Original article

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Which route of antibiotic administration should be used for third molar surgery? A split-mouth study to compare intramuscular and oral intake

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Abstract

Objectives. To compare the effectiveness of two different routes of antibiotic administration in preventing septic complications in patients undergoing third molar extraction.

Materials and Methods. Twenty-four healthy patients requiring bilateral surgical removal of impacted mandibular third molars were successfully enrolled for this study. Depth of impaction, angulation, and relationship of the lower third molars with the mandibular branch had to be overlapping on both sides. A split-mouth design was chosen, so each patient underwent both the first and second surgeries, having for each extraction a different antibiotic route of administration. The second extraction was carried out 1 month later. To compare the effects of the two routes of antibiotic administration, inflammatory parameters, such as edema, trismus, pain, fever, dysphagia and lymphadenopathy were evaluated 2 and 7 days after surgery. Side effects of each therapy were evaluated 48h after surgery.

Results. oral and intramuscular antibiotic therapies overlap in preventing post-operative complications in dental surgery (p>0.05), even if the oral intake, seems to promote the onset of significant gastrointestinal disorders (p=0.003).

Conclusions. This study could help dentists in their ordinary practice to choose the right route of antibiotic administration in the third molar surgery. At the same effectiveness, the higher cost and the minor compliance of the patient seem not to justify a routine antibiotic intramuscular therapy, reserving it for patients with gastrointestinal disorders. ***Clin Ter 2014; 165(1):e12-16. doi: 10.7417/CT.2014.1665***

Key words: *antibiotics, intramuscular therapy, oral intake, third molar surgery*

Introduction

Third molar extraction is usually considered a clean-contaminated surgery; therefore, routine antibiotic administration is a controversial topic.

Piecuch et al. (1) identified five reasons to justify the use of antibiotics: 1) presence of infection at the time of surgery; 2) compromised patients; 3) the patient or the patient's family demand for antibiotics; 4) presence of a standard of care in oral surgery that requires antibiotic therapy; 5) presence of a high risk of postoperative infection necessitating antibiotic prophylaxis.

Several authors (2-6) reported a lower incidence of postoperative infections after systemic antibiotic therapy that proved effective in reducing the incidence of alveolar osteitis.

On the other hand, several studies (7-9) evaluating the effectiveness of different antibiotics in preventing alveolar osteitis and postoperative pain after the extraction of third molars showed no statistically significant differences between antibiotic therapy and placebo.

In addition, no clear and precise guidelines regarding the route of antibiotic administration have been assessed.

The aim of the present study was to compare the effects of two routes of beta-lactam antibiotic administration after surgical removal of impacted mandibular third molars.

Materials and Methods

This study was performed in the School of Dentistry, University of Bari, Italy, in accordance with the provisions of the Declaration of Helsinki. Patients requiring bilateral surgical removal of impacted mandibular third molars were enrolled.

The following parameters were assessed to determine the spatial position of the single tooth and the difficulty of its extraction:

1. Depth of inclusion, according to Pell and Gregory classification (10), measured in relation to the occlusal plane.
2. Relationship with the mandibular branch, according to Pell and Gregory classification (10).
3. Angulation of the third molar, according to Winter classification, measured in degrees with respect to the axis of the second molar (11).

A total score for the difficulty of intervention was obtained according to the Pederson (12) and Checchi-Monaco index (13).

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The inclusion criteria were age >18 years or <40 years and good health. Depth of impaction, angulation, and relationship of the lower third molars with the mandibular branch had to be overlapping on both sides.

Exclusion criteria were age <18 years or >40 years, compromised subjects, smokers, pregnancy, allergy to beta-lactam antibiotics, lower third molars with bilateral different characteristics and indications for extraction, consumption of antibiotics or anti-inflammatory drugs in the 2 weeks prior to the intervention, and subjects with clinical signs of infection and inflammation around lower third molars at the time of surgery.

Thirty-six patients (18 males and females each) with a mean age of 27.5 ± 7 years were initially recruited for this study. Each patient gave written informed consent to participate and was allowed to withdraw from the trial at any time.

