Do perioperative antibiotics reduce complications of mandibular third molar removal? A double-blind randomized controlled clinical trial

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Objective. The aim of this study was to compare the effects of different antibiotic prophylaxis regimens versus placebo in relation to possible postoperative complications derived from the surgical extraction of impacted lower third molars.

Study Design. The final study sample of this double-blind randomized controlled trial comprised 92 Caucasian volunteers. Patients were assigned to 3 groups by using a randomization table. Group 1 (n = 30) received 750 mg oral amoxicillin both before and after the surgery; group 2 (n = 32) received the same oral dose after surgery alone; and group 3 (n = 30) received placebo both before and after surgery. Infectious complications, postoperative pain, and inflammation intensity were measured. The requirement for and the timing of rescue medication were also measured.

Results. Postoperative pain and inflammation intensity were significantly higher ($P < .05$) in group 3 than in groups 1 or 2 at 48 hours, 72 hours, and 1 week. A significantly higher proportion of group 3 required rescue medication (analgesics and rescue antibiotics) ($P = .013$) compared with groups 1 or 2.

Conclusions. Greater pain and inflammation were experienced by patients receiving placebo before lower third molar extraction than by those receiving antibiotics either before surgery or both before and after surgery. Other options, such as use of local antibiotics, should be considered to reduce the problems, including bacterial resistance, caused by overuse of systemic antibiotics. (Oral Surg Oral Med Oral Pathol Oral Radiol 2021;131:286−294)

Impacted mandibular third molar extraction, considered class II (clean-contaminated) surgery, is one of the most frequent procedures in oral and maxillofacial surgery.[1,2] The rates of serious complications and of morbidity after third molar extraction are low, especially when performed prophylactically[3]; nevertheless, this surgery can sometimes be followed by pain, inflammation, or trismus,[4] and infectious complications are also relatively frequent. The presence of oral infection is associated with edema, trismus, fever, pus, localized infection (e.g., alveolitis), and pain.[5] The risk of infection after third molar extraction is around 10% in young and healthy patients but increases to 25% in patients with disease or reduced immunity.[5] Therefore, although the prevalence of infection in healthy patients is low, infections can significantly affect patient quality of life, especially in the immediate postoperative period.[6]

Given the high frequency of third molar extraction in the general population, it is important to reduce this type of complication, which causes substantial morbidity and economic costs.[7] Infection appears to be more likely if the surgery is complex and prolonged or if the surgical site has a history of frequent infections.[8,9]

Prophylactic antibiotic treatment is administered before, during, or after a diagnostic or therapeutic procedure to prevent infectious complications, whereas the aim of therapeutic antibiotic treatment is to clear infection caused by a colonizing microorganism.[10] There is debate on the value of antibiotic prophylaxis in this context, and its benefits must be weighed against possible adverse effects, such as diarrhea, intestinal pain, and nausea.[11] One must take account of the need to reduce the occurrence of bacterial resistance, which has become a global public health problem.[12] In this regard, recent randomized controlled trials (RCTs) have shown that there is no need for systemic antibiotics after third molar surgery because local antibiotics are effective in reducing postoperative complications, thereby avoiding adverse effects of their systemic administration, including the appearance of bacterial resistances.[13,14]

Recent systematic reviews have called for further RCTs to resolve these questions[5,15] and have pointed to lack of evidence on the timing of antibiotic administration: preoperative, postoperative, or both.[5]

Statement of Clinical Relevance

The findings of this study suggest that antibiotic prophylaxis is effective in preventing postoperative complications.

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The objectives of this study were to evaluate the effectiveness of antibiotic therapy (750 mg amoxicillin) as a preventive measure against possible complications (pain, inflammation, infection) of impacted mandibular third molar extraction, comparing outcomes between its administration before surgery and both before and after surgery.

MATERIALS AND METHODS

Study design and patient selection

This single-center, double-blind RCT was undertaken in patients undergoing scheduled surgical extraction of impacted mandibular third molar at the Clinic of the School of Dentistry of the University of Granada (Granada, Spain) between January 2018 and December 2018.

