MedNEXT
Journal of Medical an Health Sciences

REVIEW ARTICLE

DOI: 10.54448/mdnt23S301

Major evidence and guidelines for antibiotic therapy in implant dentistry: a systematic review

Melannye Sophia Ponce Vera[1*], Martha Elizabeth Criollo Jimenez[2], Fabio Alarcon Idalgo[3,4], Silvio Antonio dos Santos Pereira[3,4], Alexandre Gomes Nunes[3,4], Elias Naim Kassis[3,4], Alvaro José Cicareli[3,4]

[1] Dental care office. Ecuador, Manabí, city Portoviejo. Calle Antonio Menéndez and Av. Reales Tamarindos, Ecuador.
[2] Martha Criollo office. Ecuador-Store-Store. Calle Zoilo Rodríguez y Victor Vivar corner, Ecuador.
[3] UNORTE - University Center of Northern São Paulo, Dentistry department, São José do Rio Preto, São Paulo, Brazil.
[4] UNIPOS - Post graduate and continuing education, Dentistry department, São José do Rio Preto, São Paulo, Brazil.

*Corresponding author: Melannye Sophia Ponce Vera.
Dental care office. Ecuador, Manabí, city Portoviejo.
Calle Antonio Menéndez and Av. Reales Tamarindos, Ecuador.
Email: mela.ponce@hotmail.com

DOI: https://doi.org/10.54448/mdnt23S301
Received: 05-18-2023; Revised: 07-07-2023; Accepted: 07-14-2023; Published: 07-21-2023; MedNEXT-id: e23S301

Abstract

Introduction: Dentistry was favored by the discovery of osseointegration, which has become important in the treatment of partially and edentulous patients. Initially, osseointegration was used only to treat edentulous patients in the maxilla and mandible, using a single type of implant, prosthetic abutment, and rehabilitation protocol. However, as the applications of osseointegration evolved, complications also increased, which became more numerous and are no longer the result of surgical and mechanical problems of the components of a single care protocol, requiring more research, studies, and care. In this scenario, the use of antibiotics in implantology is very common and the abuse of antibiotics is more and more frequent. The rational use of antibiotics in the oral implantology process needs the support of evidence-based medicine. The prophylactic use of antibiotics in dental implantology was reviewed in the present study, including the summary of different risks of infection, such as peri-implantitis and maxillary sinusitis after lifting the maxillary sinus floor. **Objective:** To carry out a systematic review of the literature on the real effects of antibiotic therapy on implantology, especially in the pre-procedure phase. The present study was based on studies of guidelines, with emphasis on the German directive. **Main findings and conclusion:** The current evidence of antibiotic prophylaxis from oral and maxillofacial surgery was summarized by the planned German S3 guideline "antibiotic prophylaxis in surgery". Perioperative prophylactic antibiotics can reduce SSI in major procedures, such as head and neck cancer surgery, and prophylaxis is only beneficial for 24 hours. In orthognathic surgery, preoperative antibiotics can reduce SSI with good quality evidence, but it benefits prolonged therapy, and which regimen is most effective remains uncertain. In traumatology, perioperative antibiotic prophylaxis for mandibular fractures and Lefort-1/2 can reduce the SSI, but antibiotic regimens should not be prolonged in the postoperative period by 24 hours. For dentoalveolar surgery, the evidence is more ambivalent. For dental implants, perioperative antibiotics as single injection prophylaxis before placement can reduce dental implant failure, but not SSI. For the removal of third molars, antibiotic therapy in the perioperative period is of uncertain benefit for healthy patients, but it was not possible to obtain evidence to evaluate antibiotic therapy for patients with pre-existing conditions.

Keywords: Antibiotics. Therapy. Implant dentistry. Guidelines.

Introduction

Dentistry was favored by the discovery of osseointegration, which became important in the treatment of partially and completely edentulous patients. Initially, osseointegration was only used to

treat patients who were completely edentulous in the maxilla and mandible, through a single type of implant, prosthetic abutment, and rehabilitation protocol [1]. Surgeons, as soon as they started using osseointegration, only sought to obtain and maintain implant anchorage, without worrying too much about aesthetics [1].

Over time, the basic principle of osseointegration was proven, to allow its application in the most varied clinical situations of dental failure, both single and partial. New concepts, principles, and technologies must be discovered and improved [1]. However, as the applications of osseointegration evolved, so did the complications, which became more numerous and are no longer the result of surgical and mechanical problems of the components of a single care protocol, requiring more research, studies, and care [1].

In this scenario, the use of antibiotics in implant dentistry is very common and the abuse of antibiotics is increasingly frequent [2]. The rational use of antibiotics in the oral implantology process needs the support of evidence-based medicine. The prophylactic use of antibiotics in dental implantology was reviewed in the present work, including the summary of different risks of infection, such as peri-implantitis and maxillary sinusitis after lifting the maxillary sinus floor [2].

Therefore, the present study carried out a systematic review of the literature on the real effects of antibiotic therapy in implant dentistry, especially in the pre-procedure phase. The present study was based on guideline studies, with an emphasis on the German guideline.

Methods

Study Design

The systematic review rules of the PRISMA Platform were followed. Available at: www.prisma-statement.org/). Accessed: 04/28/2023. A search protocol was developed to identify the evidence related to determinants for good aesthetics in implantology. Thus, the study included should report different aspects and may involve different tissues (gum and bone), surgical techniques, materials, and expectations of the patient and report them with getting a nice aesthetic when rehabilitation involved anterior regions.

