THEMATIC ABSTRACT REVIEW

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It's a Brave New World: How Should We Use Antibiotics?

Risk management of postoperative complications with dental implant placement and bone grafting procedures has long relied upon prophylactic antibiotics.^{1,2} Most reports have supported antibiotic use preoperatively but are still limited in defining a clear advantage for antibiotic coverage relative to the many potential confounding factors that may influence outcomes for infection or implant failure.³ More recently, two publications supported antibiotics as an important adjunct to implant therapy, but also questioned the benefits of clindamycin in limiting postoperative complications.^{4,5}

These findings remind us of the importance of considering both the goals of antibiotic therapy as well as the risks facing our patients. The goals of reduced surgical site infection and implant failure must be weighed against possible allergic reactions, as well as microbial resistance and dysbiosis. Antibiotic resistance was evaluated by Patini et al (2020) through a systematic review of the literature to evaluate the effects of different antibiotic regimens. With limited evidence, this study found that transient microbial antibiotic resistance may be a consequence of antibiotic therapy, even with shortterm use or with reduced dosages.

Klinge et al (2020) performed a complex systematic review to assess the benefits of prophylactic antibiotic use for implant therapy and bone grafting. This review concluded that the current evidence was limited, resulting in insufficient evidence available to guide this clinical decision. However, looking at two of the stronger studies identified, it appeared that clindamycin had a similar complication rate to that of amoxicillin, and the use of clindamycin as a single preoperative dosage or with a 24-hour postoperative regimen resulted in similar levels of postoperative infection.

Given these mixed outcomes, how do we use antibiotics? A recent survey of dentists in the UK (Williams, 2020) showed that 55% of respondents routinely prescribe antibiotics, while 13% never do so. The primary reasons cited for antibiotic prescriptions were to reduce the risk of postoperative infection and implant failure. Amoxicillin was the first choice, with metronidazole and erythromycin as primary alternatives for penicillin allergies. A similar survey in Spain (Salgado-Peralvo et al, 2021) also showed 55% of respondents routinely prescribing antibiotics, but with clindamycin being the most commonly used alternative for penicillin allergies.

Dominiak et al (2020) evaluated antimicrobial practices across four European countries and found that 54% of patients were given preoperative antibiotics, with > 80% of patients also given postoperative antibiotics. Importantly, this survey also considered the use of local antimicrobial agents, highlighting these otherwise underrepresented factors in this discussion. Bernabeu-Mira et al (2021) systematically evaluated studies covering nine countries across three continents and found that 77% of practitioners routinely prescribed antibiotics with implant placement, while 14% did not prescribe antibiotics prophylactically.

While these reports suggest similar patterns of antibiotic use, a four-country evaluation of prescribing patterns for dental practitioners from Australia, England, Canada, and the United States identified distinct usage patterns (Thompson et al, 2021). Dentists in the United States had the highest rate of prescribing, doubling that of Australia, which had the lowest prescribing rate. Amoxicillin was the most-used antibiotic in all four countries, while clindamycin was the second-mostprescribed antibiotic in the United States and Canada, and metronidazole was the second-most common in Australia and England.

It becomes clear that many questions remain as to the best approach to address our concerns with risk reduction for postoperative infections and implant failures relative to added risks for allergic reactions, microbial dysbiosis, and resistance. These questions include whether we should use antibiotics at all, the timing of the use, and which antibiotics we should use. Interestingly, there are different approaches among clinicians and distinct patterns of use in different countries. Further confounding our considerations, we do see a small subset of practitioners who do not use antibiotics. Fortunately, the rates of postoperative infection generally appear low, but they remain an important clinical consideration. Our conventional thinking certainly suggests antibiotics offer important benefits toward our postoperative outcomes, but as we expand our understanding of the risks of prophylactic antibiotics to including microbial dysbiosis and antibiotic resistance, as well as greater consideration

of the many factors influencing postsurgical outcomes, it will be critical to remain diligent in following the evidence as it unfolds. Will we be brave enough to follow the evidence?

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Patini R, Mangino G, Martellacci L, Quaranta G, Masucci L, Gallenzi P. The effect of different antibiotic regimens on bacterial resistance: A systematic review. Antibiotics (Basel) 2020;9:22.

