DOI: https://doi.org/10.2298/SARH220124049S
UDC: 616.314.5-089.23; 615.33.035.1

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Use of antibiotics after lower third molar surgery – useful or harmful procedure? A randomized, double-blind, placebo-controlled trial

Branimir Stošić[1,2,3], Ivan Šarčev[1], Siniša Mirković[1], Deana Medić[4,5], Milica Novaković[6,7], Ivan Soldatović[8], Branislav Bajkin[1]

[1]University of Novi Sad, Faculty of Medicine, Dental Clinic of Vojvodina, Department of Oral Surgery, Novi Sad, Serbia;
[2]Dr. Draga Ljočić Health Center, Šabac, Serbia;
[3]University of Travnik, Faculty of Pharmacy and Health, Travnik, Federation of Bosnia and Herzegovina, Bosnia and Herzegovina;
[4]University of Novi Sad, Faculty of Medicine, Institute of Public Health of Vojvodina, Center for Microbiology, Department of Bacteriology, Novi Sad, Serbia;
[5]University of Novi Sad, Faculty of Medicine, Department of Microbiology with Parasitology and Immunology, Novi Sad, Serbia;
[6]University of Belgrade, School of Dental Medicine, Belgrade, Serbia;
[7]University of Illinois at Chicago, College of Dentistry, Department of Endodontics, Chicago, IL, USA;
[8]University of Belgrade, Faculty of Medicine, Institute of Medical Statistics and Informatics, Belgrade, Serbia

SUMMARY

Introduction/Objective The aim of the present study was to investigate the effects of moxifloxacin and cefixime in preventing postoperative infection following mandibular third molar surgery.

Methods Double-blind study was completed by 157 patients undergoing surgical removal of mandibular third molars. The patients were randomly assigned to the following three groups: moxifloxacin (M), cefixime (C), and placebo (P). Patients in each group were classified into two subgroups: subgroup (a), without previous history of pericoronitis, and subgroup (b), with previous history of pericoronitis. All the patients were evaluated at the postoperative follow-ups on the first, second, and seventh postoperative day.

Results Postoperative infections were registered only in patients with a history of pericoronitis. Antibiotic prophylaxis with cefixime and moxifloxacin reduced the occurrence of postoperative infection. Overall incidence of postoperative infections was 6.4%. All postoperative infections were registered in the placebo-group, where the incidence of postoperative infection was 19.2%. Microbiological tests verified the clinically obtained results. Isolated microflora was resistant to penicillin-derived antibiotics in 50% of the cases.

Conclusion Prophylactic use of antibiotics after third molar surgery should be weighed against potential risks and benefits and could be considered in cases with previous history of pericoronitis, when complicated surgical extraction is performed.

Keywords: third molar surgery; antibiotic prophylaxis; postoperative complications; drug resistance; microbial susceptibility tests

INTRODUCTION

Amoxicillin (alone or in combination with clavulanic acid), as well as clindamycin and metronidazole, have a long history of success in the treatment of odontogenic infections. These are still the most commonly used antibiotics in oral surgery due to the fact that oral microorganisms are mostly susceptible to them. Therefore, it is not surprising that the majority of published studies related to the use of antibiotics in oral and maxillofacial surgery, both for prophylaxis and treatment of odontogenic infections, have been done with amoxicillin or antibiotics of similar antimicrobial spectrum [1].

However, due to the growing number of patients being allergic to penicillin derivatives as well as the increasing occurrence of oral microorganisms resistant to penicillin and several other antibiotics, there is a growing need for research directed towards antibiotics that could be an alternative to amoxicillin and other antibiotics with similar antibacterial spectrum in prevention and treatment of oral infections [2, 3]. Among novel antibiotics, it seems that fluoroquinolones (especially moxifloxacin) and the third generation of cephalosporins (especially cefixime) are promising in that regard. Both are effective against many microorganisms resistant to other antibiotics, including amoxicillin [4, 5]. Moreover, they have different pharmacokinetic properties from penicillin derivatives and may demonstrate (especially moxifloxacin) some anti-inflammatory and immunomodulatory effects, which is desirable in prophylaxis or treatment of odontogenic infections [6].

On the other hand, inadequate prescribing accelerates the development of bacterial resistance to a large number of antibiotics, which could have unforeseeable consequences for health care worldwide in the future. Antibiotic resistance is currently one of the biggest public

Received • Примљено: January 24, 2022
Revised • Ревизија: May 12, 2022
Accepted • Прихваћено: May 16, 2022
Online first: May 18, 2022

Correspondence to:
Branimir STOŠIĆ
University of Novi Sad
Faculty of Medicine
Dental Clinic of Vojvodina
Department of Oral Surgery
12 Hajduk Veljkova Street
Novi Sad 21000, Serbia
brankoddm@gmail.com

health problems today, resulting in significant decreases in infection treatment efficiency, an increase in multidrug-resistant bacterial strains, and increased morbidity and mortality, with repercussions for the health system as a whole [7]. The World Health Organization report makes it clear that this is not a phenomenon in poor or developing countries – the problem of bacterial resistance is now being observed around the world [8].

