Extraction Socket Grafting and Ridge Augmentation Failures Associated with Clindamycin Antibiotic Therapy: A Retrospective Study

Hussein S. Basma, DDS, DESS, MS[1]/Craig M. Misch, DDS, MDS[2]

Purpose: The aim of this retrospective study was to determine if penicillin allergy and/or clindamycin therapy may contribute to a higher incidence of postsurgical infections after bone augmentation. ***Materials and Methods:*** This retrospective study analyzed patients between 2014 and 2019 who received bone augmentation procedures (socket grafting [SG]; ridge augmentation [RA]) prior to placement of dental implants. All the grafting procedures were performed under preoperative and postoperative oral antibiotic coverage with either amoxicillin or clindamycin for patients who reported penicillin allergy. Infections associated with the bone augmentation procedures were recorded. ***Results:*** In this study, 1,814 patients received 2,961 bone augmentation procedures (2,530 SG, 431 RA). In the 2,530 SG procedures, 270 (10.7%) were associated with a penicillin allergy. Infections occurred in 91 of the 2,530 SG sites (3.6%). However, the infection rate was 10.7% (29 SG sites) for clindamycin and only 2.7% (62 SG sites) for amoxicillin ($P < .02$). In the 431 RA procedures, 71 (16.5%) were associated with a penicillin allergy. Overall infections occurred in 31 of the 431 sites (7.2%). However, the infection rate was 22.5% (16 RA sites) for clindamycin and only 4.2% for amoxicillin (15 RA sites; $P < .01$). Penicillin-allergic patients taking clindamycin demonstrated a higher risk of infection with a risk ratio of 6.9 (95% CI) and 4.5 (95% CI) compared with nonallergic patients taking amoxicillin for RA and SG, respectively. ***Conclusion:*** Penicillin allergy and the use of clindamycin following SG and RA procedures was associated with a higher rate of infection and may be a risk factor for bone augmentation complications. *Int J Oral Maxillofac Implants 2021;36:122–125. doi: 10.11607/jomi.8461*

Following tooth extraction, alveolar ridge alterations can occur due to bone resorption.[1,2] As a result, insufficient bone volume may compromise implant placement. To minimize this dimensional loss, alveolar ridge preservation procedures are performed following tooth extraction.[3] Compared with unassisted healing, socket bone grafting has been shown to reduce overall alveolar bone resorption.[4] In cases of ridge atrophy, reconstruction of the ridge is important to allow for implant placement satisfying both functional and esthetic criteria. Guided bone regeneration (GBR) can be used to augment the ridge and provide adequate supporting bone. The survival rate of implants placed in GBR augmented sites has been reported in the literature to be 95.5%.[5]

[1]Department of Periodontology, University of Alabama at Birmingham, Birmingham, Alabama, USA.
[2]University of Alabama at Birmingham School of Dentistry, Birmingham, Alabama, USA; Private Practice, Sarasota, Florida, USA.

Correspondence to: Dr Hussein Basma, University of Alabama at Birmingham, SDB 412, 1530 3rd Avenue South, Birmingham, AL 35294-0007, USA. Fax: (205) 934-7901 Email: basma86@uab.edu

Submitted March 30, 2020; accepted May 25, 2020.

The risk of postoperative infection is a potential complication with all surgical procedures. When infection occurs, it can compromise the healing of bone grafting procedures.[6] An overall prevalence of 2.09% has been reported for postsurgical infections, encompassing a spectrum of periodontal surgical procedures that includes GBR and dental implant surgery.[7] According to the same study, no relationship was found between the types of procedures and the infection rates.[7] Preoperative antibiotic prophylaxis has been utilized to restrict the colonization of potential pathogens within the surgical site.[8,9] The general principle of antibiotic prophylaxis is to achieve an adequate concentration of the antibiotic systemically before bacterial contamination occurs.[10]

However, the widespread use of antibiotics raises concerns for adverse drug reactions and may contribute to selection of antibiotic-resistant microorganisms.[11,12] Despite the routine use of antibiotics in dentistry, no one drug or drug regimen has been found to be the most effective for prophylaxis.[11,13,14]

