The Effect of Duration of Antibiotic Prophylaxis on Infections Following Open Reduction and Internal Fixation of Mandibular Fractures: A Prospective Randomized Clinical Trial

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Aim: To evaluate the benefits of a long-term prophylactic antibiotic regimen following treatment of fractured mandibles with open reduction and internal fixation.

Material and Methods: A prospective, randomized controlled trial was undertaken at Wits Oral Health Centre. Patients with mandibular fractures who were managed with open reduction and internal fixation using miniplates were randomized into 2 groups. The control group, the perioperative antibiotic (POA) group, was composed of patients who received intravenous (IV) antibiotic cover intraoperatively and a further 3 IV doses 24 hours postoperatively. The study group, the extended postoperative antibiotic (EPOA), was composed of patients who received similar doses as the control group but with an additional 5 days of oral antibiotics upon discharge. The patients were then evaluated for evidence of infection 1, 4, and 6 weeks postoperatively.

Results: A total of 77 patients were included in the study, 41 in the POA and 36 in the EPOA groups. Fourteen patients had evidence of infection noted within the 6-week follow-up period (10 in the POA and 4 in the EPOA groups). Statistical analysis with the Pearson Chi-square and Student *t* test showed no statistically significant difference ($P=0.399$) between POA and EPOA groups. There were no significant differences between the groups with respect to site and etiology of fracture, duration of operation, and presence of infection ($P>0.05$) during the 6-week review period.

Conclusions: The extended use of antibiotic prophylaxis when managing mandibular fractures with open reduction and internal fixation offers no additional benefit in reducing postoperative infections.

Key Words: Antibiotics, duration, fractures, infection, mandible

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Although the efficacy of prophylactic antibiotics in the management of facial fractures has been demonstrated in several studies, there is, however, great variability in practice.[1,2] The practices vary from using antibiotics preoperatively, intraoperatively, and postoperatively or in combination. In particular, the appropriate duration of prophylactic antibiotics remains a controversial subject in the management of traumatic mandibular fractures.[3]

Despite the long-standing evidence that perioperative prescription is not required for more than 24 hours postoperatively, many units anecdotally still prescribe longer courses[3–10] (Supplemental Digital Content, Table 1, http://links.lww.com/SCS/F556). Because the most common reason for misuse of prophylactic antibiotics is the excessive duration, we conceived this prospective, randomized-controlled clinical study to assess whether extended postoperative course of oral antibiotics in addition to perioperative intravenous antibiotics offer better prevention of postoperative infections than perioperative antibiotics (POA) in patients with mandibular fractures.

MATERIALS AND METHODS

Study Population

To answer the research question, we designed and implemented a prospective randomized-controlled study whose sample consisted of patients treated by open reduction and internal fixation (ORIF) for compound mandibular fractures at the University of the Witwatersrand Oral Health Centre in Johannesburg, South Africa, between January 1, 2019, and December 31, 2019. The study was approved by the institution's Human Research Ethics Committee (clearance number M181035). All the participants were given an explanation about the study and signed an agreement of informed consent.

To be included in the study, patients needed to have been at least 18 years of age, with isolated compound mandibular fractures treated by ORIF via a transoral approach. Also, a minimum of 6-week follow-up data post-treatment was required for inclusion in the study.

Compound fractures were defined as fractures communicating with the oral cavity through a periodontal ligament space or intraoral laceration. Patients were excluded if they presented with fractures older than 2 weeks, associated fractures (zygoma

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This randomized study was approved by the University's Human Research Ethics Committee; (clearance number M181035) and written informed consent was obtained from all patients.

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or maxillary fractures), complex mandibular fractures requiring transcervical approach, gunshot wounds, pathological fractures, fracture site infections present at the time of initial presentation, closed mandibular fractures, compromised host defenses (immunosuppression, uncontrolled diabetes), or received antibiotics for any other indication.