We intended to test the efficacy of moxifloxacin and cefixime in preventing postoperative infection after mandibular third molar surgery [9, 10]. The goal of our study was to investigate whether prophylactic use of moxifloxacin and cefixime has significant impact on the rate of postoperative infections after third molar removal. Having an increased antibiotic resistance in mind, our goal was also to determine under what circumstances recommendations on their prophylactic use can be justified.

METHODS

This clinical research, approved by the Ethics Committee of the Dental Clinic of Vojvodina, with the decision number 01-33/8-2019 and registered with the NIH – ClinicalTrials.gov with ID NCT05027893, was carried out as a double-blind, prospective, placebo-controlled clinical study. All patients included in the study were ≥ 18 years old, indicated for surgical removal of the impacted mandibular third molars, with good systemic health (classified as ASA I and ASA II) [11]. Exclusion criteria were as follows: hypersensitivity to study drugs; history of systemic antibacterial therapy within six months prior to randomization; pregnancy or breastfeeding; fluoroquinolone-related tendon disorder; clinically relevant cardiac conditions or current use of QT interval prolonging drugs; severe hepatic insufficiency (Child–Pugh C); cases where, in addition to removing the impacted mandibular third molar, some other oral surgical procedure was performed; patients with currently present pericoronitis.

It was assumed that the percentage of infection in the prophylactic groups would be similar and no more than 1%, while in the placebo group it would be higher – approximately 15%. Sample size was calculated as a difference between the two proportions (1% and 15%). Using 80% power and alpha = 0.05, 56 patients per group was determined sufficient to achieve 80% to detect significant differences between the groups.

The patients were randomly and equally assigned to treatment groups. Randomization was performed using a complete randomization algorithm (R software for Windows, package "randomizeR"), allocation ratio 1:1:1, and a sample size of 165 (55 per group). The randomization list was created with three groups and consequent numbers from 1 to 165. The medication boxes were marked using a specific ID consisting of three digits and two letters, generated by R software. The IDs were randomly assigned to the randomization list numbers and the final randomization list consisted of ID and list number. Consecutive patients were assigned to a specific group by reading the list number and giving the medication box with specific ID for that number. Only third-party members, who were not involved in patient care, had all the lists in one place and could identify the medication (to be used for emergency unblinding purposes if needed). That person was available 24/7 via mobile phone number provided to the participants.

The manufacturers (Hemofarm DOO, Vršac, Serbia, and Alkaloid DOO, Skopje, North Macedonia) created the boxes for medications to be identical by instruction of the research team. The boxes with film-coated tablets were the same shape, size, color, and taste. Placebo tablets were created using the same instructions (PhytoNet DOO, Belgrade, Serbia).

After the screening, all participants that fulfilled the enrollment criteria (inclusion/exclusion) were blindly assigned to a specific group by the randomization list. Eight patients were classified as dropouts due to either non-compliance (n = 4) or failure to appear for the control visit (n = 4).

Mandibular third molar surgeries were performed by five oral surgeons (Figure 1). All surgeries were performed under local anaesthesia, using 4 ml of 2% lidocaine with adrenaline 1:80,000. Flaps were elevated, bone was removed with surgical burrs, and third molars sectioned as needed to facilitate removal. All wounds were sutured with non-resorbable 3-0 black silk sutures. The sutures were removed on the seventh postoperative day. The patients were advised to take an analgesic containing 200 mg of ibuprofen and 325 mg of paracetamol if needed.

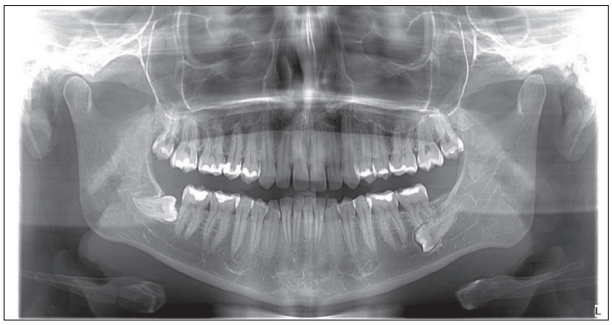


Figure 1. Panoramic radiograph of a patient included in this study (lower right third molar with previous history of pericoronitis was removed)

All the patients postoperatively received film-coated tablets with either 400 mg of moxifloxacin or 400 mg of cefixime *per os*. One-third of the patients received placebo tablets containing indifferent substances with no antimicrobial action (99% microcrystalline cellulose, 0.5% silicon dioxide, and 0.5% magnesium stearate). Surgeons who performed surgery were blinded to the type of tablet which patients received. All used film-coated tablets were administered for the first five days postoperatively, once a day, in a double-blind manner. All the patients were evaluated at the postoperative follow-ups on the first, second, and seventh postoperative day.

