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Antibiotic prophylaxis to prevent local infection in Oral Surgery: Use or abuse?

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Abstract

Antibiotics have a well-documented efficacy in the treatment of established infections and as prophylactic agents in medically compromised patients. However, the systematic administration of antibiotics to prevent local infections in fit patients is much more controversial. The aim of this paper is to reflect on the justification for prophylactic usage of antibiotics to prevent wound infection and to reason out the most appropriate antibiotic guidelines taking into account available scientific data and studies by other authors. Numerous clinical trials question the efficacy of antibiotics in preventing wound infection. While some studies establish that antibiotics reduce the incidence of postoperative infections, others compare their efficacy to that of placebo. Thus, scientific literature suggests that every oral surgical intervention is not tributary of systematic antibiotic prophylaxis to prevent local infections. Intrinsic surgical risk factors and the patient's individual circumstances must be taken into account. Even though the efficacy of other antibiotics cannot be ruled out due to our limited comprehension of the bacteriologic interrelations intervening in the pathogenesis of postextraction local infection, the amoxicillin-clavulanic acid combination theoretically covers the complete odontogenic bacterial spectrum in Spain. When the prophylactic use of antibiotics is indicated, this should be performed preoperatively, at high doses, and its extent should not exceed 24 hours. Special attention should be paid to antiinfectious local measures that can minimize infection risk during the wound's healing period.

Key words: *Antibiotic, prophylaxis, local infection.*

Introduction

"Antibiotic prophylaxis" is a broadly used term that can nevertheless cause misunderstanding due to its ambiguity. "Prevention using antibiotics" would be the most succinct definition. However, what is expected to be prevented? Prevention can be made for distant site infection as well as for surgical wound infection in the early postoperatory period. On the other hand, if antibiotic prophylaxis refers to prevention using an antimicrobial agent, various procedures can be understood with this term: A single preoperative antibiotic dose to prevent distant site infection (for instance, bacterial endocarditis) would be considered antibiotic prophylaxis, but so would the use of pre- or postoperative topic antiseptics or antibiotics to prevent local infection. Therefore, when referring to antibiotic prophylaxis, the process that is meant to be prevented and the strategy employed should always be specified. This review will focus on the administration of antibiotics to prevent postoperative wound infection.

Tooth extraction is probably the most frequently performed procedure in Oral Surgery practice. Hence, numerous bibliographic references related to technical aspects and possible complications are available. Among the latter, infectious complications outstand due to their clinical relevance. Antibiotic therapy to treat established infections or as a prophylactic strategy to prevent distant site infections in risk patients is a broadly accepted indication with documented efficacy. However, although tooth extraction could be considered clean-contaminated surgery and occasionally dirty surgery, the systematic employment of antibiotic prophylaxis in patients who are free from individual infectious risk factors is not scientifically justified and therefore controversial. The great variability in pharmacologic treatment guidelines among practitioners illustrates the lack of consensus on antibiotic antiinfectious prophylaxis even though it is routinely prescribed after third molar removal.

It seems evident that antibiotic prophylaxis guidelines for dentoalveolar surgery should be revised. In fact, this topic has been largely discussed within the scientific community in an attempt to reach consensus. In this sense, several reviews based on clinical trials questioning the value of antibiotics in the prevention of local infection have been elaborated. What's more, a Cochrane Review about antibiotic prophylaxis and third molar surgery is currently being carried out, based on the uncertain infection risk and frequency of this procedure (1).

Antibiotic use in medical fields (as well as in agriculture or stockbreeding) has been under inspection by sanitary authorities during the last decade. The need to reduce antibiotic abuse has been acknowledged. Rational use of antibiotics seeks to preserve antibiotic effectiveness against severe infections, reduce the emergence of bacterial resistance and minimize possible serious adverse reactions derived from antibiotic intake. Strategies to accomplish this aim comprise evidence-based critical analyses of antibiotic use in different clinical situations, improved prescription training for the medical staff, and measures to upgrade the population's educational level.