Research Strategy, Quality of Studies and Risk of Bias

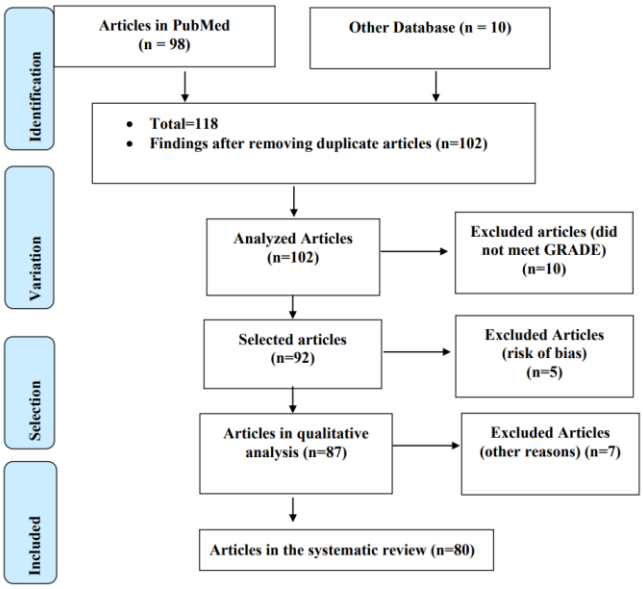
The search strategies for this systematic review were based on the keywords (MeSH Terms): *Antibiotics. Therapy. Implant dentistry. Guidelines.* The research was carried out from January to March 2023 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. In addition, a combination of keywords with the Booleans "OR", "AND" and the operator "NOT" were used to target scientific articles of interest. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument.

Results

Summary of Findings

A total of 118 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, resulting in 102 articles. A total of 87 articles were evaluated in full and 80 were included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 5 studies with a high risk of bias and 10 studies that did not meet GRADE.

Figure 1. Flowchart - Article Selection Process.



Source: Own authorship

In the context of implant dentistry, perioperative antibiotics are generally used in surgery to prevent surgical site infections (SSI). By definition, an SSI is an infection that develops within 30 days of an operation or within 1 year of implant placement, where the infection appears to be related to surgery [3]. SSI prevalence greatly depends on the variety of the procedure.

The American Society of Health-System Pharmacists categorizes surgery into four different classes which, in the context of this study, are further listed with examples of respective procedures in oral and maxillofacial procedures surgery: clean (e.g., atraumatic procedures or where neither gastrointestinal

tract, genitourinary nor respiratory tract is violated, such as cervical lymph node excisions), cleanly contaminated (e.g., procedures that violate the gastrointestinal system or respiratory tract, such as parotidectomy, submandibular gland excision, third molar removal), contaminated (e.g., surgery in a situation of acute inflammation, such as open jaw fracture repair with osteosynthesis) and dirty (for example, procedures involving pus or compound/open lesions, odontogenic incision of the abscess) [4,5].

Unlike therapeutically used antibiotics, perioperative treatment aims to reduce contamination of the (physiological) bacterial forums in the specific surgical area. The basic aim of antibiotic prophylaxis is therefore to provide an adequate level of drug in the tissues before, during, and for the shortest possible time after the procedure [6]. Prophylactic antibiotic treatment is defined as the use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications. Here, the Scottish Intercollegiate Network guideline 'Antibiotic prophylaxis in surgery' defines two regimens; short-term prophylaxis given at any time before or after surgery for up to 24 hours after surgery. Longterm that is continued for more than 24 h. In contrast, therapeutic antibiotic treatment is used to reduce the growth or reproduction of bacteria, including eradication therapy. Antimicrobial therapy is prescribed to clear an infection by an organism or to clear an organism that is colonizing a patient but not causing an infection [7].

Still, in Europe and the USA, SSI represents the second most common nosocomial infection and is highly responsible for prolonged stay and lethality [8]. Especially in head and neck surgery and maxillofacial procedures, where the aerodigestive tract is involved and operations are often considered to be contaminated, SSI represents a serious health burden with an incidence of up to 10 to 15% [6]. However, overuse and overuse of antibiotics is not only uneconomical but also involves the risk of developing multi-drug resistance in bacteria, which is claimed to be a major cause of therapy failure in many infections [9]. Therefore, the appropriate use of antibiotics is seen as a national health priority to prevent morbidity from infections and the development of resistant organisms [10]. It has been estimated that approximately half of SSIs are preventable by applying evidence-based strategies [11-14].

To minimize SSI and the emergence of multidrug resistance mechanisms in head and neck surgery, the Association of Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften and 25 collaborating medical societies initiate an update of the existing S1 guideline "Antibiotics in surgery" to a consensusdriven S3 guideline [7].

The systematic literature search is based on the research chain of the SIGN guideline "Antibiotic prophylaxis in surgery" from 2014 [7]. The most recent evidence for antibiotic therapy in oral and maxillofacial and dentoalveolar surgery is summarized. As a suitable substance, cefazolin seems to be more effective than penicillin and clindamycin but with a high risk of bias [15,16]. Furthermore, the number needed to treat was relatively high, which leads to uncertainty regarding the preferred antibiotic compound and optimal range of prophylaxis [17,18]. In addition, 16 studies evaluated antibiotic prophylaxis in maxillofacial trauma but differed in quality of study design with low to high risk of bias. A 1-day postoperative course of antibiotics is effective in preventing infectious complications.