The benefit of using prophylactic antibiotics for dental implant therapy is controversial. Several systematic reviews have shown a significant reduction in early implant failures when patients are given antibiotic prophylaxis.[11,14,15] However, other studies have demonstrated no significant differences in clinical outcomes when comparing antibiotic prophylaxis and control

groups, particularly in patients who are systemically healthy.[11,14,15] A systematic review on the effect of prophylactic antibiotics on the outcome of bone augmentation concluded that the scientific evidence is very limited, and the infection risk, preferred drug, and optimal duration of therapy are still unknown.[16] Lindeboom and van den Akker evaluated antibiotic prophylaxis for patients undergoing intraoral bone augmentation.[17] There was a statistically significant increased risk of having an infection after bone grafting without antibiotic prophylaxis. A subsequent prospective randomized study on patients undergoing intraoral bone grafts showed no significant difference between a prophylactic single dose of clindamycin (600 mg) and a 24-hour regimen of clindamycin (600 mg, then 300 mg every 6 hours) with regard to postoperative infection.[10]

The most commonly prescribed antibiotic for oral surgical procedures is amoxicillin.[9,12] Amoxicillin is a first-choice drug, as it has nontoxic bactericidal properties that are effective against both aerobic and anaerobic microorganisms usually associated with oral infections.[8–10] In cases of penicillin allergy, which ranges from 8% to 12%,[8,18] clindamycin is the most commonly used alternative.[9] Clindamycin, a lincosamide antibiotic with bacteriostatic properties, binds to 50S ribosomal and inhibits bacterial protein synthesis. At higher concentrations, it can also exhibit bactericidal properties.[8]

Several studies have reported that the use of clindamycin is a possible risk factor for infection following dental implant and sinus augmentation procedures.[8,9,18] The aim of this retrospective study was to determine if clindamycin therapy contributed to a higher incidence of postsurgical infections with socket bone grafting and ridge augmentation procedures.

MATERIALS AND METHODS

A retrospective chart review study was performed for patients who underwent socket grafting (SG) or ridge augmentation (RA) procedures prior to dental implant placement between 2014 and 2019 in the graduate periodontal clinic at the University of Alabama at Birmingham School of Dentistry. The University Institutional Review Board approved the study protocol (IRB-300004539). The following exclusion criteria were applied: patients with systemic conditions that alter bone healing (uncontrolled diabetes, IV bisphosphonates, chemotherapy, immunosuppressive medications), poor oral hygiene, and heavy smokers (> 10 cigarettes a day). Patients who were not prescribed antibiotics or took a different antibiotic, other than amoxicillin or clindamycin, were not included. Any patients who had records lacking information regarding other study variables were also excluded. The following data were recorded from the patient charts: patient sex and age, allergy to penicillin, type of bone augmentation (SG or RA), and presence or absence of complications including infection.

Patients who did not report a penicillin allergy received 2 g amoxicillin, 1 hour prior to surgery, and continued postoperative coverage for 1 week (amoxicillin 500 mg, 3 times a day). Patients who self-reported a penicillin allergy were prescribed 600 mg clindamycin, 1 hour before surgery, and continued postoperative coverage for 1 week (clindamycin 300 mg, 2 times a day). All patients were recalled for a follow-up visit at 2 and 4 weeks postsurgery. Bone augmentation failures and/or complications that occurred in the first month of healing, including infection, were recorded. Patients who underwent SG had implants placed after 3 to 5 months, while those who underwent RA had implants placed at 6 to 9 months postaugmentation.

Statistical Analysis

The patient age was summarized as a mean and standard deviation. All the categorical variables were summarized as frequency and proportion and presented in contingency tables. To account for multiple procedures on the same patient, the association between the infection and penicillin allergy status was assessed using a generalized estimating equations (GEE) model with a sandwich variance estimator, controlling for the patient age and sex. The odds ratio (OR) and its 95% confidence interval (CI) were calculated for the strength of association. All the tests were two-tailed with a significance level of .05. All the analyses were conducted using SAS 9.4.

RESULTS

Between 2014 and 2019, a total of 1,814 patients received 2,961 bone augmentation procedures (SG, RA). There were 834 (46%) men and 980 (54%) women, with a mean age of 61 years. Of the 2,961 procedures, 2,530 (85.4%) were socket grafting, and 431 (14.6%) were RA. Patients reported no penicillin allergy for 2,620 bone augmentation procedures (88.5%; Table 1). In 341 bone augmentation procedures, patients reporting a penicillin allergy took clindamycin (11.5%). No complications were reported in 2,839 of 2,961 sites (95.9%). Postsurgical infections were found in 122 of 2,961 sites (4.1%; Fig 1).