Postoperative infection was diagnosed based on the presence of local signs of inflammation and systemic signs

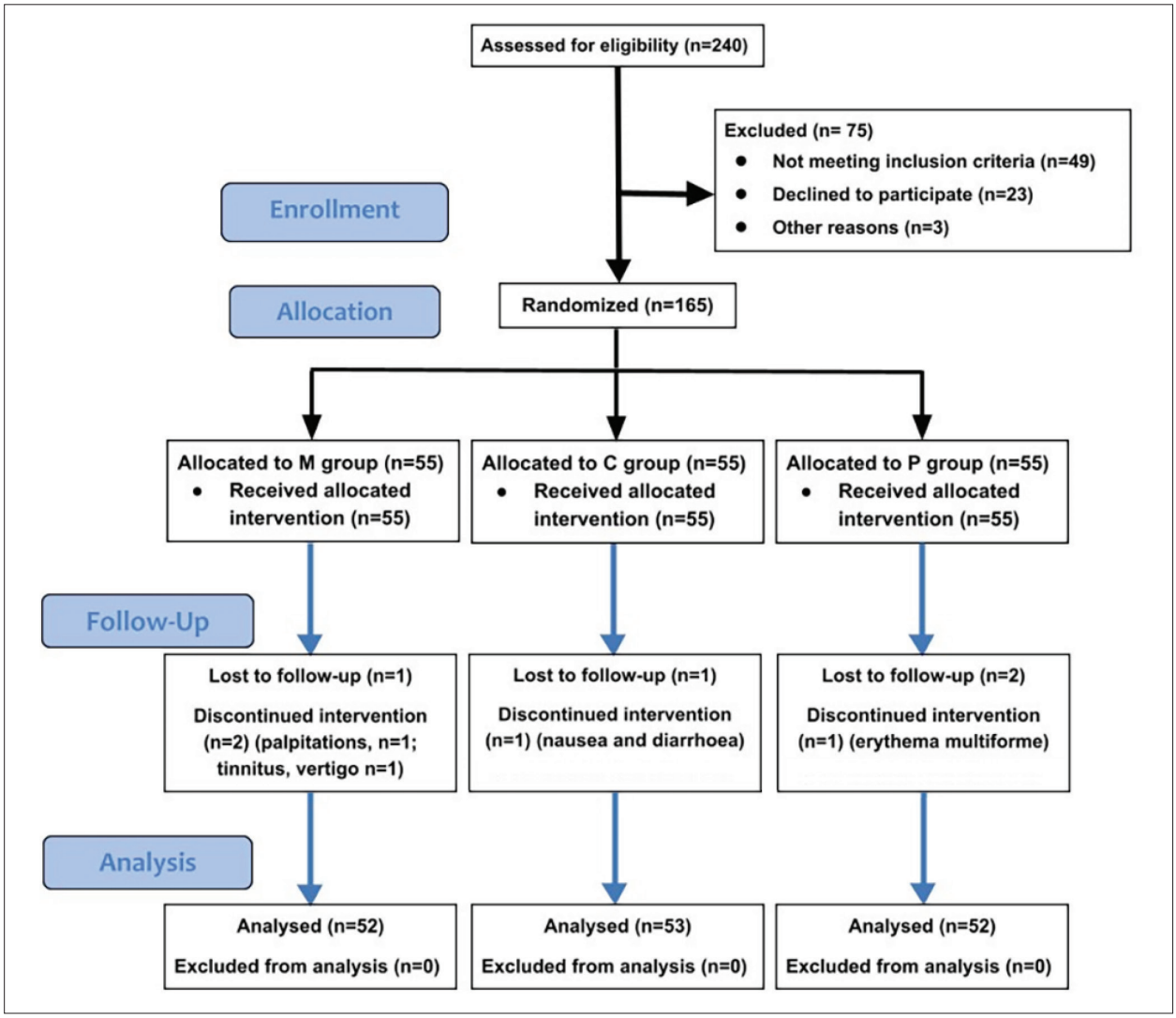


Figure 2. Flow diagram of the progress through the phases of a three-group parallel randomized trial [12]; [downloaded Sep 2, 2021]; available from: http://www.consort-statement.org/

of infection (elevated body temperature, accelerated erythrocyte sedimentation, leucocytosis).

Swab samples were obtained from surgical wounds of patients with signs of postoperative infection, and microbiologically analysed. The susceptibility of isolated microorganisms to moxifloxacin, cefixime, and other antibiotics commonly used in oral and maxillofacial surgery was tested by culture on antibiotic-containing media. Regarding the susceptibility to antimicrobial drugs, bacteria were classified according to the growth inhibition zone, into three categories: susceptible (S), intermediate (I), and resistant (R).

After the study was completed and the codebook was opened, the results were grouped by type of treatment into three groups: moxifloxacin (M), cefixime (C), and the placebo (P). Based on the previous history of pericoronitis, the patients in each group were classified into two subgroups: patients without previous history of pericoronitis (a) and patients with previous history of pericoronitis (b).

The manuscript was reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement [12]. Primary outcome was identified as occurrence of postoperative infection. Secondary outcomes were the subgroup analysis (previous history of pericoronitis or not) and identified as susceptibility of isolated microorganisms to antibiotics (in cases where swab samples were obtained).