Infections caused by resistant bacteria are a growing public health problem that is linked to many different causes; among them, the antibiotics' incorrect use plays an important role. According to the World Health Organization (WHO), the most dangerous behaviors are the early interruption of antibiotic therapy and the use of molecules without appropriate prescription. The authors conducted a systematic review to assess if antibiotic prescription with different regimens is connected to the onset of bacterial resistance. The authors performed an electronic and manual literature search on four databases (Web of Science, Scopus, PubMed, and Cochrane Register of Controlled Trials) from their inception to June 15, 2019. The date of the last search was November 27, 2019. Any article comparing cultural or genic analysis of resistance in patients who took antibiotics with at least two different regimens was included. No language restrictions were applied. Risk of bias for randomized controlled trials (RCTs) was assessed using the Cochrane collaboration's tool, whereas case-control and cohort studies were evaluated through the Newcastle-Ottawa scale. The initial search resulted in a total of 1,744 titles. After careful evaluation of all results, only three studies satisfied the outcome of the present review. From the qualitative analysis of data, it emerges that even if antibiotics are administered for a shorter period than the conventional one, the species that inhabit the oral cavity can adapt quickly and express genes of antibiotic resistance. Additional evidence from this analysis is that not only does the proportion of resistant bacteria increase in the oral cavity, but also in more distant districts such as the intestine. Despite the great number of studies retrieved by electronic databases, only few studies investigated the target of this review. The reason for this evidence is that it is not ethical to investigate and compare different antibiotic regimens that are shorter or longer than the appropriate one. This evidence is applicable both to prophylactic administrations and to those aimed at treating infections. Besides this, the WHO affirms that, in the absence of infective complications, the prescription of antibiotics after every type of surgical intervention cannot be admitted and studies dealing with antibiotic regimens that do not comply with the drug's pharmacodynamics characteristics cannot be ethically admitted.

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Klinge A, Khalil D, Klinge B, et al. Prophylactic antibiotics for staged bone augmentation in implant dentistry. Acta Odontol Scand 2020;78:64–73.

The objective of the study was to assess the effect of prophylactic antibiotics on the outcome of bone augmentation and subsequent dental implant placement by combining the recommended quality assessment methods for systematic reviews and primary studies. This is a complex systematic review in which systematic reviews as well as primary studies are scrutinized. A search of Medline (OVID), The Cochrane Library (Wiley), and Embase, PubMed, and Health technology assessment (HTA) organizations as well as a complementary hand search was carried out. Selected primary studies were assessed using GRADE. Each study was reviewed by three authors independently. Abstract screening yielded six potential systematic reviews allocated for full-text inspection. A total of 10 primary studies were read in full text. No relevant systematic reviews regarding the topic of this article were found. The quality assessment resulted in two primary studies with a moderate risk of bias. Of the two studies with a moderate risk of bias, one compared a single dose of clindamycin 600 mg preoperatively with the same preoperative dose followed by four doses of 300 mg every 6 hours. The second study compared a single-dose prophylaxis of two different types of antibiotic compounds. In conclusion, the scientific evidence regarding the use of antibiotic prophylaxis for reducing the risk of infection in conjunction with bone augmentation procedures during dental implant placement is very limited. The infection rate compared with nonusage of prophylactic antibiotics, selection of the most suitable compound, and the optimal duration of prophylactic treatment are still unknown.

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Williams R. Antibiotic prophylaxis during dental implant placement in the UK. Br Dent J 2020;229:787–792.

Antimicrobial resistance is a growing concern globally. It has previously been demonstrated that antibiotic prescribing for dental implants within the U.K. is varied, with an apparent lack of guidance. This study aimed to establish current use of antibiotic prophylaxis during dental implant placements in the U.K. An anonymous validated online questionnaire was distributed to members of BAOS, BSSPD, BSP, ADI, and ITI. Data were then collated and analyzed. Two hundred twenty-nine responses were received during April to July 2018. Fifty-five percent of dentists routinely prescribed antibiotics during implant placement. One-third sometimes prescribed antibiotics, but not routinely. Thirteen percent never prescribed. Reported protocols contained 61 different drug/dose combinations given over 124 different regimens. Those who prescribed routinely had significantly higher levels of training/qualification (P = .008), placed more implants (P = .014), and undertook more complex placements (P = .002) than nonprescribers. Seventy-three percent believed that antibiotics decrease postoperative infection. One in 10 felt they gave no benefit. Half believed they decrease implant failure. More than 90% would like national guidelines. Significant variance in practice is clear. Almost half of practitioners did not routinely prescribe. Those who did were significantly more experienced, were highly trained, and did more complex placements. There was a difference between practitioners' perceived benefits of antibiotic prophylaxis and the evidence in the literature. There was a great desire for clearer guidance.

