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Antibiotic prophylaxis for mandibular advancement with bilateral sagittal split osteotomy: A comparison of three versus four doses Penicillin V

Running title: Antibiotic prophylaxis for BSSO

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Abstract

Aim: Compare two regimens of antibiotic prophylaxis on the development of surgical site infection (SSI) following mandibular advancement with bilateral sagittal split osteotomy (BSSO).

Materials and methods: In total, 176 patients were included. Two antibiotic regimens were administered intravenously. The first 114 patients were given Penicillin V (PcV) in three doses every eight hours (PcV3-group), and the next 62 patients were given PcV in four doses every six hours (PcV4-group). The same surgical protocol was followed for all patients. Development of SSI was registered at follow-up two months and one year after surgery.

Results: A significant reduction in the rate of SSI was found in the PcV4 group compared to the PcV3-group ($p=0.012$). The infection rates were 4.8% and 19.3% respectively. A higher prevalence of SSI was found when mandibular wisdom teeth were present, but this was not statistically significant. There were no correlations between gender, age, intraoperative bleeding and operation time and the development of SSI. None of the patients developed severe infection.

Conclusion: The infection rate was significantly reduced when PcV was administered in four doses, suggesting that an extended regimen of antibiotic prophylaxis is beneficial when performing mandibular advancement with BSSO.

Keywords: orthognathic surgery, surgical site infection, sagittal split osteotomy, mandibular advancement, antibiotic prophylaxes

Clinical relevance

Scientific rationale for study: Identify effective antibiotic prophylaxis to reduce the risk of surgical site infection (SSI) after mandibular advancement with bilateral sagittal split osteotomy (BSSO).

Principal findings: Two regimens of Penicillin V (PcV) prophylaxis were compared. The infection rate was significantly reduced when PcV was administered in four doses compared to three doses ($p=0.012$).

Practical implications: Extended antibiotic prophylaxis can be considered for mandibular advancement with BSSO to reduce the risk of SSI.

Introduction

Severe postoperative infections after orthognathic surgery are very rare, but also low-grade surgical site infections (SSI) result in pain and discomfort for patients, and many cases require a second surgical procedure to remove osteosynthesis-material[1]. The reported prevalence of SSI after orthognathic surgery varies from 2% to 33,4%, and mandibular osteotomies are more prone to develop postoperative infections, possibly due to the reduced blood supply compared to the maxilla[2-5]. Overall, administration of prophylactic antibiotics is broadly accepted practice in orthognathic surgery to prevent SSI. The prophylactic antibiotic regimes administered vary greatly, from restricted use of narrow-spectrum antibiotics to extended protocols of broad-spectrum agents[6]. Limiting the use of broad-spectrum antibiotics is an important measure to reduce the risk of antimicrobial resistance[7]. The aim of antibiotic prophylaxis is to provide an adequate drug concentration in the tissue before, during and for a short time after the procedure, and excess use of antibiotics should be avoided[8]. Long term antibiotic prophylaxis has been found to reduce the risk of postoperative SSI by some authors[6,9], but not by others[10]. To minimize the risk of complications, it is important to identify the variables that increase the risk and optimize the surgical routine. Also, identifying effective antibiotic prophylaxis is needed to reduce the risk of postoperative infections. Orthognathic surgery is elective and standardised procedures and consensus regarding the preferred type of prophylactic antibiotic, as well as the dose and duration it is administered, is warranted. The aim of this study was to compare two regimens of narrow-spectrum Penicillin on the development of SSI following mandibular advancement with bilateral sagittal split osteotomy (BSSO).

Materials and methods

Inclusion of patients and antibiotic protocol

We performed a retrospective cohort study of consecutive patients undergoing mandibular advancement with BSSO at the Department of Maxillofacial Surgery, Haukeland University Hospital from 2013-2019. The work was presented to a regional ethics committee which considered it a quality assessment study that did not require additional ethical approval. All other orthognathic surgery procedures performed in the same period, including double-jaw surgery were excluded from the study. Patients with a known allergy towards Penicillin were also excluded. A total of

176 consecutive patients were included, and the first 114 patients were given an antibiotic regimen of Penicillin V (PcV) 2 million international units (1,2g) administered intravenously in three doses (PcV3-group). The first dose was given 15 minutes before the start of the operation, and the two following doses eight and 16 hours after surgery. The next 62 patients were given four doses of PcV (PcV4-group) 2 million international units (1,2g). Also here, the first dose was given 15 minutes before the start of the operation, but the following three doses six, 12 and 18 hours after surgery. Inclusion to the PcV4-group was stopped at June 30th 2019 to allow for one year follow-up of all patients.

Surgical procedure

The same surgical protocol was followed for all patients. Total intravenous anaesthesia (TIVA) with nasotracheal intubation was administered, supplemented with 10ml lidocaine 2% with adrenalin local infiltration. Bilateral incisions were made from the ascending ramus and buccal to the second molar. Subperiostal dissection was performed laterally and medially to identify the mandibular foramen. The osteotomies were performed with an oscillating saw and the split completed with osteotomes. The distal fragment was mobilized and advanced to the planned occlusion and ostesynthesis with microplates (Biomet Microfixation LLC, Jacksonville, FL, USA) was performed. No autologous bone grafts were used. The incisions were closed with a continuous polyglactine suture (Vicryl Rapid, Ethicon, Somerville, NJ, USA), and an active drain on each side was kept until the following day.

