Comparison of the efficacy of amoxicillin-clavulanic acid with metronidazole to azithromycin with metronidazole after surgical removal of impacted lower third molar to prevent infection

Shermil Sayd¹, Suresh Vyloppilli², Krishna Kumar³, Pramod Subash⁴, Nithin Kumar⁵, Sarfras Raseel⁶

¹Department of Oral and Maxillofacial Surgery, Kannur Dental College, Anjarakandy Integrated Campus, Kannur;
²Department of Oral and Maxillofacial Surgery and Dentistry, Malankara Orthodox Syrian Church Medical College & Hospital, Kolenchery, Kochi;
³Department of Cleft and Craniofacial Surgery, Aster MIMS Hospital, Calicut;
⁴Department of Craniofacial Surgery, Amrita School of Dentistry, Kochi;
⁵Department of Oral and Maxillofacial Surgery, KMCT Dental College, Calicut, India

Abstract (J Korean Assoc Oral Maxillofac Surg 2018;44:103-106)

Objectives: The goal of the study was to investigate the clinical effects of amoxicillin-clavulanic acid (500+125 mg) with metronidazole 400 mg administered three times daily (Group I) versus azithromycin 500 mg administered once daily and with metronidazole 400 mg three times daily (Group II) for the prevention of postoperative infection following mandibular third molar surgical removal.

Materials and Methods: The study design was a single-center prospective study. Patients who reported to the Department of Oral and Maxillofacial Surgery between February 2015 and January 2017 for removal of mandibular third molar were screened, and 108 patients were chosen. One surgeon carried out all procedures. Patients were prescribed antibiotics until the two groups contained a similar number of cases.

Results: Our data showed that Group II had fewer incidences of surgical site infection, but with no statistical significance.

Conclusion: Although both treatments are used routinely after removal of the mandibular third molar, neither is significantly better than the other.

Key words: Impacted third molar removal, Antibiotic prophylaxis, Amoxicillin, Azithromycin, Metronidazole

[paper submitted 2017. 9. 30 / revised 1st 2017. 12. 21, 2nd 2018. 1. 5 / accepted 2018. 1. 22]
ary 2017 for removal of a mandibular impacted third molar were selected. The sample size was determined as the number of patients consenting for the procedure and participation during the period of study.

The inclusion criteria were as follows: (1) male or female patient between the ages of 18-30 years; (2) mesioangular impacted tooth; (3) Pell and Gregory classification: Position A, Class I; (4) absence of follicular space; and (5) absence of infection involving the mandibular impacted third molar.

The exclusion criteria were as follows: (1) patient with co-morbidities; (2) pregnant or lactating mother; (3) patient with acute infection; (4) history of recent antibiotic therapy; and (5) history of allergy or intolerance to the drugs used in this study.

One surgeon performed all procedures under local anaesthesia. Assuring meticulous asepsis, a full thickness rhomboid flap was raised to aid in bone removal and odontectomy, as required, using rotary instruments. The full duration of the proceedings, from the time of the first incision to the final suture, was recorded. Post-surgical alveolus irrigation was performed using chlorhexidine-digluconate (0.12%) solution for 1 minute in all cases. Wound closure was achieved using 4-0 silk sutures.

Drugs were prescribed as either a course of amoxicillin-clavulanic acid (500+125 mg) with metronidazole 400 mg three times daily (Group I) or azithromycin 500 mg once daily with metronidazole 400 mg three times daily (Group II). Uniform analgesics were prescribed for all combinations of aceclofenac and acetaminophen. All patients were directed to an emergency review or to a seven-day review. Patients were prohibited from taking other drugs and from seeking medical attention unless it was from our oral surgery department. The diagnosis was made by prior established clinical criteria. On the seven day review, the parameters were recorded accordingly. Patients who underwent emergency care were re-evaluated seven days later.

A total of 150 patients who fulfilled the criteria were selected for this study; after exclusion, the final sample size was 108 patients.

The statistical analyses were performed using IBM SPSS Statistics (ver. 20.0; IBM Co., Armonk, NY, USA). $P<0.05$ was considered as statistically significant.

III. Results

The sample of 108 patients was composed of 50 males with a mean age of 25.42 years and 58 females with mean age of 24.15 years. The mean age for the total study group was $24.00\pm6.39$ years.