Study exclusion criteria were age less than 18 years; pregnancy or breastfeeding; presence of systemic disease (the study only included American Society of Anesthesiologists [ASA] class I patients); allergy to the study medication or related drugs (allergy to penicillin); use of antibiotics in the week before surgery; and the presence of pericoronitis or apical radiolucency in the tooth to be extracted. Assessments of the indication for third molar extraction were based on the Clinical Practice Guidelines of the Spanish Society of Oral Surgery (2018)[16] and the American Association of Oral and Maxillofacial Surgeons (2007).[17]

All participants provided signed informed consent to participate in the study, which followed the tenets of the Helsinki Declaration and was approved by the ethics committee of the University of Granada (No. 533 CEIH/2018). The trial has been registered in the Australian New Zealand Clinical Trials Registry (ANZCTR; No. ACTRN12619000149167).

Of the 103 Caucasian volunteers initially included in the study, 11 were excluded for incorrect use of the study medication or failure to attend their follow-up appointments. The final study sample comprised 92 volunteers (37 males and 55 females) age 18 to 63 years.

A randomization table was used to allocate participants to group 1 (pre- and postoperative antibiotics); group 2 (postoperative antibiotics); or group 3 (placebo). Group 1 (n = 30) received 750 mg oral amoxicillin (Amoxicillin; Normon SA, Madrid, Spain) every 8 hours for 2 days before surgery and for 5 days after surgery; group 2 (n = 32) received 750 mg oral amoxicillin every 8 hours for 5 days after surgery; and group 3 (n = 30) received placebo (methylcellulose tablet) for 2 days before surgery and for 5 days after surgery. Surgeons and patients were double-blinded to the use of antibiotic or placebo tablets, which were of the same size and color and administered by a physician not involved in the perioperative evaluation capsule, according to a randomization sequence. All data were recorded by the main researcher blinded to group allocations.

Surgical protocol

The surgeon and the assistant scrubbed and put on sterile gowns and gloves. Patients were fully covered with sterile drapes, and their lips and perioral facial skin were disinfected with 10% povidone iodine (Corsodyl; SmithKline Beecham, Brendford, UK). Immediately before surgery, the patients rinsed their mouths for 2 minutes with 10 mL 0.12% chlorhexidine mouthwash (Perio-Aid; Dentaid SL, Barcelona, Spain), which was delivered via sterile injectors. All surgical procedures were performed under supervision by graduate students in their last year of training, with the patients placed under local anesthesia by using 4% articaine with 1:100,000 epinephrine (Ultracain; Normon SA, Madrid, Spain).

A scalloped or releasing incision was made, depending on the radiologically evaluated difficulty of the extraction, and a full-thickness flap was then elevated to reveal the molar and the adjacent bone. Osteotomy was carried out with a hand piece and a round drill, or when appropriate, odontosection was performed with a turbine. The wound was closed with 3.0 silk sutures (Normon SA, Madrid, Spain).

After extraction, gauze with 0.20% chlorhexidine gel (Lacer SA, Barcelona, Spain) was maintained in place for 30 minutes. Patients were instructed to use 0.12% chlorhexidine mouthwash (Perio-Aid; Dentaid SL, Barcelona, Spain) after brushing for 1 week after surgery and to attend an appointment for suture removal after 1 week.

All patients were prescribed 600 mg ibuprofen every 8 hours for 2 days after surgery; if adequate pain relief was not obtained within 1 hour, patients were permitted to take 1 g paracetamol as rescue analgesic.

Patients with postoperative signs or symptoms of infection were prescribed one tablet of 875 mg amoxicillin/125 mg clavulanic acid every 8 hours for 1 week as rescue antibiotic.

Study variables

Study variables were classified as predictor variables and outcome variables.[18] Predictor variables were divided among those related to patients, teeth, and surgery. All variables were evaluated by the main researcher.

Patient-related variables were gender, age, oral hygiene (good/bad), presence of periodontal disease (yes/no), bruxism (yes/no), and tobacco smoking (yes/no).

Tooth-related variables were extracted third molar (38/48); degree of extraction difficulty according to the Pedersen index[19,20] (Figure 1); and cause of extraction (preventive extraction, orthodontic cause, or damage of adjacent tooth (37/47).

Surgical variables were surgery duration (in minutes); osteotomy degree (none, mesial-vestibular, mesial-distal-vestibular, mesial-distal-vestibular-lingual/occlusal); coronal section (yes/no); and number of sutures.