In the 2,530 SG procedures, 270 (10.7%) were associated with a penicillin allergy and clindamycin use. Infections occurred in 91 of the 2,530 SG sites (3.6%). However, the infection rate was 10.7% (29 SG sites) for clindamycin and only 2.7% (62 SG sites) for amoxicillin (Fig 2). For SG procedures, the GEE analysis suggested a significant association between infection and clindamycin use (OR = 4.5 [2.3, 8.7]; $P < .02$) during SG procedures, controlling for patient age and sex.

Table 1 Demographic Characteristics of Included Subjects

Variable	Mean (SD) or N (%)
Patients	1,814
Age	61 (14.2)
Sex	
Men	834 (46.0%)
Women	980 (54.0%)
Procedures	2,961
Procedure type	
Ridge augmentation	431 (14.6%)
Socket grafting	2,530 (85.4%)
Type of antibiotic	
Clindamycin	341 (11.5%)
Amoxicillin	2,620 (88.5%)

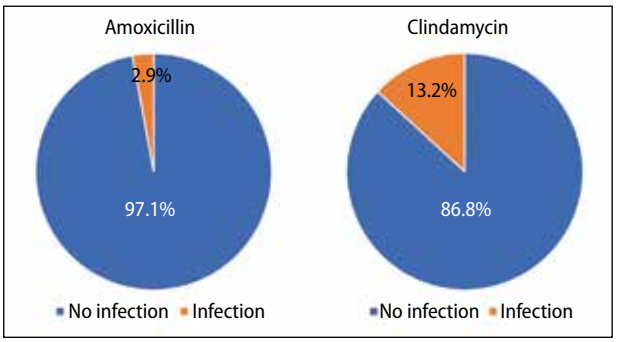

Fig 1 Infection rates for amoxicillin and clindamycin in all bone augmentation procedures.

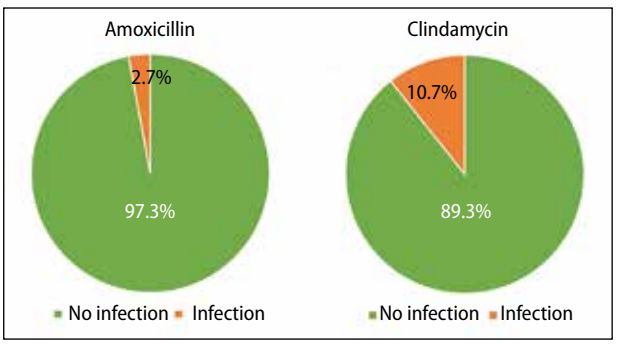

Fig 2 Infection rates in SG procedure for amoxicillin and clindamycin.

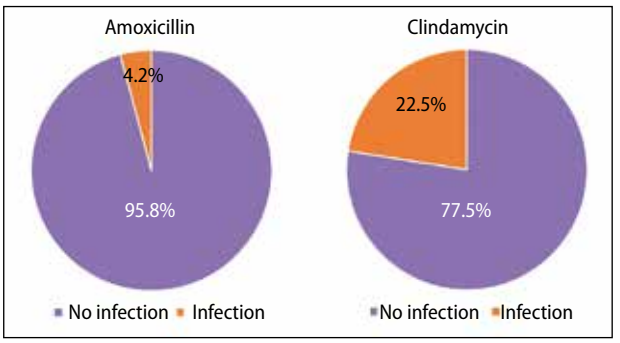

Fig 3 Infection rates in RA procedures for amoxicillin and clindamycin.

Specifically, the odds of infection given clindamycin use were 4.5 times higher than the odds of infection given amoxicillin use during SG procedures.

In the 431 RA procedures, 71 (16.5%) were associated with clindamycin use. Overall infections occurred in 31 of the 431 sites (7.2%). However, the infection rate was 22.5% (16 RA sites) for clindamycin and only 4.2% for amoxicillin (15 RA sites; Fig 3). For RA procedures, the GEE analysis suggested a significant association between infection and clindamycin use (OR = 6.9 [3.2, 14.8]; $P < .01$) during RA procedures, controlling for patient age and sex. Specifically, the odds of infection given clindamycin use were 6.9 times higher than the odds of infection given amoxicillin use during RA procedures.