No additional benefit of postoperative antibiotic prophylaxis could be found [19-28]. As a suitable antibiotic compound, ampicillin/sulbactam appears to be superior to clindamycin [29]. Furthermore, a retrospective study with a high risk of bias found no statistically significant difference between penicillin and cefotaxime regimens [30]. Another retrospective study even questions the use of prophylactic antibiotics in orbito-zygomatic fractures [31]. For temporomandibular joint replacement, perioperative prophylaxis is efficient in reducing SSI [3]. In cleft palate surgery, three studies could be found, but no benefit of postoperative antibiotics was observed to prevent SSI [32-34]. Two studies, retrospectively only at high risk of bias, found long-term antibiotic treatment helpful in preventing the recurrence of drugrelated necrosis of the jaw. Here, ampicillin/sulbactam may be superior to clindamycin [35,36].

In clean oncology interventions, anti-infective therapy for as little as 24 hours is effective in five reviews and 1 retrospective study [37-42]. In contrast, a retrospective study and a controlled clinical trial prolonged protective therapy against SSI [7,43,44]. In cases of microvascular reconstruction, a regimen of 3 to 5 days can reduce SSI [38,45]. Here, clindamycin appears not suitable for preventing SSI [46]. For parotid gland surgery, singledose cefazolin prophylaxis is sufficient to reduce SSI [47]. However, infection rates after dermatologic procedures and nose and ear grafting did not differ significantly between patients receiving single-dose versus placebo prophylaxis [48].

Nineteen studies were evaluated evaluating perioperative prophylaxis in the removal of third molars

with low to high risk of bias. The use of prophylactic antibiotics did not significantly reduce SSI in nine clinical trials [49-57] and two retrospective analyzes [58,59]. Three meta-analyses concluded that routine prescribing is not supported for healthy people undergoing third molar removal [60-64]. In contrast, two clinical trials showed significantly higher SSI where no antibiotics were administered [65, 66] and three reviews found systemic antibiotics effective in reducing dry socket and SSI significantly [67-69]. A clinical trial did not show significant results with the use of antibiotics in intra-alveolar extraction dental procedures [70].

For dental implants, five studies with a low risk of bias demonstrate that perioperative antibiotics as a single-shot prophylaxis before placement can reduce dental implant failure but not SSI [71-75]. However, single-dose prophylaxis may be beneficial in preventing postoperative pain [76] A retrospective study with a high risk of bias found antibiotics for 7 days effective in implant survival [77] Other studies with low risk of bias, no statistically significant differences were found between single-dose prophylaxis and prolonged postoperative course [75, 78-80].

If peri-implantitis occurs, antibiotics adjunctive to surgical treatment have not shown improvement in outcomes [80]. In the treatment of odontogenic and inflammatory abscesses, moxifloxacin was found to reduce pain more effectively than clindamycin, but the mean length of stay did not show significant differences in the two groups. One study was found that evaluated the benefit of single-dose prophylaxis versus prolonged antibiotics in general maxillofacial surgery [80].

Especially in oral and maxillofacial surgery, where procedures involving the aerodigestive tract are considered cleanly contaminated, SSI represent a serious healthcare burden. To improve the implementation and methodological standard, an upgrade from the existing S1 guideline to a consensus-driven S3 guideline was initiated by the Association of Scientific Medical Societies of Germany and 25 collaborating medical societies. Thus, a systematic literature search, on the guideline "Antibiotic prophylaxis in surgery" from 2014. In total, 80 clinical trials, retrospective studies, reviews, and meta-analysis were analyzed. For orthognathic surgery, a prolonged antibiotic regimen may reduce the risk of SSI, but there is a lack of evidence of short-term and long-term effects of therapy. For maxillofacial trauma, antibiotic prophylaxis may reduce SSI, but prolonged postoperative dosing does not show benefit. For both clean and contaminated oncology interventions, anti-infective therapy for 24 h may only reduce SSI; patients may not benefit from the extended regimen. On the other hand, for dentoalveolar procedures, such as implantology or removal of third molars, the literature reveals ambivalent results. Therefore, the planned S3 guideline consensus process is needed to transfer the indecisive results of antibiotic prophylaxis in dentoalveolar surgery into clinical practice and encourage adherence to the guidelines [1].

Discussion

In general, SSI depends on patient-related risk factors such as poor nutritional status, smoking, diabetes, and impaired immune system. Other significant variables for wound infection, for example, in oncology are tumor stage, previous chemotherapy, preoperative hospital stay, permanent tracheotomy, and presence of hypopharyngeal cancer [38].

Additionally, rates of antibiotic resistance are increasing and are directly related to the proportion of the population receiving antibiotics and total antibiotic exposure. Thus, increased use of antibiotics leads to more resistance [7]. In this context, organisms such as various streptococci (both aerobic and anaerobic species), other oral anaerobes including Bacteroides species, Peptostreptococcus species, Prevotella species, Fusobacterium species, Veillonella species, Enterobacteriaceae and staphylococci are pathogens of special interest that can lead to antibiotic resistance. Up to 95% remain susceptible to metronidazole and co-amoxiclav, but penicillin alone can no longer be used [7].