Results are presented as count and percent (where appropriate). Group comparisons were performed using Fisher's exact test. P values less than 0.05 were considered significant. All data were analyzed using the IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA) statistical software.

RESULTS

The clinical study included 165 patients who were indicated for surgical removal of an impacted mandibular third molar. Eight patients were excluded from the study due to non-compliance with the postoperative instructions or not showing up to the follow-up exams. The template for the CONSORT flow diagram is shown in Figure 2 [12]. The study, in accordance with the described method, was

completed by a total of 157 patients, so that the first study group, group (M), consisted of 52 patients [subgroup (a) of 39 patients, subgroup (b) of 13 patients], the second study group (C) of 53 patients [subgroup (a) of 39 patients, subgroup (b) with 14 patients], and the control group (P) of 52 patients [subgroup (a) of 39 patients, subgroup (b) of 13 patients]. Mean patient age was 26.7 years, with standard deviation of 8.85 years in group M; 24.2 years with standard deviation of 5.11 years in group C, and 25.5 years with standard deviation of 5.44 in group P. Gender distribution in groups was as follows: group M (59.6% female, 40.4% male); group C (73.6% female, 26.4% male), group P (75% female, 25% male).

In our study, the overall incidence of postoperative infections was 6.4%. Interestingly, we did not register any *de novo* infection – all cases of postoperative infection occurred in patients who had preoperative history of pericoronitis (subgroup b), and all these cases belonged to the placebo group (P) (Table 1).

Table 1. Incidence of postoperative infection in the research groups

Research groups			Postoperative infection		Total
			no	yes	
Group	M	n	52	0	52
		%	100	0	100
	C	n	53	0	53
		%	100	0	100
	P	n	42	10	52
		%	80.8	19.2	100
Total		n	147	10	157
		%	93.6	6.4	100

Group M – research group receiving moxifloxacin;
Group C – research group receiving cefixime;
Group P – control group receiving placebo

The difference between each of the study groups (groups M and C) and the control placebo group (group P) regarding the occurrence of postoperative infection was confirmed with Fisher's test of exact probability ($p < 0.001$).

There is a statistically significant difference in the predisposition to infection with previous history of pericoronitis (Table 2). Patients of the group P, subgroup (b), had a postoperative infection in 77% of the cases (10/13 patients). Patients without previous history of pericoronitis remained infection-free following surgery (0%, 0/39 patients).

Table 2. History of pericoronitis and postoperative infection

Parameter	Moxifloxacin (n = 52)	Cefixime (n = 53)	Placebo (n = 52)	p
History of pericoronitis	13 (25%)	14 (26.4%)	13 (25%)	0.982a
Postoperative infection	0	0	10 (19.2%)	< 0.001b

[a]Pearson χ^2;
[b]Fisher's exact test

Patients with diagnosed postoperative infection were under close supervision for three weeks after surgery. In cases where postoperative infection was diagnosed in the placebo group, standard therapy was administered – amoxicillin with clavulanic acid (or in case of allergy to amoxicillin, azithromycin was used). After the microbial identification of the causative agent(s), and in case of its resistance to amoxicillin with clavulanic acid or azithromycin, antibiotic therapy was modified in accordance with microbiological susceptibility.

Out of 23 analysed samples, five were taken preoperatively from the examinees from each of the study groups (M and C), who had a history of pericoronitis (subgroups b). A total of 13 samples were taken from the control placebo group (P); three samples were taken preoperatively around the tooth with a history of pericoronitis, and 10 samples were taken from the operative wound of the patients with signs of postoperative infection before giving antibiotic therapy. The samples were tested for susceptibility to the researched antibiotics, as well as to other antibiotics usually used in oral surgery (Table 3).

As shown in Table 3, all the swabs were susceptible to moxifloxacin. It is interesting to note that three swabs with strictly pathogenic *Staphylococcus aureus* were resistant to ampicillin, amoxicillin, amoxicillin with clavulanic acid, and had intermediate susceptibility to clindamycin. Resistance to moxifloxacin was not observed in any of the samples taken, and resistance to cefixime was noted in only one case.

DISCUSSION

Justification for the use of antibiotics relative to mandibular third molar surgery has been a controversial topic. Lang et al. [13] found as many as 42 different protocols for antibiotic administration following this procedure (in terms of type, dose, timing, and mode of delivery). Many authors conducted prospective, placebo-controlled clinical trials, with similar methods, and in most studies the antibiotic in the study group was amoxicillin (with or without clavulanic acid), administered in a single preoperative dose or three to five days after surgery. The conclusions are mainly reduced to the common consensus that there is sufficient evidence for the use of these antibiotics for third molar surgery, because the benefit does not outweigh the risk of side effects [14]. Recently, Cervino et al. [15] proposed a modified protocol based on the administration of amoxicillin or amoxicillin with clavulanic acid before and after intervention, but, again, many questions were left unanswered. The conclusion was that it was necessary to find an alternative to existing, especially penicillin-derived antibiotics [15].