For all bone augmentation procedures (SG, RA), the GEE analysis suggested a significant association between infection and clindamycin use (OR = 5.5 [3.1, 9.6]; $P < .01$), controlling for patients' age and sex. Specifically, the odds of infection given clindamycin use were 5.5 times higher than the odds of infection given amoxicillin use.

DISCUSSION

In this study, the overall prevalence of postsurgical infection following SG and RA was 4.1%. This percentage compares favorably with other studies on periodontal and implant surgery that reported an infection rate of 1% to 5.4%,[7,19,20] and supports that these procedure have a low risk of postsurgical infection. Several factors have been reported to influence the success of bone augmentation procedures, including surgeon experience, flap design, primary tension-free closure, graft material, smoking, and patient compliance.[21,22] The use of prophylactic antibiotic therapy may reduce the risk of developing postoperative infection following bone augmentation procedures.

Clinicians are more likely to prescribe antibiotics with bone augmentation and as complexity of the bone grafting procedure increases.[23] Clindamycin is often the first antibiotic option selected for patients with a reported penicillin allergy. However, several studies have reported higher infection rates with the use of clindamycin for dental implant and sinus augmentation surgeries.[8,9,18] French et al[9] found that the odds of failure for dental implants placed in penicillin-allergic patients were 3.1 times higher and 10 times higher for immediate implant placement. Salomó-Coll et al[18] showed similar outcomes where penicillin-allergic patients receiving clindamycin had a risk ratio of 3.84 (95% CI) of implant failure compared with nonallergic patients. Khoury et al[8] performed a retrospective observational study and found that antibiotic prophylaxis with clindamycin therapy could be a risk factor for

infection following a sinus augmentation procedure. To the authors' knowledge, no studies have been done on the association between penicillin allergy and/or clindamycin use with RA and SG. In the present study on bone augmentation procedures, penicillin-allergic patients using clindamycin demonstrated a higher risk of infection with a risk ratio of 6.9 (95% CI) and 4.5 (95% CI) compared with nonallergic patients for RA and SG, respectively.

There may be other variables in the present study that also contributed to higher rates of infection with bone augmentation procedures. The procedures were performed by residents in postgraduate periodontal training, so operator experience may be a contributing factor. Although graft material was not evaluated in this study, there may be a higher risk of infection with the use of intraorally harvested bone from salivary contamination.[24] Smoking can interfere with postoperative wound healing. Patient compliance with taking antibiotics and following postoperative instructions must also be considered. Well-designed studies are needed to validate that penicillin allergy and/or clindamycin administration are associated with a higher risk of infection with bone augmentation procedures. Furthermore, the need for routine antibiotic prophylaxis, preferred drug, and continued drug therapy after SG and RA also need to be investigated.

CONCLUSIONS

Prophylactic antibiotic therapy can assist in reducing the risk of postoperative infections following bone augmentation procedures. In this study, penicillin allergy and clindamycin therapy following SG and RA procedures was associated with a higher rate of infection and may be a risk factor for bone augmentation complications. Further studies should evaluate the most suitable antibiotic regimen for penicillin-allergic patients.

ACKNOWLEDGMENTS

The authors would like to thank Dr Peng Li for his support for statistical analysis and Dr Kenneth Liu, Dhara Patel, and Vishnupriya Kurukundu for their collaboration on this project. The authors state that they do not have any financial or personal relationships with people or organizations that could inappropriately influence this study.