Six patients, however, did not want to extract the second lower third molar, other two patients did not follow the prescription and consumed oral antibiotic after both interventions because of needle fear and finally two more patients complained of side effects such as nausea, diarrhea, stomach pain, headache, and insomnia during oral intake of amoxicillin, therefore, it was necessary to discontinue this therapy and replace it with intramuscular therapy in both surgeries. Two patients complained of severe pain at the injection site and difficulties in deambulation. In this case, intramuscular therapy was replaced with oral administration.

Finally, 24 patients were successfully enrolled for the study. They underwent two surgical intervention, for a total of 48 partially impacted lower third molars extracted (Fig. 1).

For all patients, the extractions were performed by the same operator according to the following steps: disinfection of the surgical site with iodine, alveolar nerve block by means of mepivacaine without a vasoconstrictor (30 mg/ml cartridges), infiltration of buccal soft tissues with mepivacaine 1.8-ml solution (20 mg/ml) with 1:100.000 epinephrine, incision of triangular mucoperiosteal flap, corticotomy by a water-cooled bur in a surgical drill, odontotomy by a water-cooled bur, tooth extraction by a straight or a Barry lever, surgical curettage by a Volkmann spoon, irrigation of postextraction sites with a saline solution, and 2/0 polyglactin (Vicryl) interrupted sutures.

Random sampling by means of sealed envelopes was used to determine the route of drug intake after the first extraction. The second extraction was carried out one month later using a route not employed till then. This "*wash out*" period of one month spaced out the two therapies in order to eliminate the effects of the first drug, thus bringing the patient in the initial conditions.

Amoxicillin + clavulanic acid 1 g tablets (1 tablet every 12 h for 5 days) were given in the oral therapy, whereas sodium cefazolin, vials 1 g (1 g i.m. twice a day for 5 days) in the intramuscular intake.

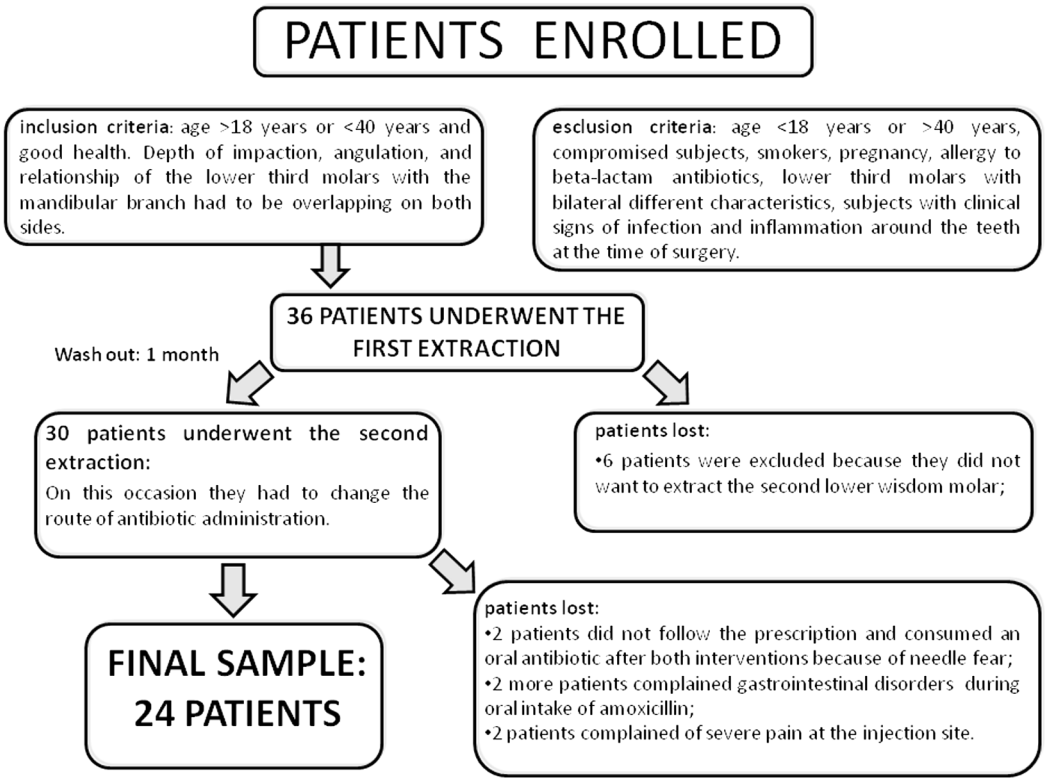

Fig. 1. Flow chart of sampling.