This work intends to analyze the justification of antibiotic prophylaxis in Oral Surgery and to establish antibiotic guidelines based on scientific data and previous studies elaborated by other authors.

When is antibiotic prophylaxis to prevent local infection indicated?

The main issue is: Which conditions should a surgical procedure comprise to make it tributary of antibiotic prophylaxis to avoid local infection? It seems obvious that any preoperative sign of active infection in the surgical field calls for effective therapeutic antibiotic doses. In these cases, antibiotic use is not prophylactic but rather therapeutic. However, when considering surgical fields that are apparently free from infection, antibiotic prescription becomes much more controversial.

The principles that every antibiotic prophylaxis should follow were classically defined by Peterson (2). Firstly, he established the local infection risk of any surgical procedure had to be greater than 10% in order to be tributary of antibiotic prophylaxis. The mainstream of authors agree that the infection risk after surgical removal of third molars is low (precisely between 1 and 6%), (3), being even lower when considering other teeth (4). However, some study groups have reported an infection risk of up to 45% (5). In our opinion, these important discrepancies in incidence numbers probably respond to inter-study methodological differences and inaccurate diagnoses of postoperative complications that erroneously label other processes (such as acute swelling secondary to surgical trauma or cicatrisation alterations as dry socket) as "local infections". These imprecisions complicate the real risk estimation of this process.

Another broadly accepted indication of antibiotic prophylaxis is any clinical situation with an inherently low infection risk but whose possible complications are potentially stern. A representative example of this circumstance is a total hip arthroplasty, where although the intrinsic infection risk is very low, a hypothetical infection could require leg amputation or even cause the patient's death. In the field of Oral Surgery, Indresano et al. (6) studied the dissemination of odontogenic infection to deep anatomic spaces. They proved that the amount of complications after mandibular third molar removal was minimal, highlighting that every infection dissemination case was preceded by an active pericoronaritis episode at surgery time; no infectious dissemination occurred when asymptomatic third molars were extracted. Besides, Arteagoitia et al. (7), who described a 12.9% incidence of postoperative infection incidence after mandibular third molar removal in the group without antibiotic prophylaxis, asserted that every case of infection was resolved with rescue antibiotics without further complications. Subsequently, potential postoperative infectious complications usually relate to teeth with previously underlying infectious pathology. Furthermore, even in cases where an infection arises after the extraction of an

asymptomatic tooth, it cannot be considered severe due to its minor clinical relevance and easy resolution; thus, routine antibiotic prophylaxis is probably unjustified.

Consequently, numerous recent clinical studies question the significance of antibiotic prophylaxis. While some state that prophylactic antibiotics can reduce the incidence of postoperative infection, others assure comparable results between the group receiving antibiotics and the placebo-controlled group. In this sense, Poeschl et al. (8) elaborated a prospective clinical study over 523 lower third molars assessing the prophylactic efficacy of the postoperative administration of clindamicin or a combination of amoxicillin and clavulanic acid against a control group who received no antibiotic treatment. They concluded the global surgical infection incidence was 3.9%, without any statistically significant differences between groups. In another study with similar features, Happonen et al. (9) affirmed that neither penicillin nor tinidazol had benefits over a placebo-controlled group in avoiding post-surgical local infection after inferior third molar removal. Sekhar et al. (10) completed a double blind randomized placebo-controlled clinical trial to compare the effectiveness of different metronidazol doses in the prevention of postoperative infection incidence after third molar removal; they found no benefits to justify pre- or postoperative antibiotic administration to reduce the risk of surgical wound infection.