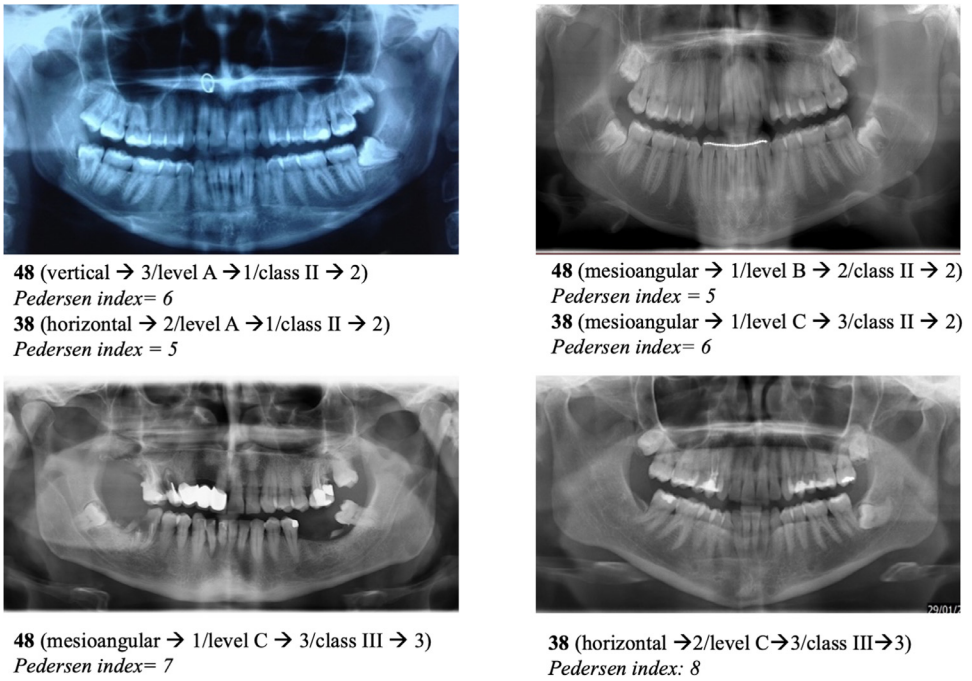

Fig. 1. Examples of orthopantomograms depicting localization of extracted teeth and the degree of difficulty, according to the Pedersen index.

The primary outcomes of this study were the presence of infection and the need for rescue antibiotic therapy after surgery. Secondary outcomes were related to inflammation and pain. Baseline inflammation was measured immediately before surgery, according to the method described by Gabka and Matsumura, from the mandibular angle to lateral canthus of eye, tragus to pogonion, and tragus to lip oral commissure.[21] Maximum jaw opening (in millimeters) was measured, from the incisal margin of maxillary to mandibular incisors, before the intervention.

During the postoperative period (7 days after extraction), each patient completed a data collection form with the following outcome variables: *pain intensity* at the time of surgery and at 1, 12, 24, 48, and 72 hours and 7 days after surgery by using a horizontal visual analogue scale (VAS) with "no pain" and "worst pain imaginable" as endpoints; *postoperative swelling* of the treated area using a similar VAS scale with "no swelling" and "worst swelling imaginable" as endpoints; *need for rescue analgesia* with 1 g paracetamol (yes/no); *need for rescue antibiotic* (yes/no), previously determined in agreement with the main researcher; *possible adverse effects* (nausea, vomiting, drowsiness, motion sickness, tremors, sweating, dyspepsia, diarrhea, bleeding, or dizziness); and patients' *global perception of the medication* (1 = poor, 2 = average, 3 = good, 4 = very good).

Patients returned to the clinic on postoperative day 7 for follow-up, suture removal, and return of the completed questionnaire. At this appointment, the main researcher measured the postoperative swelling (in millimeters), according to the method of Gabka and Matsumara, and the maximum jaw opening (in millimeters) and recorded the presence/absence of infection or alveolitis in the surgical wound.