In addition, procedure-related risk factors summarized in the surgery classification alter the rate of infection. As postoperative surgical site infections occur in <1% of patients undergoing clean head and neck operations, antibiotic prophylaxis is not considered beneficial [37]. On the other hand, the use of antibiotic prophylaxis in cases of clean facial contamination after surgery is well established [22]. As the intraoral mucosa is exposed to oropharyngeal secretions, saliva, and bacteria, the incidence of infections in head-contaminated neck and neck surgery without preoperative antibiotics is reported to be 30-80% [38].

Perioperative antibiotic prophylaxis is therefore of fundamental importance in maxillofacial surgery. Here, some studies suggest that short-term antibiotic therapy may increase the number of resistances. For head and neck injuries, significantly fewer patients were found with MRSA-infected wounds in the short-term group. This is why SIGN guidelines and others recommend the duration of single-dose prophylactic AT except in

special circumstances, such as prolonged surgery or massive blood loss [7].

In dentoalveolar surgery, the literature is ambivalent towards antibiotic therapy. One of the main points of interest was the third molar removal. Overall, there is evidence that the use of prophylactic antibiotics cannot significantly reduce the presence of surgical site infections [49-57, 61]. Given the low risk of infection versus the potential development of resistant bacteria and infection control, there is no evidence to support the routine prescription of antibiotic prophylaxis to healthy people undergoing third molar extraction [55,60,64].

Even in anatomically difficult cases, measured with the difficulty index described by Pederson et al, there were no significant associations between antibiotic prophylaxis and postoperative complications, although a small but insignificant increase in the number of dry sockets and infections was observed [49]. Only two trials (a retrospective analysis with a high risk of bias included) were found where postoperative infections were significantly correlated with the placebo group [65,66].

The effectiveness of perioperative prophylactic antibiotics in preventing postoperative wound infections after cleanly contaminated head and neck surgery where the aerodigestive tract is violated has been established in clinical trials [41,80] There was no need for prolonged antibiotic therapy, but risk factors such as tracheotomy have been associated with increased risk for SSI [80].

In orthognathic surgery, postoperative infection rates range from 1.4 to 33.4%, but the use of antibiotics remains controversial [15]. In this study, good quality evidence that preoperative antibiotic prophylaxis appears to be effective in reducing the rate of postoperative infection in orthognathic surgery can be presented [13,14].

Conclusion

Current evidence for antibiotic prophylaxis of oral and maxillofacial surgery was summarized by the planned German S3 guideline "antibiotic prophylaxis in surgery". Perioperative prophylactic antibiotics can reduce SSI in major procedures such as head and neck cancer surgery, and prophylaxis is only beneficial for 24 hours. In orthognathic surgery, preoperative antibiotics can reduce SSI with a good quality of evidence, but the benefit from prolonged therapy and which regimen is most effective remains unclear. In traumatology, perioperative antibiotic prophylaxis for mandibular fractures and Lefort-1/2 may reduce SSI, but one should not prolong postoperative antibiotic regimens beyond 24 h. For dentoalveolar surgery, the evidence is more ambivalent. For dental implants, perioperative antibiotics as single injection prophylaxis before placement can reduce dental implant failure, but not SSI. For third molar removal, perioperative antibiotic therapy is of uncertain benefit to otherwise healthy patients, but it was not possible to obtain evidence evaluating antibiotic therapy for patients with pre-existing conditions.

Acknowledgement

Not applicable.

Funding

Not applicable.

Ethical Approval

Not applicable.

Informed consent

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

It was applied by Ithenticate[@].

References

1. Brivio A, Al-Jabri T, Martin J, Barrett D, Maffulli N. Debridement, antibiotics and implant retention (DAIR) is successful in the management of acutely infected unicompartmental knee arthroplasty: a case series. Ann Med. 2023 Dec;55(1):680-688. doi: 10.1080/07853890.2023.2179105.
2. Okafor CE, Nghiem S, Byrnes J. One-stage revision versus debridement, antibiotics, and implant retention (DAIR) for acute prosthetic knee infection: an exploratory cohort study. Arch Orthop Trauma Surg. 2023 Apr 27. doi: 10.1007/s00402-023-04891-1.
3. Torof E, Morrissey H, Ball PA. Antibiotic Use in Dental Implant Procedures: A Systematic Review