Chugha et al. [9] observed heterogeneity in the design of the studies and the method of antibiotics administration. Better evidence and justification are needed in this area, as many strong recommendations are currently made on the basis of weak evidence [16].

Moxifloxacin and cefixime have been labelled by many authors as a realistic therapeutic alternative to existing antibiotics widely used in oral and maxillofacial surgery [5,

Table 3. Susceptibility of samples obtained from the infected postoperative wounds or from the space around the tooth to test antibiotic

Antibiotic	Research group												Total
	Moxifloxacin (M)			Cefixime (C)			Placebo (P)						
	History of pericoronitis			History of pericoronitis			History of pericoronitis			Postop. infection			
	S	I	R	S	I	R	S	I	R	S	I	R	
Moxifloxacin	5			5			3			10			23
Cefixime	5			5			2		1	9		1	23
Ampicillin	4		1	5			1		2	5		5	23
Amoxicillin	4		1	5			1		2	5		5	23
Amoxicillin + CA	4		1	5			2		1	6		4	23
Tetracycline	5			4		1			3	6		4	23
Clindamycin	5			4	1		3			8		2	23
Total samples	5			5			3			10			23

S – susceptible; I – intermediate; R – resistant; CA – clavulanic acid

17]. Cachovan et al. [18] demonstrated that moxifloxacin penetrates very well into oral tissues, reaches high concentrations in bone, and is well resorbed after oral administration. Moreover, moxifloxacin is very effective against oral pathogens, especially against the periopathogen *Aggregatibacter actinomycetemcomitans*, as well as against *Porphyromonas gingivalis*, *Prevotela intermedia* and *Tannerella forsythia* [19]. Efficacy of oral treatment with moxifloxacin and amoxicillin with clavulanic acid on oral function and quality of life after third molar surgery demonstrated that moxifloxacin shortened the period of postoperative recovery [20].

In our study, the frequency of postoperative infection in group P was extremely high (19.2%). Data on the frequency of infection after this surgery vary depending on the assessment method. Most studies indicate that the prevalence of postoperative infection is in 1–10% range, which is lower than in our study [21]. Patients with a previous history of pericoronitis had postoperative infection in 77% of cases, while none of the patients without previous history of pericoronitis developed postoperative infection (0%). All the cases of postoperative infection occurred in the group that did not receive antibiotics postoperatively. Some studies suggest that randomized controlled trials should be performed and a cause-and-effect relationship between a previous history of pericoronitis and more frequent postoperative infection after mandibular third molar surgery should be established, while others have shown that postoperative infection is statistically higher in patients with previous history of pericoronitis [22, 23].

We also observed three postoperative infections where *Staphylococcus aureus* was isolated from the sample; in all other cases we registered polymicrobial flora dominated by viridians streptococci. The results of microbiological analysis verified the results of clinical trials, because the microorganisms isolated from all swab samples were susceptible to moxifloxacin. All samples were susceptible to cefixime, except one case with coagulase-negative staphylococci. Also, in 50% of the samples taken, resistance to ampicillin, amoxicillin, and amoxicillin with clavulanic acid was registered, which is very concerning (Table 3). Microbiological analysis of samples obtained from odontogenic abscesses concluded that odontogenic infections are polymicrobial. Moxifloxacin had promising *in vitro* activity against odontogenic pathogens such as the viridans and hemolytic streptococci, *Strep. anginosus* and *Strep. mitis* group and *Neisseria spp.* [4]. Moxifloxacin was also effective against more than 90% of isolated strict anaerobes, predominantly *Prevotella spp.* [24]. Treatment of severe odontogenic infections comparing moxifloxacin, amoxicillin with clavulanic acid, and clindamycin, in the mixed aerobic-anaerobic bacterial flora, showed at least one of the pathogens was resistant to penicillin in 50% of the patients, and a rate of increase in resistance to clindamycin was also noticeable [4, 25]. Due to its high tissue penetration and concentration in bone tissue, moxifloxacin has shown promising results [18, 24]. Because of the broader activity and reduced dosing frequency (administration only once daily), the use of moxifloxacin instead of clindamycin in penicillin-allergic patients seems worth considering [4, 24].

Antibiotic prophylaxis with moxifloxacin and cefixime reduced the occurrence of postoperative inflammatory sequelae (pain, swelling, and trismus). It is interesting that both antibiotics, especially moxifloxacin, also contributed to reducing the incidence of postoperative dry socket, which is not provoked by inflammation [26].

Adequate antibiotic treatment comprises the administration of the appropriate antibiotic in optimal dose through the correct route of administration [27]. Nevertheless, antibiotics have been associated with considerable side effects, thus their use should be adequate and according to guidelines. Our finding that several patients in group P did not have postoperative infections confirms that antibiotics are not an absolute requirement in all surgical cases.

Side effects of fluoroquinolones include headaches, tendonitis, and transient neurological effects in elderly population [28]. In addition, some relatively benign side-effects are observed, such as nausea, vomiting, and diarrhea [29].