Infection was defined according to clinical criteria: abscess, diagnosed by fluctuation or pus discharge; body temperature greater than 37.8°C for longer than 24 hours with no other identifiable cause; and severe pain or swelling at 48 hours or later after surgery, with no other identifiable cause that could be alleviated with antibiotic treatment.[5,22]

Sample size

The primary outcome of this study was the presence of infection and the need for rescue antibiotic after surgery. On the basis of data from previous studies, a difference of 2 points in these variables was considered to be of clinical relevance. The sample size was calculated by using the Sample Sizer Release statistical program (Microsoft Office Excel 2011; Microsoft Corp., Redmond, WA), with an alpha value of 0.05, statistical power of 80%, and assumed loss to the follow-up of 15%. According to this calculation, the number of patients required per group was 30.

Statistical analysis

In a descriptive analysis, means, standard errors of the mean, standard deviations, quartiles, and minimum and

maximum values were calculated for quantitative variables, and frequency and contingency tables were constructed for qualitative variables. The Shapiro-Wilk test was applied to check the normality of variable distribution and the Levene test to determine the homogeneity of variance. Qualitative variables were analyzed by using the χ^2 test with Fisher's correction for 2 × 2 tables. Pearson's gamma coefficient was calculated to assess the direction of associations for ordinal variables. Analysis of variance (ANOVA) was used to compare quantitative variables among treatments, and Dunnett's, Games-Howell, and Bonferroni's tests were applied for multiple comparisons. A value of $\alpha = 0.05$ was considered significant (alpha* = xxx for Bonferroni's test). SPSS software version 21.0 (SPSS Inc., Chicago, IL) was used for statistical analyses.

RESULTS

The mean ± standard deviation of participant age was 27.5 ± 10.71 years in group 1 (pre- and postoperative antibiotic); 24.72 ± 5.18 years in group 2 (postoperative antibiotic); and 24.5 ± 5.81 years in group 3 (placebo). Of the participants, 37 were males and 55 were females. The remaining predictor variables are summarized in Table I.

No significant differences were found among the groups in mean age ($P = .236$), gender ($P = .85$), oral hygiene ($P = .923$), or bruxism ($P = .789$); however, there was a significantly ($P = 0.048$) higher proportion of patients with periodontal disease in the antibiotic groups (groups 1 and 2). There was also a significant difference ($P = .03$) in the proportion of smokers: 3 in group 1 (pre- and postoperative antibiotic); 0 in group 2 (postoperative antibiotic); and 6 in group 3 (placebo). A review of clinical records showed that only 1 smoker (from group 3) had signs of infection after extraction. The groups did not significantly differ in tooth-related or surgical variables.

As shown in Table II, VAS-measured pain intensity was significantly higher ($P < .05$) in the placebo group than in either of the antibiotic groups at 48 hours ($P = .011$); 72 hours ($P = .002$); and 1 week ($P = .003$). No statistically significant differences were found in pain intensity between the antibiotic groups, except for a significantly ($P = .019$) lower VAS score at 1 week in group 2 (postoperative antibiotic alone). Analgesic rescue medication was required by 36.7% of patients in group 1 and 34.4% of those in group 2 versus 60% in group 3; however, these differences were not statistically significant ($P = .083$).

Significantly higher swelling values were recorded in group 3 (placebo) than in groups 1 or 2 (antibiotic prophylaxis) for VAS-measured inflammation (Table III) at 48 hours ($P = .012$); 72 hours ($P = .001$); and 1 week ($P = .02$) and for inflammation measurements at the tragus−pogonion ($P = .016$) and the tragus−lip commissure ($P = .018$); and jaw opening values ($P = .046$). No significant differences in inflammation were found between group 1 (pre- and postoperative antibiotic) and group 2 (postoperative antibiotic), although there was a close-to-significant trend ($P = .069$) toward lower inflammation values at 1 week in group 2. The VAS-measured pain and inflammation intensity values are depicted in Figure 1.

There was a trend ($P = .064$) toward a higher percentage of infection cases in group 3 (placebo group) (Table IV), whereas a significantly higher proportion of this group received rescue antibiotic ($P = .013$) compared with the antibiotic groups.

Groups 1 and 2 did not significantly differ in inflammation, pain, or risk of infection variables, except for lower inflammation and pain values at 1 week in group 2.

