of wound infection and alveolar osteitis (AO) [8].

OHIP-NL14 questionnaire

The participants completed a version of the OHIP-14 that has been translated into Dutch (OHIP-NL14) and evaluated by Van der Meulen et al. [21]. The OHIP-NL14 shows very good internal consistency and reliability (Cronbach's alpha = 0.90; intraclass correlation coefficient = 0.80) [22]. The questions from the OHIP questionnaire are answered on a 5-point scale that varies from never (0) to very often (4). The total score of the OHIP-14 ranges from 0 to 56, and the separate domain scores provide information regarding the level at which the consequences of the oral problem occur. A higher score on the OHIP-14 indicates a lower quality of life of the patient.

Pain intensity

We measured pain intensity using an 11-point pain intensity numerical rating scale (PI-NRS). Patients were asked to enter their pain score, ranging from 0 (no pain) to 10 (worst possible pain) on each day of the first postoperative week. Several studies have provided strong support of the validity and reliability of the PI-NRS for detecting changes in pain intensity [23–24].

Self-care and discomfort

Self-care and discomfort were measured daily during the first postoperative week. Patients also recorded their intake of prescribed and over-the-counter (OTC) medications. On postoperative day 1 (POD1), the patient reported the number of hours that they used ice packs to cool their cheek on the side of surgery. Patients were also asked to keep a daily record of the presence of swelling, trismus, pain, or inflammatory complications—giving a response of "yes" or "no" for each.

Statistical analysis

The sample was characterized using conventional descriptive statistics. The Chi^2-test was used to examine associations between categorical variables. Mean scores of multiple measurements in the same subjects were compared using ANOVA for repeated measures. The mean scores between two repeated measurements were compared using the paired-samples *t*-test. For skewed data (number of painkillers), analysis was repeated using the Friedman test and the Wilcoxon signed-rank test. An alpha of 5% was set as the level of significance.

Results

Description of subjects

A total of 87 subjects participated in this study, including 52 women and 35 men, with an average age of 26.47 years (SD, 6.36 years). These participants were randomly allocated to the experimental group (iodine tampon) or control group (Monoject® syringe). A chi-square test showed that the distribution of men and women did not significantly differ between the two conditions (Table 1). An independent-samples *t*-test revealed that the average age was significantly higher in the experimental group compared to the control group. Correlation analysis (Pearson's) for the age variable and the seven mean OHIP-14 sum scores (repeated measurements of OHIP-14 over seven postoperative days) did not reveal statistically significant correlations; therefore, age was not included as a covariate in follow-up analyses.

Table 2 presents a frequency table showing the Pell & Gregory classification for both groups [25]. The Mann-Whitney U test was used to analyze differences in impaction grade between the two conditions. The results showed that impaction grade did not significantly differ between the iodine tampon group and the Monoject® syringe group (U = 735.00, z = −1.91, $p = 0.56$).

Table 1: Characteristics of examined groups

	Iodine tampon (N = 44)	Monoject® syringe (N = 43)	Difference test
Men	17	18	$\chi^2 = 0.94$, df = 1, $p = 0.76$
Women	27	25	36
Average age (SD)	28.11 (7.27)	24.79 (4.80)	$T = -2.51$, $df = 74.73$, $p = 0.014$

Table 2: Frequency Pell & Gregory classification of impaction of examined groups

Impaction grade	Iodine tampon (N = 44)	Monoject® syringe (N = 43)	Total
2a	2	3	8
2b	5	5	10
3a	12	20	32
3b	22	15	37
3c	3	0	3
Total	44	43	87

OHIP-14: iodine tampon versus Monoject® syringe

To determine whether the mean OHIP-14 sum score changed during the first postoperative week in the iodine tampon group and the Monoject® syringe group, we carried out two separate repeated measures ANOVA (RMA) comparing the means on each postoperative day (Table 3). The results showed a significant effect of time in the iodine tampon group [F (6, 258) = 61.58, $p < 0.001$, $\eta p^2 = 0.59$], as well as in the Monoject® syringe group [F (6, 252) = 108.99, $p < 0.001$, $\eta p^2 = 0.72$]. For each group, pairwise comparison of the mean OHIP-14 sum scores from the seven postoperative days showed that all measurements declined over time and significantly differed from each other ($p < 0.001$).

We next assessed the extent to which the mean OHIP-14 sum scores differed between the two interventions across the multiple measurements, by performing a repeated measures ANOVA between-subjects factor. The results indicated that there was a statistically significant interaction effect between the factor of time and each intervention (iodine tampon and Monoject® syringe) [$F (df = 6, 510) = 3.27$, $p = 0.004$, $\eta p^2 = 0.037$]. This meant that the changes in the mean OHIP-14 score over time differed between the two conditions (Figure 1).

To investigate the source of the significant interaction effect between the two groups, first, we calculated a mean difference score (i.e., change over time) between the first and second postoperative day, between the second and third postoperative day, etc. Next, we compared the two patient groups with regards to the mean changes for each calculated difference score. Table 4 presents the comparison of differences between the mean OHIP-14 sum scores for the two conditions. The independent-samples *t*-tests revealed that the difference $\Delta 7\text{-}6$ was statistically significant ($p = 0.048$). The independent-samples *t*-test enabled examination of whether the conditions differed in the mean OHIP-14 sum scores for the 7 post-operative days (Table 3). We found that the mean OHIP-14 sum scores were significantly lower in the iodine tampon group than in the Monoject® syringe group, except on postoperative days 6 and 7.

Figure 1: OHIP-14 sum scores on the seven postoperative days for both conditions

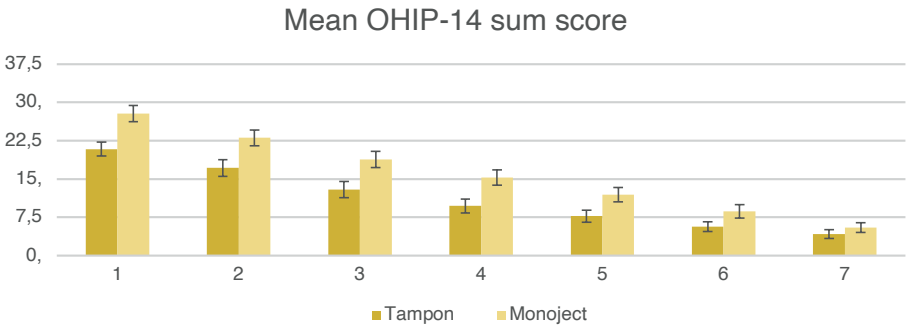

Table 3: Mean OHIP-14 sum scores in the iodine tampon and Monoject® syringe conditions

Intervention OHIP-14 Mean (SD)	Iodine tampon (N = 44)	Monoject® syringe (N = 43)	*p* value[a]
Day 1	20.84 (9.11)	27.79 (10.19)	0.001
Day 2	17.16 (11.15)	23.07 (10.08)	0.011
Day 3	12.91 (10.69)	18.84 (10.25)	0.010
Day 4	9.72 (9.09)	15.29 (9.51)	0.006
Day 5	7.71 (7.73)	11.93 (9.13)	0.022
Day 6	5.64 (6.48)	8.66 (8.35)	0.064
Day 7	4.19 (5.93)	5.50 (6.20)	0.319

[a] *p* value from independent-samples *t*-test for differences in mean OHIP-14 sum scores for each of the 7 post-operative days between the iodine tampon and Monoject® syringe conditions.

Table 4: Independent-sample *t*-tests of differences in mean delta OHIP-14 between the iodine tampon and Monoject® syringe conditions

Intervention Differences between POD	Iodine tampon (N = 44) Mean (SD)	Monoject® syringe (N = 43) Mean (SD)	*p* value
D 2-1	−3.68 (9.32)	−4.72 (5.21)	0.52
D 3-2	−4.25 (4.24)	−4.23 (4.50)	0.99
D 4-3	−3.19 (4.84)	−3.55 (4.94)	0.74
D 5-4	−2.01 (3.96)	−3.36 (5.02)	0.17
D 6-5	−2.06 (3.22)	−3.27 (4.58)	0.16
D 7-6	−1.46 (3.69)	−3.16 (4.24)	0.048*

* $p < 0.05$

PI-NRS: iodine tampon versus Monoject® syringe

To assess the use of an iodine tampon compared with the Monoject® syringe in terms of the measured pain intensity score during the first postoperative week, we carried out two separate RMA and independent-samples *t*-tests, comparing the PI-NRS scores for both groups on each postoperative day. RMA analysis revealed a statistically significant effect of time in the iodine tampon group [$F (6, 258) = 46.48$, $p < 0.001$, $\eta p^2 = 0.52$] as well as in the Monoject® syringe group [$F (6, 252) = 57.64$, $p < 0.001$, $\eta p^2 = 0.58$]. A pairwise comparison of the PI-NRS score over seven postoperative days in the iodine tampon group revealed that all measurements declined over time and significantly differed from each other, except between postoperative days 1–2 ($p = 0.065$). Pairwise comparison of the mean PI-NRS score over seven postoperative days in the Monoject® syringe group showed that the mean scores declined over time, with significant differences between all days ($p <0.05$).

We additionally carried out a repeated measures ANOVA between-subjects factor analysis to evaluate differences in the PI-NRS between the two conditions. The results revealed that the mean PI-NRS significantly differed between the iodine tampon group (3.33; SE, 0.27) and Monoject® syringe group (4.46; SE, 0.27) [$F (1, 85) = 8.16$, $p < 0.01$], and we found no interaction effect between time and condition on the PI-NRS [$F (6, 510) = 1.26$, $p = 0.28$].

To determine the effect of the iodine tampon compared to use of the Monoject® syringe, we performed independent-samples *t*-test analysis on PI-NRS scores for the seven postoperative days. Table 5 shows the differences in mean PI-NRS scores between the iodine tampon and Monoject® syringe conditions on each postoperative day. The results showed that the mean PI-NRS scores in the iodine tampon group were significantly lower from post-operative day 1 up to and including postoperative day 4. The two groups did not significantly differ on the subsequent postoperative days.

Table 5: Mean PI-NRS scores in the iodine tampon and Monoject® syringe conditions

Intervention PI- NRS Avg. (SD)	Iodine tampon (N = 44)	Monoject® syringe (N = 43)	*p* value[a]
Day 1	5.22 (2.32)	6.61 (1.70)	0.002
Day 2	4.74 (2.50)	5.84 (1.94)	0.025
Day 3	3.94 (2.58)	5.40 (1.78)	0.003
Day 4	3.16 (2.41)	4.69 (1.91)	0.002
Day 5	2.73 (2.41)	3.56 (2.14)	0.093
Day 6	2.14 (2.26)	3.02 (2.33)	0.075
Day 7	1.41 (2.08)	2.12 (2.10)	0.116

[a] *p* value from independent *t*-test for differences in mean PI-NRS scores for 7 post-operative days between the iodine tampon and Monoject® syringe conditions

Discomfort and self-care

Table 6 presents the results concerning the variables on self-care and discomfort, which clearly demonstrated a superior effect of iodine-containing tampons during the first postoperative week after extraction. Notably, on postoperative day 4, 57% of patients in the intervention group used the prescribed medication, compared to 84% in the control group. Similar results were found with regards to the presence of limited mouth opening (trismus), chewing problems, swollen cheek, and pain. Additionally, "no discomfort at all" was reported on postoperative day 4 by 2% of patients in the intervention group compared to 0% of the control group, and on postoperative day 7 by 45% of the intervention group compared to 30% of the control group. The two groups reported a similar number of hours that they cooled their cheek with an ice pack on the first day after surgery, and an independent-samples *t*-test showed no significant difference groups in the mean number of cooling hours [t (85) = .97, $p = 0.33$; mean, 5.3 h; range, 0–12 h].

Duration of surgery

The mean duration of surgery in the control group was 11.07 min (SD, 1.10 min). The mean surgery duration in the intervention group was significantly longer: 12.18 min (SD, 2.64 min).

Table 6: Percentage of patients who answered 'yes' on the self-care and discomfort questions

Question (yes)	Intervention	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Did you use the prescribed medication?	Monoject	100	93	91	84	65	49	40
	Tampon	98	89	86	57	48	34	25
Did you cool with an ice package?	Monoject	100	51	23	14	14	2	0
	Tampon	100	45	25	14	9	5	5
Did you use additional medication other than that prescribed?	Monoject	26	16	19	14	19	14	7
	Tampon	18	14	16	18	11	9	9
Did you follow the same routine as always?	Monoject	0	2	5	12	26	47	60
	Tampon	2	11	20	32	50	64	73
Did you experience limited mouth opening?	Monoject	100	98	93	79	70	42	37
	Tampon	98	93	86	73	57	39	23
Did you experience reduced chewing ability?	Monoject	93	91	91	81	72	42	30
	Tampon	91	80	70	73	57	45	30
Did you experience a swollen cheek?	Monoject	93	95	95	86	63	37	26
	Tampon	82	93	93	77	43	23	11
Did you experience pain as a result of surgery?	Monoject	98	93	88	79	65	63	47
	Tampon	86	84	80	64	59	45	25
Did you experience any discomfort?	Monoject	0	0	0	0	0	12	30
	Tampon	0	0	0	2	16	25	45

Postoperative complications

There were no cases of postoperative infection or AO. Temporary hypoesthesia occurred in two cases (0.5%) in the control group after surgical removal of the third molar. Full recovery of sensibility was observed in both patients after the 6 months.

Discussion

In the present study, we aimed to assess how the use of an alveolar iodine-containing tampon affected postoperative oral health-related quality (OHRQoL) following third mandibular molar surgery. In accordance with previous findings, surgical removal of the impacted mandibular third molar significantly affected OHRQoL during the first postoperative days [1–8]. Postoperative sequelae, such as pain, trismus, swelling, and chewing problems, commonly arise after tissue injury. Numerous researchers have studied the effects of various preoperative, intraoperative, and postoperative intervention strategies to avoid or decrease the degree of discomfort due to inflammation induced by tissue injury during the surgical removal of mandibular third molars [26–34]. Here, we demonstrated that the application of an iodine-containing tampon reduced the amount of perceived postoperative discomfort, and thus improved the OHRQoL.

We used the OHIP-14 questionnaire to evaluate the effects of iodine-containing tampons on the physical, social, psychological, and functional aspects of daily life. Daily measurement of the mean OHIP-14 sum scores in the iodine tampon group revealed that the scores significantly decreased each day from the first postoperative day to the seventh. In the Monoject® syringe group, the mean OHIP-14 sum scores for postoperative days 1 and 2 were similar to the values in a 2012 study by Kieffer et al. [20]. However, on postoperative day 3, the mean OHIP-14 sum score was lower in the Monoject® syringe group in our study compared with the Kieffer's study. This indicated that postoperative irrigation of the extraction socket was beneficial to decrease the amount of discomfort. Ghaeminia et al. previously reported benefits of the use of a Monoject® syringe after mandibular third molar surgery [18]. In the present study, the postoperative extraction sockets were not primarily closed, and thus remained a vulnerable site for debris accumulation.

The other major primary outcome measure in our study was the effect of alveolar iodine-containing tampons on postoperative pain intensity. For pain relief, the patients were prescribed ibuprofen 600 mg, commencing immediately after the surgery. Bailey and colleagues proposed that NSAIDS, such as ibuprofen, should be considered the first choice of pain relief medication [35]. In addition

to the prescribed ibuprofen 600 mg, the patients in our study also reported the type and dosage of any other over-the-counter (OTC) medications used. Most patients reported the intake of paracetamol 1000 mg in combination with their prescribed medication. This combination is reportedly beneficial for pain relief after third molar surgery.

Both study groups reported pain on postoperative day 1. The Monoject® syringe group exhibited a slightly higher pain score on the 1st postoperative day, and the two study groups significantly differed in pain perception on the following days. Additionally, the Monoject® syringe group had a higher percentage of patients with intake of prescribed medications on all assessed postoperative days. On the 4th postoperative day, less than 60% of patients in the iodine tampon group were taking prescribed medications, compared with over 80% of the patients in the Monoject® syringe group. The two groups also showed differences in other clinical parameters commonly induced as the result of inflammatory responses, such as swelling, trismus, and chewing problems. The differences in these clinical parameters appeared to be higher after the 3rd postoperative day. From these results, it was obvious that the iodine-containing tampon group suffered less postoperative inconvenience.

Several factors have been identified as risk factors for the severity of postoperative sequelae [31, 36], including patient's age, gender, anatomical and surgical variables (e.g., degree of impaction), wound closure techniques, operator experience, and the procedure duration. In the present study, the two groups did not significantly differ in the distribution of men and women, but a *t*-test for independent observations revealed a significant between-group difference in age. However, Pearson's correlation analysis did not reveal a statistically significant correlation between age and mean OHIP-14 sum scores. This finding is in accordance with results presented by Benediktsdóttir et al. [37]. Moreover, the independent *t*-test showed no statistically significant correlation between gender and mean OHIP-14 sum scores. All procedures were performed by one specialized oral and maxillofacial surgeon; therefore, operator experience did not influence the results, and could be eliminated as a variable adversely effecting OHRQoL [7, 38-40]. The mean operating duration was significantly lower for the control group (11.07 min) compared to the intervention group (12.18 min), but the difference was clinically irrelevant.

Many prior studies have evaluated how different wound closure techniques influence the degree of discomfort after the surgical removal of third molars. There remains considerable controversy, with some studies suggesting that an open wound may be beneficial [41–44], while others found that primary closure of the wound is more convenient [45]. In both groups of our present study, the postoperative extraction sockets were left open for healing by means of secondary intention. The patients in the Monoject® syringe group were instructed to irrigate the post-extraction socket with saline at 48 hours postoperatively. For patients in the experimental group, an iodine-containing tampon was placed in the extraction socket after molar extraction. Wound healing by secondary intention and administration of an alveolar iodine-containing tampon in the post-operative extraction socket is a form of surgical drainage.

Over the past three decades, multiple studies have examined the administration of various foreign agents in a post-extraction socket [14-17] and have evaluated how these agents impact the degrees of pain, swelling, trismus, and chewing problems. Additionally, several prior studies have evaluated the effects of surgical drainage on wound healing, postoperative sequelae, and pain. Hollander et al. observed reduced postoperative pain and swelling when using a bismuth iodoform paraffin paste-impregnated (BIPP) ribbon gauze dressing with partial closure, compared to a primary closure technique [14]. Similarly, Egbor et al. reported reduced postoperative swelling and trismus in patients treated with a Whitehead's Varnish dressing in the socket, compared to primary closure [15]; however, the measured pain score did not significantly differ between these study populations. Notably, all patients received oral administration of 500 mg amoxicillin and 200 mg metronidazole for 5 days postoperatively, and thus it is unclear whether the positive effects can be fully attributed to the dressing intervention. Consistent findings were also described by Chukwuneke et al. [46] and Chaudhary et al. [47].

Liu et al. [17] performed a systematic review of ten randomized controlled trials to evaluate the effectiveness of surgical drainage after mandibular third molar surgery. They concluded that surgical drainage has a positive effect on postoperative sequelae, resulting in less swelling and trismus during the early and late stages, and significantly less pain during the early stage. They also

evaluated three types of drainage methods and concluded that the tube drain group showed better results than the rubber drain and gauze drain groups, due to a stronger drainage effect. Akota et al. [16] assessed the post-surgical effects of locally applied gauze drain impregnated with chlortetracycline ointment and concluded that the impregnated drain effectively reduced alveolar osteitis. However, they did not find any beneficial effects on postoperative pain, swelling, or trismus. Rakprasitkul et al. [48] compared primary closure with placement of a tube drain after surgery, and found that surgical drainage did not influence pain but had a significant positive effect on postoperative swelling and trismus, which is in agreement with the finding of Egbor et al. [15].