The enrolled patients were randomly allotted into 2 groups representing those who were to receive POA only or those to receive extended postoperative antibiotics (EPOA). A research assistant balloted for the first patient into one of the 2 groups and allotted subsequent consecutive patients to the opposite group in alternation until exhaustion of patients who met the inclusion criteria. Group 1 or control group was composed of patients who received an intravenous (IV) antibiotic cover intraoperatively and further 3 doses postoperatively (8 hourly) before being discharged. Group 1 patients received POA only and was also called POA group. Group II or study group was composed of patients who received similar doses as the control group but with an additional 5 days of oral antibiotics following discharge. Group II patients received EPOA and was also called the EPOA group. The antibiotics for the purpose of the study given were as follows:

Patients in the POA group received Amoxicillin/clavulanic acid 1.2 g IV intraoperatively and then 3 intravenous doses postoperatively (no>24 hours) while they were still in the hospital. Patients in the EPOA were given Amoxicillin/clavulanic acid 1.2 g IV intra-operatively and then 3 intravenous doses postoperatively plus Amoxil 500 mg capsules 3 times a day orally for an additional 5 days.

Patients allergic to penicillin received Clindamycin 600 mg IV intraoperatively and the 3 doses postoperatively, and Clindamycin 300 mg orally 6 hourly for 5 days.

Surgical Procedure

All patients were managed under general anesthesia with nasotracheal intubation. Sterile protocols were observed. A prophylactic dose of Amoxicillin/clavulanic acid 1.2 g stat was administered intravenously before the incision was made, and patients allergic to penicillin were given Clindamycin 600 mg. Local anesthetic was administered, followed by placement of eyelet wires or arch bars.

The fracture sites were exposed through intraoral incisions. Fractures were mobilized and debrided under direct vision. To establish proper occlusion, maxillomandibular fixation was established by fixing the mandible against the maxilla with stainless steel wires around the extensions of the arch bars or eyelet wires. The fractured segments were then reduced and fixated with 2.0 mm standard titanium miniplates according to the Champy principle. Two miniplates were fixated in the symphysis and parasymphyseal regions, whereas fractures in the angle and body regions were fixated with single plates. The miniplates were secured with monocortical titanium screws, with at least 2 screws on either side of the fracture. Adequacy of fixation and occlusion were verified after placement of the miniplates.

Maxillomandibular fixation was released after fixation of the fracture segments and after copious irrigation with saline and achievement of adequate hemostasis, the incisions were closed in layers with 3-0 chromic. Guiding elastics were used postoperatively for occlusal guidance.

Patients were discharged from the hospital after receiving a further 3 intravenous doses of antibiotics 24 hours postoperatively and were reviewed during 1-, 4-, and 6-week follow-up visits from date of discharge, or as needed. At each visit, a surgeon who was blinded to the antibiotic schedule administered reviewed the patients. Patients were evaluated for presence or absence of postoperative infection.

Criteria for infection included purulent discharge (with or without microbiologic confirmation), abscess formation, or deliberate opening of the wound by a surgeon in the presence of signs and symptoms of infection such as localized pain, tenderness, or fever ($>38°C$).

Sample Size

The estimated sample size was calculated based on a previous study, using obtained prevalence of infection rates in the intervention (36%) and control groups (64%).[9] We estimated that a sample size of 49 in each group would be adequate for a power of 80% and type 1 error of 5% (2-tailed).

Data Analysis

The data were collected and tabulated in Microsoft Excel worksheets (Microsoft Office 2013; Microsoft Corporation, Redmond, WA). Statistical analysis of results was performed using SPSS v.25 (IBM Corporation, Armonk, NY). Descriptive statistics of median and interquartile range was used to summarize the continuous variables (age, date of injury—presentation and date of injury-operation) and percentage and frequency was used to report the categorical variables (gender, site of fracture, and presence of infection). The significant difference between the continuous variables was measured by using the Mann–Whitney *U* test for nonparametric data and the measure of association between the categorical variables was determined by using the 2-tailed Fisher exact test. A *P* value ≤ 0.05 was considered significant.

RESULTS

A total of 98 patients were enrolled in the study, of which 77 patients with isolated mandibular fractures met the inclusion criteria. The median age was 32, ranging from 26 to 38 years, and the majority (92.2%) of the participants were males. The etiology of the fracture was alleged assault in 57 patients (74%), motor vehicle accident in 11, and pedestrian vehicle accident in 5. The most common site of fracture was the angle (35.1%), followed by angle and body (26%) and parasymphysis and angle (10.4%) fractures.

Of the 77 patients, 41 were randomized into the POA group and 36 into the EPOA group. The difference between POA and EPOA 2 at baseline is summarized in Table 2 (Supplemental Digital Content, http://links.lww.com/SCS/F557). There were no significant differences between the groups at baseline in all the variables except for the days between injury and presentation and the duration of surgery. Patients in the EPOA group had a significantly higher number of days before presentation compared to the patients in the POA group ($P=0.04$). The mean duration of surgery was 70 minutes (range 55–90 min) and 82 minutes (range 65–124 min) for the POA and EPOA groups, respectively ($P=0.04$).