The prescribed medication caused adverse effects in 4 patients: 1 in group 1, 1 in group 2, and 2 in group 3.

There was no significant difference among groups in patients' global perception of the drug, as shown in Table IV, although it was described as "excellent" by a smaller proportion of the placebo group than of the antibiotic groups, and this difference was close to significant ($P = .096$).

DISCUSSION

This RCT addressed the controversial issue of antibiotic prophylaxis for impacted mandibular third molar extraction.[5,10] It was designed to minimize random and systematic errors, randomly assigning individuals to 1 of 3 study groups and considering patient-, tooth-, and surgery-related variables. According to a 2006 consensus, published evidence on the indication of antibiotics for surgical procedures has been conflicting and should be based on assessment of the risks and benefits for patients.[23]

Compared with the 2 antibiotic groups, the controls reported significantly higher VAS-assessed pain and inflammation values at 48 hours, 72 hours, and 7 days after surgery; the degree of their inflammation was higher at 7 days, according to the Gabka and Matsumara scale; and their jaw opening capacity was lesser. A higher proportion of controls required rescue analgesics and showed signs of infection, but the differences did not reach statistical significance.

A significantly higher proportion of controls also required rescue antibiotic therapy ($P = .013$). Lacasa et al. published similar results,[24] observing a nonsignificantly higher infection rate in the placebo group (16%) than in the groups receiving preoperative (5.3%) or postoperative (2.8%) amoxicillin. They associated the presence of infection with the difficulty and duration of surgery, finding a greater effect of antibiotic prophylaxis against infection risk when osteotomy was required.

Table I. Summary of predictor variables: patient-related, tooth-related, and surgery-related variables

Variable	*Pre- and postoperative antibiotic group*	*Postoperative antibiotic group*	*Control group*	*P value*	*Variable*	*Pre- and postoperative antibiotic group*	*Postoperative antibiotic group*	*Control group*	*P value*
Patient-related variables (n = 92)					Tooth extracted [n (%)]				.605
Age (years) [x ± s]	27.5 ± 10.71	24.72 ± 5.18	24.5 ± 5.81	.236	*48	16 (53.3)	19 (59.4)	14 (46.7)	
Gender [n(%)]				.85	*38	14 (46.7)	13 (40.6)	16 (53.3)	
- *Male	12 (40)	14 (43.8)	11 (36.7)		Cause of extraction [n (%)]				.972
- *Female	18 (60)	18 (56.3)	19 (63.3)		*Prophylactic	17 (56.7)	20 (62.5)	17 (56.7)	
Oral hygiene [n(%)]				.923	*Orthodontic	9 (30)	9 (28.1)	10 (33.3)	
- *Good	20 (66.7)	20 (62.5)	20 (66.7)		*Damage in 37/47	4 (13.3)	3 (9.4)	3 (10)	
- *Bad	10 (33.3)	12 (37.5)	10 (33.3)		Extraction difficulty [x ± s]	6.03 ± 1.13	5.94 ± 1.08	6.20 ± 1.06	.634
Periodontal disease [n (%)]				**.048**	Duration of surgery (minutes) [x ± s]	45.43 ± 24.28	43.44 ± 24.3	41.6 ± 15.6	.794
- *No	25 (83.3)	30 (93.8)	30 (100)		Osteotomy [n(%)]				.570
- *Yes	5 (16.7)	2 (6.3)	0 (0)		*No osteotomy	11 (36.7)	16 (50.0)	9 (30)	
Bruxism [n(%)]				.789	*Mesial/Vestibular	6 (20)	2 (6.3)	5 (16.7)	
- *No	26 (86.7)	26 (81.3)	26 (86.7)		*Distal	11 (36.7)	11 (34.4)	14 (46.7)	
- *Yes	4 (13.3)	6 (18.8)	4 (13.3)		*Lingual/Occlusal	2 (6.7)	3 (9.4)	2 (6.7)	
Smoker [n(%)]				**.03**	Coronal section [n (%)]				.425
- *No	27 (90)	32 (100)	24 (80)		*No	16 (53.3)	22 (68.8)	17 (56.7)	
- *Yes	3 (10)	0 (0)	6 (20)		*Yes	14 (46.7)	10 (31.3)	13 (43.3)	
Tooth- and surgery-related variables (n = 92)					No. of stitches [x ± s]	3.76 ± 1.52	3.28 ± 1.28	3.23 ± 1.08	.128