Chlorhexidine 0.12% mouthwashes were prescribed twice a day for 10 days following the operation.

To compare the effectiveness of these two different routes of antibiotic administration in pain control and prevention of septic complications, a "split-mouth" design was chosen (14-17). This is a popular design in oral health research where each of two treatments is randomly assigned to either the right or left halves of the same patient's dentition. By making within-patient comparisons, rather than between-patient comparison, the error variance (noise) of the experiment can be reduced, thereby obtaining a more powerful statistical test. The attractiveness of the design is that it removes a lot of inter-individual variability from the estimates of the treatment effect.

Each patient was evaluated 2 and 7 days after surgery to check the presence and intensity of signs and symptoms of inflammation.

In this regard, parameters evaluated were:

– Edema: measured in cm as the distance between the lower insertion of the auricular lobe and the chin medium point.
– Trismus: measured in cm as the distance between the incisal edges of the upper and the lower central incisors.

For the above-mentioned parameters, three measurements were performed (6): a) before surgery, b) 2 days after surgery, and c) 7 days after surgery. Their variations were evaluated as difference respect to the pre-operatory state.

– Pain: measured by a visual analogical scale (VAS), a sensitive and reliable method for recording pain intensity, with the anchor points "0 = no pain" and "10 = the worst pain imaginable" (18). Two measurements were performed 2 and 7 days after surgery.
– Fever: measured in °C (6) at 2 and 7 days after surgery.
– Dysphagia: evaluated during the first and the second control. The following score was assigned (6):
  0 point: absence of dysphagia.
  1 point: dysphagia to solid foods only
  2 point: dysphagia to both solid and liquid foods.
– Lymphadenopathy: evaluated during the first and the second control. The following score was assigned (9):
  0 points: lymph nodes not examinable and not painful
  1 point: lymph nodes movable and examinable but not painful
  2 points: lymph nodes examinable, movable, and painful.

Side effects of antibiotic therapy reported by patients, such as gastrointestinal disorders (nausea, constipation, diarrhea, stomachache, vomiting), headache, weakness and insomnia, were considered.