and Meta-Analysis. Medicina (Kaunas). 2023 Apr 5;59(4):713. doi: 10.3390/medicina59040713.
4. Saleh AM, Torres KM, Murad MH, Erwin PJ, Driscoll CL. Prophylactic perioperative antibiotic use in endoscopic sinus surgery: a systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2012;146:533–8. https://doi.org/10.1177/01945 99811434117.
5. Wahab PU, Narayanan V, Nathan S, Madhulaxmi. Antibiotic prophylaxis for bilateral sagittal split osteotomies: a randomized, double-blind clinical study. Int J Oral Maxillofac Surg. 2013;42:352–5. https://doi.org/10.1016/j.ijom.2012.10.036.
6. SIGN SIGN. Antibiotic prophylaxis in surgery. (SIGN publication no104) 2014; 2008.
7. Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidencebased global perspective. Lancet Infect Dis. 2016;16:e276–87. https://doi.org/10.1016/s1473-3099(16)30398-x.
8. Lu Q, Xie SQ, Chen SY, Chen LJ, Qin Q. Experience of 1166 thyroidectomy without use of prophylactic antibiotic. Biomed Res Int. 2014;2014:758432. https://doi.org/10.1155/2014/75843 2.
9. Langerman A, Ham SA, Pisano J, Pariser J, Hohmann SF, Meltzer DO. Laryngectomy complications are associated with perioperative antibiotic choice. Otolaryngol Head Neck Surg. 2015;153:60–8. https://doi.org/10.1177/0194599815583641.
10. Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA Surg. 2017. https://doi.org/10.1001/jamasurg.2017.0904.
11. Boccia G, Di Spirito F, D'Ambrosio F, Di Palo MP, Giordano F, Amato M. Local and Systemic Antibiotics in Peri-Implantitis Management: An Umbrella Review. Antibiotics (Basel). 2023 Jan 8;12(1):114. doi: 10.3390/antibiotics12010114.
12. Tan SK, Lo J, Zwahlen RA. Perioperative antibiotic prophylaxis in orthognathic surgery: a systematic review and meta-analysis of clinical trials. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011;112:19–27. https://doi.org/10.1016/j.tripleo.2010.07.015.
13. Oomens MA, Verlinden CR, Goey Y, Forouzanfar T. Prescribing antibiotic prophylaxis in orthognathic surgery: a systematic review. Int J Oral Maxillofac Surg. 2014;43:725–31. https://doi. org/10.1016/j.ijom.2014.01.012.
14. Danda AK, Ravi P. Effectiveness of postoperative antibiotics in orthognathic surgery: a meta-analysis. J Oral Maxillofac Surg. 2011;69:2650–6. https://doi.org/10.1016/j.joms.2011.02.060.
15. Davis CM, Gregoire CE, Steeves TW, Demsey A. Prevalence of surgical site infections following orthognathic surgery: a retrospective cohort analysis. J Oral Maxillofac Surg. 2016;74:1199–206. https://doi.org/10.1016/j.joms.2016.01.040.
16. Posnick JC, Choi E, Chavda A. Surgical site infections following bimaxillary orthognathic, osseous genioplasty, and intranasal surgery: a retrospective cohort study. J Oral Maxillofac Surg. 2017;75:584–95. https://doi.org/10.1016/j.joms.2016.09.018.
17. Davis CM, Gregoire CE, Davis I, Steeves TW. Prevalence of surgical site infections following orthognathic surgery: a double-blind, randomized controlled trial on a 3-day versus 1-day postoperative antibiotic regimen. J Oral Maxillofac Surg. 2017;75:796–804. https://doi.org/10.1016/j.joms.2016.09.038.
18. Naimi-Akbar A, Hultin M, Klinge A, Klinge B, Tranaeus S, Lund B. Antibiotic prophylaxis in orthognathic surgery: a complex systematic review. PLoS ONE. 2018;13:e0191161. https://doi. org/10.1371/journal.pone.0191161.
19. Morris LM, Kellman RM. Are prophylactic antibiotics useful in the management of facial fractures? Laryngoscope. 2014;124:1282–4. https://doi.org/10.1002/lary.24364.
20. Schaller B, Soong PL, Zix J, Iizuka T, Lieger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomized, double-blind, placebo-controlled pilot clinical study. Part 2: mandibular fractures in 59 patients. Br J Oral Maxillofacial Surg. 2013;51:803–7. https://doi.org/10.1016/j. bjoms.2013.08.008.
21. Mottini M, Wolf R, Soong PL, Lieger O, Nakahara K, Schaller B. The role of postoperative antibiotics in facial fractures: comparing the efficacy of a 1-day versus a prolonged regimen. J Trauma Acute Care Surg. 2014;76:720–4. https://doi.org/10.1097/TA.0000000000000123.
22. Lauder A, Jalisi S, Spiegel J, Stram J, Devaiah A. Antibiotic prophylaxis in the management of complex midface and frontal sinus trauma. Laryngoscope. 2010;120:1940–5. https://doi.