Table II. VAS-measured pain intensity in groups at all time points

	Group 1 (n = 30)		*Group 2 (n = 32)*		*Group 3 (n = 30)*		
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*P value**
Surgical duration	1.63	1.96	1.44	2.37	1.93	2.66	.707
1 hour	3.33	2.89	3.53	3.14	3.1	3.28	.862
12 hours	4.43	2.65	5.0	2.9	4.4	3.23	.663
24 hours	4.73	2.88	4.75	2.86	5.23	2.76	.739
48 hours	3.6	3.0	3.44	2.46	5.4	2.77	.011
72 h	2.93	2.66	2.19	2.36	4.7	3.23	.002
1 week	1.7	2.1	0.72	1.22	2.63	2.86	.003

ANOVA, analysis of variance; *SD,* standard deviation; *VAS,* visual analogue scale.
**P* value, ANOVA.

Table III. Swelling assessed by VAS and Gabka and Matsumara scale and jaw opening measurement by study group at all time points

	Group 1 (n = 30)		*Group 2 (n = 32)*		*Group 3 (n = 30)*		
VAS scale	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*P value**
Time of surgery	1.9	2.25	1.5	2.18	1.3	2.02	.549
1 hour	3.6	3.0	2.97	2.78	2.7	2.58	.442
12 hours	4.53	2.87	4.75	2.65	5.1	3.0	.738
24 hours	4.6	3.18	5.28	2.98	5.27	3.04	.615
48 hours	3.73	2.97	3.94	2.92	5.83	3.01	.012
72 hours	2.87	2.3	2.5	2.45	4.77	2.8	.001
1 week	1.13	1.5	0.59	1.01	1.8	2.27	.020
Gabka & Matsumara scale (in millimeters)							
Mandibular angle− lateral canthus/eye	3.77	4.75	2.06	3.22	4.67	4.97	.062
Tragus−pogonion	3.43	5.42	1.06	2.17	5.67	9.03	.016
Tragus−lip commissure	2.87	3.97	1.88	4.02	5.17	5.52	.018
Jaw opening	5.5	4.92	4.56	5.35	8.77	9.40	.046

ANOVA, analysis of variance; *SD,* standard deviation; *VAS,* visual analogue scale.
**P* value, ANOVA.

Table IV. Presence of infection, use of rescue antibiotic, and global drug perception by study group

	Presence of infection [n(%)]		*Rescue antibiotic [n(%)]*		*Drug perception [n(%)]*		
	No	*Yes*	*No*	*Yes*	*Average*	*Good*	*Excellent*
Pre- and postoperative antibiotic group (n = 30)	27 (90)	3 (10)	27 (90)	3 (10)	3 (10)	22 (73.3)	5 (16.7)
Postoperative antibiotic group (n = 32)	32 (100)	0 (0)	32 (100)	0 (0)	2 (6.3)	19 (59.4)	11 (34.4)
Control group (n = 30)	25 (83.3)	5 (16.7)	23 (76.7)	7 (23.3)	6 (20)	21 (70)	3 (10)
*P value	.064		.013		.096		

**P* value, χ^2 test.

Ramos et al.,[25] in their meta-analysis, found that antibiotic prophylaxis achieved a 57% reduction in the infection risk of third molar extraction and that penicillin was significantly more effective than nitroimidazoles. In contrast, no difference between the use of antibiotics and that of placebo was found by Milani et al.,[15] who administered amoxicillin preoperatively and postoperatively, or by Bortoluzzi et al.,[26] who administered amoxicillin and/or corticoids preoperatively. In addition, Calvo et al.[27] performed extractions in 110 patients who were not given antibiotics and observed no postoperative complications. Antibiotics were found to reduce the risk of pain, inflammation, and infection in a clinical trial[22] and meta-analysis[28] by Arteagoitia et al. and in a Cochrane review[5] by Lodi et al.; however, these authors concluded that the risk of adverse effects outweighed the benefits of antibiotics in this type of surgery, except for the risk of bacterial resistance. Susarla et al.,[29] in their review, drew the opposite conclusion, which was based on the reduction in infection rates achieved by antibiotic prophylaxis and the low frequency (1%−3%) of adverse effects (e.

g., diarrhea, nausea, skin eruptions, vomiting, or vaginitis). In our study, there were no significant differences among the groups with regard to the adverse effects of medications, which were only reported by 4 participants. Additionally, there was a nonsignificant trend toward a more negative perception of their medications by the placebo group compared with the antibiotic groups.