Benediktsdóttir et al. reported that the use of an ice pack to cool the masseteric region, starting immediately after surgery, resulted in significantly reduced swelling and trismus ($p < 0.05$) on postoperative days one, two, and seven [37]. However, Van der Westhuijzen et al. [49] and Zandi et al. [50] did not find any significant difference in postoperative sequelae with the application of an ice pack after third mandibular surgery in their studies. In our present study, immediately after the operation, patients in both groups were given an ice pack and instructed to apply it to the cheek on the side of intervention in 10-min intervals. Although both groups used ice packs, the two groups in our study exhibited significantly different degrees of swelling, based on the overall mean OHIP-14 sum scores measured on the first three days postoperatively. Notably, Benediktsdóttir et al. reported that level of impaction was correlated with postoperative pain [37]. In our present study, the Mann-Whitney U-test showed that no significant differences in impaction grade between the iodine tampon group and the Monoject® syringe group ($U = 735.00$, $z = -1.91$, $p = 0.56$). However, the iodine tampon group included more patients with a higher impaction grade compared to the Monoject® syringe group. Thus, with all other things being equal, the iodine tampon group was at a greater risk for postoperative pain. Considering that patients in the iodine tampon group perceived less postoperative sequelae, it is likely that the effect of an alveolar iodine tampon on OHRQoL would have been even greater than in our present results if both groups had been equal.

Chlorhexidine (CHX) has an antimicrobial effect that can last up to 24 hours. Several studies have evaluated the effect of a CHX rinse on the incidence of AO [12–13]. Rinsing preoperatively and up to seven days postoperatively with CHX 0.12% significantly reduces the incidence of AO. On the other hand, a single preoperative rinse with CHX was not associated with a significant reduction in AO incidence [51]. Adverse side effects, such as tooth discoloration and alteration in taste, have been reported with prolonged use of CHX [52–53]; therefore, it is advised that CHX use should be limited to a short period. In our present study, the incidence of surgical site infection (SSI) and AO was 0%. These results were positive compared to the prevalence rates reported in other studies, which vary between 1–30% and 3.9–29.6% respectively [54–55].

Despite much effort to objectify our present results, there are several limitations that must be considered when interpreting the results. All third molars removed in the present study were asymptomatic and without pathology; therefore, no statements can be made about the effectiveness of placing an iodine-containing tampon in the post-extraction socket in cases of active pathology. Additionally, this study only measured the effects of the iodine-containing tampon after surgical removal of the mandibular third molars; therefore, our results cannot be extrapolated to other extraction sites in the tooth arch. Another limitation is that there is a lack of data regarding the correct usage of the Monoject® syringe by the patients. Failing to correctly rinse the post-operative extraction socket after surgery may lead to food impaction, infection, and delayed healing time. Ghaeminia et al. reported that 42% of the patients were unable to irrigate the post-operative extraction socket, despite having received instructions [18]. This issue may have resulted in more postoperative sequelae for the control group, and thus adversely affected patients' QoL. Finally, the data regarding the postoperative days were filled in by the patients themselves. Although self-assessment or self-reporting is a preferred method for data acquisition, the data are subjective, and the assessment of self-reported data is not immune to potential bias [56]. A recall on postoperative day three or four would have been helpful for objective assessment of the clinical parameters.

Conclusion

The results of our present study indicated that the administration of an alveolar iodine-containing tampon in the post-operative extraction socket, after removal of an impacted mandibular third molar, resulted in improved OHIP-14 and PI-NRS scores. The use of an iodine tampon also had positive effects on post-operative sequelae, and thereby resulted in less postoperative inconvenience and discomfort following the surgical removal of an impacted mandibular third molar.

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Chapter 6

Oral Health-related quality of life after coronectomy for impacted mandibular third molar in the first postoperative week

This chapter is based on the publication:
Oral Health-related quality of life after coronectomy for impacted mandibular third molar in the first postoperative week

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Published: Medicina Oral, Patología Oral y Cirugía Bucal, 2021

Abstract

Background: Coronectomy of a mandibular impacted third molar is a surgical treatment to minimize the risk for inferior alveolar nerve damage. We aimed to determine whether this procedure affected the oral health-related quality of life (OHRQoL) within the first postoperative week.

Material and Methods: This prospective study included 50 patients that underwent a coronectomy for an impacted mandibular third molar. The patients completed the Oral Health Impact Profile-14 (OHIP-14) questionnaire and questions about pain and analgesic intake on every day during the first postoperative week.

Results: Mean OHIP-14 scores were highest during the first three postoperative days; the highest mean score (26.40, SD: 8.67) was observed on the first postoperative day. Mean OHIP scores gradually declined during the first postoperative week, and the mean OHIP-14 score was 9.82 (SD: 9.15) on the seventh day. Physical pain was the highest contributor to the overall OHIP-14 score. Pain gradually declined with time; the lowest mean pain score (3.38, SD: 2.2) was observed on the seventh day. OHIP-14 and pain scores were not significantly different between sexes or between different grades of impaction. OHIP-14 scores were positively correlated with pain scores.

Conclusions: A mandibular third molar coronectomy had a strong effect on patient OHRQoL, particularly during the first three postoperative days.

Introduction

Surgical removal of the mandibular third molar is a very common oral surgical procedure. Postoperative inflammatory conditions, like alveolar osteitis and surgical site infections, are frequent complications after this procedure, but they are typically easy to manage. A less common, but more serious complication is an inferior alveolar nerve (IAN) injury, which can lead to a neurosensory deficit. In 1-3.6% of IAN injuries, the neurosensory disturbance is permanent.[1-3] This can cause long-term effects, such as persistent sensory loss, chronic pain, and depression.[4,] The risk of damaging the IAN is high during surgical removal of a third mandibular molar, due to the close relationship between the molar roots and the IAN. The IAN is located deep in the mandible; thus, a coronectomy can minimize the risk of IAN injury.[5-11] The fundamental objective of a coronectomy is to prevent trauma to the IAN by removing only the crown of an impacted mandibular third molar. Thus, the roots remain in place, and the IAN is untouched.[12] Previous reports on the mandibular third molar coronectomy were mainly focused on the surgical technique, root migration, postoperative IAN function, socket healing, and postoperative inflammatory parameters.[3,6,13] Little emphasis has been placed on the postoperative quality of life (QoL). As in any surgery, the coronectomy of a mandibular third molar causes tissue damage, and as such, it will have an impact on the oral health-related quality of life OHRQoL.

The present study aimed to investigate whether an impacted mandibular third molar coronectomy would affect the OHRQoL during the first postoperative week. We surveyed patients with the Oral Health Impact Profile-14 (OHIP-14) questionnaire. Previous studies have demonstrated the effect of surgical removal of mandibular third molars on OHRQoL with the OHIP-14 questionnaire, but no study focused on the mandibular third molar coronectomy.[14-15] In addition, we assessed postoperative pain, swelling, trismus, alveolar osteitis, and infection in the week after a third mandibular molar coronectomy.

Materials and methods

Participants

Eligible patients were referred by their dentist to the Department of Oral and Maxillofacial Surgery of the Amstelland hospital in Amstelveen, The Netherlands, for removal of an impacted mandibular third molar. Patients with asymptomatic impacted mandibular third molars that underwent a coronectomy between January 2019 and December 2019 were included. Inclusion criteria were age 18 years or older, healthy (American Society of Anesthesiologists (ASA) 1), willing to participate, and able to read, understand, and answer the questionnaire. Exclusion criteria were: known allergies to ibuprofen or chlorhexidine; smoker; periodontitis; a medical history involving renal failure, blood diseases, or chronic liver disease; taking anti-aggregants or corticosteroids, currently, or in the 15 days prior to surgery; breastfeeding or pregnant; local infection, preoperatively or in the 15 days prior to surgery; previous radiation therapy to the maxillofacial region; uncontrolled diabetes; taking antibiotic prophylaxis for endocarditis; or any local pathology.

This prospective study was reviewed and approved by the institutional Medical Ethics Committee of the Amsterdam University Medical Center. The study was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki, as amended in Somerset West, Republic of South Africa, in 1996. Patients were provided with information to explain the study, and all patients consented to participate in the study. Patients also agreed to attend two appointments (the surgery and a control visit). All patients were fully informed about the surgical procedure, postoperative care, possible complications, and follow-up examinations. Each patient was informed that they had the opportunity to withdraw from the study at any time, without consequences regarding the treatment.

Study procedure

This study included 50 patients. Preoperatively, patient demographic and medical information was recorded, and the patients were labeled patient 1 to patient 50, to ensure confidentiality of patient information during the study. We recorded the location of the impacted third molar, and we performed an X-ray orthopantomogram to assess the degree of impaction (Pell and

Gregory's classification). We also recorded the proximity of the IAN to the third molar roots. With 3-dimensional computed tomography, we confirmed the relationship between the IAN and the roots of the impacted mandibular third molar.

Surgical procedure

The impacted mandibular third molar coronectomy was performed with the patient under local anesthesia. All surgeries were performed by one surgeon in a standardized fashion, with a similar technique in all cases. All patients received a standardized, mandibular nerve block injection, with additional local infiltration of the buccal nerve. The location, temperature, type, and amount of anesthetic (40 mg articaine/hydrochloride with .01 mg epinephrine, administered with a 1.7-mL syringe, Ultracain D-S forte; Sanofi-Aventis, Netherlands BV, Gouda, the Netherlands), and the type of needle (27 gauge/.40 × 35 mm) were all standardized, according to the hospital protocol. A triangular flap was used in all patients. Briefly, an incision was started at the distobuccal edge of the second molar, then dropped at a slight oblique angle, and then curved forward into the mandibular vestibule. The second part of the incision started from the mandibular ramus and ended at the distobuccal aspect of the second molar. Any bone overlying the crown of the impacted third molar was removed with a round surgical bur, which exposed the cementoenamel junction of the tooth. Next, a fissure bur was used to separate the crown from the roots. The root was shortened to 3-4 mm below the bony margin and checked for mobility. Copious irrigation with sterile saline was performed with rotary instrumentation. Dental follicular soft tissue was removed, and the socket was thoroughly irrigated with saline. The surgical site was primarily closed with 3/0 Undyed Vicryl Rapide (Ethicon, Somerville, MA, USA). Immediately after surgery, the details of the procedure were recorded.

Postoperative management

After surgery, all patients were instructed to bite on gauze for 30 min. They were also instructed not to rinse or spit during the first 24 h postoperatively. Ibuprofen (600 mg Brufen, Abbot BV, Hoofddorp, the Netherlands) was prescribed three times a day. No postoperative antibiotics were prescribed. The day after surgery, patients began rinsing the mouth with a 0.12% aqueous chlorhexidine mouth rinse for 1 min twice per day for 7 days. Patients were

given verbal and written postoperative instructions, and they were recalled for follow-up at 1 week.

Follow-up

One week after surgery, patients were examined to assess surgical site wound healing and to check for alveolitis and wound infection. At that time, the completed OHIP-14 questionnaires were collected.

Outcome measurements

The outcome measurements included the OHIP-14 score, the pain score, based on the numeric rating scale (NRS) and the daily analgesic intake. OHRQoL was assessed with the OHIP-14 questionnaire. It involved the following parameters: problems pronouncing words, altered sense of taste, difficulty in chewing, pain/aching, worry about dental problems, psychological discomfort, problems affecting the diet, interruptions in meals, difficulty relaxing, feeling embarrassed, feeling irritable, job-related difficulties, less satisfaction in life, and functional inabilities. The short form of the OHIP-14 consisted of 14 items within 7 domains, including: functional limitations, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicaps.[15-16] Patients rated each item on a 5-point scale, with 4=very often, 3=fairly often, 2= sometimes, 1=hardly ever, and 0=never. The total score ranged from 0 (minimum impact) to 56 (maximum impact). Scoring high on the OHIP-14 questionnaire indicated that the surgery had a strong impact on the OHRQoL. Pain assessment was measured by rating pain intensity with an 11-point NRS, which ranged from 0 (no pain) to 10 (worst possible pain). Patients self-rated their pain on each day of the first postoperative week.[14-16] The questionnaires were completed daily at the end of the day.

At the 1-week control visit, an independent assessor evaluated wound infection, alveolitis, and the sensory function of the IAN. The patients were assessed for sensory disorders, such as pain, numbness, dysesthesia, or paresthesia, based on a 2-point discrimination and static light touch detection test.[3]

Data management

All patient data on infection, alveolitis, analgesic intake, pain scores and OHIP-14 scores were collected between January 2019 and December 2019 and

imported into a database. The data also included two demographic variables: the age at surgery (years) and sex. Gregory and Pell's classification of the third molar position was used to describe the degree and type of mandibular impaction.

Statistical analysis

Conventional descriptive statistics were performed to characterize the patient sample. The Shapiro-Wilk test showed that all the outcome variables in this study were normally distributed ($p>0.05$). Repeated measures ANOVA was used to assess the mean differences of OHIP- and pain scores over time from day 1 to day 7. If the overall p-value of the repeated measures ANOVA was smaller than 0.05, pairwise comparison was used to test differences between any two time points. Pearson's correlation test was performed to analyze correlations between different variables. The independent sample t-test was used to determine if there was a significant difference in OHIP-14 scores, pain scores and analgesic intake between the male and female variables on each postoperative day. The one-way ANOVA tests were used to determine if there were statistically significant differences in the means of pain and OHIP-14 scores between the different categories of the Pell and Gregory degrees of impact, separately.

Results

Data from 50 patients were available for analysis, including 13 (26%) males and 37 (74%) females. The mean ages were 25 years (range: 19 to 35) for males and 25 years (range: 18 to 36) for females. The treated third molar was on the left side in 30 patients and on the right side in 20 patients. The treated molar alignments included 60% mesioangular, 24% horizontal, and 16% vertical (Table 1). The degree of impaction varied from grades 1A to grade 3B, according to Gregory and Pell's classification.

Table 1: Patient demographics and mandibular third molar characteristics

Gender	
Male	13 (26%)
Female	37 (74%)
Age (yrs), mean, (range)	25 (18-36)
Pattern of impaction (%)	
Vertical	16%
Horizontal	24%
Mesioangular	60%

OHIP-14 and Pain scores

Table 2 and Table 3 show the mean pain- and OHIP-14 scores on each postoperative day. On the first postoperative day, pain was the highest (mean score; 6.40 SD 2.07). Pain gradually declined with time, being the lowest on the seventh day (mean score: 3.38, SD 2.24). Result from the repeated measures ANOVA test showed this decline in pain score was significant ($p<0.01$) and the pairwise comparisons revealed a statistically significant difference ($p<0.05$) between the means of each different postoperative day, except between day 1 and 2 and day 2 and 3. The repeated measures ANOVA test also showed this decline over time in the mean OHIP-14 scores ($p<0.01$). This decline over time was statistically significant on each postoperative day ($p<0.05$). The independent sample t-test showed that there were no significant differences between males and females in the total OHIP-14 scores and the pain scores on each postoperative day ($p>0.05$; Table 1). Figure 1 shows the mean pain scores on each postoperative day.

Table 2: Means and standard deviations (SD) of total OHIP-14 scores for males, females, and total samples on postoperative days (POD's) 1 to 7 (n=50).

	Males (n=13)		Females (n=37)		All (n=50)	
POD	Mean	SD	Mean	SD	Mean	SD
1	28.77	5.15	25.56	9.52	26.40	8.67
2	23.13	9.34	23.92	10.54	23.72	10.09
3	23.37	9.44	21.49	12.16	21.98	11.46
4	19.52	9.2	18.77	12.82	18.97	11.9
5	17.35	8.48	15.88	12.82	16.26	11.78
6	14.27	9.78	13.88	11.4	13.47	10.92
7	11.34	8.98	9.29	9.27	9.82	9.15

OHIP-14: Oral Health Impact Profile-14 questionnaire

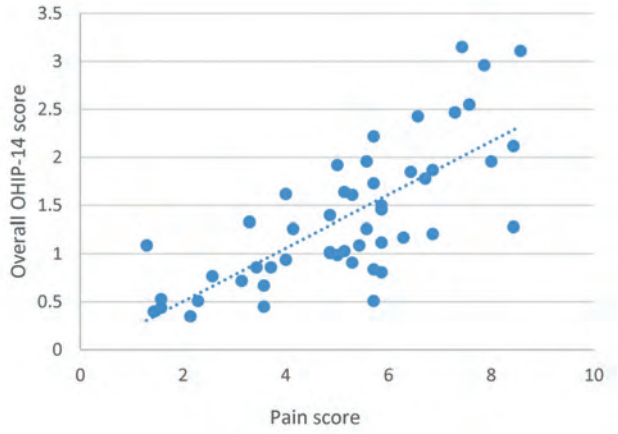
Table 3: Means and standard deviations (SD) of total pain scores for males, females, and total samples on postoperative days (POD's) 1 to 7 (n=50).

	Males (n=13)		Females (n=37)		All (n=50)	
POD	Mean	SD	Mean	SD	Mean	SD
1	6.62	2.06	6.32	2.1	6.40	2.07
2	5.77	1.97	6.14	2.12	6.04	2.07
3	5.38	2.06	6.00	2.10	5.84	2.08
4	4.92	2.02	5.46	2.39	5.32	2.29
5	4.38	1.76	4.86	2.61	4.74	2.41
6	4.38	1.90	4.27	2.75	4.30	2.53
7	3.38	2.06	3.38	2.33	3.38	2.24

Correlation between pain and OHIP-14 scores

The correlation between the pain scores and the overall OHIP-14 scores were analyzed with Pearson's correlation. We found a positive correlation between these variables ($r=0.743$, $n=50$, $p<0.05$; Figure 1).

Figure 1: Scatterplot of pain scores vs. OHIP-14 scores. The dotted line shows a significant positive correlation ($r=0.743$, $n=50$, $p<0.05$).



Pell and Gregory classification

Analyzing the means of OHIP-14 scores and pain scores between the different categories of the third molar impaction grades for any postoperative day, we found that the impaction grade did not influence the OHIP-14 and pain scores.

Analgesic intake

No differences were found for the postoperative mean analgesic intake, except for the first day were more painkillers were used by females than males. However, this difference was not statistically significant.

Postoperative complications

One case of postoperative infection occurred during the first postoperative week. After 3 days, an abscess appeared and was drained. Subsequently, the patient was given amoxicillin 3 times per day for 5 days. Postoperative alveolitis did not occur in any patient, and no sensory disturbances of the IAN were detected at the 1-week follow-up visit.

Coronectomy versus surgical removal OHIP-14 and pain scores

Table 4 compares the OHIP-14 and pain scores from the present study with the data from an earlier prospective cross-over, randomized controlled study where patients underwent surgical removal of an impacted third molar.[14] The data from the control group were compared to the coronectomy group in the present study. The basic characteristics of the two groups was comparable (mean age of 25 years, all impacted molars required bone removal).

The mean OHIP-14 scores were comparable for the first postoperative day but were higher in the coronectomy group for the remainder of the week. Mean pain scores were higher in the coronectomy group compared to the surgical removal group for each day of the postoperative week.