org/10.1002/lary.21081.
23. Soong PL, Schaller B, Zix J, Iizuka T, Mottini M, Lieger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomised, double-blind, placebo-controlled pilot clinical study. Part 3: Le Fort and zygomatic fractures in 94 patients. Br J Oral Maxillofac Surg. 2014;52:329–33. https://doi.org/10.1016/j.bjoms.2014.01.010.
24. Gaal A, Bailey B, Patel Y, Smiley N, Dodson T, Kim D, et al. Limiting antibiotics when managing mandible fractures may not increase infection risk. J Oral Maxillofac Surg. 2016;74:2008–18. https://doi.org/10.1016/j.joms.2016.05.019.
25. Campos GB, Lucena EE, da Silva JS, Gomes PP, Germano AR. Efficacy assessment of two antibiotic prophylaxis regimens in oral and maxillofacial trauma surgery: preliminary results. Int J Clin Exp Med. 2015;8:2846–52.
26. Habib AM, Wong AD, Schreiner GC, Satti KF, Riblet NB, Johnson HA, et al. Postoperative prophylactic antibiotics for facial fractures: a systematic review and meta-analysis. Laryngoscope. 2018. https://doi.org/10.1002/lary.27210.
27. Hammond D, Parmar S, Whitty J, McPhillips M, Wain R. Prescription of antibiotics: does it alter the outcome for patients who have fractures of the angle of the mandible? Br J Oral Maxillofac Surg. 2017;55:958– 61. https://doi.org/10.1016/j.bjoms.2017.09.015.
28. Perepa A, Sinha R, Agarwal A, Khan TA. Protocol for antibiotic administration in mandibular trauma: a prospective clinical trial. J Maxillofac Oral Surg. 2018;17:19–23. https://doi.org/10.1007/ s12663-016-0964-9.
29. Schaefer EHT, Caterson EJ. Antibiotic selection for open reduction internal fixation of mandible fractures. J Craniofac Surg. 2013;24:85–8. https://doi.org/10.1097/scs.0b013e318275ef21.
30. Adalarasan S, Mohan A, Pasupathy S. Prophylactic antibiotics in maxillofacial fractures: a requisite? J Craniofac Surg.2010;21:1009–11. https://doi.org/10.1097/SCS.0b013e3181e47d43.
31. Huang W, Lynham A, Wullschleger M. Orbitozygomatic fracture repairs: are antibiotics necessary? Craniomaxillofac Trauma Reconstr. 2015;8:271–6. https://doi.org/10.1055/s-0034-1399795.
32. Aznar ML, Schonmeyr B, Echaniz G, Nebeker L, Wendby L, Campbell A. Role of postoperative antimicrobials in cleft palate surgery: prospective, double-blind, randomized, placebo-controlled clinical study in India. Plast Reconstr Surg. 2015;136:59e– 66e. https://doi.org/10.1097/PRS.0000000000001324.
33. Rottgers SA, Camison L, Mai R, Shakir S, Grunwaldt L, Nowalk AJ, et al. Antibiotic use in primary palatoplasty: a survey of practice patterns, assessment of efficacy, and proposed guidelines for use. Plast Reconstr Surg. 2016;137:574–82. https://doi.org/10.1097/01.prs.0000475784.29575.d6.
34. Schonmeyr B, Wendby L, Campbell A. Early surgical complications after primary cleft lip repair: a report of 3108 consecutive cases. Cleft Palate Craniofac J. 2015;52:706– 10. https://doi.org/10.1597/14-158.
35. Zirk M, Kreppel M, Buller J, Pristup J, Peters F, Dreiseidler T, et al. The impact of surgical intervention and antibiotics on MRONJ stage II and III—retrospective study. J CranioMaxillofac Surg. 2017;45:1183–9. https://doi.org/10.1016/j.jcms.2017.05.027.
36. Hoefert S, Eufinger H. Relevance of a prolonged preoperative antibiotic regime in the treatment of bisphosphonate-related osteonecrosis of the jaw. J Oral Maxillofac Surg. 2011;69:362–80. https://doi.org/10.1016/j.joms.2010.06.200.
37. Koshkareva YA, Johnson JT. What is the perioperative antibiotic prophylaxis in adult oncologic head and neck surgery? Laryngoscope. 2014;124:1055– 6. https://doi.org/10.1002/lary.24226.
38. Kruse AL, Luebbers HT, Gratz KW, Obwegeser JA. Factors influencing survival of free-flap in reconstruction for cancer of the head and neck: a literature review. Microsurgery. 2010;30:242–8. https://doi.org/10.1002/micr.20758.
39. Russell MD, Goldberg AN. What is the evidence for use of antibiotic prophylaxis in clean-contaminated head and neck surgery? Laryngoscope. 2012;122:945–6. https://doi.org/10.1002/lary.22484.
40. Man LX, Beswick DM, Johnson JT. Antibiotic prophylaxis in uncontaminated neck dissection. Laryngoscope. 2011;121:1473–7. https://doi.org/10.1002/lary.21815.
41. Vila PM, Zenga J, Jackson RS. Antibiotic prophylaxis in cleancontaminated head and neck surgery: a systematic review and meta-analysis. Otolaryngol Head Neck Surg. 2017;157:580–8. https://doi.org/10.1177/0194599817712215.
42. Cannon RB, Houlton JJ, Mendez E, Futran ND.

Methods to reduce postoperative surgical site infections after head and neck oncology surgery. Lancet Oncol. 2017;18:e405–13. https://doi.org/10.1016/ s1470-2045(17)30375-3.