However, other authors plead for the use of antibiotics but only in certain situations, not indiscriminately. After a thorough bibliographic review, Sands et al. (11) advocate for antibiotic prophylaxis in complicated cases, such as total osseous impaction. In a double blind randomized clinical trial comparing the efficacy of tinidazol versus placebo for the prevention of surgical wound infection following third molar removal, Mitchell et al. (5) detected an incidence reduction in the tinidazol group, nevertheless recommending to restrict antibiotic prophylaxis to deep intraosseous included molars. Similarly, a Spanish study (7) comparing the value of amoxicillin-clavulanic acid versus placebo in preventing postoperative wound infection concluded that the combination of 500 mg amoxicillin and 125 mg clavulanic acid was effective in reducing infectious complications, although it should not be prescribed routinely but rather when certain risk factors are present.

Classically, certain circumstances are recognized as infection risk factors. These include long-lasting surgical procedures, significant ostectomy degree, previous pericoronaritis episodes, placement of foreign bodies in the surgical wound (haemostatic materials or even sutures) and patients' immune or metabolic disruptions.

Benediksdottir et al. (12) evaluated the complications and secondary effects of 388 lower third molar removals in a prospective study and tried to identify risk factors for postoperative infection. They emphasized complete intraosseous molar inclusion and intraoperative inferior alveolar nerve visualization were related to a higher incidence of postoperative infection. Contrasting with other studies (13, 14), extended surgical time periods did not seem to be an indicator of postoperative complications. Similar opinions are defended by Monaco et al. (15), who underline that the operator's surgical experience has a greater weight in the outcome of the procedure than the actual time needed to perform surgery. In addition, they highlight tobacco use is directly related with the emergence of some postoperative complications such as fever and local pain. Likewise, Arteagoitia et al. (7) assert that the degree of molar inclusion, and therefore the access ostectomy necessary for extraction of the impacted tooth, is a risk factor for postoperative wound infection. Furthermore, they stress age as a major risk factor. Hence, while a 20-year-old patient has a 10% risk of postoperative infectious complications, a 40-year-old exceeds 30%. In a retrospective evaluation of 6,713 third molars, Piecuch et al. (16) assessed the relationship between third molar removal, local infection and antibiotic therapy and obtained a series of recommendations catalogued according to the nature of the surgical procedure. As a result of the low global infection rate in upper third molar extractions (0.27%), independently of the inclusion degree, these authors do not find antibiotic prophylaxis justified in these situations. Neither do they justify prophylaxis in erupted lower third molars. They only recommend antibiotic prophylaxis in partially or totally bony included lower third molars, declaring intraalveolar topic antibiotic therapy (tetracycline) more effective than systemic administration.

When defining a risk factor that is indisputably tributary of antibiotic prophylaxis, it seems the meeting point between authors is the existence of metabolic or immunologic diseases that reduce patients' defensive capacity. These circumstances include uncontrolled metabolic disorders (diabetes mellitus), congenital or acquired immunodeficiencies (agammaglobulinemia, HIV-AIDS infection) and immunosuppressant drugs (prolonged corticosteroid therapy, chemotherapics). Even in cases where surgical aggression is mild and wound contamination low, patients with severe immunitary compromise need antibiotic prophylaxis (2).

Which antibiotic should be prescribed to prevent local infection?

When the aforementioned infection risk factors are present and antibiotic prophylaxis is deemed necessary, drug selection as well as administration guidelines have to be strategic. Therefore, the decision to administer antibiotic prophylaxis should be based on the drug's coverage spectrum, its intrinsic activity against implicated bacteria, its capability to select resistant bacteria and hence its environmental impact, and tolerance degree and safety for the patient (17).

According to prevalence studies, the most prevalent microorganisms in the oral cavity are anaerobic bacteria. Therefore, it seems coherent that these bacteria are the main etiologic agents of the odontogenic infection (18). Studies assessing bacterial prevalence in odontogenic infection evidence slight

discrepancies in their results, possibly due to a deficient acquaintance with the pathogenesis of local infection and the flora's biologic complexity and dynamism. In some series, facultative anaerobic Gram-positive cocci continue being the most prevalent, with *Streptococcus viridans* as the protagonist; in others, strict anaerobic Gram-negative rods, primarily represented by *Porphyromona* and *Prevotella* spp. species, are predominant. Strict anaerobic Gram-positive cocci (*Peptostreptococcus* spp.) and other strict anaerobic Gram-negative anaerobic bacilli as the *Fusobacterium* spp can also be found in similar proportions.