Comparison of Presence of Infection Between the POA and EPOA Groups

The number of infections at weeks 1, 4, and 6 in the POA group was 4, 10, and 4, respectively. In the EPOA group, the figures at weeks 1, 4, and 6 were 4, 4, and 1, respectively. As shown in Figure 1, there was an equal number of patients with infection at week 1 in both groups. In the POA group, the number of patients with infection increased to 10 (24.39%) by week 4, and the number of patients with infection in the EPOA group remained at 4. At 6 weeks, the number of patients with infection in the POA and the EPOA groups had reduced to 4

(9.76%) and 1 (2.78%), respectively. Using Fisher exact test, there was no significant association between the presence of infection and the 2 groups ($P>0.05$).

The differences between the number of infections in both groups at weeks 1, 4, and 6 were not statistically significant ($P=1$, $P=0.15$, and $P=0.36$, respectively) (Fig. 1 and Supplemental Digital Content, Table 3, http://links.lww.com/SCS/F558).

There was no significant difference between these groups with respect to age and gender. The mean delay in time from injury to receiving treatment was 9 days (range 6–11 d) and 10 days (range 8–13) for POA and EPOA, respectively. There was also no significant difference between delay in treatment, site of fracture, etiology of fracture, duration of operation, and presence of infection ($P>0.05$) during the 6-week review period.

Further analysis using binary logistic regression showed that the odds of presenting with infection is 19.2 times higher in the patients with comorbidities than in patients without comorbidities.

Patients who developed infections were treated differently depending on their signs and symptoms. Five of the infections resolved with oral antibiotics alone, 8 required an incision and drainage procedure (either intraoral or extraoral depending on the presentation) as well as oral antibiotics, and 8 required hardware removal with concomitant antibiotic administration. The remaining infection, presented as a nonunion requiring hardware removal, incision and drainage, and treatment with oral antibiotics.

DISCUSSION

We designed this study to evaluate the benefit of an EPOA regimen following ORIF of the fractured mandible as compared to a POA regimen. We hypothesized that there is no significant difference between patients receiving short-term antibiotics and those that received an extended antibiotic regimen. After a 6-week follow-up, we found that the extended use of antibiotic prophylaxis when managing mandibular fractures with ORIF offers no additional benefit in reducing postoperative infection.

The findings of this study that there is no significant difference between POA and EPOA confirm our hypothesis of no difference between a short and extended antibiotic regimen and correspond with the findings of Miles et al.[9] The limitation to the study by Miles et al[9] was that the duration of postoperative antibiotics was not consistent and that patients received unknown preoperative antibiotics (not mandated by the study protocol) until the day of surgery. This is a common problem in that most patients with mandibular fractures receive antibiotics prophylaxis at the initial consultation. Gaal et al[6] have, however, shown that there is no increase in surgical site infections secondary to a lack of preoperative antibiotics from the time of consultation to when surgery is performed. Unless there is an infection noted, preoperative antibiotic prophylaxis is not deemed necessary.[11]

Studies by Schaller et al,[3] Lovato et al,[8] Abubaker and Rollert,[10] and Andreasen et al[12] have also concluded that the use of extended postoperative oral antibiotics in the management of mandibular fractures has no benefit in reducing postoperative surgical site infections.

A similar study design by Dogra et al,[13] which analyzed 39 patients with mandibular fractures undergoing ORIF, concluded that there was no significant difference between the short and extended antibiotic groups ($P=0.58$). The study, however, was more focused on the surgical site infection and assessing microbial load at the suture site, which was analyzed at 3- and 7-day reviews. There was no record of further follow-up on the patients. A bigger sample size would have strengthened the findings of this study.

Systematic review and meta-analyses have also reported that there is no significant difference in infection at the surgical site between patients who were given antimicrobials for 24 hours postoperatively and those who take them for longer.[14–16]

Miles et al[9] also reported a statistically significant ($P=0.021$) increase in the risk of postoperative infections in patients who abused tobacco and alcohol simultaneously, citing local and systemic effects of alcohol and tobacco on soft tissue/bone healing, poor nutrition, and poor compliance with postoperative instructions. Our study did not investigate the relationship between the independent or combined use of alcohol and smoking and the infection rate.