43. Bartella AK, Kamal M, Teichmann J, Kloss-Brandstatter A, Steiner T, Holzle F, et al. Prospective comparison of perioperative antibiotic management protocols in oncological head and neck surgery. J Cranio-maxillofac Surg. 2017;45:1078–82. https://doi.org/10.1016/j.jcms.2017.04.001.
44. Murphy J, Isaiah A, Dyalram D, Lubek JE. Surgical site infections in patients receiving osteomyocutaneous free flaps to the head and neck Does choice of antibiotic prophylaxis matter? J Oral Maxillofac Surg. 2017;75:2223–9. https://doi. org/10.1016/j.joms.2017.02.006.
45. Shkedy Y, Alkan U, Roman BR, Hilly O, Feinmesser R, Bachar G, et al. Role of perioperative antibiotic treatment in parotid gland surgery. Head Neck. 2016;38:E1876–80. https://doi. org/10.1002/hed.24339.
46. Rosengren H, Heal CF, Buttner PG. Effect of a single prophylactic preoperative oral antibiotic dose on surgical site infection following complex dermatological procedures on the nose and ear: a prospective, randomised, controlled, double-blinded trial. BMJ Open. 2018;8:e020213. https://doi.org/10.1136/bmjop en-2017-020213.
47. Lee JY, Do HS, Lim JH, Jang HS, Rim JS, Kwon JJ, et al. Correlation of antibiotic prophylaxis and difficulty of extraction with postoperative inflammatory complications in the lower third molar surgery. Br J Oral Maxillofac Surg. 2014;52:54–7. https://doi.org/10.1016/j.bjoms.2013.08.010.
48. Iglesias-Martin F, Garcia-Perla-Garcia A, Yanez-Vico R, AcedJimenez E, ArjonaGerveno E, Gonzalez-Padilla JD, et al. Comparative trial between the use of amoxicillin and amoxicillin clavulanate in the removal of third molars. Med Oral Patologia Oral y Cirugia Bucal. 2014;19:e612–5.
49. Arteagoitia I, Ramos E, Santamaria G, Barbier L, Alvarez J, Santamaria J. Amoxicillin/clavulanic acid 2000/125 mg to prevent complications due to infection following completely boneimpacted lower third molar removal: a clinical trial. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015;119:8–16. https://doi.org/10.1016/j.oooo.2014.08.014.
50. Bezerra TP, Studart-Soares EC, Scaparo HC, Pita-Neto IC, Batista SH, Fonteles CS. Prophylaxis versus placebo treatment for infective and inflammatory complications of surgical third molar removal: a split-mouth, double-blind, controlled, clinical trial with amoxicillin (500 mg). J Oral Maxillofac Surg. 2011;69:e333–9. https://doi.org/10.1016/j.joms.2011.03.055.
51. Xue P, Wang J, Wu B, Ma Y, Wu F, Hou R. Efficacy of antibiotic prophylaxis on postoperative inflammatory complications in Chinese patients having impacted mandibular third molars removed: a split-mouth, double-blind, self-controlled, clinical trial. Br J Oral Maxillofac Surg. 2015;53:416–20. https://doi. org/10.1016/j.bjoms.2015.02.001.
52. Pasupathy S, Alexander M. Antibiotic prophylaxis in third molar surgery. J Craniofac Surg. 2011;22:551–3. https://doi. org/10.1097/SCS.0b013e31820745c7.
53. Martin-Ares M, Barona-Dorado C, Martinez-Rodriguez N, Cortes-Breton-Brinkmann J, Sanz-Alonso J, Martinez-Gonzalez JM. Does the postoperative administration of antibiotics reduce the symptoms of lower third molar removal? A randomized double blind clinical study. J Clin Exp Dent. 2017;9:e1015–22. https://doi.org/10.4317/jced.54024.
54. Sayd S, Vyloppilli S, Kumar K, Subash P, Kumar N, Raseel S. 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;44:103–6. https:// doi.org/10.5125/jkaoms.2018.44.3.103.
55. Milani BA, Bauer HC, Sampaio-Filho H, Horliana AC, Perez FE, Tortamano IP, et al. Antibiotic therapy in fully impacted lower third molar surgery: randomized three-arm, double-blind, controlled trial. Oral Maxillofac Surg. 2015;19:341–6. https://doi. org/10.1007/s10006-015-0521-6.
56. Prajapati A, Prajapati A, Sathaye S. Benefits of not prescribing prophylactic antibiotics after third molar surgery. J Maxillofac Oral Surg. 2016;15:217–20. https://doi.org/10.1007/s12663-015-0814-1.
57. Reiland MD, Ettinger KS, Lohse CM, Viozzi CF. Does administration of oral versus intravenous antibiotics for third molar removal have an effect on the incidence of alveolar osteitis or postoperative surgical site infections? J Oral Maxillofac Surg. 2017;75:1801–8.