Statistical analysis

Continuous normally distributed data were expressed as

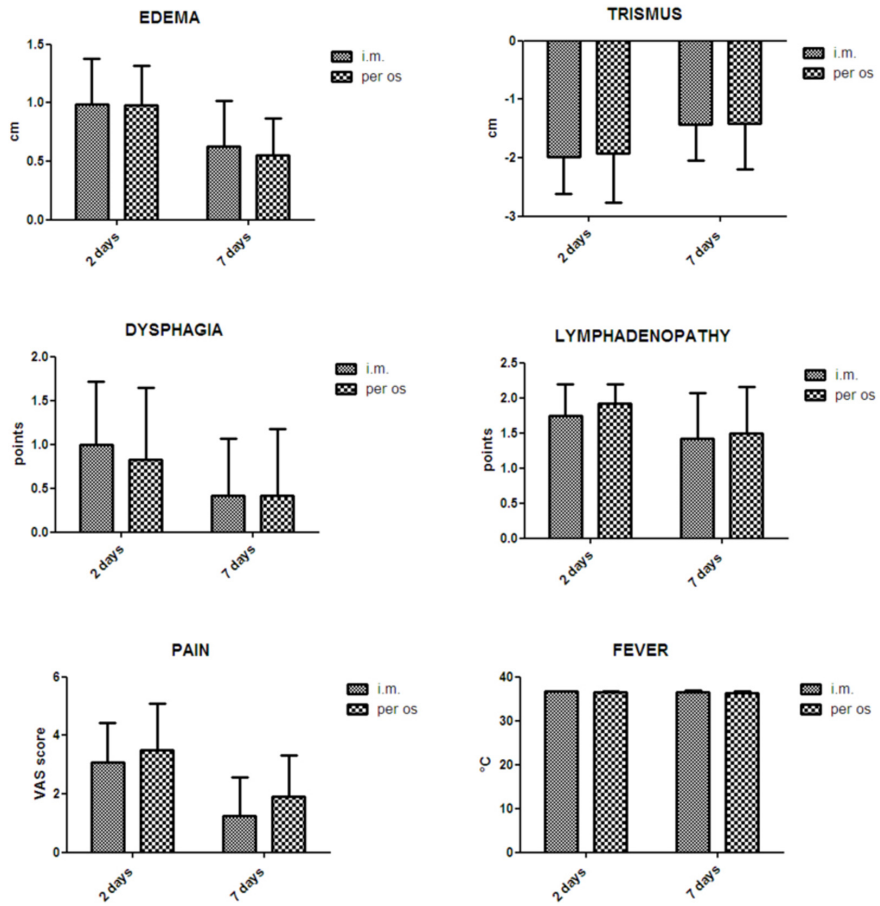

Fig. 2. Mean values (±SD) of facial edema, trismus, dysphagia, lymphoadenopathy, pain and fever in intramuscular (i.m.) and oral (per os) therapy at the 2nd and 7th postoperative days. (paired Student t test; n=24, p>0.05).

mean ± standard deviation (SD) and compared using paired Student *t* test.

Categorical data were compared using chi-squared (χ^2) or Fisher exact tests. In all comparison, a *p* value ≤0.05 was considered statistically significant. (PRISM® version 5.0 GraphPad Software, 1994-2007).

Results

Inflammatory parameters

Mean values (±SD) about inflammatory parameters demonstrated no statistically significant differences between the two route of antibiotics compared by using paired Student's *t* test (Fig. 2).

Facial edema increased about 1 cm and 0.6 cm at the second and the seventh days after surgery respectively. There were no statistically significant differences between the two therapies at the first (p=0.87) and the second control (p=0.54), although the injection therapy seems to be slightly more effective in reducing the amount of postoperative swelling seven days later.

About trismus, mouth opening showed a mean reduction of about 2 cm and 1.4 cm respectively at the second and the seventh postoperative days in both therapies. No statistically significant difference between the two treatments at the first (p=0.91) and the second (p=0.94) evaluations was found.

Postoperative pain score (VAS), two days after surgery, was 3.08 points for the injection therapy and 3.5 for the oral therapy. Seven days after surgery, the values recorded were 1.3 and 1.9 for the injection therapy and the oral therapy respectively. Also in this case, no statistically significant differences between the two typologies of administration at the first (p=0.30) and the second controls (p=0.09) were detected. However, it would seem that injection therapy was more effective in reducing pain.

The mean value of dysphagia registered was 1.0 points two days after surgery for injective therapies and 0.83 for oral ones. On the seventh postoperative day, dysphagia decreased in both therapies and was even absent in most cases. No statistically significant differences between the two typologies of administration at the first (p=0.38) and the second assessments (p>0.99) were found.

The assessment of lymphadenopathy demonstrated both therapies were very similar at the second and the seventh day after surgery. No statistically significant differences between the two therapies at the first (p=0.16) and the second controls (p=0.60) were observed.

Finally, regarding fever, a temperature >37°C was recorded only in four cases on the second day after surgery for both therapies. The mean values of temperature show no differences between the two therapies (p=0.659).

Side effects

Data showed a significant increase of gastrointestinal disorders in the oral therapy (p=0.003), whereas the other side effects (i.e., headache, weakness and insomnia) did not reveal any differences.

The side effects of therapy between the two typologies of administration were evaluated by χ^2 test and reported in Figure 3.

Discussion

At present, there is no agreement in literature about the effectiveness of antibiotics in preventing septic complications after dental surgery. Timing and protocol of antibiotic use are still controversial: antibiotic prophylaxis or cover, topical or systemic application, oral or intramuscular administration.