Table 4: Comparison of means and standard deviation (SD) of total OHIP-14 scores for coronectomy versus surgical removal of impacted mandibular third molars on postoperative days (POD's) 1 to 7

	Total OHIP-14 score				Pain Intensity Score			
	Coronectomy (n=50		Surgical Removal (n=54)		Coronectomy (n=50)		Surgical Removal (n=54)	
POD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	26.4	8.67	26.3	10.6	6.4	2.07	6.09	2.11
2	23.72	10.09	20.6	11.6	6.04	2.07	5.41	2.29
3	21.98	11.46	18.0	12.1	5.84	2.08	5.13	2.42
4	18.97	11.9	13.3	10.7	5.32	2.29	4.07	2.34
5	16.26	11.78	10.9	10.3	4.74	2.41	3.42	2.42
6	13.47	10.92	7.5	9.1	4.3	2.53	2.67	2.22
7	9.82	9.15	5.2	7.6	3.38	2.24	2.06	2.11

OHIP-14: Oral Health Impact Profile-14 questionnaire

Discussion

This study investigated the OHRQoL in patients that underwent a coronectomy for an impacted mandibular third molar. Mean OHIP-14 scores were highest during the first three postoperative days and gradually declined during the first postoperative week. Pain was the highest on the first postoperative day and declined gradually. Pain occurs with tissue injury, which leads to the formation of prostaglandins from the enzymatic degradation of arachidonic acid in the lipid membrane by cyclooxygenase (COX).[17] Then, as the membrane lipids are restored by tissue repair mechanisms, pain is gradually reduced each day. Analgesics inhibit the COX enzyme, and thus, inhibit the production of prostaglandins, which minimizes pain sensation. Therefore, analgesics affect the pain score. In the present study, patients received 600 mg ibuprofen 3 times per day, and when necessary they were instructed to combine the 600 mg of ibuprofen with 1000 mg of acetaminophen (paracetamol). The analgesic intake in this study was highest on the third day (mean: 3.76) and lowest on the seventh day postoperative (mean: 1.86).

In the present study, we found no significant differences in OHIP-14 and pain scores between males and females. Our findings were in contrast with those of Fillingim et al.18, who reported that some forms of pain were more prevalent among females than among males. They found that women experienced more pain than men in oralrelated issues, such as tooth pain and jaw joint pain.18 Another study found that women reported more pain then men after an invasive oral surgical procedure.19 However, other studies reported no differences in pain between the sexes after oral surgery.20,21

We found that the degree of impaction, according to Gregory and Pell's classification of the third mandibular molar, did not impact the pain score. In contrast to the expectation that surgery on more deeply impacted mandibular third molars would have a more significant impact on the OHRQoL, we did not find any significant difference in the degree of pain experienced for different degrees of impaction. Nevertheless, we found a high positive correlation between physical pain and the OHRQoL, consistent with our findings regarding the pain domain of the OHIP-14 questionnaire.[22] Indeed, 'physical pain' was the highest contributor to the overall OHIP-14 score. Therefore, the pain score could be used to predict the effects of pain on the QoL after a coronectomy.

After the coronectomy, patients exhibited a reduced ability to chew and enjoy food. They experienced limited mouth opening and had to adjust their diet. In particular, during the first few postoperative days (days 1 to 3), patients had difficulties in opening the mouth or chewing. Most patients required liquified or soft foods that could be swallowed without much chewing.

An important question is whether a coronectomy of an impacted mandibular third molar might impact the QoL or pain score more than the surgical removal of an impacted mandibular third molar. Only one previous study reported on QoL after a coronectomy. Manor et al (2016) compared 34 patients that underwent a coronectomy and 35 that underwent surgical removal of the mandibular third molar.[23] Similar to the present study, they administered a OHRQoL questionnaire to patients during the first postoperative week. They found no differences in QoL scores between the groups. For both groups, the first three days were the most difficult, regarding pain, swelling, and oral and general functions. Tuk et al (2019) studied 54 patients that underwent the surgical removal of impacted mandibular third molars.[14] They found lower scores for the total OHIP-14 and pain than we found in the present study, where patients underwent a coronectomy. Additionally, they found lower analgesic intakes on each postoperative day than those observed in the present study. A potential explanation of these differences in the OHIP-14 and pain scores between these studies might be that, in some cases, a coronectomy might require greater surgical invasiveness compared to a complete surgical removal. Indeed, Zola (2010) pointed out the concern that the postoperative course was more protracted for a coronectomy than for a surgical removal.[24] One reason for this difference might have been that a larger flap and greater bone removal was required to complete the coronectomy compared to the surgical removal. Consequently, patients might have experienced greater immediate postoperative discomfort after a coronectomy. In addition, after the coronectomy, the exposure of pulp tissue might increase the risk of infection or prolong sensitivity or pain. Previous studies have described increased pain in patients after a coronectomy compared to a surgical removal.[78] However, other studies found that the incidences of pain and swelling after a coronectomy were lower than those reported after the surgical removal of a partially or completely impacted mandibular third molar.[6,12] Frenkel et al (2015) reported that 15% of patients that underwent a coronectomy complained of pain at a

follow-up conducted one month after surgery.[13] However, the severity of the pain was not specified. In most cases, the cause of the protracted period of pain was due to enamel retention, and a reoperation was performed. Kang et al (2019) compared surgical removal and coronectomy, and found that the pain experienced postoperatively in the coronectomy group resolved more rapidly than the pain experienced in the surgical removal group.[3] In that study, the mean duration of pain was 2.61 days (SD 1.95) for a coronectomy and 3.40 days (SD 1.55) for a surgical removal.[3]

In the present study, no patient experienced sensory impairment of the IAN after the mandibular third molar coronectomy. Previously, a randomized study compared surgical removals to coronectomies in 128 patients. They found that 19% of the surgical removal group sustained IAN damage and no IAN symptoms were reported among the successful coronectomies.[25] Other studies confirmed that no IAN injury occurred with a coronectomy.[3,8,10] In the largest prospective study on coronectomies, among 612 coronectomies of impacted mandibular third molars, the prevalence of IAN deficits was only 0.16%.[11]

In the present study, only one patient experienced a postoperative infection: an abscess occurred on the third postoperative day. The abscess was drained, and amoxicillin was given 3 times per day for 5 days. Postoperative infection rates after a mandibular third molar coronectomy have varied between 3.2 and 5.8 %.[6,25] The infections were always treated with antibiotics and debridement. Leung and Cheung (2016) showed that, among 612 coronectomies, infections occurred in 2.9%.[11] However, Cilasun et al (2011) found no postoperative infections in a coronectomy group.[8]

In a coronectomy, the roots remain in place; over time, this situation can lead to symptoms and pain. Due to this potential complication, some patients and oral surgeons might hesitate in selecting this treatment.[5] On the other hand, the significant reduction in the risk of neurosensory disturbances after a coronectomy can offset the risk of a future second surgery; indeed, the need to remove migrated roots was only reported in 3.3% of cases.[11] The coronectomy is typically performed on healthy teeth without pathology; consequently, the retained roots should pose less of an issue compared to teeth with some form of pathology, which is frequently observed in erupted teeth.

In the present study, no cases of alveolitis were observed. The incidence of dry socket after a coronectomy was previously reported to be relatively low, due to the facts that the wounds were small, little alveolar bone was exposed, and primary wound closure was performed.[7] Leung & Cheung (2009) reported no cases of dry socket in a coronectomy group, compared to 2.8% cases of alveolitis in a surgical removal group.[6] In a later study, among 612 coronectomies on lower third molars in 458 patients, only one coronectomy (0.16%) resulted in a dry socket in the first postoperative week.[11] However, Renton et al (2005) reported a 12.1% incidence of postoperative alveolitis in a coronectomy group, which was comparable to the 9.6% postoperative alveolitis observed in a surgical removal group.[25] In that study, the high incidence of alveolitis observed after a coronectomy might have been due to the fact that the mucoperiosteal flaps were replaced with a single suture; thus, compared to other studies, they did not achieve a 'water-tight' closure. Another explanation might be that, in that study, a high proportion of patients were treated for difficult, deeply impacted teeth with pericoronitis.[25]

It remains controversial whether antibiotics are necessary in a coronectomy. The lack of postoperative antibiotic therapy is believed to increase the risk of postoperative complications after a mandibular third molar coronectomy. However, the need for antibiotic prophylaxis or postoperative administration remains controversial for both a coronectomy and the surgical removal of an impacted mandibular third molar. In the original description of a coronectomy by Pogrel et al (2004), patients were prescribed preoperative prophylactic antibiotics, which were continued for at least 3 days.[5] Other studies use different antibiotic protocols, ranging from 3 to 7 days, however, no scientific evidence exists to support the use of antibiotics for a coronectomy.[3,8,13]

Kouwenberg et al (2016) instructed patients to rinse with chlorhexidine 0.12% 3 times per day, starting from the first postoperative day and continuing until normal dental hygiene was achieved.[10] However, no data were given on postoperative infections, alveolitis, or pain after the coronectomy.

Another important question is whether endodontic treatment or vital pulp therapy is necessary, and whether these treatments might influence pain or the QoL. Histological evaluation of mandibular third molar roots retrieved after

coronectomy have shown that the roots remained vital without degenerative changes.[26-27] Moreover, a long-term study showed no evidence to support the notion that retained roots required an endodontic procedure.[11] A pilot study by Sencimen et al (2010) compared coronectomies with and without endodontic treatment. They concluded that intraoperative root canal therapy did not add any benefit to the outcome, but considerably increased the complication and infection rates; therefore, it was not recommended.[28]

The main limitation of this study was that we included only 50 participants. Although the procedure was similar in all cases, a small sample size increases the margin of error and affects the reliability of the study results.

Another potential limitation was that, although the OHIP-14 questionnaire was a reliable, useful tool for assessing OHRQoL, it was based on self-reports completed by patients after oral surgery. Therefore, the data could not be controlled, and we could not rule out a certain degree of bias.

In conclusion, the results of the present study showed that a coronectomy of an impacted mandibular third molar affected the OHRQoL of patients, particularly in the first three postoperative days. This information should be considered, when assisting patients in planning their schedules and preparing themselves psychologically. A coronectomy seems to have a greater impact on the OHRQoL than the total surgical removal of mandibular third molars.

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Chapter 7

Effect of periapical surgery on oral health-related quality of life in the first postoperative week using the Dutch version of Oral Health Impact Profile-14

This chapter is based on the publication:

Effect of periapical surgery on oral health-related quality of life in the first postoperative week using the Dutch version of Oral Health Impact Profile-14
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Published: Oral and Maxillofacial Surgery, 2021

Abstract

Objective: To evaluate whether periapical surgery affects oral health-related quality of life (OHRQoL) within the first postoperative week.

Study Design: The primary outcomes in 133 patients (54 men, 79 women; mean age 50.8 years) undergoing periapical surgery were the Oral Health Impact Profile-14 (OHIP-14) score and postoperative sequelae, including pain, analgesic intake, swelling, limited mouth opening, chewing difficulties, and postoperative infection.

Results: We found a significant effect on OHIP-14, pain, and analgesics, which decreased throughout the week. We found no significant differences in mean OHIP-14, pain scores, or analgesic use for gender, medical history, surgical flaps, operation time, or location of the operated teeth. Younger patients had a higher OHIP-14 score in the first 2 days after surgery and more pain on the first postoperative day. Women experienced more pain during the first 3 days. Smokers had a higher OHIP-14 score on the first postoperative day and greater pain during the first 3 days compared to non-smokers.

Conclusion: We identified a low incidence of pain and reduced OHRQoL following periapical surgery. The postoperative reduction in OHRQoL and pain were of short duration, with maximum intensity in the early postoperative period and rapidly decreasing with time.

Introduction

Periapical surgery is a therapeutic surgical procedure to treat teeth with periapical inflammation, particularly when orthograde retreatment is problematic or fails to lead to regression of the apical pathology [1-2]. As with any surgery, periapical surgery causes tissue damage and can have both a local and systemic impact that deteriorates the patient's quality of life (QoL). There has been little emphasis on immediate postoperative outcomes, such as pain, swelling, and the patient's well-being after periapical surgery, but the number of studies evaluating the influence on QoL during the period following endodontic surgery is growing [3-17]. In the decision-making process regarding endodontic surgery, clinicians need to consider patients' postoperative discomfort. Pain and swelling are common following periapical surgery, but postoperative pain is reported to be of short duration, with a maximum intensity in the first 48 hours.[3-13] Routine daily activities, function, and loss of work are reported to be only moderately impaired.[14] Several studies have investigated additional interventions to ameliorate the effect of periapical surgery on postoperative pain and QoL [9,15-17]. The use of corticosteroids has been reported as a pain relief measure in periapical surgery [9], although another study failed to find an effect of submucosal injection of 4 mg dexamethasone on pain, bruising, and wound healing [16]. Conflicting outcomes have also been reported for the use of platelet concentrates in periapical surgery. Del Fabbro et al. [15] found a significant beneficial effect of adjunct platelet concentrate on postoperative QoL, whereas a recent study evaluating the impact of adjunct leukocyte and platelet-rich-fibrin on QoL after periapical surgery found no significant improvement during the first postoperative week [15-17].

The aim of the present study was to investigate whether periapical surgery affects oral health-related quality of life (OHRQoL) during the first postoperative week. Patients were surveyed using the Oral Health Impact Profile-14 (OHOP-14) questionnaire. In addition, we assessed postoperative pain, analgesic intake, and infection in the first postoperative week.

Materials and Methods

Patient selection

Patients referred by their dentists for periapical surgery at the Department of Oral and Maxillofacial Surgery of Amstelland Hospital in Amstelveen, the Netherlands, during 2017 and 2018 were eligible for inclusion in this prospective study. The study was reviewed and approved by the institutional Medical Ethics Committee of the Academic Medical Centre of the University of Amsterdam and conducted in accordance with Good Clinical Practice and the Declaration of Helsinki, as amended in Somerset West, Republic of South Africa, in 1996. Patients were fully informed about the surgical procedure, postoperative care, follow-up examinations, and alternative treatment options. Each patient was informed that they could withdraw from the study at any time without consequences regarding their treatment.

Inclusion and exclusion criteria

Patients with apical periodontitis in a root canal-treated tooth were included in this study. Asymptomatic patients aged ≥18 years and in good health (American Society of Anesthesiologists [ASA] I or II) who were willing to participate and able to read, understand, and answer the questionnaire were considered for inclusion if they had periapical periodontitis with no possibility of root canal retreatment or the ability to achieve better results with a nonsurgical approach. Patients underwent a clinical and radiographic examination, and a panoramic radiograph and periapical radiograph were taken. The tooth to be treated had to have an adequate final restoration without clinical evidence of coronal leakage. No acute symptoms were present, and the diameter of the periapical lesions had to be <10 mm as measured on the periapical radiograph.

Exclusion criteria were other causes related to root pathology other than apical re-infection, such as root fractures, teeth with an inadequate coronal restoration, perforations and bone loss (periodontal pockets deeper than 7 mm), and defects of the buccal and lingual cortical bone, as suggested by Zuolo et al [18]. Other exclusion criteria were antibiotic prophylaxis, a history of a recent and/or symptomatic peptic ulcer, antiplatelet or anticoagulant therapy, pregnancy or lactation, recent (< 15 days) acute local infection before

surgery, previous radiation therapy to the maxillofacial region, or lack of consent to undergo the procedure or participate in the study.

Surgery

The surgery was performed by two surgeons (JT and JL). Patients received local anesthesia with 40 mg of articaine/hydrochloride and 0.01 mg epinephrine (Ultracain D-S Forte, Sanofi-Aventis Netherlands BV, Gouda, the Netherlands). The surgical technique consisted of a mid-level, rectangular or triangular, full-thickness mucoperiosteal flap. The surgical flap was reflected, and bone removed by a round burr with continuous sterile distilled water irrigation to expose the root apex. After debridement of the pathological tissue, the root was resected approximately 3 mm from the apex using a cylinder burr with minimal or no bevel. Using glasses with 5.0 magnification loupes and a PureLight Headlamp with 140 mm spot size (SL Company, London, UK), the root end was prepared using ultrasound to a 2-3 mm depth with ultrasonic retro-tips (Mectron S.p.A., Carasco, Italy). Intermediate Restorative Material (IRM, Dentsply, Konstanz, Germany) was placed into a dried cavity after adequate hemostasis. Before wound closure, the bone cavity was cleaned with 10 ml of 0.9% NaCl solution (B Braun, Melsungen, Germany). The wound was closed by re-approximating the soft tissue to the original position and sutured with Vicryl 4/0 (Johnson and Johnson; Somerville, NJ) before taking final radiographs.

Postoperative instructions

After surgery, patients were given verbal and written instructions, including information about swelling, using an ice pack for cooling the cheek to reduce swelling and pain relief, avoiding mouth rinsing and spitting, practicing caution when eating and drinking hot food and beverages and, to avoid physical activities. Patients <50 years of age with an ASA I classification were prescribed 600 mg ibuprofen (Brufen; Abbot BV, Hoofddorp, the Netherlands) three times a day postoperatively, whereas patients ≥50 years old or with an ASA II classification were prescribed 1000 mg paracetamol 3-4 per day postoperatively. No antibiotics were prescribed. The day after surgery, patients began using a 0.12% aqueous chlorhexidine mouth rinse twice a day for 1 minute for 7 days. Patients were informed to contact the surgeon if they experienced severe pain, swelling, fever, bleeding, or any concerns after surgery.

Follow-up

One week after surgery, patients were examined by an independent assessor to assess surgical site wound healing and to check for wound infection. Remaining resorbable sutures were removed. Infection was defined as the presence of purulent discharge and/or excessive swelling with fluctuation, with or without pain; presence of a local abscess; or onset of facial or cervical cellulitis plus other signs suggesting infection, such as pain, increased heat, temperature, erythema, and/or fever [19]. In patients in whom infection was diagnosed, drainage was followed by a 5-day course of amoxicillin three times a day. The number of postoperative visits, type and amount of analgesic, type and dosage of antibiotic, and interventions were documented. The completed OHIP-14 questionnaires and pain scores were collected.

Outcome measurements

The primary outcome measures were the OHIP-14 questionnaire and pain score based on the numeric rating scale (NRS). Each patient was asked to complete a questionnaire in the first 7 days postoperatively. The questionnaire was translated into Dutch, comprising 14 questions to evaluate the OHRQoL on a 5-point scale ranging from 0 ("never") to 4 ("very often") [20-21]. Higher scores on the OHIP-14 (range 0-56) indicated a worse OHRQoL. The questionnaire was supplemented with additional questions on analgesic use and postoperative symptoms, such as limited mouth opening, limited chewing, and swelling. The patients were asked to complete the daily OHIP-14 questionnaire, to evaluate pain and analgesic intake at the end of each day. Pain assessment was measured by rating pain intensity with an 11-point NRS, which ranged from 0 (no pain) to 10 (worst possible pain). The daily analgesic intake was self-reported, by filling in the number of used painkillers on each postoperative day.

Data were collected and imported into a database. Variables included patient age, gender, medical history, and smoking habits. Age at surgery was computed in years as the difference between the date of operation and the patient's date of birth. Furthermore, the location of the treated tooth, surgical flap design, and operation times were recorded.

Statistical analysis

Data were analyzed using SPSS version 25 (SPSS Inc., Chicago, IL, USA). Significance was set at α=0.05. To obtain the overall mean OHIP-NL14 score, all 14 questions were averaged for each day, and this score was used to compare changes over time and between groups. Repeated measures ANOVA within subjects was performed to assess the change over time (day 1 - day 7). Additional analyses were conducted to determine the relationship between OHRQoL and the other study variables (age, gender, smoking, ASA classification, and tooth position) over time by means of univariate analysis of variance. Between-group comparisons were performed by means of independent t-tests.

Results

A total of 133 patients (54 [40.6%] males and 79 [59.4%] females) participated in this study, and all questionnaires were included in the study. The mean patient age was 50.8 years (SD 14.7) for the whole population, 50.7 years (SD 14.8) for the males, and 51 years (SD 14.7) for the females. Surgery was performed in 22 maxillary anterior teeth (16.5%), 29 maxillary premolars (21.8%), 37 maxillary molars (27.8%), 3 mandibular anterior teeth (2.3%), 5 mandibular premolars (3.8%), and 37 mandibular molars (27.8%).