Discrepancies among studies may be attributed to the differences in study type, design, or antibiotic regimen.[30,31] Furthermore, the diagnostic criteria for infection are not always clearly defined, and the complexity/duration of the surgery is not always reported.[25,27]

The decision to prescribe prophylactic treatment is based on the possibility of wound infection during surgery, commonly caused by staphylococci, streptococci, and/or anaerobic rods. For this reason, broad-spectrum antibiotics are typically prescribed in odontogenic infections,[32] traditionally B-lactam antibiotics alone or in combination with a B-lactamase inhibitor.[33] Amoxicillin and other penicillin derivatives are widely selected by clinicians for this purpose.[34] We selected amoxicillin for this study, in agreement with many other authors.[15,26] Antibiotics used in other studies have included amoxicillin/clavulanic acid,[24,35] macrolides,[36] nitroimidazoles,[37] clindamycin,[38] or even intravenous amoxicillin.[39]

It should be borne in mind that macrolides and fluoroquinolones exert anti-inflammatory action beyond their antimicrobial activity,[40-43] attributed to their effects on inflammatory cells, transcription factors, cytokines, and inflammatory mediators.[40] However, it has not been clarified whether these antibiotics have a primarily antimicrobial or anti-inflammatory impact, and this action is not clear in beta-lactam antibiotics.[42]

Chlorhexidine, one of the most effective antiseptics, is widely administered prophylactically before oral surgery and also appears to protect against dry postextraction socket,[44] although this effect has not been definitively established.[31] All patients in our study (antibiotic and placebo groups) were prescribed a mouthwash with chlorhexidine immediately before and after the extraction and after toothbrushing for 1 week after surgery. Some authors have described the occurrence of bacterial resistance after exposure to clohexadine,[45] which may also favor the development of cross-resistance to antibiotics,[46] although this hypothesis has been rejected by other researchers.[47] Further clinical research is needed on the occurrence of resistance as a function of the dose and duration of treatment with chlorhexidine.

With regard to the timing of antibiotic therapy, we found no difference in its effects on pain, inflammation, or infection risk between postoperative administration alone (5 days after surgery) and the combination of preoperative (2 days before surgery) and postoperative administration. This finding suggests that a preoperative antibiotic regimen is unnecessary in healthy patients with no previous history of infection and that a postoperative 5-day course of antibiotics is sufficient. Kaczmarzyk et al.[38] described that a single preoperative antibiotic dose is as effective as multiple postoperative doses, whereas other authors[24] found amoxicillin to be more effective when administered preoperatively than when administered postoperatively for 5 days.

The effectiveness of other types of antibiotics, such as nitroimidazoles, was not examined in this study. A further limitation is that in comparing outcomes, we did not include a group that received a preoperative dose alone, which would have revealed whether the same benefits could be achieved with a shorter course of treatment, thus reducing the amount of antibiotics consumed. Further research is warranted on the need for and timing of antibiotic prophylaxis in patients undergoing impacted mandibular third molar extraction. The results of our RCT support the use of antibiotics to avoid postoperative complications and shows that their administration both before and after this surgery offers no advantage over their administration only after its performance. However, there is a need to evaluate whether postoperative complications are serious and frequent enough to justify the routine administration of antibiotics. It is also necessary to consider other options, such as the administration of local antibiotics, to avoid the complications of systemic antibiotics, including the occurrence of bacterial resistance.[13,14] We found more adverse effects in the placebo group, probably because of the rescue analgesics used in those patients for their high pain and inflammation.

CONCLUSIONS

This study confirmed that antibiotic prophylaxis is effective against postoperative complications of impacted mandibular third molar extractions. The achievement of an evidence-based consensus on the use and timing of antibiotic prophylaxis requires further high-quality RCTs that take known risk factors and clinical outcomes into account.

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