A distinction between the authors favoring (2-6) and those not favoring (7-9) a prescription of the antibiotic therapy for the lower third molar extraction is, however, too schematic, because a different approach should be followed, depending on different variables such as the difficulty of surgery, need of ostectomy and crown sectioning, dental depth, and angulation.

The lack of precise guidelines about the use of antibiotic therapy in healthy patients after oral surgery makes the dentists to rely solely on their own experience.

The study compared the effectiveness of two different routes of antibiotic administration for prevention of septic complications in healthy patients undergoing third molar extraction.

A split-mouth study design (14-17) was performed to reset all bias. Thanks to this sampling method, all the confounding factors linked to the characteristics of the subjects are eliminated, thus ensuring a high power of the test that we are going to run and obtaining conclusive results even with small samples.

However, this protocol has the problem of sample size, due to the difficulty in finding similar characteristics in collaborating patients. In fact, several subjects were excluded from the study because they did not comply with the requi-

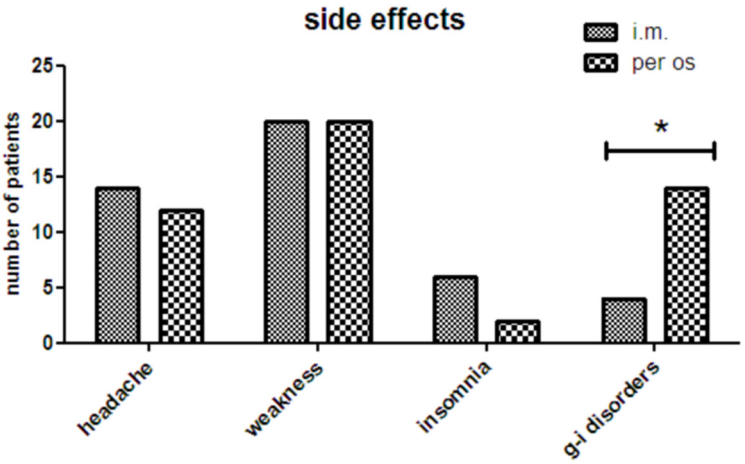

Fig. 3. Side effects of therapies 48 h after surgery: the oral therapy (per os) reveals a higher incidence of gastrointestinal (G-I) disorders as nausea, constipation, diarrhea, stomachache, vomiting. (χ^2 test; n=24; *p=0.003). The remaining side effects do not show any differences (p>0.05).

rements, were absent from the appointments, or decided to withdraw. This attitude has been reported in patients whose first extraction was particularly difficult and traumatic, or in subjects who developed infectious complications at the end of the surgery. In fact, after a case of dry socket and a case of significant swelling, patients refused to remove the contralateral lower third molar.

Results obtained by the evaluation of all the inflammatory parameters demonstrated that both therapies proved effective. However, there has been a trend, though not statistically significant, of the intramuscular therapy in the control postoperative pain.

Data about side effects showed only a significantly increased incidence of gastrointestinal disorders associated to the oral therapy.

Among the enrolled patients, there were no cases of secondary infection who have requested prolongation of antibiotic therapy or a new alveolar curettage. This could support the efficacy of antibiotic cover to prevent postoperative infectious complications after the lower third molar surgery, irrespective of the type of drug administration.

For this reason, in the daily routine, dentists can either prescribe one or the other route of drug administration, except for some situations such as needle fear or gastrointestinal problems. However, at the end of follow-up, each patient was asked: which was the preferred route of administration. Most of them indicated oral therapy for the following reasons: easier and cheaper administration and absence of pain at the time of drug consumption. All these aspects should be taken into account by the dental surgeon to increase patients' compliance and their response to the requirements.

In conclusion, the analysis of the data shows that oral and intramuscular antibiotic therapies almost overlap in preventing postoperative complications in dental surgery. However, the higher cost and the minor compliance of the patient do not justify a routine antibiotic intramuscular therapy, reserving it for patients with gastrointestinal disorders.

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