OHIP-14 scores

Of the 133 returned questionnaires, the mean overall OHIP-14 score was determined for postoperative day 1 to 7 (Table 1). Repeated measures ANOVA was used to analyze the mean overall OHIP-14 scores collected each day during the first postoperative week, indicating a significant effect for the repeated measurements ($F(6, 792) = 72.8$, $p < 0.001$). Subsequent pairwise comparisons indicated that the mean OHIP-14 scores decreased significantly throughout the week. Only the mean scores from day 5 and day 6 did not differ significantly ($p=0.11$), whereas all the mean scores on the other days differed significantly from each other ($p<0.05$). No significant differences in mean OHIP-14 scores were found for gender, ASA score, surgical flaps, or operation time. Smokers had a significantly higher OHIP-14 score on the first postoperative day than non-smokers. Patients who had a postoperative infection had a significantly higher OHIP-14 score on the fifth postoperative day. Younger patients had a

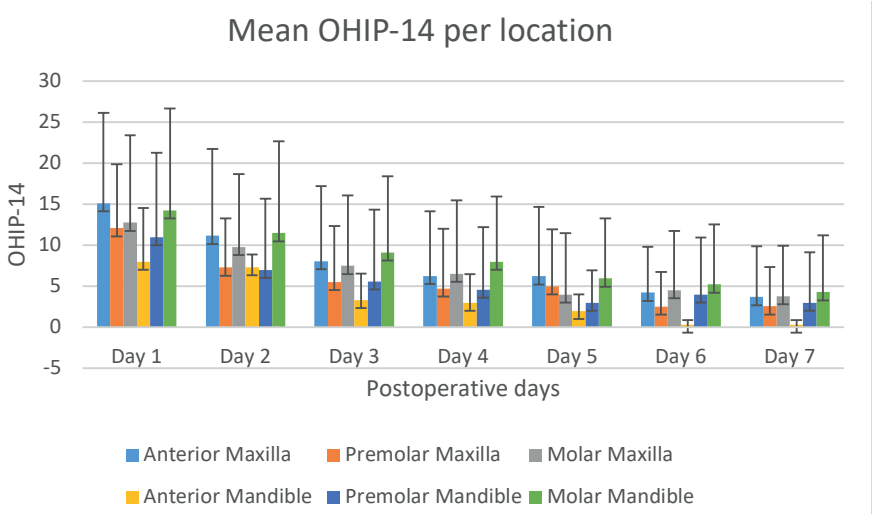
Table 1: OHIP-14 scores on postoperative days 1-7.

Group	N	Mean SD	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Men	54	Mean	11.48	8.26	6.11	5.44	4.83	3.91	3.43
		SD	10.31	9.34	8.59	7.71	6.22	6.63	6.37
Women	79	Mean	14.47	10.86	8.35	6.97	5.20	4.28	3.61
		SD	10.61	9.17	8.31	8.19	7.97	6.21	5.80
ASA I	88	Mean	13.63	10.01	7.52	6.75	4.78	4.43	3.97
		SD	10.93	9.21	8.37	8.10	6.94	6.49	6.62
ASA II	45	Mean	12.53	9.40	7.29	5.58	5.58	3.53	2.69
		SD	9.86	9.54	8.75	7.84	7.99	6.14	4.55
Smokers	17	Mean	**18.59***	11.76	8.12	5.88	4.82	3.35	2.47
		SD	11.48	8,58	7.60	5.70	6.12	4.85	4.14
Non-smokers	116	Mean	**12.47***	9.52	7.34	6.42	5.09	4.24	3.69
		SD	10.23	9.39	8.61	8.31	7.47	6.57	6.24
age 18-25 yrs	5	Mean	**19.20***	**12.00***	9.00	10.00	0.20	2.40	1.60
		SD	12.46	7.81	5.61	8.28	0.45	2.61	1.82
Age 26-45 yrs	45	Mean	**17.60***	**12.78***	9.91	7.91	6.67	5.71	4.89
		SD	11.31	10.95	9.84	8.55	7.47	7.48	7.46
age 46-65 yrs	61	Mean	**11.13***	**8.64***	6.18	4.90	4.18	3.05	2.75
		SD	9.24	7.90	6.86	5.99	6.87	4.95	4.85
age > 65 yrs	22	Mean	**8.91***	**6.55***	5.55	6.36	5.27	4.27	3.36
		SD	8.74	8.12	9.22	10.94	8.29	7.52	6.03
Postop infection	7	Mean	15.00	14.14	13.29	11.57	**10.43***	8.00	7.43
		SD	14.40	14.37	11.60	6.06	3.51	4.20	5.68
No postop infection	126	Mean	13.16	9.56	7.12	6.60	**4.75***	3.91	3.32
		SD	10.37	8.95	8.20	8.00	7.34	6.41	5.98
Quadr. flap	63	Mean	13.65	10.17	8.06	6.94	5.19	4.67	4.02
		SD	12.01	10.70	9.31	7.99	7.21	7.06	6.80
TRIANG. FLAP	60	Mean	12.23	8.85	6.38	5.32	4.32	3.25	2.70
		SD	8.31	7.10	7.12	7.62	6.54	5.39	4.43
MIDLEVEL FLAP	10	Mean	16.90	13.20	9.90	8.90	8.60	6.00	5.50
		SD	12.81	11.31	10.25	10.12	11.11	7.04	8.55
SURGERY									
<20 min	63	Mean	14.78	10.68	7.97	6.59	5.29	4.11	3.25
		SD	10.43	10.02	9.27	8.79	7.62	5.97	5.34
20-25 min	18	Mean	12.22	8.72	6.33	5.56	5.28	4.50	4.17
		SD	9.21	6.68	7.23	7.00	6.43	6.65	6.45
26-30 min	44	Mean	12.63	9.55	7.72	6.84	5.23	4.41	3.84
		SD	11.48	9.54	8.28	7.78	7.75	7.28	6.82
> 30 MIN	8	Mean	7.00	6.75	4.25	3.63	1.75	1.88	2.63
		SD	7.05	7.05	4.95	4.63	2.12	2.85	6.30
OVERALL	133	Mean	13.26	9.80	7.44	6.35	5.05	4.13	3.53
		SD	10.55	9.87	8.47	8.00	7.29	6.37	6.01

*p<0.05; quadr, quadrangular; triang, triangular; SD, standard deviation

significantly higher OHIP-14 score on the first 2 postoperative days compared to the older patient groups. Figure 1 shows the mean OHIP-14 scores per location. No significant interaction effect between time and OHIP-14 score was found for anterior teeth, premolars, and molars in the upper or lower jaw. Comparing the second molar region with the other locations, no significant differences were found during the week for the mean OHIP-14 scores during the first 3 days (day 1, p=0.84; day 2, p=0.34; day 3, p=0.27).

Figure 1: Mean OHIP-14 score per location during the 1st postoperative week. Error bars indicate SD.



Pain scores

Repeated measures were used to determine mean scores over time for pain from postoperative day 1 to 7. Repeated measures ANOVA was used to analyze mean NRS scores collected each day during the first postoperative week (Table 2). We found a significant effect for the repeated measurements ($F(6, 792) = 61.3$, $p < 0.001$). Subsequent pairwise comparisons showed that the mean NRS scores decrease significantly throughout the week. Only the mean scores from day 3 and day 4 did not differ significantly (p=0.15), whereas all the mean scores on the other days differed significantly from each other ($p<0.05$).

Women and smokers experienced significantly more pain during the first 3 days. Younger patients had a higher pain score compared to older patients on the first postoperative day. We found no significant interaction effect during

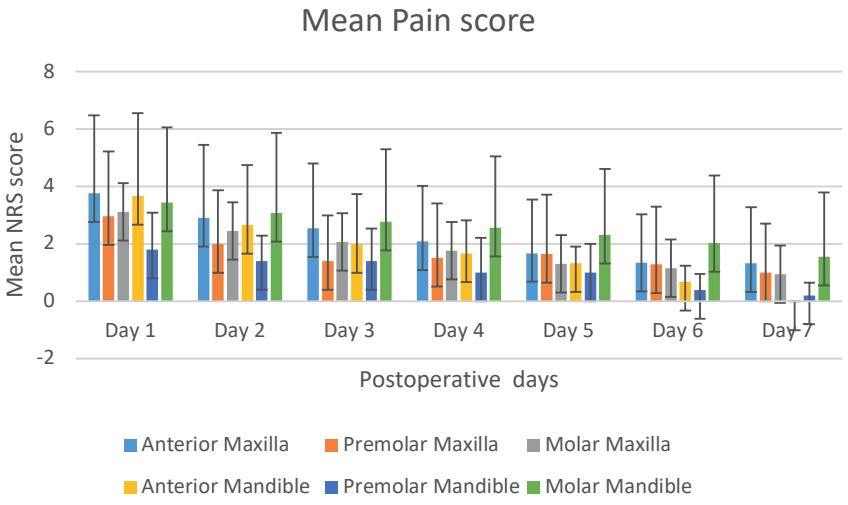
Table 2: NRS pain scores for the 1st postoperative week.

Group	N		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Men	54	Mean	**2.50***	**2.06***	**1.72***	1.64	1.72	1.52	1.94
		SD	2.31	2.29	2.06	2.13	2.18	2.37	2.26
Women	79	Mean	**3.75***	**2.92***	**2.48***	2.17	1.71	1.35	1.11
		SD	2.45	2.46	2.25	2.21	2.01	1.69	1.58
ASA I	88	Mean	3.40	2.60	2.23	2.06	1.80	1.53	1.24
		SD	2.45	2.40	2.13	2.24	2.12	2.09	1.99
ASA II	45	Mean	2.94	2.51	2.06	1.76	1.57	1.19	0.94
		SD	2.50	2.47	2.36	2.09	1.99	1.77	1.64
Smokers	17	Mean	**4.76***	**3.65***	**3.24***	2.47	1.65	1.29	1.06
		SD	2.54	2.42	2.17	1.91	1.58	1.40	1.52
Non-smokers	116	Mean	**3.03***	**2.41***	**2.02***	1.88	1.73	1.44	1.16
		SD	2.39	2.39	2.17	2.22	2.14	2.06	1.93
age 18-25 yrs	5	Mean	**4.80***	3.40	3.00	3.00	1.20	1.00	0.70
		SD	1.92	1.34	1.87	2.55	1.10	1.22	1.10
Age 26-45 yrs	45	Mean	**3.70***	2.91	2.57	2.19	1.90	1.76	1.38
		SD	2.28	2.52	2.28	2.16	1.98	2.10	2.10
age 46-65 yrs	61	Mean	**3.22***	2.62	2.14	1.88	1.69	1.30	1.16
		SD	2.71	2.54	2.29	2.23	2.15	1.87	1.91
age > 65 yrs	22	Mean	**2.05***	1.55	1.27	1.45	1.55	1.14	0.73
		SD	1.81	1.79	1.55	2.04	2.30	2.21	1.39
Postop infection	7	Mean	2.29	2.14	2.14	2.29	3.00	**2.86***	2.29
		SD	1.80	2.19	1.77	2.21	2.08	2.41	2.63
No postop infection	126	Mean	3.30	2.60	2.17	1.94	1.65	**1.34***	1.08
		SD	2.49	2.44	2.22	2.19	2.06	1.94	1.82
Quadr. flap	63	Mean	3.52	2.71	2.42	2.06	1.81	1.47	1.20
		SD	2.55	2.71	2.51	2.31	2.16	2.09	2.07
TRIANG. FLAP	60	Mean	2.78	2.30	1.97	1.80	1.59	1.34	1.09
		SD	2.32	2.09	1.78	2.10	2.05	1.96	1.76
MIDLEVEl FLAP	10	Mean	4.40	3.30	2.90	2.20	1.90	1.55	1.10
		SD	2.46	2.31	2.13	1.99	1.85	1.64	1.45
SURGERY									
<20 min	63	Mean	3.51	2.81	2.17	2.02	1.97	1.64	1.24
		SD	2.60	2.47	2.17	2.23	2.25	2.22	1.85
21-25 min	18	Mean	3.06	2.11	1.83	1.58	1.33	1.22	1.28
		SD	2.53	2.47	2.43	1.85	1.61	1.90	2.37
26-30 MIN	44	Mean	3.11	2.57	2.45	2.15	1.69	1.27	0.98
		SD	2.34	2.42	2.27	2.38	2.06	1.71	1.72
> 30 min	8	Mean	2.38	1.75	1.38	1.25	0.75	0.88	1.00
		SD	2.00	1.83	1.19	1.39	1.39	1.99	2.07
OVERALL	133	Mean	3.25	2.57	2.17	1.95	1.72	1.42	1.14
		SD	2.47	2.42	2.20	2.19	2.07	1.99	1.88

*p<0.05; quadr, quadrangular; triang, triangular; SD, standard deviation

the first postoperative week for pain scores and ASA group, surgical flaps, location of teeth, or operation time. Comparing the second molar region with the other locations, we found no significant differences during the week for the NRS pain scores, or even during the first 3 days (day 1, p=0.30; day 2, p=0.32; day 3, p=0.29). Figure 2 shows the pain scores versus the location of the operated teeth.

Figure 2: Mean numeric rating scale (NRS) pain score per location during the 1st postoperative week. Error bars indicate SD.



Analgesic intake

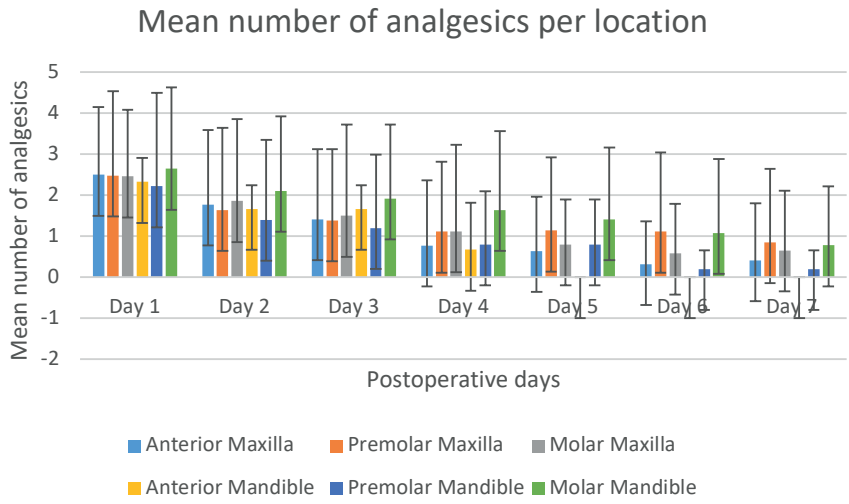
Repeated measures were used to determine mean scores over time for pain from postoperative days 1 to 7. Repeated measures ANOVA was used to analyze mean analgesic intake each day during the first postoperative week (Table 3). We found a significant effect for the repeated measurements ($F(6, 127) = 26.8$, $p < 0.001$). Subsequent pairwise comparisons show that the mean analgesic use decreased significantly throughout the week. Only the mean scores from day 4 and 5, and day 6 and 7 did not differ significantly (p=1.00), whereas all of the mean scores on the other days differed significantly from each other ($p<0.05$). We found no significant interaction effect during the first postoperative week for mean analgesic intake and gender, ASA group, smokers, surgical flaps, operation time, or location of teeth. Figure 3 shows the mean number of analgesic intake for the location of the operated teeth. On the first postoperative day, 14.3% of patients reported not using any analgesics. This percentage increased to 30.8% on day 2 and 42.1% on day 3. On the seventh day, 23.3% of the patients used analgesics.

Table 3: Analgesic intake during the 1st postoperative week.

Group	N		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Men	54	Mean	2.24	1.58	1.25	0.87	0.85	0.77	0.62
		SD	1.82	1.74	1,53	1.41	1.45	1.64	1.51
Women	79	Mean	2.70	1.96	1.79	1.40	1.09	0.75	0.68
		SD	1.80	1.88	2.04	2.07	1.72	1.48	1.45
Smokers	17	Mean	2.53	2.47	2.12	1.12	0.47	0.47	0.53
		SD	1.70	2.15	1.93	1.69	1.18	1.18	1.50
Non-smokers	116	Mean	2.51	1.76	1.50	1.20	1.07	0.80	0.68
		SD	1.84	1.83	1.85	1.88	1.64	1.58	1.47
ASA I	88	Mean	2.40	1.85	1.61	1.27	1.03	0.86	0.69
		SD	1.77	1.80	1.89	1.94	1.56	1.56	1.38
ASA II	45	Mean	2.73	1.84	1.49	1.02	0.93	0.58	0.59
		SD	1.90	2.04	1.83	1.67	1.68	1.48	1.64
age 18-25 yrs	5	Mean	2.60	2.00	2.50	2.50	0.50	0.10	1.20
		SD	1.95	1.00	3.32	4.24	0.87	0.22	2.68
Age 26-45 yrs	45	Mean	2.53	2.02	1.75	1.20	1.09	0.86	0.56
		SD	1.74	1.95	2.05	1.79	1.80	1.65	1.30
age 46-65 yrs	61	Mean	2.36	1.82	1.34	0.93	0.82	0.75	0.66
		SD	1.84	1.94	1.60	1.58	1.45	1.61	1.57
age > 65 yrs	22	Mean	2.86	1.54	1.64	1.54	1.41	0.73	0.73
		SD	1.96	1.79	1.81	1.87	1.66	1.28	1.24
infection	7	Mean	2.71	2.29	2.00	1.43	1.14	1.29	1.00
		SD	2.21	1.60	1.63	1.40	0,90	1.50	1.73
No infection	126	Mean	2.50	1.82	1.55	1.17	0.99	0.73	0.64
		SD	1.80	1.90	1.88	1.87	1.63	1.54	1.46
Quadr. flap	63	Mean	2.48	1.79	1.55	1.20	0.93	0.73	0.65
		SD	1.87	1.92	2.13	2.04	1.57	1.56	1.45
TRIANG. FLAP	60	Mean	2.53	1.92	1.55	1.22	1.10	0.85	0.70
		SD	1.86	1.95	1.62	1.70	1.65	1.59	1.55
MIDLEVEl FLAP	10	Mean	2.60	1.80	1.70	0.80	0,70	0.30	0.30
		SD	1.26	1.23	1.57	1.48	1.49	0.95	0.95
SURGERY									
< 20 min	63	Mean	2.56	1.86	1.59	1.16	1.03	0.81	0.67
		SD	1.94	2.01	1.81	1.77	1.68	1.64	1.60
21-25 min	18	Mean	2.17	1.39	0.94	0.61	0.56	0.33	0.67
		SD	1.34	1.20	1.30	0.98	0.92	0.69	1.53
26-30 min	44	Mean	2.66	2.14	1.89	1.48	1.13	0.89	0.61
		SD	1.92	1.98	2.17	2.27	1.77	1.70	1.32
> 30 min	8	Mean	2.13	1.25	0.94	0.94	0.81	0.56	0.63
		SD	1.82	1.16	1.15	1.02	0.84	0.90	1.19
OVERALL	133	Mean	2.51	1.85	1.56	1.18	0.99	0.76	0.65
		SD	1.82	1.87	1.86	1.84	1.59	1.53	1.46

quadr, quadrangular; triang, triangular; SD, standard deviation

Figure 3: Mean analgesic consumption score per location during the 1st postoperative week. Error bars indicate SD.



Postoperative swelling, mouth-opening, and chewing difficulties

Table 4 and 5 show the effect of periapical surgery on postoperative swelling, limitations in mouth opening, and chewing difficulties. Swelling was significantly different between genders on postoperative days 1 and 4, with women reporting more swelling. On the first postoperative day, more swelling was reported in the patients with an ASA I classification.

