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

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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 only used 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.

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. Long-term 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 consensus-driven 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/sublactam 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 drug-related necrosis of the jaw. Here, ampicillin/sublactam 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 [7,42,44]. 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 adjuncive 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.

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