We did not include a group with amoxicillin (with or without clavulanic acid) due to a different dosing regimen, which makes double-blind design impossible, which is a relative limitation of the study. Another limitation of our study is a relatively small sample size, which should be considered when estimating the strength of data given here in. Finally, even though isolated microorganisms have demonstrated resistance to penicillin and its derivatives, we cannot claim with certainty that those species/strains have caused the infection, considering that all specimens contained polymicrobial flora.

Our study also indicates that antibiotics should not be prescribed generally in all cases. Overprescribing is fueling a global increase in bacterial resistance, which is becoming a major public health challenge around the world [7]. Considering the increase in antimicrobial resistance,

a growing awareness on the search for new antibacterial agents is essential, and the choice of moxifloxacin and cefixime to prevent postoperative infections after third molar surgery seems appropriate, not only because of the aforementioned benefits, but also because of the simplified dosing regimen, avoiding drug interactions in polymedicated patients (patients who use multiple medications), monotherapy options, and thus better compliance and adherence [30].

Ultimately, the decision to prescribe antibiotics, should be made on the case-by-case basis, considering the complexity of the surgical case as well as risks and benefits of antibiotic prophylaxis.

CONCLUSION

We found a cause-and-effect relationship between a previous history of pericoronitis and frequent postoperative infections after mandibular third molar surgery, while no infections were observed in patients without such history. This indicates that prior history of pericoronitis may be a decisive risk factor, and that prescribing prophylactic antibiotics may be unwarranted in cases where such a history is absent. Restraint and appropriate practices in antibiotics prescribing would be very helpful in limiting further spread of microbial resistance, and in maintaining efficacy of existing drugs. However, our study did not include the analysis of time elapsed between the last pericoronitis episode (in cases with history of pericoronitis) and date when surgery was performed, which may influence the relative risk of postoperative infection.

While strong recommendations require a more powerful study with a larger number of patients, our data provide evidence that in cases where prophylactic antibiotics are warranted, moxifloxacin and cefixime provide good protection against postoperative infection, and should be considered for use in that context.

ACKNOWLEDGEMENTS

We thank all participants for their help, especially Prof. Karmen Stankov (University of Novi Sad, Faculty of Medicine, Department of Biochemistry and Clinical Center of Vojvodina, Department of Clinical Pharmacology, Novi Sad, Serbia), Bojan Pavlović, PhD (chief operating officer PhytoNet AG, Zürich Area, Switzerland), and Miloš Babić, PhD (director of Single Cell Genomics at Celldom, Inc. San Diego, Metropolitan Area, California, United States).

The authors did not receive support from any organization for the submitted work – specific grant from any funding agency in the public, commercial, or not-for-profit sectors. PhytoNet DOO, Belgrade, Serbia, donated the placebo tablets to the study.

Conflict of interest: None declared.

REFERENCES

1. Sologova D, Diachkova E, Gor I, Sologova S, Grigoreviskikh E, Arazashvili L, et al. Antibiotics Efficiency in the Infection Complications Prevention after Third Molar Extraction: A Systematic Review. Dent J. 2022;10(4):72. [DOI: 10.3390/dj10040072] [PMID: 35448066]
2. Blumenthal KG, Lu N, Zhang Y, Walensky RP, Choi HK. Recorded Penicillin Allergy and Risk of Mortality: a Population-Based Matched Cohort Study. J Gen Intern Med. 2019;34(9):1685–7. [DOI: 10.1007/s11606-019-04991-y] [PMID: 31011962]
3. Ardila CM, Bedoya-García JA. Antimicrobial resistance of Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis and Tannerella forsythia in periodontitis patients. J Glob Antimicrob Resist. 2020;22:215–8. [DOI: 10.1016/j.jgar.2020.02.024] [PMID: 32169683]
4. Sobottka I, Wegscheider K, Balzer L, Böger RH, Hallier O, Giersdorf I, et al. Microbiological analysis of a prospective, randomized, double-blind trial comparing moxifloxacin and clindamycin in the treatment of odontogenic infiltrates and abscesses. Antimicrob Agents Chemother. 2012;56(5):2565–9. [DOI: 10.1128/AAC.06428-11] [PMID: 22354306]
5. Dukić S, Matijević S, Daković D, Čutović T. Comparison of cefixime and amoxicillin plus metronidazole in the treatment of chronic periodontitis. Vojnosanit Pregl. 2016;73(6):526–30. [DOI: 10.2298/vsp150326133d] [PMID: 27498443]
6. Assar S, Nostrabadi R, Khorramdel Azad H, Masoumi J, Mohamadi M, Hassanshahi GA. A Review of Immunomodulatory Effects of Fluoroquinolones. Immunol Invest. 2021;50(8):1007–26. [DOI: 10.1080/08820139.2020.1797778] [PMID: 32746743]
7. Dadgostar P. Antimicrobial Resistance: Implications and Costs. Infect Drug Resist. 2019;12:3903–10. [DOI: 10.2147/IDR.S234610] [PMID: 31908502]
8. Organization WH [Internet]. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015 [cited 2021 Sep 4]. Available from: https://apps.who.int/iris/handle/10665/193736.
9. Chugha A, Patnanaa AK, Kumara P, Chugha VK, Kherab D, Singh S. Critical analysis of methodological quality of systematic reviews and meta-analysis of antibiotics in third molar surgeries using AMSTAR 2. J Oral Biol Craniofac Res. 2020;10(4):441–9. [DOI: 10.1016/j.jobcr.2020.07.011] [PMID: 32884898]
10. Ramos E, Santamaría-Zuazua JA, Santamaría G, Barbier L, Arteagoitia MI. Do systemic antibiotics prevent dry socket and infection after third molar extraction? A systematic review and meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;122(4):403–25. [DOI: 10.1016/j.oooo.2016.04.016] [PMID: 27499028]
11. Mayhew D, Mendonca V, Murthy BVS. A review of ASA physical status – historical perspectives and modern developments. Anaesthesia. 2019;74(3):373–9. [DOI: 10.1111/anae.14569] [PMID: 30648259]
12. Liu X, Cruz Rivera S, Moher D, Calvert MJ, Denniston AK. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI Extension. BMJ. 2020;370:m3164. [DOI: 10.1136/bmj.m3164] [PMID: 32909959]
13. Lang MS, Gonzalez ML, Dodson TB. Do antibiotics decrease the risk of inflammatory complications after third molar removal in community practices? J Oral Maxillofac Surg. 2017;75(2):249–55. [DOI: 10.1016/j.joms.2016.09.044] [PMID: 28341449]
14. Lupi SM, Olivieri G, Landini J, Ferrigno A, Richelmi P, Todaro C, et al. Antibiotic Prophylaxis in the Prevention of Postoperative Infections in Mandibular Third Molar Extractions: Systematic Review and Meta-Analysis. Appl Sci. 2021;11(20):9449. [DOI: 10.3390/app11209449]
15. Cervino G, Cicciù M, Biondi A, Bocchieri S, Herford AS, Laino L, et al. Antibiotic Prophylaxis on Third Molar Extraction: Systematic Review of Recent Data. Antibiotics (Basel). 2019;8(2):53. [DOI: 10.3390/antibiotics8020053] [PMID: 31052566]
16. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ.