A significant difference in mouth opening was found on days 2, 3, and 4 for teeth surgically treated in the lower jaw. Postoperative swelling persisted longer in mandibular locations, especially the molars, and was significant on days 5, 6, and 7. Limitations in mouth opening were reported significantly more in females on the first postoperative day and in the ASA I group on the third postoperative day.

Table 4: Number of patients with select complications during the 1st postoperative week.

		Day 1			Day 2			Day 3			Day 4			Day 5			Day 6			Day 7		
Group	n	S	M	C	S	M	C	S	M	C	S	M	C	S	M	C	S	M	C	S	M	C
Male	54	36*	27*	29	38	20	23*	31	16	17*	22*	16	15	20	11	11	16	7	12	13	7	10
Female	79	66*	52*	54	66	37	52*	57	35	42*	52*	25	32	36	21	28	31	17	20	24	13	18
ASA I	88	73*	57	57	72	42	51	61	39*	43	50	30	35	40	24	30	34	17	25	26	14	21
ASA II	45	29*	22	6	32	15	24	27	12*	16	24	11	12	16	8	9	13	7	7	11	6	7
Smokers	17	14	11	13	15	8	12	14	8	8	12	6	6	8	4	6	7	5	4	5	3	4
Non-smokers	116	88	68	70	89	49	63	74	43	51	62	35	41	48	28	33	40	19	28	32	17	24
Quadr flap	63	52	38	41	51	29	37	46	26	30	37	23	26	27	18	19	26	14	14	22	11	13
Triang flap	60	43	34	37	46	24	33	36	21	26	33	15	18	25	11	17	18	8	16	12	6	14
Midlev flap	10	7	7	5	7	4	5	6	4	3	4	3	3	4	3	3	3	2	2	3	3	1
OT < 20 MIN	63	45	36	41	46	25	35	36	19	25	32	18	21	26	12	17	20	11	17	13	10	15
OT 20-25 MIN	18	16	11	11	13	5	8	10	3	8	8	3	6	3	2	5	3	2	4	3	1	4
OT 26-30 MIN	44	34	28	25	38	25	28	36	25	22	28	19	18	23	16	15	20	10	10	19	8	8
OT > 30 MIN	8	7	4	6	7	2	4	6	4	4	6	1	2	4	2	2	4	1	1	2	1	1
TOTAL	133	102	79	83	104	57	75	88	51	59	74	41	47	56	32	39	47	24	32	37	20	28

S, swelling; M, limited mouth opening; C, chewing difficulties; OT, operation time quadr, quadrangular; triang, triangular; * p<0.05

Table 5: Number of patients experiencing select complications during the 1st postoperative week per location.

		Day 1			Day 2			Day 3			Day 4			Day 5			Day 6			Day 7		
Location	n	S	M	C	S	M	C	S	M	C	S	M	C	S	M	C	S	M	C	S	M	C
Anterior Maxilla	22	15	14	14	16	7*	10	12	4*	6	9	4*	6	6*	2	6	3*	1	3	2*	1	2
Premolar Maxilla	29	22	19	16	24	11*	15	18	8*	11	15	8*	9	9*	5	7	9*	4	8	7*	3	8
Molar Maxilla	37	26	24	19	24	11*	21	23	13*	15	17	9*	13	12*	11	11	12*	7	9	7*	6	9
Anterior Mandible	3	3	1	3	3	3*	2	3	3*	2	3	3*	2	3*	2	1	2*	2	1	2*	2	1
Premolar Mandible	5	5	3	3	4	3*	3	3	2*	3	3	2*	3	1*	1	2	1*	1	2	0*	0	2
Molar Mandible	37	31	22	24	33	22*	24	29	21*	22	27	15*	14	25*	11	12	20*	9	9	19*	8	6
Total	133	102	83	79	104	57	75	88	51	59	74	41	47	56*	32	39	47	24	32	37	20	28

S, swelling; M, limited mouth opening; C, chewing difficulties.

* significant<0.05

Postoperative complications

Seven (5.3%) patients with a postoperative infection presented with increasing swelling at the surgical site on postoperative day 6. The abscess was drained, followed by a 5-day oral course of 500 mg amoxicillin three times a day. The patients with a postoperative infection had a significantly higher OHIP-14 score on the fifth postoperative day and a significantly higher pain score on the sixth postoperative day, which corresponded with the day that the abscess was drained (Tables 1 and 2).

Discussion

In the present study, we assessed how periapical surgery affects postoperative OHRQoL and found the greatest effect of periapical surgery on OHRQoL and NRS pain scores during the first postoperative day, gradually decreasing through the first postoperative week. Compared to earlier studies on postoperative OHRQoL and pain after third molar surgery, periapical surgery only had a mild to moderate effect during the first postoperative week [19-21]. This finding is supported by other studies that found maximal postoperative symptoms on days 1 to 3, which then generally subsided [5-6]. In the present study, we found no significant differences in mean OHIP-14 scores between males and females.

Postoperative pain is not uncommon following periapical surgery, and is usually of short duration, with a maximum intensity either on the day of the surgical procedure or the next day [3,7,9,14]. In the present study, the mean NRS pain score was highest during the first 3 days. The mean NRS pain score was 3.25 (SD 2.47) on day 1, decreasing to 2.57 (SD 2.42) on day 2 and gradually decreasing through the week. Iqbal et al. [11] reported a mean pain score on day 1 of 3.17 (SD 2.03), and other studies have reported mean peak visual analog scale (VAS) scores of approximately 30, which is comparable to the present study [3-4]. Garcia et al. found the highest pain score on day 2 [10].

The postoperative mean pain score is influenced by the analgesics taken by patients and, as such, do not truly reflect the real pain caused by the surgery. To obtain a real measurement of the pain after periapical surgery, patients

should refrain from taking analgesics; however, as pointed out by Seymour et al., this approach would be unethical [3].

The NRS pain score exhibited a significant gender difference in the first 3 days, with women experiencing more pain, but this did not affect the OHRQoL. The mean differences in OHIP-14 score were not significantly different between males and females; however, the slightly higher pain with less impact on OHRQoL observed in women may be explained by women being better at managing pain than men [22]. Therefore, the OHIP-14 score may reflect the notion that pain did not hinder day-to-day life in women as much as it did in men [22]. Interestingly, Penarrocha et al. [8] found higher pain scores for males after periapical surgery until the third postoperative day, whereas other studies reported no significant differences in pain scores between males and females after apical surgery [3, 5-6].

In the present study, the younger age group (<25 years) experienced a greater effect of periapical surgery during the first 2 days and more pain during the first postoperative day. This finding is in contrast to other studies that did not find any significant effect of age on postoperative symptoms after periapical surgery [3,5-6,9-10]. However, Iqbal et al. found more postoperative discomfort in younger patients [11].

In the present study, ibuprofen was used as an analgesic in younger patients and paracetamol in the ASA II group and older patients. No significant differences were found in the use of analgesics between gender, age groups, smokers or non-smokers, flap design, or location. In the present study, 85.7% of the patients reported using analgesics on the first postoperative day. This decreased during the week and, on the seventh postoperative day, 23.3% of the patients used analgesics. Earlier studies reported that 63-67% of the patients took analgesics, which meant that some patients did not take them even though pain was reported [4,7].

Surgical operation time, ASA classification, and flap design did not significantly impact OHRQoL and NRS pain scores during the first postoperative week. Seymour et al. also failed to find a correlation between operating time and postoperative pain. Studies have reported great variety in operation time,

from a mean of 25 minutes to a time of 140 minutes for a single rooted tooth [3,8,12,14]. However, no significant correlation between operation time and postoperative pain and swelling were found. Penarrocha et al. found that trapezoidal flaps caused greater pain than triangular flaps, particularly in the first 2 days [8].

We found that smokers had a significantly higher OHIP-14 score on the first postoperative day than non-smokers. In addition, smokers experienced significantly more pain during the first 3 days. Garcia et al. also found that smokers experienced greater pain throughout almost the entire first postoperative week [10].

In the present study, the operation site had no significant influence on postoperative OHRQoL or pain. This finding is in agreement with other studies [5-6, 8, 12, 14]. One would expect more postoperative discomfort after periapical surgery in second molars, but we found no significant effect in regard to the postoperative OHRQoL or pain scores. Other studies have found greater pain after periapical surgery of maxillary anterior teeth [11], molars [9], or the lower incisors and canines [8].

Swelling is common following surgical periapical treatment. In the present study, swelling was significantly different between genders on postoperative days 1 and 4, with women reporting more swelling. Postoperative swelling persisted longer in mandibular locations and was significant on days 5, 6, and 7. Previous reports found that the maximum swelling is experienced on the first postoperative day [4, 11] and patients were more likely to experience swelling than pain [11]. Garcia et al. [10] reported that 40.3% of their patients had no or only mild postoperative swelling on the first postoperative day, whereas Tsesis et al. [5] found that 64.7% of their patients did not report any swelling; however, patients in that study received dexamethasone, which influences the postoperative outcome with regard to swelling. We found that limitations in mouth opening were significantly more common in females on the first postoperative day and in the ASA I group on the third postoperative day. A significant difference in mouth opening was also found on days 2, 3, and 4 for teeth surgically treated in the lower jaw. Swelling, chewing, and phonetic impairment were the worst 1 and 2 days after surgery [8, 14].

Several earlier studies used some form of antibiotic prophylaxis for periapical surgical procedures [9, 11-12, 17]. In the present study, however, no antibiotics were prescribed. A previous randomized double-blind placebo-controlled trial comparing oral placebo and a preoperative dose of 600 mg clindamycin in 256 patients [23] reported an infection rate of 1.6% in the antibiotic prophylaxis group versus 3.2% in the placebo group. In the present study, 7 (5.3%) cases of postoperative infection occurred, which were treated with drainage and a 5-day course of amoxicillin. Patients with a postoperative infection had a significantly higher OHIP-14 score on day 5 and more pain on day 6.

This study has some limitations. First, only asymptomatic cases were included; therefore, no conclusions can be drawn about the impact on OHRQoL in cases of acute periapical surgery. Second, we did not use an operating microscope in the periapical procedure. An operating microscope is used for optimal identification of root canals, fractures, and isthmuses [17], and some studies have reported that the use of microsurgical techniques is associated with less postoperative pain [1, 5-6]. Magnification was used in the present study, but the 5x magnification with the surgical loupes does not compare to visualization of 16 to 32 times as with the microscope. Although an earlier study did find that patients undergoing periapical surgery using a surgical microscope recovered sooner with respect to pain, no significant difference was found in postoperative swelling [1]. A disadvantage of performing periapical surgery with a microscope is that the procedure takes twice as long. Tsesis et al. [5] reported an average operating time of 20 minutes for periapical surgery without a microscope versus 40 minutes for periapical surgery using a microscope [6]. Moreover, in that study, the patients from the group operated on using a microscope experienced more difficulty in mouth opening, mastication, and the ability to speak during the first 2 days after surgery. In addition, no significant differences in pain were observed in those first 2 days. The differences in pain became clear starting with the fourth postoperative day, but the mean pain scores were ~2 on a 5-point scale. In contrast, in the present study, the mean pain scores were ≤2 on an 11-point NRS.

Another limitation of the present study is that, although the OHIP-14 is a reliable and validated tool to measure OHRQoL, data acquired from the patients are self-reported. The usual disadvantage with questionnaires is that data

acquisition is subjective, and the data cannot be controlled. As such, some bias may be present [19, 24]. Facial swelling as such was not measured but reported on the OHIP-14 questionnaire, so the OHIP-14 scores were used to subjectively assess postoperative swelling. Objective methods for assessing the degree of postoperative swelling are more accurate than the estimations made by patients themselves, but as stated by Happonen et al.[25], there is no real objective way to assess the degree of intraoral swelling, which is experienced by the patients as being at least as unpleasant as extraoral swelling. Moreover, the amount of postoperative swelling is inter-individually different and the absence of a control group in the present study makes it difficult to draw a significant conclusion.

Conclusions

We identified a low incidence of postoperative pain and reduced OHRQoL following periapical surgical treatment. The postoperative reduction in OHRQoL and pain were of short duration, with maximum intensity in the early postoperative period and decreasing with time.

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Chapter 8

Impact of orthognathic surgery on quality of life in patients with different dentofacial deformities: longitudinal study of the Oral Health Impact Profile (OHIP-14) with at least 1 year of follow-up

This chapter is based on the publication:

Impact of orthognathic surgery on quality of life in patients with different dentofacial deformities: longitudinal study of the Oral Health Impact Profile (OHIP-14) with at least 1 year of follow-up
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Published: Oral and Maxillofacial Surgery, 2022

Abstract

Purpose: The objective of this study was to assess the impact of orthognathic surgery for dental facial deformities on oral health-related quality of life (OHRQoL) in the immediate postoperative period up to at least 1 year after surgery.

Methods: This prospective study evaluated data from 85 patients. OHRQoL was assessed using the Dutch version of the Oral Health Impact Profile questionnaire (OHIP-14NL) preoperatively (T_0), each day for 7 days postoperatively (T_1-T_7), 4 weeks (T_8), 6 months (T_9), and at least 1 year (T_{10}) after surgery. The total OHIP score was calculated for each patient, with higher OHIP scores indicating a worse impact on oral health. The patients also completed an extra questionnaire about self-care, discomfort, and experienced pain (rated on a 10-point scale) in the postoperative period (T_1-T_{10}).

Results: The mean OHIP score increased sharply at T_1 compared to T_0, but it decreased significantly in the first postoperative week. The mean OHIP score at T_8 was still higher than before surgery. However, at T_9 and T_{10} the mean OHIP score was significantly lower than at T_0 ($P < .05$). No significant difference in OHIP score was found between gender, age, type of surgery, or indication for surgery. Pain significantly decreased from T_6 compared to T_{10}. The OHIP and pain scores significantly positively correlated at every time point except T_9.

Conclusion: The findings indicate that OHRQoL is reduced from baseline in the immediate postoperative period but improves over time. By 1 year, OHRQoL improves significantly after orthognathic surgery in patients with different dentofacial deformities.

Introduction

Many studies have found lower oral health-related quality of life (OHRQoL) in patients with dentofacial deformities.[1-7]

Patients with dentofacial deformities are characterized by various irregularities of the face and dental bone structures, such as hyperplasia, hypoplasia, and asymmetries of the maxilla, mandible, or chin. An abnormal position of the jaws can manifest in the dentition as a class II or III malocclusion and cause aesthetic and functional problems, including difficulty chewing, sleeping, breathing, speaking, or overall oral health problems.[8] Some patients experience psychological and emotional problems.[9]

Orthognathic surgery is a common treatment for dentofacial deformities. The procedure involves repositioning the maxilla, mandible, or both, sometimes in combination with correction of the chin. The functional and aesthetic goals are to achieve a class I dental occlusion and facial balance and proportion. Traditionally, orthognathic surgery involves preoperative and postoperative orthodontics to achieve dentofacial correction by aligning the dental arches. The main surgical techniques are Le Fort I osteotomy, bilateral sagittal split osteotomy (BSSO), and bimaxillary osteotomy (BIMAX), which are sometimes combined with an osseous genioplasty.

Patients seek orthognathic surgery for various reasons. Their primary motivations are aesthetic concerns and improved QoL.[10, 11] Some studies have found that oral function, including bite, pain, smile, and speech, is a primary motivation.[12-14] A recent systematic review[15] showed physiological and psychological improvement in QoL following orthognathic surgery. A study with a 5-year follow-up found significant improvement and stabilization after 2-5 years in regards to the general health-related QoL, OHRQoL, and psychosocial function after BSSO.[16]

The Oral Health Impact Profile (OHIP-14) is a standardized questionnaire that measures the OHRQoL. The questionnaire is a short version of the OHIP-49 that includes 14 questions representing 7 domains.[17, 18] The Dutch version of the questionnaire, OHIP-14NL, was reported in 2011 to be a reliable and valid

questionnaire for measuring the impact of oral health on QoL.[19] Other validated questionnaires commonly used in orthognathic studies are the Orthognathic Quality of Life Questionnaire (OQLQ) and the Short Form Health Survey (SF-36).[15]

It is important to provide patients with realistic and accurate information prior to the start of orthognathic treatment. The temporary discomfort in the initial postoperative period, such as problems related to oral function, pain, numbness of the lower lip and chin, postoperative bleeding and swelling, should be explained to patients prior to the treatment, and they should also be given a realistic idea of the final facial appearance.[20-22] This knowledge would lead to greater satisfaction after surgery.[12,23,24]

The aim of this study was to evaluate the impact of orthognathic surgery on the QoL of patients with various dentofacial deformities in the immediate postoperative period and during at least 1 year of follow-up using the OHIP-14 questionnaire. The hypothesis is that the QoL of patients with different dentofacial deformities improves with orthognathic surgery. This knowledge would be useful in improving preoperative, perioperative, and postoperative care and could lead to greater satisfaction for patients.

Materials and MethodStudy design and ethical approval

This prospective observational study was approved by the Medical Ethics Committee (METC W17_083#17.102) of Amsterdam University Medical Center (Amsterdam UMC, location AMC). It was granted a non-WMO status (Medical Research Involving Human Act).

Patients

Patients were eligible for the study when they had facial skeletal malformations that required elective combined treatment with preoperative and postoperative orthodontic corrections and orthognathic surgery at Amsterdam UMC, location AMC between September 2016 and March 2020. The patients were selected for the study by an oral facial maxillary surgeon. The inclusion criteria were age ≥ 18 years; ASA class 1 and 2; no congenital anomalies, including cleft lip and/or palate; and sufficient command of the Dutch language. Exclusion criteria were obstructive sleep apnea syndrome as the reason for treatment, craniofacial syndromes, and previous history of orthognathic surgery. All participants were informed about the aims and protocol of the study and provided informed consent.

Planning and surgery

Each patient underwent preoperative orthodontic alignment with fixed orthodontic braces for approximately 18 months. They also received postoperative orthodontic alignment with fixed orthodontic braces for another 6 months. Analysis and treatment planning were carried out with study models mounted on an adjustable articulator to facilitate three-dimensional planning and manufacturing of the interocclusal positioning wafers. Patients in the study received one of the following surgical corrections: Le Fort 1 osteotomy, bilateral sagittal split osteotomy (BSSO), bimaxillary osteotomy (BIMAX), or osteotomy combined with genioplasty. Postsurgical stabilization was achieved with elastics during the first 2 weeks of healing. The patients were followed up for at least 1 year after surgery.

Data collection

Demographic information (gender, date of birth) and information about the surgery (date of surgery, type of surgery, indication for surgery, blood loss, and time of surgery) were collected from the medical records for each patient included in the study. The patients were asked to complete a questionnaire before the operation (T_0, baseline) and every day for the first 7 days after the surgery (T_1-T_7). The next questionnaires were completed postoperatively at 4 weeks (T_8), 6 months (T_9), and at least 1 year (T_{10}). During the first 6 months of the study, the patients received a written questionnaire; thereafter, online questionnaires were sent by email. As a result, some patients received all of the questionnaires online, whereas others received only the last one online. Lime Survey 2.6.4. was used as a tool for online surveys and quota management (LimeSurvey GmbH. LimeSurvey (2.6.4.).

Patients received two reminders if they did not respond after 1 week.

The questionnaire used for this study was OHIP-14NL.[19] This questionnaire focuses on the impact of a person's oral health on QoL, evaluating the following domains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. Answers to each question indicated the frequency of occurrence, with five possible answers: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, 4 = very often. The total OHIP score was the sum of the answers to the 14 questions. Scores ranged from 0-56, with higher scores indicating

a worse impact on oral health. In addition to the OHIP-14 questions, patients responded to four relevant questions that covered pain experienced (rated on a 10-point scale), self-care applied, discomfort experienced, and the use of pain medications.