Traditionally, β-lactamic antibiotics have been used as first-line therapy in odontogenic infections because of their bactericidal effect over etiologic microorganisms, low percentage of adverse reactions and relatively inexpensive price (19). Currently, while some authors (20) continue defending natural penicillins or aminopenicillins as first-line agents, others have published studies suggesting that their antimicrobial activity against some bacteria involved in the odontogenic infection is declining. Among these emergent resistant bacteria, two large groups are the most noticeable: 1) *Streptococcus viridians* group, due to modifications in penicillin-binding proteins (PBP), and 2) strict anaerobic Gram-negative rods such as *Porphyromona, Prevotella* and *Fusobacterium* species, as a result of an increasing β-lactamase synthesis capacity (19). Even though bacterial resistance caused by PBP modification can be overcome increasing the penicillin dose, that caused by β-lactamase production requires the addition of a drug that specifically inhibits these enzymes. Consequently, some authors currently consider the combination of a β-lactamic antibiotic with a β-lactamase inhibitor, such as amoxicillin plus clavulanic acid, an up-to-date first-line treatment option (21,22).

Nonetheless, other clinicians prefer other antibiotics as first-line agents to prevent local odontogenic infection. While clindamicine is popularly considered the alternative treatment option in penicillin-allergic patients (22,23), some doctors opt initially for this antibiotic to treat odontogenic infections in all patients. They latter justify their choice arguing that, besides its bactericidal power, clindamicine owes an elevated oral absorption, a notable tissue distribution (achieving high bone drug concentrations), as well as a low resistance rate. Other studies support the use of azitromicine as an alternative to penicillins, defending an antibiotic rotation protocol meant for controlling the emergence of bacterial resistances (24).

Plenty of works have studied bacterial resistances in Dentistry. However, we believe a rational selection of applicable studies is crucial in order to extract accurate conclusions. Selected studies should be based on designs that make them comparable to the population upon which preventive strategies are aimed. Therefore, in our case, relevant studies are those performed recently over the Spanish population. Among these, Brescó et al. (20) studied antibiotic susceptibility of bacteria involved in the odontogenic infection in its different stages (cellulitis, abscess, pericoronaritis, acute apical periodontitis). They concluded that 68% of the isolated stocks corresponded to facultative anaerobic Gram-positive cocci, 30% to strict anaerobic Gram-negative rods, and only 2% to facultative anaerobic Gram-positive rods. Independently of the odontogenic infection's origin, the authors stated that the best results with respect to high sensibility and low resistance rates were obtained with amoxicillin+clavulanic acid and amoxicillin, respectively. When studying bacterial resistance to different antibiotics prescribed routinely in Spain, Maestre et al. reported similar results (25). In this work, samples were obtained introducing sterile paper points in the periodontal sulcus with a probing depth greater than 4 mm. The study comprised adult patients diagnosed and treated for periodontal disease in the Complutense University Dental School of Madrid. They concluded that, while amoxicillin covers every isolated *Streptococcus viridians* stock, the resistance rate for different *Prevotella* species ranged from 17.1% to 26.3%. On the other hand, every isolated bacterium was sensible to the amoxicillin-clavulanic acid combination; clindamicin, conversely, presented a greater resistance rate than the aforementioned β-lactamic antibiotics for both the *Streptococcus* group (8.1-11.4%) and *Prevotella* spp. (9.1-21%).