Outcome measures

All patients were evaluated two months and one year after surgery. A clinical evaluation on the presence of SSI was performed according to established criteria[11]. To be registered with SSI, the patient had to present with pain, swelling, redness, purulence, fistula or dehiscence, in addition to a clinical diagnosis of infection. Panoramic and cephalometric radiographs were taken the day before surgery, the day after surgery, and one year after surgery. The treating orthodontist performed additional follow-up during and after the postoperative orthodontic treatment, and if clinical signs of infection or symptoms occurred, additional follow-up was scheduled. Patients meeting the criteria for SSI required antibiotic treatment in addition to the

standard protocol, and all patients registered with SSI had additional surgery to remove osteosynthesis-material. Secondary parameters age, gender, blood loss, operation time, presence of wisdom teeth and prevalence of bad splits were registered at the day of surgery.

Statistical analysis

The two groups were compared with a two-sided Fisher's exact test. Statistical evaluations were performed using SPSS version 25 (IBM, Armonk, NY, USA). Results with a p-value <0.05 were considered statistically significant.

Results

None of the patients developed severe infection, and all SSI were adequately managed with orally administered antibiotics, drainage and removal of osteosynthesis-material. A significant reduction in the rate of SSI was found in the PcV4 group compared to the PcV3-group (p=0.012) (Table 1). The infection rates were 4.8% (3/62) in the Pcv4 group compared to 19.3% (22/114) in the Pcv3 group. A higher prevalence of SSI was found when mandibular wisdom teeth were present, in particular when the wisdom teeth were not removed during the BSSO-procedure. However, this was not statistically significant (Table 2). The overall prevalence of bad split was 5.1% (9/176), and none of these patients developed SSI. There were no correlations between gender, age, intraoperative bleeding and operation time and the development of SSI (Table 3).

Discussion

Administration of prophylactic antibiotics is accepted practice in orthognathic surgery to reduce the risk of postoperative infections. There is however a lack of consensus regarding the preferred type of antibiotic, dose and duration. It has been suggested that the risk of SSI can be decreased by long term antibiotic prophylaxis compared to short term[6,9]. Others have not found a beneficial effect of extended postoperative administration of antibiotics on the development of SSI, compared to a single dose regimen[10]. The scientific evidence for any prophylactic antibiotic protocol is uncertain, as the majority of primary studies and systematic reviews have a high risk of bias[12]. Due to increasing antibiotic resistance, use of narrow-spectrum agents is preferred, in particular for prophylactic applications. Phenoxymethylpenicillin or Penicillin V is a

narrow-spectrum antibiotic effective against gram-positive cocci, gram-positive bacilli and gram-negative cocci. It is the initial antibiotic of choice against orofacial infections, although ineffective against streptococci with altered penicillin binding proteins, as well as β-lactamase producing anaerobes[13]. The duration of unbound drug concentration above the minimum inhibitory serum concentration (MIC) largely determines the efficacy of β-lactam antibiotics, and the dose and frequency of which the antibiotic is administered are the most important determinants for the time above MIC[14]. Administration of PcV in four doses every six hours resulted in a significantly reduced infection rate compared to three doses with eight hour intervals. Due to the pharmacokinetics of PcV, a dosing regimen of four times daily provides a better target attainment compared to three times daily, even when a lower dose is administered[15]. Clean-contaminated operations in the oral cavity have a reported infection rate of 8-25% without the use of antibiotics[16]. Previous work has found an infection rate as high as 52.6% in a placebo-treated group of orthognathic patients[17], and duration of procedures and placement of osteosynthesis-material are factors that may increase the risk of postoperative infection[18]. However, few studies have been performed with placebo-controls for ethical reasons as this can potentially lead to high infection rates. Most studies have compared different regimens of antibiotic prophylaxis. Also, inclusion of patients is variable, and often a mixture of single- and double jaw surgery, or BSSO with setback or advancement is included in the same study, making comparisons difficult[6]. We only included single-jaw BSSO procedures for mandibular advancement in order to have comparable experimental groups. Although the same surgical protocol was followed for all patients, the main shortcoming of the study is that consecutive patients were assigned to the two groups without being randomised. No correlation between gender, age, blood loss and operation time was found, which is in line with previous work[19].

The prevalence of SSI in the PcV3-group was 19.3%. A potential contributing factor to the high infection rate is the presence of mandibular wisdom teeth, which was more common for patients developing SSI in the PcV3-group, although this was not statistically significant. In total, 41.2% of the patients in the PcV3-group (47/114) had mandibular wisdom teeth present at the time of surgery, compared to 30.6% in the PcV4-group (19/62). However, no significant correlations between the presence of wisdom teeth and development of SSI could be observed for either experimental group. It has been shown that the presence and simultaneous removal of third

molars during orthognathic surgery is not a risk factor for developing SSI[20, 21]. Others have found that removal of third molars during BSSO does increase the risk of developing SSI[22]. In the PcV3-group, although not statistically significant, a lower infection rate was registered if wisdom teeth were removed during BSSO compared to if they were present but not removed. This tendency was not found in the PcV4-group. It is generally recommended that mandibular wisdom teeth are removed minimum six months prior to BSSO, mostly because weakening of the retromolar part of the distal segment is related to bad splits, and wisdom teeth may also complicate placement of screw fixation, in particular bicortical screws. Also the presence of third molars influence the procedures level of difficulty, in particular impacted teeth[21]. In the present work, a correlation between the presence of wisdom teeth and prevalence of bad splits could not be found. Overall, 37.5% of patients had mandibular wisdom teeth present at the time of surgery, suggesting that a better collaboration between orthodontists and surgeons could be beneficial, mainly to decrease the level of difficulty of the surgical procedure, but also to potentially reduce the infection rate.

Conclusions

The infection rate was significantly reduced when PcV was administered in four doses, suggesting that an extended regimen of antibiotic prophylaxis is beneficial when performing mandibular advancement with BSSO.

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