Statistical analysis

The Shapiro-Wilk test was applied to verify the data distribution and normality. The data were not normally distributed, so nonparametric tests were used. Friedman two-way analysis for variance and a post hoc test was performed to investigate the change from baseline over 1-7 days after surgery. The Wilcoxon signed rank test was used to investigate the change between two time points (4 weeks (T_8), 6 months (T_9), or 1 year (T_{10}) compared to baseline and the change per OHIP question between baseline (T_0) and at least 1 year (T_{10}). Correlations were analyzed by the Spearman rank correlation coefficient. The Kruskal-Wallis test was used to analyze the difference between the OHIP score and type of surgery or indication for surgery. A P-value $< .05$ was considered significant. SPSS Statistics (version 26.0 IBM Inc., Armonk, New York) for Mac was used for statistical analyses.

Results

Demographic data

A total of 94 patients were included in the study. Nine patients were excluded during the study because they did not respond to any of the questionnaires. The final data were based on answers from 85 patients (48 females and 37 males). The patient characteristics are given in Table 1. No difference was found between men and women in regards to age, type of surgery, indication for surgery, blood loss, or duration of surgery. Blood loss correlated with the duration of surgery ($r = 0.542$, $P < .000$, $n = 83$), with more blood loss occurring with a longer time in surgery. All data were anonymized.

Table 1: Demographic data.

	Total	Female	Male	*P*-value
Patients	85 (100)	48 (56.5)	37 (43.5)	
Age, years				.496
	28.6 ± 10.6	27.9 ± 10.7	29.5 ± 10.5	
Range	18-60			
Type of surgery				.139
Le Fort I Osteotomy	15 (17.6)	8 (16.7)	7 (18.9)	
BSSO	33 (38.8)	21 (43.8)	12 (32.4)	
BIMAX	24 (28.2)	15 (31.3)	9 (24.3)	
Osteotomy with genioplasty	13 (15.3)	4 (8.3)	9 (24.3)	
Indication for surgery				.132
Class II	55 (64.7)	34 (70.1)	21 (56.8)	
Class III	29 (34.1)	14 (29.1)	15 (40.5)	
Class I (anterior open bite)	1 (1.2)	0	1 (2.7)	
Blood loss, mL	275.5 ± 240.7	247.2 ± 244.4	312.5 ± 234.25	.223
Duration of surgery, min				
	151.8 ± 66.3	145.8 ± 66.3	159.7 ± 66.3	.341

Data are given as n (%) or mean ± standard deviation unless otherwise noted,
n: number, min: minutes Significance at P<.05

OHIP scores

Table 2 shows the mean OHIP score measured over all time points. Higher OHIP scores indicate lower OHRQoL. The range of T_{10} is 1-3 years. A correlation was found between the duration of surgery and the OHIP score on the first 7 days after surgery ($r = 0.3 - 0.4$, $P < .05$). The longer the surgery, the higher the OHIP score in the first week. No significant correlation was found between age, gender, blood loss, or OHIP score.

The Friedman test was used to assess the mean OHIP scores over baseline (T_0) and the first 7 days after surgery (T_1-T_7). The overall P-value < .00 indicates a significant overall difference in mean OHIP scores between the first 7 days. The mean OHIP score increased from T_0 to T_1 but tended to decrease from T_1-T_7. A post hoc pairwise comparison indicated that the OHIP score from T_1-T_6 was significantly higher than at T_0, but there was no significant difference between T_0 and T_7 (Table 3).

According to the Wilcoxon signed rank test, the mean OHIP score was still higher 4 weeks after surgery compared to baseline (P = .002) but lower at 6 months and 1 year compared to baseline (P = .000; Table 4).

The statistical analysis of the changes in the total OHIP score over time (Figure 1) indicates that the OHRQoL decreases sharply immediately 1 day after surgery, and then improves slowly but is still lower than the baseline at 4 weeks. At 6 months, the OHRQoL was better than before surgery and continues to improve for at least 1 year.

When the change in mean OHIP-14 score was examined per question after at least 1 year (T_{10}) compared to baseline (T_0), the Wilcoxon signed rank test showed a significant reduction for all questions except question 14 (Table 5). Question 14, which concerns inability to function, had a mean score of 0.4 at the baseline. This low score indicates that patients do not or hardly ever experience problems with function before surgery.

The Kruskal Wallis test was used to assess the difference in the mean OHIP score across the different types of surgery and indications for surgery at a single time point (P > .05). We found no significant difference in the mean OHIP score between the four types of surgeries (Table 6) and between the two indications for surgery (class II vs. class III; Table 7) at any single time point. Class I with anterior open bite was not analyzed because only one patient had this deformity. Two-way ANOVA test was used to assess the average difference between the types of surgeries and types of deformities across four time points. No significant difference was found in the mean OHIP scores between the different types of surgeries over time (P = .783) and all time points together (P = .305). There was also no significant difference between class II and class III patients over time (P = .905) and all time points together (P = .860).

Table 2: Mean OHIP score (SD) over all time points.

Time point	Mean ± *SD*	*n*
Preoperative (T_0)	15.3 ± 10.4	76
Day 1 (T_1)	32.4 ± 12.5	63
Day 2 (T_2)	33.3 ± 13.3	58
Day 3 (T_3)	33.6 ± 12.9	60
Day 4 (T_4)	31.2 ± 12.5	59
Day 5 (T_5)	32.1 ± 12.0	59
Day 6 (T_6)	30.0 ± 12.7	60
Day 7 (T_7)	27.8 ± 13.3	57
4 weeks (T_8)	22.2 ± 12.5	69
6 months (T_9)	9.2 ± 7.8	46
≥ 1 year (T_{10})	7.2 ± 7.8	40

SD: standard deviation

Table 3: Mean difference in OHIP score in the first week compared to baseline (n=49).

	Mean difference	*P*-value
T_0-T_1	17.1	.000
T_0-T_2	18.0	.000
T_0-T_3	18.3	.000
T_0-T_4	15.9	.000
T_0-T_5	16.8	.000
T_0-T_6	14.7	.011
T_0-T_7	12.5	.279

Significant at P< .05

Table 4: OHIP score at 4 weeks, 6 months, and 1 year compared to baseline.

	Mean difference	*P*-value	*n*
Baseline (T_0) - 4 weeks (T_8)	6.9	.002	58
Baseline (T_0) - 6 months (T_9)	-6.1	.000	46
Baseline (T_0) - at least 1 year (T_{10})	-8.1	.000	38

n: number

Significant at P < .05

Figure 1: Mean OHIP-14 score over time (N=46). Error bars indicate standard deviation.

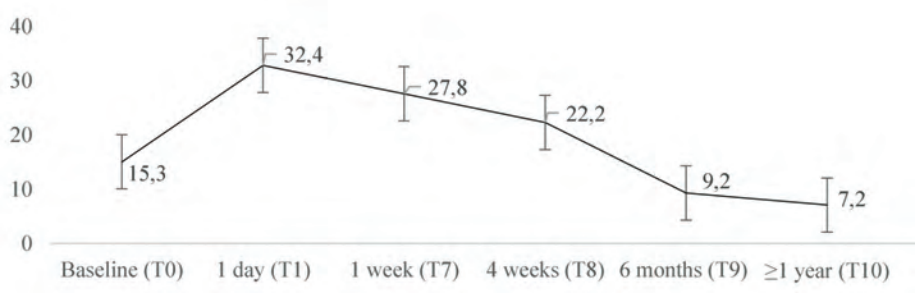


Table 5: OHIP score per question: at least 1 year after surgery compared to baseline.

Question in Table 1	Problem	Mean T_0 (*SD*)	Mean T_{10} (*SD*)	Mean difference (*SD*)	*P*-value
1	Pronunciation	1.1 (1.1)	0.6 (0.8)	0.7 (1.0)	.001
2	Reduced taste	0.4 (0.7)	0.1 (0.3)	0.3 (0.9)	.015
3	Painful aching	1.3 (1.3)	1.0 (1.0)	0.6 (1.4)	.026
4	Discomfort in eating	1.5 (1.4)	0.7 (1.0)	0.5 (1.7)	.000
5	Self-consciousness	1.8 (1.2)	0.9 (1.1)	1.3 (1.4)	.000
6	Feeling tense	1.5 (1.1)	0.7 (1.0)	1.0 (1.2)	.000
7	Unsatisfactory diet	0,9 (1.1)	0.4 (0.9)	0.3 (1.9)	.001
8	Interruption of meals	0,6 (0,9)	0.3 (0.6)	0.3 (1.0)	.012
9	Difficulty relaxing	1.0 (1.2)	0.7 (0.9)	1.9 (1.2)	.013
10	Embarrassment	2.0 (1.2)	0.5 (1.1)	1.8 (1.4)	.000
11	Irritability	0,7 (0,9)	0.4 (0.7)	1.3 (1.2)	.002
12	Difficulty with normal tasks	0.7 (1.0)	0.3 (0.7)	0.6 (1.1)	.000
13	Life less satisfying	1.2 (1.1)	0.5 (0.7)	1.0 (1.1)	.000
14	Totally unable to function	0.4 (0.7)	0.2 (0.5)	0.2 (0.1)	.091

SD: standard deviation

Significance at P< .05

Table 6: OHIP scores and type of surgery over time (± SD).

	Le Fort I osteotomy	BSSO	BIMAX	Osteotomy with genioplasty	*P*-value	N
Baseline (T_0)	14.5 ± 8.6	17.7 ± 11.8	18. 8 ± 12.4	8.7 ± 6.0	.073	76
4 weeks (T_8)	20.1 ± 11.7	21.4 ± 11. 8	26.1 ± 14.1	20.9 ± 12.4	.612	59
6 months (T_9)	9.1 ± 7.0	11.6 ± 8.7	8.9 ± 8.6	7.3 ± 7.1	.612	46
1 year (T_{10})	6.5 ± 7.7	8.6 ± 10.6	8.1 ± 8.0	7.2 ± 7.8	.941	40

SD: standard deviation; N, numbers of patients

Significance at P < .05

Table 7: OHIP scores and indication for surgery over time (± SD).

	Class II	Class III	*P*-value	N
Baseline (T_0)	14.2 ± 10.3	17.6 ± 10.3	.161	76
4 weeks (T_8)	23.5 ± 13.0	19.9 ± 11.5	.388	59
6 months (T_9)	9.2 ± 7.5	9.1 ± 8.6	.905	46
1 year (T_{10})	7.0 ± 7.8	7.7 ± 7.9	.766	40

SD: standard deviation, significance at P < .05; N, number of patients

Pain score

The pain score was measured on a scale from 0-10 from day 1 (T_1) to at least 1 year (T_{10}) after the operation. Because of the low response rate to the questionnaire, it was analyzed from day 1 to week 4 (Figure 2). The Friedman test was used to analyze the data, showing a significant decrease in the mean pain score from day 6 compared to day 1 (n = 46). Pain scores significantly positively correlated with OHIP scores for every time point except for 6 months (T_9) (Table 8).

No correlation was found between pain and age, gender, blood loss, time of surgery, indication for surgery, or type of surgery (P > .05).

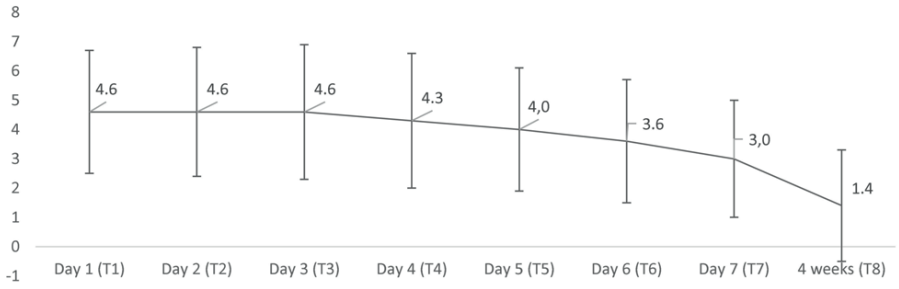
Table 8: Correlation between OHIP score and pain score for all time points.

Time point	*n*	*R*	*P*-value
Day 1 (T_1)	63	0.528	.000
Day 2 (T_2)	58	0.484	.000
Day 3 (T_3)	59	0.424	.001
Day 4 (T_4)	58	0.394	.002
Day 5 (T_5)	58	0.427	.001
Day 6 (T_6)	59	0.312	.016
Day 7 (T_7)	56	0.522	.000
4 weeks (T_8)	59	0.494	.000
6 months (T_9)	46	0.135	.371
≥ 1 year (T_{10})	40	0.315	.048

n: number R: correlation coefficient

Significance at P < .05

Figure 2: Mean pain score over time (N=46). Error bars indicate standard deviation.



Additional questions about self-care and discomfort

The additional questions about self-care, pain, and discomfort were filled in by the patients for time points T_1-T_{10} using 'yes' or a 'no' (Table 9). Chi-squared indicated no significant difference between men and women. The need for self-care and presence of discomfort were high in the immediate postoperative period. More than 50% of the patients needed pain medication for the first 7 days and cooling with ice for the first 3 days. After 4 weeks, more patients were able to do without any extra self-care measures (men: 74%, women: 73%). In addition, a high percentage of patients experienced discomfort in the immediate postoperative period. More than 50% of the patients felt some discomfort 6 months after the surgery. After 1 year, limitations in mouth opening, swelling of the cheeks, and pain resulting from the surgery were absent in almost all patients, though some patients experienced other discomfort.

Table 9: Percentage of patients answering self-care and discomfort questions after surgery.

Question		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	4 weeks	6 months	≥ 1 year
	Male (*n*)	28	26	25	25	26	25	24	27	20	18
	Female (*n*)	35	32	34	33	32	34	32	33	27	23
Did you use any pain medication?	Male	100	89	88	84	89	84	79	27	6	0
	Female	92	91	94	91	85	86	70	24	0	4
Did you cool with an ice pack?	Male	71	50	48	32	27	32	21	4	0	0
	Female	74	56	53	61	38	12	9	0	4	4
No extra self-care was needed	Male	0	8	12	16	12	16	25	74	95	89
	Female	3	6	6	6	9	18	31	73	96	96
Did you experience limited mouth opening?	Male	96	100	100	96	100	92	96	67	25	0
	Female	94	100	88	94	91	91	88	70	22	13
Did you experience reduced chewing ability?	Male	93	96	88	92	96	92	96	85	20	0
	Female	83	94	94	97	87	91	88	79	19	4
Did you have a swollen cheek?	Male	89	100	96	96	96	96	96	48	5	0
	Female	97	100	97	97	94	85	81	39	4	4
Did you have pain as a result of surgery?	Male	82	85	76	76	77	68	58	22	5	6
	Female	69	75	76	70	69	59	56	18	7	4
Did not experience any discomfort	Male	4	0	0	0	0	4	4	7	45	50
	Female	3	0	0	0	0	0	0	9	48	52
Other discomfort	Male	4	15	12	12	8	8	8	11	15	50
	Female	17	16	9	9	9	12	13	12	30	34

Discussion

The aim of this study was to investigate the impact of orthognathic surgery on OHRQoL in the immediate postoperative period until at least 1 year, as measured by the OHIP-14NL questionnaire. The OQLQ is another commonly used questionnaire in orthognathic studies. A comparison of the OQLQ with the OHIP-14NL has shown that both tools are able to discriminate differences in QoL over time and between patient groups. The OQLQ is more specific for orthognathic surgery.[24] The English version of the OQLQ was developed in 2000 and validated in 2002.[6,25] However, the current study did not use the OQLQ because the Dutch version has not yet been validated. The SF-36 is also used in some orthognathic studies, but it focuses more on one's physical and mental status.[27] The SF-36 was not used in this study because this questionnaire is not restricted to the orofacial area.

Previous studies have reported a lower QoL in patients with dental facial deformities compared to a control group.[28-30] The present study did not have a control group. The preoperative OHIP score in this study was higher than the OHIP scores of control groups in other studies. Thus, in general, one can conclude that the OHRQoL of persons with dentofacial deformities is worse overall than in patients without a dentofacial deformity.

The current study found significant deterioration of the OHRQoL 1 day after surgery compared to baseline. However, the OHRQoL improved significantly in the first week. The OHRQoL was still significantly lower after 4 weeks, but after 6 months had improved. Comparable results after orthognathic surgery have been reported in other studies.[27-34] Deterioration in the immediate postoperative period has also been described in patients who suffer from pain, swelling, limited mouth opening, reduced masticatory efficiency, and numbness of the lower lip.[27,28,35] The answers to the additional questions in our study indicate that a high proportion of patients experience discomfort and need more self-care in the immediate postoperative period. This study also found a significant positive correlation between duration of surgery and OHIP score the first 7 days after surgery. There was no significant correlation between OHIP score and age or gender.

Some studies have described female patients experiencing better improvement in self-esteem and a greater reduction in depression after orthognathic surgery compared to male patients.[3,31,32] Corso et al. found, in both the dentofacial deformities group and control group, a lower perception of QoL by women compared to men. However, some studies did not find a difference in OHIP core between men and women.[31,32,35] The present study also found no difference in OHIP score between men and women.

This study found no difference in regards to the type of surgery. However, some investigators have found better improvement in patients who underwent BIMAX compared to single jaw surgery (Le Fort I or BSSO).[29] Another study evaluated whether a combination of BIMAX and genioplasty for females with prognathism and maxillary hypoplasia has a greater positive impact on QoL than BIMAX alone; genioplasty led to significantly greater QoL after surgery.[36]

The current study did not find a significant difference between indications for surgery. Some other studies also found no significant association between the indication for surgery and OHIP-14 scores.[28,35] However, other studies have found that skeletal class III patients had more positive effects form surgery than class I and class II patients.[29,32] Baherimoghaddam et al. found an improvement in both class II and class III patients, but the pattern of change was different; class II patients experience deterioration in QoL during the preoperative stage and improvement in function rather late in the postoperative stage. Class III patients exhibited more significant changes in the domains concerning appearance and psychological issues.[34]

Another finding in this study was that the OHIP score for every question was significantly lower at least 1 year after the operation compared to baseline, except for question 14, which refers to total oral dysfunction. The fact that the OHIP score for question 14 was only 0.4 at baseline indicates that people with various dentofacial deformities do not or hardly suffer from total oral dysfunction. This could explain why no improvement was noted after 1 year. The patients recruited for this study may have more problems with their facial appearance psychologically than with function.

The pain score significantly decreased after day 5 and was very low after 4 weeks. In the first week, a high percentage of patients said that they had taken painkillers. This could influence the perceived pain, so the actual pain score may have been higher. There was a significant positive correlation between pain scores and OHIP scores for every time point except 6 months, but no association was found between pain and age, gender, blood loss, time of surgery, indication for surgery, or type of surgery.

A major limitation of this study is that only 22 of the 85 patients completed all the questionnaires. A paper version of the questionnaires was used only in the first 6 months of this study. After that, the questionnaire was sent by email; patients may have perceived the questionnaires received by email as less important, despite the reminders that were sent. Consequently, the number of patients was too low for all 11 time points (T_0-T_{10}). Therefore, we applied the Friedman test for only the first 7 days after surgery and separately tested the later time points using the Wilcoxon signed rank test.