2008;336(7650):924–6. [DOI: 10.1136/bmj.39489.470347.AD] [PMID: 18436948]
17. Ogle OE. Odontogenic Infections. Dent Clin North Am. 2017;61(2):235–52. [DOI: 10.1016/j.cden.2016.11.004] [PMID: 28317564]
18. Cachovan G, Nergiz I, Thuss U, Siefert HM, Sobottka I, Oral O, et al. Penetration of moxifloxacin into rat mandibular bone and soft tissue. Acta Odontol Scand. 2009;67(3):182–6. [DOI: 10.1080/00016350902787564] [PMID: 19306136]
19. Ardila CM, Hernández-Casas C, Bedoya-García JA. Effects on clinical outcomes of adjunctive moxifloxacin versus amoxicillin plus metronidazole in periodontitis patients harbouring Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis and Tannerella forsythia: exploratory analyses from a clinical trial. Quintessence Int. 2021;52(1):20–9. [DOI: 10.3290/j.qi.a44927] [PMID: 32696031]
20. Limeres J, Sanromán JF, Tomás I, Diz P. Patients' Perception of Recovery After Third Molar Surgery Following Postoperative Treatment With Moxifloxacin Versus Amoxicillin and Clavulanic Acid: A Randomized, Double-Blind, Controlled Study. J Oral Maxillofac Surg. 2009;67(2):286–91. [DOI: 10.1016/j.joms.2008.06.061] [PMID: 19138601]
21. Blatt S, Al-Nawas B. A systematic review of latest evidence for antibiotic prophylaxis and therapy in oral and maxillofacial surgery. Infection. 2019;47(4):519–55. [DOI: 10.1007/s15010-019-01303-8] [PMID: 30945142]
22. Poeschl PW, Spusta L, Russmueller G, Seemann R, Hirschl A, Poeschl E, et al. Antibiotic susceptibility and resistance of the odontogenic microbiological spectrum and its clinical impact on severe deep space head and neck infections. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;110(2):151–6. [DOI: 10.1016/j.tripleo.2009.12.039] [PMID: 20346713]
23. Kotarac Knežević A, Knežević D, Kuna T, Granić M, Grgić N, Gabrić D. Does A Single Dose Of Systemic Antibiotic Prevent Postoperative Inflammatory Complications After Lower Third Molar Surgery? A Randomized Controlled Trial. Res J Pharm Biol Chem Sci. 2018;9(6):1223–33.
24. Gómez-Arámbula H, Hidalgo-Hurtado A, Rodríguez-Flores R, González-Amaro AM, Garrocho-Rangel A, Pozos-Guillén A. Moxifloxacin versus Clindamycin/Ceftriaxone in the management of odontogenic maxillofacial infectious processes: A preliminary, intrahospital, controlled clinical trial. J Clin Exp Dent. 2015;7(5):e634–9. [DOI: 10.4317/jced.52627] [PMID: 26644841]
25. Arteagoitia I, Sánchez FR, Figueras A, Arroyo-Lamas N. Is clindamycin effective in preventing infectious complications after oral surgery? Systematic review and meta-analysis of randomized controlled trials. Clin Oral Investig. 2022;26(6):4467–78. [DOI: 10.1007/s00784-022-04411-2] [PMID: 35235059]
26. Stošić B, Šarčev I, Mirković S, Bajkin B, Soldatović I. A comparative analysis of the efficacy of moxifloxacin and cefixime in the reduction of postoperative inflammatory sequelae after mandibular third molar surgery. Vojnosanit Pregl. 2022;79(4):359–67. [DOI: 10.2298/VSP200909122S]
27. Póvoa P, Moniz P, Gonçalves Pereira J, Coelho L. Optimizing Antimicrobial Drug Dosing in Critically Ill Patients. Microorganisms. 2021;9(7):1401. [DOI: 10.3390/microorganisms9071401] [PMID: 34203510]
28. Scavone C, Mascolo A, Ruggiero R, Sportiello L, Rafaniello C, Berrino L, et al. Quinolones-Induced Musculoskeletal, Neurological, and Psychiatric ADRs: A Pharmacovigilance Study Based on Data From the Italian Spontaneous Reporting System. Front Pharmacol. 2020;11:428. [DOI: 10.3389/fphar.2020.00428] [PMID: 32351386]
29. Motamendi H, Fathollahi M, Abiri R, Kadivarian S, Rostamian M, Alvandi A. A worldwide systematic review and meta-analysis of bacteria related to antibiotic-associated diarrhea in hospitalized patients. PLoS One. 2021;16(12):e0260667. [DOI: 10.1371/journal.pone.0260667] [PMID: 34879104]
30. Muller C. Antibiotics and Antimicrobials Resistance: Mechanisms and New Strategies to Fight Resistant Bacteria. Antibiotics (Basel). 2022;11(3):400. [DOI: 10.3390/antibiotics11030400] [PMID: 35326863]