Salgado-Peralvo AO, Kewalramani N, Peña-Cardelles JF, et al. Preventive antibiotic prescribing habits among professionals dedicated to oral implantology: An observational study. Antibiotics (Basel) 2021;10:301.

The prescription of preventive antibiotics in oral implantology is a controversial issue. This study aimed to determine the prescribing habits of preventive antibiotics in professionals dedicated to oral implantology in various treatments in healthy and at-risk patients. This is a cross-sectional observational study based on the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. An electronic survey consisting of four blocks of questions was sent to members of the Spanish Society of Implants. The data were analyzed using descriptive analysis. A total of 303 participants (20.8%) responded to the questionnaire. One percent never prescribed preventive antibiotics, 55.4% always prescribed them, and 43.6% sometimes prescribed them. Ninety-six percent administered them preoperatively, while 92.4% administered them postoperatively. The most commonly used antibiotic is amoxicillin followed by amoxicillin with clavulanic acid (875/125 mg). Clindamycin is the most commonly administered antibiotic in patients with allergies. Professionals dedicated to oral implantology frequently prescribe preventive antibiotics in both healthy and at-risk patients, especially perioperatively. Immediate implant placement, sinus elevations, bone regeneration, and multiple implant placement are the treatments in which preventive antibiotics are most commonly prescribed, as well as in patients with heart valve prostheses or a history of bacterial endocarditis and immunodeficiency.

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Dominiak M, Shuleva S, Silvestros S, Alcoforado G. A prospective observational study on perioperative use of antibacterial agents in implant surgery. Adv Clin Exp Med 2020;29:355–363.

Dental implant surgery has become routine practice for replacing missing teeth. Little is known about the use of local antisepsis to control the development of bacterial plaque and to facilitate healing, as current practice guidelines do not address this issue. The objectives of this study were to describe antiseptic practices for implant surgery and to assess plaque control at the operative site as well as the investigator's satisfaction. This prospective, observational study conducted in four European countries enrolled 911 adult patients receiving a single implant or multiple implants on the day of inclusion. Any medication prescribed during the preoperative or postoperative periods was documented, particularly antibiotics, antiseptic mouthwashes, and topical antiseptic gels. At a follow-up visit, the presence of plaque was documented on teeth adjacent to the implant and its extent determined using the Silness-Löe index. Oral antibiotics were prescribed prior to surgery in 53.8% of the patients. Antiseptic mouthwashes were prescribed to patients (49.6% to 65.7%) according to country. Following dental implant placement, 84.1% to 94.7% of patients were prescribed oral antibiotics, 45.6% to 86.5% of patients were prescribed antiseptic mouthwash, and 72.8% to 100% of patients were prescribed an antiseptic gel. At the follow-up visit, plaque was observed in 45.4% of the patients. The mean Silness-Löe Plaque Index was 0.7 or 0.8, indicating a low level of plaque accumulation. The Löe and Silness Gingival Index was 0.6 or 0.7, which is consistent with a low level of gingival inflammation. Use of antibiotics presurgery and postsurgery is frequent in implant surgery, despite it being discouraged in practice guidelines. Use of antiseptic mouthwashes and topical antiseptic gels is widespread, although treatment paradigms vary widely. Practice guidelines covering antisepsis provision would be useful, since those products could be used as an alternative to antibiotics to facilitate wound healing.

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Bernabeu-Mira JC, Peñarrocha-Diago M, Peñarrocha-Oltra D. Prescription of antibiotic prophylaxis for dental implant surgery in healthy patients: A systematic review of surveybased studies. Front Pharmacol 2021;11:588333.