In this study, some patients mentioned numbness of the lower lip in the comments to the questionnaire, though numbness of the lower lip after surgery was not specifically requested. There may have been more patients who suffered from this complication. Damage of the inferior alveolar nerve is a common postoperative complication.[37-39] There is broad variation in the incidence of inferior alveolar nerve injury,[40,41] which could influence patient satisfaction.[42] However, some studies that report a high incidence of lip paraesthesia in patients following orthognathic surgery have shown no effect on patient satisfaction.[9, 43, 44] Most patients, especially in the younger age group, seem to adapt to this complication.[42]

Another limitation of this study was that the first questionnaire was completed before surgery, but this was not the baseline for orthodontic treatment. Patients already had orthodontic braces for a few months, which can influence the OHRQoL when they filled out the first questionnaire. Huang et al. compared surgery-first and orthodontic-first treatments. The orthodontic-first group experienced deterioration before surgery and suggested that pre-orthodontics could worsen the facial deformity.[48] Therefore, our last evaluation was 1-3 years after surgery. Not every patient had finished the orthodontic

treatment. Choi et al. suggested that the best time for evaluating OHRQoL is 1 year after debonding.[38]

Notably, we did not take into account a possible second operation that may have been required as a follow-up of the first surgery due to complications or a relapse. A second surgery could result in more discomfort and lower OHRQoL, influencing the answers to the questionnaire.

Another point that could influence the answers is that the consultation and surgeries were done by different oral maxillofacial surgeons of the Amsterdam UMC. This creates variation in preoperative preparations, provided information, manner of operation, and postoperative support.

Further long-term clinical studies should investigate the impact of orthognathic surgery on psychological well-being and OHRQoL in patients. This could lead to better preoperative and postoperative guidance for patients who undergo orthognathic surgery.

Conclusion

The main aim of this study was to evaluate the impact of orthognathic surgery on the QoL in patients with various dentofacial deformities in the immediate postoperative period and during follow-up of at least 1 year using the OHIP-14NL questionnaire. The OHRQoL was lower in the immediate postoperative period but improved over time compared to baseline. OHRQoL in patients with different facial deformities improved significantly by 1 year after surgery. With this knowledge about changes in OHRQoL after orthognathic surgery, patients can be informed appropriately with realistic expectations.

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Chapter 9

General discussion and future perspectives

Quality of life (QoL), or "individuals' perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns" is now recognized as a valid parameter in patient assessment in nearly every area of physical and mental health care, including oral health. Oral health–related quality of life (OHRQoL) has important implications for the clinical practice of oral maxillofacial surgery and research. It includes a subjective evaluation of the individuals' oral health, functional well-being, emotional well-being, expectations of and satisfaction with care, and sense of self. Assessment of OHRQoL allows for a shift from traditional medical/dental criteria to assessment and care that focus on a person's social and emotional experience and physical functioning in defining appropriate treatment goals and outcomes.[1] Medical and dental research on HRQoL has flourished because of (1) the patient's more active role as a member of the treatment team; (2) the need for evidence-based approaches in health practices; and (3) the fact that many treatments for chronic diseases fail to cure the health condition, thereby elevating the importance of HRQoL as a valuable health outcome variable.[2] This has created a need for a range of instruments with which to measure oral health–related quality of life. The Oral Health Impact Profile (OHIP-49) questionnaire contains 49 questions, assessing 7 dimensions of impacts of oral conditions on people's OHRQoL, including functional limitations, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap.[3, 4] A short version, the Oral Health Impact Profile-14 (OHIP-14) was later developed and is based on a subset of 2 questions for each of the 7 dimensions. [4] It is patient centered, gives a greater weight to psychological and behavioral outcomes, is better at detecting psychosocial impacts among individuals and groups, and better meets the main criteria for the measurement of OHRQoL. [4] The OHIP responses, "never", "hardly ever", "occasionally", "fairly often", and "very often", are codified from 0 to 4, respectively. In 2011, a study showed that the Dutch version of the OHIP-14NL questionnaire is a reliable and valid tool with which to measure the impact of oral health on quality of life in the Dutch population.[5, 6]

The use of questionnaires as used in this thesis also has drawbacks. The data are self-reported and there are concerns regarding patient bias that might distort the results. The motivations and accuracy of the patients in filling out the questionnaires can be debated. They may be driven to fill out the forms just to

please the surgeon, or to fill out the form rapidly just before an appointment. In the postoperative data collection, many questionnaires were given and this could have resulted in questionnaire fatigue, making the obtained results less reliable. In our studies OHIP-14 forms were handed out in person by the surgeon or by a dental student. This can also influence the results and the willingness to fill out the questions. A trial with automatically sent questionnaires, using the Lime-Survey program, showed even less response, although 3 reminders were sent at regular times. All the factors above will influence research outcomes, and the power analyses used to design a study should reflect this.

Another consideration in the use of OHRQoL as an outcome measure is addressing and measuring clinically meaningful change. Statistical significance is used to demonstrate the importance of results, but sample and size variation within studies play a very important role in determining statistical significance. While significant results showing pre/post group change may be appropriate for use in population-based health policy, they may not be appropriate for clinical care outcomes or clinical trials measuring within-group effects.[7, 8] Larger numbers of participants can reduce the overall bias, but a prolonged study time is necessary. This makes the study more susceptible to failure due to unforeseen events in the study group—for example, researcher or student illness, closure of the institute or new legislation affecting research—making completion of the study and thus publication of its results more challenging. The advantage of the 7-days postoperative questionnaire was that patients returned to the outpatient clinic after a week for a control visit and handed over their questionnaires. The biggest challenge of the 1-year orthognathic study was to collect all the OHIP-14 questionnaires at all the time points. To our disappointment, only 22 of the 85 patients completed all the questionnaires. This could be because the patients were operated by different surgeons and received preoperative orthodontic treatment from various orthodontists. In the future, the response rate might be improved by using a different approach to collect the data. If patients were approached by just one study surgeon/researcher, personal familiarity with them might make the patients more committed to filling out all the OHIP-14 questionnaires at all time points. To acquire more information on the OHIP-14 status of nontreated patients, a future study should include patients newly visiting the orthodontist, so that the preoperative orthodontic treatment, which involves realignment of the

teeth that is necessary for the surgery but inconvenient for the patients, will not influence the OHIP-14 scores. We are also interested in the long-turn outcomes of orthognathic surgery, and currently, we are collecting data on same cohort at least 2 years after surgery. We assume that all orthodontic appliances are removed and that we can obtain information about the stability of the OHIP-14 scores and compare the outcomes with the 1-year postoperative OHIP-14 scores.

In general, performing multicenter studies could help to include more patients in a shorter time frame. In future studies on OHRQoL, the use of questionnaires dedicated to specific types of operations could help in obtaining more specific and more detailed information.

Conclusions

OHRQoL has a multitude of substantive applications in oral surgery, health care, and dental research as we move from bench to applied science and person-centered approaches to measuring treatment needs and efficacy of care. Patient-oriented outcomes like OHRQoL will enhance our understanding of the relationship between oral health and general health and demonstrate to clinical researchers and practitioners that improving the quality of a patient's well-being goes beyond simply treating dental disorders. Researchers are beginning to uncover what OHRQoL has to offer and, if recent studies are any indication, the future looks bright indeed.[1]

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Chapter 10

Summary
Samenvatting

Summary

This thesis is a result of several studies assessing the impact of oral and maxillofacial procedures on patients' oral health-related quality of life (OHRQoL). It is recognized that poor oral health status can cause considerable pain and suffering. Untreated oral symptoms can be a major source of diminished quality of life, disturbing a patient's food choices or their speech, or leading to sleep deprivation, depression, and multiple adverse psychosocial outcomes. OHRQoL is a tool with which to understand and shape clinical practice, dental research, and dental education. It is associated with functional factors, psychological factors, social factors, and experience of pain or discomfort. In this thesis we use the OHIP-14 questionnaires as a measure of OHRQoL in clinical oral and maxillofacial practice to assess the effects of different surgical procedures on patients' postoperative subjective experience.

Chapter 1 is the introduction; it outlines the thesis and provides the scientific rationales for the different studies.

In **Chapter 2**, we measured patients' physical and psychological responses to local anesthesia for the surgical removal of a third molar. We hypothesized that patients with a high pain response (>7) on a 11-point numerical rating scale (NRS), would have a higher physical response than patients from the low-pain response group (NRS <7). We used different questionnaires, such as an 11-point NRS to obtain information on the expected and experienced pain of the injection, the Dental Anxiety Inventory (S-DAI), the Profile of Mood States (POMS), the State-trait Anxiety Inventory (STAI), and the Nexus-10 device to register the heart rate, respiration, and galvanic skin response. One can argue that all the preoperative questionnaires, especially, would induce fatigue bias in the patients. When we examined the results, only 8 of the total 66 patients were found to be in the high-pain group, making a comparison with the low-pain group (N = 58) challenging. An interesting finding was the physiological response. The heart rate and sweat secretion were significantly lower, when the oral and maxillofacial surgeon was already present in the operation theatre when the patient entered.

Chapter 3 describes the use of low-level laser light therapy (LLLT) on the injection site, prior to administering local anesthesia before the removal of a third molar in the upper or lower jaw. We did not find that this technique had a positive effect on either the experienced pain or anxiety rate in our patients. We did find that women had higher rates of pain expectation and anxiety, and also experienced more pain when the injection was administered. Unfortunately, the distribution of the procedures was skewed towards the removal of the lower wisdom tooth. This could have influenced the outcomes of this technique regarding, for example, the administration of the palatal injection, which is widely known as a more painful injection than are other forms of infiltration anesthesia.

In **Chapter 4**, a cross-over study design was used to obtain data on postoperative pain after removal of the lower wisdom tooth, using iodine-tampon packing. The advantage of such a study design is that each patient is their own control. The use of an iodine tampon can lead to reduced inflammation at the extraction site, and thus less pain and swelling and fewer functional problems. In the OHIP-14 scores collected at 7 days, we found better outcomes for pain in the iodine-tampon group than in the non-tampon group. In females, we found a slightly longer recovery time than in males. Including enough patients for this study was difficult. The position of the lower impacted wisdom tooth had to meet de Gregory-Pell grade 3B criteria on both sides. In total we included 54 patients for this study. One might argue with the results on the basis of the low number of participants; finding these participants among the patients of a small outpatient clinic proved to be quite challenging.

Chapter 5 describes a randomized study. We included patients scheduled for removal of the lower wisdom tooth and randomized their selection for the treatment protocol. In the first group, we administered a 2-cm iodine-tampon packing in the extraction socket for 1 week. In the second group, patients were instructed to use a syringe, Monoject, to irrigate the wound postoperatively 2 times a day, using only tap water. We found a significant reduction in the overall OHIP-14 scores in the iodine-tampon group compared with those of the non-tampon group. Improper syringe use could have influenced our results. Improperly performed irrigation could have led to more inflammation and more pain in the syringe group. An additional control appointment after

days 3 or 4 to check wound healing and wound irrigation could have been an alternative to solve this issue, but then the patient would have had to attend yet another appointment.

Chapter 6 describes a study on the coronectomy of mandibular third molars. To obtain more information about the OHRQoL after a coronectomy, which is the removal of the crown of an impacted wisdom tooth localized near to the inferior alveolar nerve, we collected the OHIP-14 data of our patients in the first postoperative week. We found a substantial rise in the mean OHIP-14 score up to the third day, than a gradually lowering to the seventh day. The pain score was highest on the first postoperative day and declined thereafter until the seventh day. We did not find a correlation with the degree of impaction, using the Gregory and Pell classification, and the pain scores. Also, there was no difference between the pain scores of males and females. When comparing the OHIP-14 and pain scores with those of other studies involving the removal of a wisdom tooth, we found higher scores for pain and total OHIP-14 scores in the other studies. An explanation for these findings might be that after the coronectomy is performed, the remaining pulp tissue, which is localized in the roots, prolongs the sensitivity or pain. This is an interesting outcome and could help patients in the preoperative stage to choose one of these procedures.

Chapter 7 is an assessment of the effect of periapical surgery on the OHRQoL in the first postoperative week. We concluded that both OHIP-14 and NRS scores changed considerably in the first postoperative day and that the scores decreased rapidly in the first postoperative week. We found no difference between the OHIP-14 scores of women and men, but we did find higher NRS scores in female compared with male patients. We found higher pain scores in younger patients than in older patients. The operation time did not influence the postoperative pain experienced in our patients.

The last study of this thesis, described in **Chapter 8**, investigated the impact of orthognathic surgery on quality of life in patients with different dentofacial deformities. The OHIP-14 scores of 85 patients were preoperatively calculated and compared with the outcomes in the first week and at 4 weeks, 6 months, and at least 1 year after the surgery. Besides the OHIP-scores, we collected mean pain scores, using a visual analog scale (VAS). We found a major decline

in the OHIP-14 scores in the first week, and a further gradually lowering in the postoperative months. By 1 year, the OHRQoL had improved significantly. The duration of the surgery did influence the OHIP-14 outcome negatively in the first postoperative week, meaning that a longer operation time resulted in temporarily higher OHIP-14 scores compared with those of shorter operation times. Regarding the OHRQoL scores, we found the results involving facial appearance to be more important than those involving oral function. The indication for surgery, Class II or III malocclusion, had no influence on the outcomes.

Samenvatting

Dit proefschrift is het resultaat van meerdere onderzoeken naar de invloed van orale en maxillofaciale procedures op de mondgezondheid-gerelateerde kwaliteit van leven (OHRQoL). Een slechte mondgezondheid kan aanzienlijk pijn en lijden veroorzaken., en onbehandelde orale symptomen kunnen een belangrijke oorzaak zijn van een verminderde kwaliteit van leven. Deze symptomen kunnen de voedselkeuzes van patiënt beïnvloeden, de spraak verstoren, of leiden tot slaapgebrek, depressie en/of meerdere nadelige psychosociale gevolgen. De mondgezondheid-gerelateerde kwaliteit van leven is een hulpmiddel om in de klinische praktijk, tandheelkundig onderzoek en tandheelkundig onderwijs te begrijpen en vorm te geven. Het wordt in verband gebracht met functionele factoren, psychologische factoren, sociale factoren en het ervaren van pijn of ongemak. In dit proefschrift is er gebruik gemaakt van de Oral Health Impact Profile-14 (OHIP-14-NL) vragenlijsten, als maat voor de mondgezondheid-gerelateerde kwaliteit van leven in de (poli) klinische orale en maxillofaciale praktijk. Er is gekeken naar de effecten van verschillende chirurgische procedures op de postoperatieve subjectieve ervaring.

Hoofdstuk 1, de inleiding, schetst de inhoud van het proefschrift en de wetenschappelijke redenen voor het uitvoeren van de studies.

In **hoofdstuk 2** zijn de fysieke en psychologische reacties, ontstaan bij het toedienen van lokale anesthesie voor de chirurgische verwijdering van een verstandskies, gemeten. We veronderstelden, dat patiënten met een hoge pijnrespons (>7) op een 11-punts numerieke beoordelingsschaal (NRS), een hogere fysieke respons zouden hebben, dan patiënten uit de lage-pijnresponsgroep (NRS <7). We gebruikten verschillende vragenlijsten, zoals een 11-punts NRS om informatie te verkrijgen over de verwachte en ervaren pijn van de injectie, de Dental Anxiety Inventory (S-DAI), de Profile of Mood States (POMS), de State-Trait Anxiety Inventory (STAI) en het Nexus-10-apparaat om de hartslag, ademhaling en galvanische huidreactie te registreren. Men kan stellen, dat met name de vele preoperatieve vragenlijsten een vermoeidheidsbias bij de patiënten zou kunnen veroorzaken. Bij het beoordelen van de resultaten, bleken slechts 8 van de in totaal 66 patiënten, in

de hoge pijnrespons groep te vallen, waardoor een vergelijking met de groep met een lage pijnrespons (N = 58) uitdagend was. Een interessante bevinding was de fysiologische respons: de gemeten hartslag en zweetafscheiding van patiënten waren significant lager als de mond, -kaak- en aangezichtschirurg reeds in de operatiekamer aanwezig.

Hoofdstuk 3 beschrijft het gebruik van low-level laserlichttherapie (LLLT) ter plaatse van de injectieplaats, voorafgaand aan het toedienen van lokale anesthesie, ter voorbereiding van een verwijdering van een verstandskies uit de boven- of onderkaak. Wij vonden met deze methode geen positief effect op de ervaren pijn of angst constateren. Vrouwen hadden een hogere pijnverwachting en angstgevoelens voelden ook meer pijn als de injectie werd toegediend. Helaas was de verdeling van de procedures scheef in de richting van het verwijderen van de onderste verstandskies. Dit zou de uitkomsten kunnen hebben beïnvloed. De toediening van de noodzakelijke palatinale injectie, die algemeen bekend staat als een pijnlijker injectie dan andere vormen van infiltratieanesthesie, kan eveneens invloed op de uitkomst hebben gehad.

In **hoofdstuk 4** is een cross-over studiedesign beschreven. Het doel van deze studie was, om gegevens te verkrijgen over de postoperatieve pijn, na verwijdering van de onderste verstandskies, gebruikmakend van het plaatsen van een met jodium geïmpregneerde tampon in de extractiealveole. Het voordeel van een dergelijke onderzoeksopzet is, dat elke patiënt zijn eigen controle is. Het gebruik van een jodium geïmpregneerde tampon kan leiden tot verminderde ontsteking in de extractiealveole, resulterend in minder postoperatieve pijn, zwelling en functionele problemen. In de OHIP-14-uitkomsten, verzameld na 7 dagen, vonden we betere resultaten voor de ervaren pijn in de jodium geïmpregneerde tampon groep ten opzichte van de controle zijde. Bij vrouwen vonden we een iets langere tijd tot herstel. Het bleek lastig, om voor dit onderzoek voldoende patiënten te kunnen includeren. De positie van verstandskies in de onderkaak moest aan beide zijden voldoen aan de Gregory-Pell classificatie, graad 3B-criteria. In totaal hebben we voor deze studie 54 patiënten geïncludeerd. De uitkomsten kunnen, op basis van het lage aantal patiënten, worden bekritiseerd; het vinden van deelnemers, die

voldoen aan de studiecriteria, bleek in een kleinere poliklinische praktijk, een hele uitdaging.

Hoofdstuk 5 beschrijft een gerandomiseerde studie. We includeerden patiënten, die gepland waren voor de verwijdering van de verstandskies uit de onderkaak en randomiseerden deze patiënten voor één van de twee behandelprotocollen. In de eerste groep hebben we gedurende 1 week een jodium geïmpregneerde tampon van 2 cm in de extractiealveole achtergelaten. In de tweede groep kregen de patiënten de instructie om een Monoject-waterspuit te gebruiken. De instructie was om de extractie-wond postoperatief twee keer per dag met kraanwater te irrigeren. We vonden een significante vermindering van de totale OHIP-14-uitkomsten in de jodium geïmpregneerde tampon ten opzichte van de Monoject-irrigatie groep. Onjuist gebruik van de waterspuit, leidend tot meer ontsteking en pijn, kan de uitkomst van het onderzoek hebben beïnvloed. Een extra controleafspraak, 3 of 4 dagen na de ingreep, zou dit probleem kunnen oplossen. Een nadeel van deze werkwijze is, dat patiënten twee in plaats van één keer naar de praktijk moeten terugkomen.