https://doi.org/10.1016/j.joms.2017.03.038.
58. Marghalani A. Antibiotic prophylaxis reduces infectious complications but increases adverse effects after third-molar extraction in healthy patients. J Am Dent Assoc. 2014;145:476–8. https:// doi.org/10.14219/jada.2013.51.
59. Isiordia-Espinoza MA, Aragon-Martinez OH, Martinez-Morales JF, Zapata-Morales JR. Risk of wound infection and safety profile of amoxicillin in healthy patients which required third molar surgery: a systematic review and meta-analysis. Br J Oral Maxillofac Surg. 2015;53:796–804. https://doi.org/10.1016/j.bjoms.2015.06.013.
60. Cho H, Lynham AJ, Hsu E. Postoperative interventions to reduce inflammatory complications after third molar surgery: review of the current evidence. Aust Dent J. 2017;62:412–9. https://doi. org/10.1111/adj.12526.
61. Arteagoitia MI, Barbier L, Santamaria J, Santamaria G, Ramos E. Efficacy of amoxicillin and amoxicillin/clavulanic acid in the prevention of infection and dry socket after third molar extraction. A systematic review and meta-analysis. Medicina Oral Patología Oral y Cirugia Bucal. 2016. https://doi.org/10.4317/medoral.21139.
62. Ramos E, Santamaria J, Santamaria G, Barbier L, Arteagoitia I. 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;122:403–25. https://doi.org/10.1016/j.oooo.2016.04.016.
63. Marcussen KB, Laulund AS, Jorgensen HL, Pinholt EM. A systematic review on effect of single-dose preoperative antibiotics at surgical osteotomy extraction of lower third molars. J Oral Maxillofac Surg. 2016;74:693–703. https://doi.org/10.1016/j.joms.2015.11.017.
64. Sidana S, Mistry Y, Gandevivala A, Motwani N. Evaluation of the need for antibiotic prophylaxis during routine intra-alveolar dental extractions in healthy patients: a randomized double-blind controlled trial. J Evid Based Dent Pract. 2017;17:184–9. https:// doi.org/10.1016/j.jebdp.2017.04.007.
65. Ata-Ali J, Ata-Ali F, Ata-Ali F. Do antibiotics decrease implant failure and postoperative infections? A systematic review and meta-analysis. Int J Oral Maxillofac Surg. 2014;43:68–74. https://doi.org/10.1016/j.ijom.2013.05.019.
66. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: antibiotics at dental implant placement to prevent complications. Cochrane Database Syst Rev. 2013;7:CD004152. https://doi.org/10.1002/14651858.cd004152.pub4.
67. Chrcanovic BR, Albrektsson T, Wennerberg A. Prophylactic antibiotic regimen and dental implant failure: a meta-analysis. J Oral Rehabil. 2014;41:941–56. https://doi.org/10.1111/joor.12211.
68. Lund B, Hultin M, Tranaeus S, Naimi-Akbar A, Klinge B. Complex systematic review—perioperative antibiotics in conjunction with dental implant placement. Clin Oral Implant Res. 2015;26:1–14. https://doi.org/10.1111/clr.12637.
69. Sharaf B, Jandali-Rifai M, Susarla SM, Dodson TB. Do perioperative antibiotics decrease implant failure? J Oral Maxillofac Surg. 2011;69:2345–50. https://doi.org/10.1016/j.joms.2011.02.095.
70. Nolan R, Kemmoona M, Polyzois I, Claffey N. The influence of prophylactic antibiotic administration on post-operative morbidity in dental implant surgery. A prospective double blind randomized controlled clinical trial. Clin Oral Implants Res. 2014;25:252–9. https://doi.org/10.1111/clr.12124.
71. Krasny M, Krasny K, Zadurska M, Fiedor P. Evaluation of treatment outcomes and clinical indications for antibiotic prophylaxis in patients undergoing implantation procedures. Adv Med Sci. 2016;61:113–6. https://doi.org/10.1016/j.advms.2015.10.005.
72. El-Kholey KE. Efficacy of two antibiotic regimens in the reduction of early dental implant failure: a pilot study. Int J Oral Maxillofac Surg. 2014;43:487–90. https://doi.org/10.1016/j.ijom.2013.09.013.
73. Park J, Tennant M, Walsh LJ, Kruger E. Is there a consensus on antibiotic usage for dental implant placement in healthy patients? Aust Dent J. 2018;63:25–33. https://doi.org/10.1111/adj.12535.
74. Arduino PG, Tirone F, Schiorlin E, Esposito M. Single preoperative dose of prophylactic amoxicillin versus a 2-day postoperative course in dental implant surgery: a two-centre randomized controlled trial. Eur J Oral Implantol. 2015;8:143–9.
75. Carcuac O, Derks J, Charalampakis G, Abrahamsson I, Wennstrom J, Berglundh T. Adjunctive systemic and local antimicrobial therapy in the surgical treatment of periimplantitis: a randomized controlled clinical

trial. J Dent Res. 2016;95:50–7. https://doi.org/10.1177/0022034515601961.
76. Hallstrom H, Persson GR, Lindgren S, Renvert S. Open flap debridement of peri-implantitis with or without adjunctive systemic antibiotics: a randomized clinical trial. J Clin Periodontol. 2017;44:1285–93. https://doi.org/10.1111/jcpe.12805.
77. Cachovan G, Boger RH, Giersdorf I, Hallier O, Streichert T, Haddad M, et al. Comparative efficacy and safety of moxifloxacin and clindamycin in the treatment of odontogenic abscesses and inflammatory infiltrates: a phase II, doubleblind, randomized trial. Antimicrob Agents Chemother. 2011;55:1142–7. https://doi.org/10.1128/AAC.01267-10.
78. Gomez-Arambula H, Hidalgo-Hurtado A, Rodriguez-Flores R, Gonzalez-Amaro AM, Garrocho-Rangel A, Pozos-Guillen 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:e634–9. https://doi.org/10.4317/jced.52627.
79. Bartella AK, Lemmen S, Burnic A, Kloss-Brandstatter A, Kamal M, Breisach T, et al. Influence of a strictly perioperative antibiotic prophylaxis vs a prolonged postoperative prophylaxis on surgical site infections in maxillofacial surgery. Infection. 2018;46:225–30. https://doi.org/10.1007/s15010-017-1110-4.
80. Knepil GJ, Loukota RA. Outcomes of prophylactic antibiotics following surgery for zygomatic bone fractures. J Cranio-maxillofac Surg. 2010;38:131–3. https://doi.org/10.1016/j.jcms.2009.03.015.