Table 1. Patient age and gender

| Gender | Patient | Age (yr) |
|--------|---------|----------|
| Male   | 50 (46.3) | 25.42±8.63 |
| Female | 58 (53.7) | 24.15±3.44 |

Values are presented as number (%) or mean±standard deviation.

Table 2. Incidence of surgical site infection under an antibiotic regimen

| Antibiotic regimen         | Yes, n (%) | No, n (%) | Total (n) |
|----------------------------|------------|-----------|-----------|
| Amoxicillin metronidazole  | 14 (25.9)  | 40 (74.1) | 54        |
| Azithromycin metronidazole | 8 (14.8)   | 46 (85.2) | 54        |
| Total                      | 22 (20.4)  | 86 (79.6) | 108       |

$\chi^2 = 2.05, P=0.152.$

Fig. 1. Description of patients with surgical site infection under an antibiotic regimen.

Shermil Sayd et al: Comparison of the efficacy of amoxicillin-clavulanic acid with metronidazole to azithromycin with metronidazole after surgical removal of impacted lower third molar to prevent infection. J Korean Assoc Oral Maxillofac Surg 2018
which was not statistically significant.

**IV. Discussion**

The incidence of infection following impacted mandibular third molar surgical removal varies between 0% and 45%.

Despite years of clinical data with systemic antibiotics and well-designed clinical studies, a significant debate still exists over the administration of postoperative antibiotics in impacted third molar surgery.

Removal of an impacted third molar results in a higher incidence of bacteremia compared with other oral surgical procedures. Blakey et al. reported that 25% of patients with impacted mandibular third molar had asymptomatic periodontitis. The subsequent postoperative infections can cause undesirable outcomes, such as deep space infections, although the incidence is low, at 0.8%. Although there is evidence that postoperative antibiotics can lower the incidence of postoperative complications, there is equally convincing evidence to the contrary.

Previous clinical trials used postoperative antibiotics for the following reasons: (1) presence of infection; (2) medical incapacitation; (3) patient or patient family demands; (4) standard of care in the oral surgery community is to use antibiotics; and (5) high risk of postoperative infection.

Numbers 3 and 4 above are the most common reasons for the prescription of antibiotics. However, clinicians treating such cases should resist such prescription to prevent the development of resistant strains within the community. Multiple studies comparing the efficacy of antibiotics, as mentioned above, found no statistically significant differences. Although there was no control group in the present study, and multiple antibiotics were administered, no statistically significant differences in outcome were observed.

Peterson stated five principles to guide the proper administration of antibiotics for the best possible practice and patient care. These principles are as follows: (1) proper use in surgical procedures with significant risk of infection; (2) appropriate selection of antibiotics; (3) use of high antibiotic level during surgery; (4) accurate timing of antibiotic administration; and (5) shortest antibiotic exposure as is possible.

One major drawback of our study was the non-differentiation of hard and soft tissue impaction. Piecuch et al., in their study involving bony impacted third molars, found that the use of preoperative parenteral antibiotics resulted in significantly reduced postoperative infection rate. However, no advantage was found in soft tissue impaction alone. Multiple studies have reported the same, with differences in outcome when differentiation of hard tissue and soft tissue impaction was considered.

The University Dental Hospital National Health Service Trust in Cardiff (UK) audited the use of antibiotics for impacted third molar surgeries and found “the potential for saving large sums of money while apparently incurring no clinical disadvantage”, in accord with the literature and now the common belief of many surgeons. Although a discussion about the need for postoperative antibiotics is beyond the scope of this article, we concluded that the administration of antibiotics should be considered only when necessary.

**V. Conclusion**

Though both groups underwent routine surgical removal of the mandibular mesioangular impacted third molar, neither combination of prescribed antibiotics had significant advantages over the other. Further studies with different methodologies are suggested to confirm our conclusion.

**ORCID**

Shermil Sayd, https://orcid.org/0000-0002-1765-8955
Suresh Vyloppilli, https://orcid.org/0000-0002-9423-3774
Krishna Kumar, https://orcid.org/0000-0001-5599-4717
Pramod Subash, https://orcid.org/0000-0002-6526-6243
Nithin Kumar, https://orcid.org/0000-0002-5447-5875
Sarfras Raseel, https://orcid.org/0000-0002-2870-8583

**Authors’ Contributions**

S.S., S.V., N.K., and S.R. were involved in the conceptualization, data collection, study conduction and manuscript reviews. K.K. and P.S. helped by guiding, creating the protocol, manuscript and statistical correction and correlations.