In any case, although the antibiotic should theoretically be chosen considering the bacterial spectrum it is intended to cover, perhaps the optimal strategy is to simply break the established synergism between different bacteria, rather than to administer an antibiotic that fits every single possible bacteria type responsible for the infection (22). These synergisms could actually account for the success or the failure of an antibiotic treatment; with the destruction of a secondary bacteria type, the complex equilibrium established between microorganisms could be broken, even though the main etiologic bacteria type is inherently resistant to the prescribed antibiotic. Following this line of thought, given that several microorganisms intervene in the odontogenic infection in a chronological manner, the former favouring a proper microatmosphere for the latter, it seems logical to think that an effective antibiotic prophylaxis against the initiating bacteria (usually aerobic bacteria) could abort the progression of the infection. For this reason, in our opinion, more research is necessary to achieve a better understanding of bacterial interrelationships and to assess the suitability of different antibiotics in breaking synergisms and hence preventing local infection successfully.

Which administration guideline is best?

Although the fittest prophylactic modality in every surgery is probably the intravenous administration of an antibiotic bolus during anaesthetic induction, in regular dental practice antibiotics are prescribed orally and once the surgery is performed. This implies plasmatic drug levels start being therapeutic several hours after the surgery. This practice is contrary to the antibiotic prophylactic principles described by Peterson (2), which state that tissue antibiotic levels should be high during the surgery. In fact, multiple authors consider

the preoperative period the best moment to administer the antibiotic in order to significantly reduce surgical wound infection risk (26-28). Likewise, more than 50 years ago, Burke noticeably stated that the fittest antibiotic prophylaxis was achieved when the antibiotic was inside the tissues before the bacterial inoculum arrived (29). He also demonstrated that the administration of antibiotics three hours after the bacterial contamination had occurred had the same preventive effect over local infection as the absence of antibiotic treatment.

Regarding the duration of antibiotic prophylaxis, this should be as short as possible as long as it is effective. When administering the antibiotic orally, a single preoperatory dose is enough. If the surgical intervention extends in time or tissue damage is considerable, another antibiotic dose can be administered at the equator of its therapeutic interval; in other words, in the case of an antibiotic administered every 8 hours, such as amoxicillin, the second dose should be administered 4 hours after the surgical intervention has concluded (2,21). According to classic studies concerning surgery, antibiotic prophylaxis should not exceed 24 hours; an extended administration does not reduce infection rate, increases the risk of adverse pharmacologic reactions and promotes the emergence of bacterial resistances (2,27-29). Nevertheless, more specific studies attending the oral cavity should be performed to ascertain these statements.

Other considerations

Besides systemic antibiotic administration, other local antiinfectious measures play an important role, perhaps imperative, in the prevention of surgical would infection. These include an aseptic surgical technique, local applications of antiseptics such as clorhexidine in its different presentations (pre- or postoperative rinses, gel application over the surgical wound) (30), proper wound hygiene by means of effective brushing and/or irrigator employment in order to mechanically remove microorganisms, etc. In this way, local bacterial population is reduced, minimizing the incidence of surgical wound infection during the healing period.

Conclusions

The following conclusions can be derived from the analysis of the studied bibliography:

1. The indications of antibiotic prophylaxis in Oral Surgery have not yet clearly been established on the basis of scientific evidence. More studies are needed to this effect.
2. Not every procedure in Oral Surgery is tributary of antibiotic prophylaxis. The presence of several risk factors needs to be assessed. These factors include intrinsic features of the surgical technique employed (for instance, ostectomy degree) and specific characteristics of each patient (age, tobacco use, diseases and their repercussion on the patient's immune system).
3. The amoxicillin-clavulanic acid combination theoretically covers the entire bacterial spectrum of the odontogenic infection in Spain. However, the lack of knowledge about the pathogenesis and bacterial interrelationships leading to postextraction local infection does not permit the ruling out of the value of other antibiotics.
4. When antibiotic prophylaxis is indicated, a high-dose preoperatory administration should be prescribed, and its duration should not exceed the first 24 postoperative hours.
5. Special attention should be payed to other local antiinfectious measures that reduce surgical wound infection risk while the cicatrisation period lasts.

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