Systemic antibiotic prophylaxis is frequently prescribed by dentists performing dental implant surgery to avoid premature implant failure and postoperative infections. The scientific literature suggests that a single preoperative dose suffices to reduce the risk of early dental implant failure in healthy patients. A systematic review was done based on an electronic literature search in the PubMed-Medline, Embase, Web of Science, Scopus, and Open Gray databases. The review addressed the question: "Which antibiotic prophylaxis regimens are being used in dental implant surgery in healthy patients according to survey-based studies?" The identification, screening, eligibility, and inclusion phases were conducted according to the PRISMA statement by two independent reviewers. The following data were collected: country, number of surveyed dentists, number of dentists who responded (n), response rate, routine prescription of antibiotic prophylactic treatment (yes, no, or conditioned prescription), prescription regimen (preoperative, perioperative, or postoperative), and antibiotic choice (first and second choice). Cohen's kappa coefficient (k) evaluated the level of agreement between the two reviewers. The analysis of risk of bias was performed following the Joanna Briggs Institute checklist for observational studies. A descriptive statistical analysis was performed to calculate total target sample, sample size, and total mean. A total of 159 articles were identified, of which 12 were included in the analysis. Two thousand seventy-seven dentists from nine different countries on three continents were surveyed. The median response rate was low and disparate between studies. About three-quarters of the surveyed dentists claimed to routinely prescribe systemic antibiotic prophylaxis for dental implant surgery. The prescription regimen was perioperative, postoperative, and preoperative, in

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decreasing order of frequency. The most frequent first-choice drug was amoxicillin, with amoxicillin-clavulanic acid as the second choice. A majority of dentists from different countries do not prescribe systemic antibiotic prophylaxis for dental implant surgery following the available scientific evidence and could be overprescribing. Efforts are needed by dental educators and professionals to reduce the gap between the use of antibiotic prophylaxis for dental implant surgery as supported by the scientific evidence and what is being done by clinicians in actual practice.

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Thompson W, Teoh L, Hubbard CC, et al. Patterns of dental antibiotic prescribing in 2017: Australia, England, United States, and British Columbia (Canada). Infect Control Hosp Epidemiol 2021:1–8. [Epub ahead of print]

The objective of this study was to compare patterns of dental antibiotic prescribing in Australia, England, and North America (United States and British Columbia, Canada). The study design was population-level analysis of antibiotic prescription. The setting was outpatient prescribing by dentists in 2017. The participants were patients receiving an antibiotic dispensed by an outpatient pharmacy. Prescription-based rates adjusted by population were compared overall and by antibiotic class.

Contingency tables assessed differences in the proportion of antibiotic class by country. In 2017, dentists in the United States had the highest antibiotic prescribing rate per 1,000 population, and Australia had the lowest rate. The penicillin class, particularly amoxicillin, was the most frequently prescribed for all countries. The second-most common agents prescribed were clindamycin in the United States and British Columbia (Canada) and metronidazole in Australia and England. Broad-spectrum agents, amoxicillin-clavulanic acid and azithromycin, were the highest in Australia and the United States, respectively. Extreme differences exist in antibiotics prescribed by dentists in Australia, England, the United States, and British Columbia. The United States had twice the antibiotic prescription rate of Australia, and the most frequently prescribed antibiotic in the U.S. was clindamycin. Significant opportunities exist for the global dental community to update their prescribing behavior relating to second-line agents for penicillin-allergic patients and to contribute to international efforts addressing antibiotic resistance. Patient safety improvements will result from optimizing dental antibiotic prescribing, especially for antibiotics associated with resistance (broad-spectrum agents) or C diffi*cile* (clindamycin). Dental antibiotic stewardship programs are urgently needed worldwide.

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MIS ANNOUNCES NEW DATES FOR ITS 5TH GLOBAL CONFERENCE

Following the long-awaited announcement on the new dates for the 5th MIS Global Conference, the MIS team is hard at work getting ready for Marrakech, Morocco, where the company will be hosting this next event.

As major global events were affected by the COVID-19 pandemic, which led to uncertainty and rescheduling, the conference is now planned for May 19–22, 2022, and will include a three-day scientific program of lectures by world-renowned experts, hands-on workshops, as well as exciting social celebrations.

World-class speakers and experts in their field

As in previous global conferences, the scientific committee is determined to present the most relevant and important topics and cases as part of the scientific program. Speakers have been carefully selected to bring forth new concepts, breakthroughs and a view into their vast collective experience and knowledge.

Exotic views and spellbinding entertainment

With a location such as Marrakech, conference guests can count on being met with a rich pallet of beautiful and colorful sights, exotic tastes and smells, and unique experiences that will never be forgotten. The meticulously planned and spectacular evening celebrations, which are a part of every MIS global conference, are sure to be part of this next, highly anticipated event.

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