Примена антибиотика после хируршког вађења доњег трећег молара – корисна или штетна процедура? Рандомизована, двоструко слепа, плацебом контролисана студија

Бранимир Стошић[1,2,3], Иван Шарчев[1], Синиша Мирковић[1], Деана Медић[4,5], Милица Новаковић[6,7], Иван Солдатовић[8], Бранислав Бајкин[1]

[1]Универзитет у Новом Саду, Медицински факултет, Клиника за стоматологију Војводине, Служба за оралну хирургију, Нови Сад, Србија;
[2]Дом здравља „Др Драга Љочић", Шабац, Србија;
[3]Универзитет у Травнику, Фармацеутско-здравствени факултет, Травник, Федерација Босне и Херцеговине, Босна и Херцеговина;
[4]Универзитет у Новом Саду, Медицински факултет, Институт за јавно здравље Војводине, Центар за микробиологију, Одсек за бактериологију, Нови Сад, Србија;
[5]Универзитет у Новом Саду, Медицински факултет, Катедра за микробиологију са паразитологијом и имунологијом, Нови Сад, Србија;
[6]Универзитет у Београду, Стоматолошки факултет, Београд, Србија;
[7]Универзитет Илиноиса у Чикагу, Колеџ стоматологије, Катедра за ендодонцију, Чикаго, Илиноис, САД;
[8]Универзитет у Београду, Медицински факултет, Институт за медицинску статистику и информатику, Београд, Србија

САЖЕТАК

Увод/Циљ Циљ студије био је да се испита ефекат моксифлоксацина и цефиксима на сузбијање инфекције после хируршког вађења доњих трећих молара.

Метод Двоструко слепа студија спроведена је на 157 пацијената којима су хируршки уклоњени доњи трећи молари, а који су насумично распоређени у једну од три групе: моксифлоксацин (М), цефиксим (Ц) или плацебо (П). Пацијенти из сваке групе распоређени су у две подгрупе: подгрупу „а", без претходне историје перикоронитиса, и подгрупу „б", са претходном историјом перикоронитиса. Пацијенти су контролисани на постоперативним прегледима првог, другог и седмог постоперативног дана.

Резултати Постоперативна инфекција регистрована је искључиво код пацијената са претходном историјом перикоронитиса. Антибиотска профилакса цефиксимом или моксифлоксацином смањила је појаву постоперативне инфекције. Укупна инциденца постоперативних инфекција била је 6,4%. Сви случајеви постоперативне инфекције регистровани су у групи која није примала антибиотике већ плацебо, где је инциденца инфекција била 19,2%. Микробиолошке анализе потврдиле су клинички добијене резултате. Изолована микрофлора била је резистентна на деривате пеницилина у 50% случајева.

Закључак У склопу профилактичке примене антибиотика после хируршког вађења доњих трећих молара треба узети у обзир могуће ризике и добробите, а може се сматрати сврсисходном у случајевима са претходном историјом перикоронитиса, као и у случају компликованијих хируршких екстракција.

Кључне речи: хирургија трећих молара; антибиотска профилакса; постоперативне компликације; резистенција на лекове; тестови осетљивости микроорганизама