Hoofdstuk 6 beschrijft een onderzoek naar het uitvoeren van een coronectomie van de verstandskies in de onderkaak. Bij het uitvoeren van een coronectomie, wordt de kroon van de verstandskies verwijderd, en blijven de radices in de kaak achter. Deze techniek wordt toegepast, als de radices van het element (te) dicht in de buurt van de nervus alveolaris inferior gelokaliseerd zijn en volledige verwijdering mogelijk een tijdelijke of blijvende gevoelsstoornis in de lip, kin en gingiva kan veroorzaken. Om meer informatie te verkrijgen over de OHRQoL in de eerste postoperatieve week, verzamelden we de OHIP-14-uitkomsten van onze patiënten. We vonden een substantiële stijging van de gemiddelde OHIP-14 uitkomsten tot de derde dag, daarna volgde een geleidelijke daling tot aan de zevende dag. De pijnscore was het hoogst op de eerste postoperatieve dag en ook deze score nam tot de zevende dag verder af. We vonden geen correlatie voor de graad van impactie, gebruikmakend van de Pell en Gregory classificatie en de pijnscores. Er bestond geen verschil tussen de pijnscores van de mannen en vrouwen. Bij het vergelijken van de OHIP-14 uitkomsten en de pijnscores met die van andere onderzoeken, waarbij de verstandskies geheel

werd verwijderd, vonden we iets hogere scores voor de totale pijn en OHIP-14 uitkomsten. Een verklaring voor deze bevindingen kan zijn, dat bij het uitvoeren van een de coronectomie, met het achterlaten van pulpaweefsel in de radices, de gevoeligheid of pijn negatief beïnvloed. Dit is een interessante uitkomst en zou patiënten in de preoperatieve fase kunnen helpen om voor één van de twee procedures te kiezen.

In **hoofdstuk 7** werd het effect van periapicale chirurgie op de OHRQoL in de eerste postoperatieve week beoordeeld. We concludeerden dat de OHIP-14 en de NRS uitkomsten de eerste postoperatieve dag hoog scoorden, maar dat de scores daarna gedurende de eerste postoperatieve week sterk verminderden. We vonden geen verschil voor de OHIP-14 uitkomsten tussen vrouwen en mannen, maar we vonden wel hogere NRS-uitkomsten bij de vrouwelijke patiënten vergeleken met de mannelijke patiënten. Bij de jongere patiënten vonden wij hogere pijnscores dan bij de oudere patiënten. De operatieduur van de ingreep, had bij onze patiënten geen invloed op de postoperatieve pijn.

De laatste studie van dit proefschrift, beschreven in **hoofdstuk 8**, onderzocht de invloed van orthognatische chirurgie op de kwaliteit van leven bij patiënten met verschillende dentofaciale afwijkingen. De OHIP-14-uitkomsten van 85 patiënten werden preoperatief berekend en vergeleken met de uitkomsten in de eerste week, 4 weken, 6 maanden en ten minste 1 jaar na de uitgevoerde operatie. Naast de OHIP-14-uitkomsten hebben we ook de gemiddelde pijnscores verzameld, gebruikmakend van de visuele analoge schaal (VAS). We constateerde een grote daling van de OHIP-14 en VAS-scores in de eerste postoperatieve week met een verdere daling in de postoperatieve maanden. Na 1 jaar was de OHRQoL aanzienlijk verbeterd. De operatie duur had in de eerste week na de operatie een negatieve invloed op de uitkomst van OHIP-14-scores. Een langere operatieduur resulteerde in vergelijking met een kortere operatie duur tot tijdelijk hogere OHIP-14-scores . Voor de OHRQoL-scores bleken de resultaten, die betrekking op het uiterlijk hadden, een grotere invloed op de totale OHRQoL-scores te hebben, dan de waardes voor de orale functie. De indicatie voor chirurgie, Klasse II of III malocclusie, had geen invloed op onze uitkomsten.

Chapter 11

Appendices

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Chapter 2

Published as:
Anxiety and pain related to mandibular block injections: Comparison of self-reported measures and physiological response

Authors:
J.G.C. Tuk, J.A.H. Lindeboom, L. Hoogendoorn, B.W. Taylor, A.J. van Wijk

Published in:
Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 2017

Author contributions:
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Performed the study: JT, LH, BW
Analyzed the data: JT, AW
Critically revised the manuscript: JL, AW

Funding sources:
None

Conflicts of interests:
None

Chapter 3

Published as:
Analgesic effects of preinjection low-level laser/light therapy (LLLT) before third molar surgery: a double-blind randomized controlled trial

Authors:
J.G.C. Tuk, A.J. van Wijk, I.C. Mertens, Z. Keleş, J.A.H. Lindeboom, D.M.J. Milstein

Published in:
Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology, 2017

Author contributions:
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Performed the study: JT, IM, ZK
Analyzed the data: JT, AW, DM
Critically revised the manuscript: JL, DM

Funding sources:
None

Conflicts of interests:
None

Chapter 4

Published as:
Alveolar iodine tampon packing reduces postoperative morbidity after third molar surgery

Authors:
J.G.C. Tuk, J.A.H. Lindeboom, F. Sana, A.J. van Wijk, D.M.J. Milstein

Published in:
Journal of Oral and Maxillofacial Surgery, 2019

Author contributions:
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Performed the study: JT, JL, FS
Analyzed the data: AW
Critically revised the manuscript: JL, DM

Funding sources:
None

Conflicts of interests:
None

Chapter 5

Published as:
Alveolar iodine tampon packing after impacted third molar surgery improves oral health-related quality of life and postoperative sequela: a randomized study

Authors:
J.A.H. Lindeboom, J.G.C. Tuk, P. Möllenkamp, A.J. Wijk

Published in:
Oral and Maxillofacial Surgery, 2021

Author contributions:
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Performed the study: JL, JT, PM
Analyzed the data: AW
Critically revised the manuscript: JL, JT

Funding sources:
None

Conflicts of interests:
None

Chapter 6

Published as:
Oral Health-related quality of life after coronectomy for impacted mandibular third molar in the first postoperative week

Authors:
J.G.C. Tuk, L.E. Yohannes, J.P.T.F. Ho, J.A.H. Lindeboom

Published in:
Medicina Oral, Patología Oral y Cirugía Bucal, 2021

Author contributions:
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Performed the study: JT, LY, JL
Analyzed the data: JL
Critically revised the manuscript: JH

Funding sources:
None

Conflicts of interests:
None

Chapter 7

Published as:
Effect of periapical surgery on oral health-related quality of life in the first postoperative week using the Dutch version of Oral Health Impact Profile-14

Authors:
J.G.C. Tuk, J.A.H. Lindeboom, A.J. van Wijk

Published in:
Oral and Maxillofacial Surgery, 2021

Author contributions:
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Performed the study: JT, JL
Analyzed the data: JL, AW
Critically revised the manuscript: JL, AW

Funding sources:
None

Conflicts of interests:
None

Chapter 8

Published as:
Impact of orthognathic surgery on quality of life in patients with different dentofacial deformities: longitudinal study of the Oral Health Impact Profile (OHIP-14) with at least 1 year of follow-up

Authors:
J.G.C. Tuk, J.A.H. Lindeboom, M.L. Tan, J. de Lange

Published in:
Oral and Maxillofacial Surgery, 2022

Author contributions:
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Performed the study: JT, MT
Analyzed the data: JT, MT
Critically revised the manuscript: JL, JdL

Funding sources:
None

Conflicts of interests:
None

List of publications

In this thesis

Tuk JGC, van Wijk AJ, Mertens IC, Keleş Z, Lindeboom JAH, Milstein DMJ. Analgesic effects of preinjection low-level laser/light therapy (LLLT) before third molar surgery: a double-blind randomized controlled trial. Oral Surg Oral Med Oral Pathol Oral Radiol. 2017 Sep;124(3):240-247.

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Acknowledgements / Dankwoord

Ter afsluiting van mijn thesis wil ik graag een aantal personen voor hun hulp en bijdrage bedanken. Een ruime 8 jaar geleden ben ik samen met mijn begeleiders deze dissertatie gestart. Deze periode heeft vele hoogtepunten, maar ook dieptepunten gekend. Een zeer groot dieptepunt in deze periode was het overlijden van mijn vader, dr. Cees Tuk op 21 december 2017. Ik had altijd de wens om mijn proefschrift, na afronding, met trots aan hem te kunnen tonen. Hijzelf was op 16 december 1994 aan de Universiteit Utrecht gepromoveerd. De titel van zijn proefschrift: **Duitse lyriek in de Nederlandse school,** een onderzoek naar canonvorming van Duitse gedichten in het voortgezet onderwijs in de periode 1913-1990 en de receptie van gedichten uit de traditionele canon door leerlingen in het cursusjaar 1991-1992. Op deze bijzondere dag mocht ik als paranimf fungeren en later bleek deze ervaring een belangrijke stuwende kracht voor mijn eigen onderzoeksinteresse.

Zonder de hulp van de vele patiënten, was het niet mogelijk dit proefschrift te schrijven en mijn dank aan hen is zeer groot. Het onvermoeibaar invullen van de vele vragenlijsten, die na de kaakchirurgische behandeling aan hen werden verstrekt, is niet altijd een eenvoudige opgave geweest. Ook bleek het retourneren van de vragenlijsten aan het onderzoeksteam nog een hele uitdaging. Een onderdeel van de onderzoeksopzet, die ik van te voren niet zag aankomen. Hulde voor al hun inzet.

Prof. Dr. J. de Lange, hooggeleerde promotor, beste Jan. Ik wil je enorm danken voor het in mij gestelde vertrouwen en dit promotietraject met mij te willen aangaan. Jouw niet aflatende steun, geduld en ruimte voor dit enigszins langdurige proces, is tekenend voor jouw karakter als leidinggevende, maar ook als collega en vriend. Jij stimuleerde mijn gang naar het wetenschappelijk onderzoek en bracht mij in contact met de juiste collega`s voor het verder uitwerken van de verschillende studies. De tijd die jij mij hebt gegund om dit manuscript af te ronden, waardeer ik enorm. Jouw benoeming als hoofd van de nieuwe en verenigde afdeling MKA-chirurgie van het Amsterdam UMC is eveneens een enorme impuls voor het afronden van dit manuscript geweest.

Dr. J.A.H. Lindeboom, beste Jerome. Sinds 1998 kennen wij elkaar door onze samenwerking op het AMC. Jij was destijds chef de polikliniek en ik aangesteld als AGNIO op deze prachtige afdeling. Voor jou is wetenschappelijk onderzoek, naast je werk, ook je leven geworden. Jij bent altijd op zoek naar nieuwe en vernieuwde onderzoeksprojecten. Je hebt altijd de wens om nog verder door te zoeken in de onderzoeksdata en bent een ster in het formuleren van nieuwe hypothesen. Onze eerste gesprek over wetenschappelijk onderzoek dateert vanaf het begin van onze ontmoeting en duurt, ook nu het manuscript is voltooid, nog altijd voort. Toen ik het schrijven van de thesis wilde staken, was jij onvermoeibaar met het stimuleren van de juiste richting voor het voltooien van de thesis. Ik kan kort zijn over je inbreng in dit uitdagende traject: zonder jouw inzet en steun was deze thesis er zeker niet gekomen. Een enorme waardering heb ik voor je tomeloze inzet, hulp en vertrouwen in mijn begeleiding. Je vernieuwende en doortastende kijk op ons werk, zeker ook in onze Maatschap MKA-chirurgie en Implantologie in ziekenhuis Amstelland, maakt mij een betere kaakchirurg, waarbij onze patiënten de grote winnaars zijn.

Dr. A.J. van Wijk, beste Arjan. Jouw aanstekelijk enthousiasme voor wetenschappelijk onderzoek en data, heb ik altijd als zeer bijzonder en prettig ervaren. Geen statistisch probleem is voor jou te veel en jouw doortastende inzichten zijn een grote hulp in het juist opzetten van de onderzoeksvraagstelling gebleken. Een korte Power-analyse door jou vooraf, was genoeg voor ons, om het onderzoek te kunnen starten. De samenwerking was altijd uitstekend en werkte synergistisch. De snelheid, waarmee jij onze onderzoeksvragen kon beantwoorden, was fenomenaal. Hierdoor konden wij snel starten met het goed uitvoeren van een studie. Ik dank je voor je vertrouwen en steun tijdens dit traject en je bereidheid om de taak als mijn copromotor te accepteren.

Geachte leden van de leescommissie: Prof. dr. J.E. Bergsma , Prof. dr. A. de Jongh , dr. J.W. Nolte, Prof. dr. G.M. Raghoebar, Prof. dr. F.R. Rozema, Prof. dr. E.A.J.M. Schulten, ik dank u voor uw tijd, uw bereidheid dit proefschrift te willen beoordelen en om zitting te nemen in deze promotiecommissie.

Collega stafleden van het Amsterdam UMC, door jullie aanwezigheid, is mijn werkplezier altijd gegarandeerd. Jullie hulp en opbeurende woorden heeft mij de energie gegeven, dit proefschrift af te ronden. Met jullie samenwerken geeft de dag kleur en jullie enthousiasme en scherpzinnigheid polijst mijn professionele en persoonlijke vorming nog elke dag. In het bijzonder dank ik de stamgasten van kamer D2-407, met name Jean-Pierre Ho en Tom van Riet. Onze gezamenlijke wens om `het boekje` af te ronden heeft mij zeer gemotiveerd, zeker tijdens de pandemie, waar wij allemaal echte meters in de wetenschap hebben kunnen maken. Ik hoop nog zeer lang onderdeel van het Team te mogen blijven.

Beste A(N)IOS en oudgedienden van het AMC, ik dank jullie voor de niet aflatende inzet om de onderzoekdata met mij te verzamelen. Naast jullie drukke bestaan, zijn jullie bereid geweest het onderzoeksprotocol te volgen en onvermoeid de vele vragenlijsten uit te delen en weer te verzamelen. Zonder jullie hulp, was een groot deel van de beschikbare onderzoeksgegevens nooit verzamelt en was ik waarschijnlijk nog bezig de nodige data te vergaren. Onderzoek doe je nooit alleen en met jullie hulp, voelde dat ook echt zo. Ieder van jullie heeft zijn eigen inbreng en inzichten met mij gedeeld en dit heeft naast mijn eigen publicaties ook voor de nodige spin-off publicaties gezorgd.

Dan Milstein, ik dank je voor het beschikbaar stellen van de Low-level laser (light) therapy (LLLT) en de Nexus 10, waarmee wij de eerste twee onderzoeken hebben kunnen uitvoeren. Jouw positieve houding ten aanzien van mijn wetenschappelijke vorming en jouw kritische, maar zeer terechte blik op de onderzoeken en publicaties heeft zeer veel indruk op mij gemaakt.

Polikliniek MKA-chirurgie AMC, dank voor alle hulp en begrip in dit proces. Onze samenwerking is voor mij altijd plezierig geweest en jullie draaien de werkelijke organisatie. Lieve Simone Vespasiano, onze samenwerking dateert reeds vanaf het begin in 1998. Bij alle fasen van mijn opleiding ben jij aanwezig geweest en jou positieve benadering en niet aflatende energie is een voorbeeld voor een perfecte collega. Ik hoop nog heel lang met je te mogen samenwerken. Inge Oliemans, veel dank voor onze fijne samenwerking. Geen brief gaat de deur uit, zonder jouw scherp toeziend oog. Regelmatig heb jij mij geholpen, de brieven correct en met de juiste informatie aan onze verwijzers

te sturen en mij behoed voor toekomstige problemen. Drikje Geskes, ik dank je voor de zeer fijne samenwerking in de afgelopen jaren. Ook jij bent vanaf het begin betrokken geweest bij mijn opleiding en hebt mij, waar nodig, altijd perfect willen ondersteunen.

Polikliniek Ziekenhuis Amstelland, dames en heren, mijn dank naar jullie is zeer groot. Doordat jullie altijd bereid waren de vele vragenlijsten te verzamelen en de patiënten op de juiste tijden op ons programma te plaatsen, zijn vele onderzoeken in dit proefschrift een succes geworden. Dagelijks werken wij in een kleine perifere kliniek samen, maar het wetenschappelijk niveau lijkt soms toch meer op een academische instelling. Ik hoop nog heel lang met jullie te mogen samenwerken.

Studenten Linda, Byron, Ine, Zuhal, Faro, Patrick, Lily en in het bijzonder Misha Tan, mijn dank aan jullie is zeer groot. Vrijwel elk onderzoek is alleen mogelijk geweest met jullie niet aflatende steun en hulp in zowel het verzamelen van de onderzoeksgegevens als ook het opstellen van de publicaties. Met jullie samenwerken was voor mij een zeer fijne tijd. Jullie inbreng heeft geleid tot het daadwerkelijk kunnen uitvoeren van de onderzoeken en heeft zeker geleid tot hoogwaardigere resultaten. Ik wens jullie een prachtige carrière in ons boeiende vak.

Beste dr. Ruud Scheurs, Niels Klop en Julia Sabelis, zeer veel dank voor jullie niet aflatende hulp bij de planningen van de orthognatische operaties met de OPS-software en natuurlijk al jullie aanvullende hulp tijdens het schrijven van deze thesis.

Lieve mamma, jij hebt alle fasen van mijn opleiding meegemaakt en bent altijd oog en oor geweest voor alle zaken die ik toch echt met je moest bespreken. Jouw scherpe inzichten en sturende woorden hebben mij al mijn hele leven lang gesteund. Natuurlijk ben jij het controlerende oog van de praktijk op ziekenhuis Amstelland, maar je hebt mij ook enorm geholpen bij het opstellen van deze thesis. Dat ik jouw kunstwerk, dat sinds jaar en dag op de praktijk hangt, mag gebruiken voor de omslag van dit boek, vind ik fantastisch. Helaas heeft pappa deze dag niet mogen meemaken, maar ik ben er zeker van dat hij zeer trots op ons zou zijn geweest.

Lieve Yulia Marasanova, Lisa en Misha Tuk, jullie zijn de vreugde met wie ik mijn leven mag delen. Wat een voorrecht. Elke dag opnieuw beleef ik de liefde, vriendschap en ouderschap met jullie en ik geniet er enorm van. 20 jaar geleden had ik niet durven hopen, dat wij vandaag uiteindelijk samen dit feest mogen vieren. Ons gezin vormt de basis voor mijn gelukkige leven. Dikke kussen aan jullie alle drie!

Beste Erwin Willemse en Marnix Bom, jaargenoten en paranimfen, ook jullie waren 20 jaar geleden aanwezig tijdens onze duikreis in Egypte, waardoor alles in mijn leven is veranderd. Ik dank jullie voor de bereidheid om vandaag mij te willen steunen en natuurlijk voor onze niet aflatende vriendschap. Hulde voor jullie en ik wens ons samen nog vele jaren van vriendschap.

Curriculum Vitae

The author of this thesis was born in Hilversum, The Netherlands on May 22, 1974. He finished the Christelijk College Stad en Lande, Huizen and obtained his Atheneum diploma in 1992.

He received his dental degree in 1998 at the Academic Center for Dentistry (ACTA)/ University of Amsterdam (UvA), and started with his medical study at the Academic Medical Centre (AMC), UvA. During this period, he worked part-time at the department of Oral and Maxillofacial surgery, Academic Medical Center, Amsterdam, and as a dentist in different dental clinics. In the year 2000 he interrupted his medical study to become a resident in Oral and Maxillofacial surgery (head: Prof. dr. H.P. van den Akker). He finished his residency in 2004, and joined the staff of the Oral and Maxillofacial surgery department, AMC, Amsterdam, and continued his medical study. In 2005 he obtained his medical degree, and was registered as an Oral and Maxillofacial surgeon. Between 2005 and 2007, he worked as a consultant at the Oral and Maxillofacial surgery department, AMC, and different Oral and Maxillofacial clinics in the Netherlands. In 2007, he accepted a part-time position as a consultant at the Amstelland Hospital, Amstelveen and he combines this with his academic work at the Amsterdam UMC. In 2017, he completed a master course (MSc) in aesthetic facial surgery EFMZ at the University Witten/ Herdecke, Germany, and obtained a University Teaching Qualification (BKO), Faculty of Medicine (UvA).

His special interest are in the field of orthognatic surgery, dentoalveolar surgery, esthetic facial surgery, and oral implantology.

Jacco lives happily with his wife Yulia, daughter Lisa, and son Misha in Huizen.