Early treatment of mandibular fractures is reported to be associated with a decreased risk of postoperative infections.[17] Both Champy et al[18] and Cawood et al[19] recommended that ORIF must be performed within 12 to 24 hours after the injury to minimize the risk of postoperative infection. Many of our patients, however, did not present for treatment for several days after the injury. Similar to the findings by Gaal et al[6] and Dillon et al,[20] delay in treatment was not significantly associated with an increased risk of infection between the groups. Sundheepkumar et al[21] also prospectively evaluated infectious complications in 83 patients who underwent delayed (defined as ORIF beyond 72 h) ORIF (median 8, range 4–19 d) for mandibular fractures. They also concluded that delay to definitive surgical intervention was not an independent attributing factor in postoperative infectious complications of compound mandibular fractures. This finding seems to suggest that the time to actual surgical treatment does not influence the rate of infections at the surgical site, provided POA are administered when surgery is eventually performed. The rich blood supply in the head and neck region and the tolerance of the oral cavity to the normal oral flora are offered as possible reasons for this.[6] Another possible explanation for this observation in our study is that fractures older than 2 weeks were excluded from the study. Fractures older than 2 weeks often require increased anesthetic and surgical time, which together with eburnation and increased mobility of the fragments may render them susceptible to infection, especially when no intermaxillary fixation is applied postoperatively.

Our findings of lack of correlation between the duration of surgery and the infection rate is comparable to that of Miles et al[9] who reported 119.5 minutes in the perioperative group and 166.6 minutes in the EPOA group, with no significant statistical difference between the groups. Contrary to our finding, Shigeishi et al[22] reported an association between increased surgical time and risk of postoperative infections in patients who underwent head and neck surgeries. They, however, stated that this is dependent on the severity of the procedure and the surgeon's skills.

Studies have demonstrated that mandibular angle fractures, the left angle in particular, result in a greater complication rate than fractures in other locations in the mandible.[23–25] Possible explanations for this include a more severe mechanism of injury from a right-hand-dominant assailant ("right hook concept") and predominantly right-handed surgical registrars who may struggle to work on the left side of the patient early in their career. Dogra et al[13] also found that a posterior location of the fracture in the mandible was a risk factor for the development of infection. Contrary to these studies, our study was unable to show any relationship between site of fracture and presence of infection. Although there were more angle fractures in both

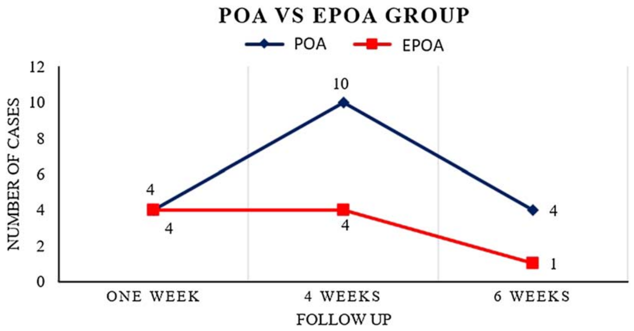

FIGURE 1. Association of the presence of infection between POA and EPOA groups. EPOA indicates extended postoperative antibiotic; POA, perioperative antibiotic.

groups, the rate of infection in the angle fractures was not significantly different from nonangle fractures. Also, we did not find that multiple or bilateral mandibular fractures resulted in an increase in the infection rate. Furthermore, the present study was unable to show any significant association between the cause of fracture and the presence of infection in both groups.

This study has several limitations. First, the degree of fracture displacement was not quantified. Second, it was not possible to monitor compliance with regard to uptake of postoperative oral antibiotics. Third, confounding factors such as smoking, seniority of the surgeon, and alcohol use were also not investigated. Last, our sample size may not have been large enough to detect the differences in infection rates necessary to reach statistical significance. Notwithstanding its limitations, this study has added valuable information to the ongoing debate on the timing and duration for antibiotics in the management of mandibular fractures.

CONCLUSION AND RECOMMENDATIONS

From the findings of the present study, revealing no difference between the brief and extended us of antibiotics, we conclude that extended use of oral antibiotics offers no additional benefit in reducing postoperative infections of mandibular fractures. Future prospective randomized-controlled studies, involving a larger number of patients, as well as longer follow-up period that will include data on smoking and the use of alcohol, teeth in the line of fracture and the treatment approach (transoral or transbuccal) are recommended to further strengthen the findings of this study.

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