REFERENCES

1. Araújo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. J Clin Periodontol 2005;32:212–218.
2. Nevins M, Camelo M, De Paoli S, et al. A study of the fate of the buccal wall of extraction sockets of teeth with prominent roots. Int J Periodontics Restorative Dent 2006;26:19–29.
3. Majzoub J, Ravida A, Starch-Jensen T, Tattan M, Suárez-López Del Amo F. The influence of different grafting materials on alveolar ridge preservation: A systematic review. J Oral Maxillofac Res 2019;10:e6.
4. MacBeth N, Trullenque-Eriksson A, Donos N, Mardas N. Hard and soft tissue changes following alveolar ridge preservation: A systematic review. Clin Oral Implants Res 2017;28:982–1004.
5. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants 2007;22(suppl):49–70.
6. Moy PK, Aghaloo T. Risk factors in bone augmentation procedures. Periodontol 2000 2019;81:76–90.
7. Powell CA, Mealey BL, Deas DE, McDonnell HT, Moritz AJ. Post-surgical infections: Prevalence associated with various periodontal surgical procedures. J Periodontol 2005;76:329–333.
8. Khoury F, Javed F, Romanos GE. Sinus augmentation failure and postoperative infections associated with prophylactic clindamycin therapy: An observational case series. Int J Oral Maxillofac Implants 2018;33:1136–1139.
9. French D, Noroozi M, Shariati B, Larjava H. Clinical retrospective study of self-reported penicillin allergy on dental implant failures and infections. Quintessence Int 2016;47:861–870.
10. Lindeboom JA, Frenken JW, Tuk JG, Kroon FH. A randomized prospective controlled trial of antibiotic prophylaxis in intraoral bone-grafting procedures: Preoperative single-dose penicillin versus preoperative single-dose clindamycin. Int J Oral Maxillofac Surg 2006;35:433–436.
11. Esposito M, Grusovin MG, Loli V, Coulthard P, Worthington HV. Does antibiotic prophylaxis at implant placement decrease early implant failures? A Cochrane systematic review. Eur J Oral Implantol 2010;3:101–110.
12. Thornhill MH, Dayer MJ, Durkin MJ, Lockhart PB, Baddour LM. Risk of adverse reactions to oral antibiotics prescribed by dentists. J Dent Res 2019;98:1081–1087.
13. Romandini M, De Tullio I, Congedi F, et al. Antibiotic prophylaxis at dental implant placement: Which is the best protocol? A systematic review and network meta-analysis. J Clin Periodontol 2019;46:382–395.
14. Esposito M, Grusovin MG, Coulthard P, Oliver R, Worthington HV. The efficacy of antibiotic prophylaxis at placement of dental implants: A Cochrane systematic review of randomised controlled clinical trials. Eur J Oral Implantol 2008;9(suppl 1):95–103.
15. Braun RS, Chambrone L, Khouly I. Prophylactic antibiotic regimens in dental implant failure: A systematic review and meta-analysis. J Am Dent Assoc 2019;150:e61–e91.
16. Klinge A, Khalil D, Klinge B, et al. Prophylactic antibiotics for staged bone augmentation in implant dentistry. Acta Odontol Scand 2020;78:64–73.
17. Lindeboom JA, van den Akker HP. A prospective placebo-controlled double-blind trial of antibiotic prophylaxis in intraoral bone grafting procedures: A pilot study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:669–672.
18. Salomó-Coll O, Lozano-Carrascal N, Lázaro-Abdulkarim A, Hernández-Alfaro F, Gargallo-Albiol J, Satorres-Nieto M. Do penicillin-allergic patients present a higher rate of implant failure? Int J Oral Maxillofac Implants 2018;33:1390–1395.
19. Gynther GW, Köndell PA, Moberg LE, Heimdahl A. Dental implant installation without antibiotic prophylaxis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:509–511.
20. Checchi L, Trombelli L, Nonato M. Postoperative infections and tetracycline prophylaxis in periodontal surgery: A retrospective study. Quintessence Int 1992;23:191–195.
21. Merli M, Migani M, Esposito M. Vertical ridge augmentation with autogenous bone grafts: Resorbable barriers supported by ostheosynthesis plates versus titanium-reinforced barriers. A preliminary report of a blinded, randomized controlled clinical trial. Int J Oral Maxillofac Implants 2007;22:373–382.
22. Chao YC, Chang PC, Fu JH, Wang HL, Chan HL. Surgical site assessment for soft tissue management in ridge augmentation procedures. Int J Periodontics Restorative Dent 2015;35:e75–e83.
23. Hai JH, Lee C, Kapila YL, Chaffee BW, Armitage GC. Antibiotic prescribing practices in periodontal surgeries with and without bone grafting. J Periodontol 2020;91:508–515.
24. Mauceri R, Campisi G, Matranga D, Mauceri N, Pizzo G, Melilli D. The role of antibiotic prophylaxis in reducing bacterial contamination of autologous bone graft collected from implant site. Biomed Res Int 2017;2017:2175019.