**Ethics Approval and Consent to Participate**

The study was approved by the ethics committee of Malankara Orthodox Syrian Church Medical College & Hospital, Kolenchery (approval no. MOSCMC/IEC/2015/02).

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.
**References**

1. Ortega G, Rhee DS, Papandria DJ, Yang J, Ibrahim AM, Shore AD, et al. An evaluation of surgical site infections by wound classification system using the ACS-NSQIP. J Surg Res 2012;174:33-8.

2. Ramu C, Padmanabhan TV. Indications of antibiotic prophylaxis in dental practice: review. Asian Pac J Trop Biomed 2012;2:749-54.

3. Lacasa JM, Jiménez JA, Ferrás V, Bosson M, Sóla-Morales O, García-Rey C, et al. Prophylaxis versus pre-emptive treatment for infective and inflammatory complications of surgical third molar removal: a randomized, double-blind, placebo-controlled, clinical trial with sustained release amoxicillin/clavulanic acid (1000/62.5 mg). Int J Oral Maxillofac Surg 2007;36:321-7.

4. Arteagoitia I, Diez A, Barbier L, Santamaria G, Santamaria J. Efficacy of amoxicillin/clavulanic acid in preventing infectious and inflammatory complications following impacted mandibular third molar extraction. Pharmacol Res 2005;52:485-90.

5. Ren YF, Malmstrom HS. Effectiveness of antibiotic prophylaxis in third molar surgery: a meta-analysis of randomized controlled clinical trials. J Oral Maxillofac Surg 2007;65:1909-21.

6. Richardson DT, Dodson TB. Risk of periodontal defects after third molar surgery: an exercise in evidence-based clinical decision-making. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;100:e11-8.

7. Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007;116:1736-54.

8. Bulut E, Bulut S, Etikan I, Koseoglu O. The value of routine antibiotic prophylaxis in mandibular third molar surgery: acute-phase protein levels as indicators of infection. J Oral Maxillofac Surg 2004;62:3-8; discussion 9.

9. Chuang SK, Perrott DH, Susarla SM, Dodson TB. Risk factors for inflammatory complications following third molar surgery in adults. J Oral Maxillofac Surg 2008;66:2213-8.

10. Yoshii T, Hamamoto Y, Muraoka S, Kohjitanai A, Teranoubo O, Furudoi S, et al. Incidence of deep fascial space infection after surgical removal of the mandibular third molars. J Infect Chemother 2001;7:55-7.

11. Susarla SM, Sharaf B, Dodson TB. Do antibiotics reduce the frequency of surgical site infections after impacted mandibular third molar surgery? Oral Maxillofac Surg Clin North Am 2011;23:541-6, vi.

12. Addy LD, Martin MV. Azithromycin and dentistry: a useful agent? Br Dent J 2004;197:141-3; discussion 138.

13. Blakey GH, Marciani RD, Haug RH, Phillips C, Offenbacher S, Pabla T, et al. Periodontal pathology associated with asymptomatic third molars. J Oral Maxillofac Surg 2002;60:1227-33.

14. Ishihama K, Kimura T, Yasui Y, Komaki M, Ota Y. Azithromycin as prophylaxis for the prevention of postoperative infection in impacted mandibular third-molar surgery. J Infect Chemother 2006;12:31-5.

15. Delibiasi C, Saracoglu U, Keskin A. Effects of 0.2% chlorhexidine gluconate and amoxicillin plus clavulanic acid on the prevention of alveolar osteitis following mandibular third molar extractions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002;94:301-4.

16. Yoshii T, Hamamoto Y, Muraoka S, Furudoi S, Komori T. Differences in postoperative morbidity rates, including infection and dry socket, and differences in the healing process after mandibular third molar surgery in patients receiving 1-day or 3-day prophylaxis with lenampicillin. J Infect Chemother 2002;8:97-93.

17. Petroner LJ. Antibiotic prophylaxis against wound infections in oral and maxillofacial surgery. J Oral Maxillofac Surg 1990;48:617-20.

18. Monaco G, Staffolani C, Gatto MR, Checchi L. Antibiotic therapy in impacted third molar surgery. Eur J Oral Sci 1999;107:437-41.

19. Thomas DW, Hill CM. An audit of antibiotic prescribing in third molar surgery. Br J Oral Maxillofac Surg 1997;35:126-8.