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Use of Prophylactic Antibiotic Therapy in Oral Surgical Procedures: A Critical Review

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ABSTRACT Despite myriad evidence-based data on the efficacy of prophylactic antibiotics in oral surgical procedures, their inaccurate use and indiscriminate abuse still continues in all clinical settings. Although controversy remains, clear-cut guidelines relying on established scientific principles do exist and must be followed. This paper provides a critical and systematic review of each principle and encourages practitioners fit to what current evidence demands.

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A great number of ambulatory minor oral surgery procedures are practiced everyday in many outpatient clinical facilities by specialists, as well as residents and general dental practitioners. Oral surgery has been usually classified as class 2 or clean-contaminated surgery (that is endogenous flora organisms are present) by some authors, thus enclosing a low percentage of infection possibility.[1-5]

For many centuries the true interest of investigators was focused on surgical wound infections prevention. The development of this topic started in 1847 when Ignacz Semmelweis inferred the power of unclean hands, instruments, and drapes, employed by obstetricians, in the transmission of puerperal fever lethal agents. This induced the introduction of a strict prophylactic surgical antisepsis protocol, which involved the scrubbing of hands and immersing the instruments in chlorine solutions.[6] Twenty years later, in 1867, Sir Joseph Lister associated airborne germs with surgical infections. He sprayed carbolic acid in the operating room and instilled it into different surgical wounds, giving a great step toward modern asepsis practices in the operating room.[6,7]

In 1876, Robert Koch demonstrated the pathogenicity of bacteria and by 1878 Louis Pasteur recognized the importance of microorganisms' presence on all different surfaces coming in direct contact with the operative field.[5] His observations led into the adoption of asepsis as a technique.[7] It passed less than a century after these authors' amazing inductions for recognizing the real role of microscopic living germs in surgical infections.

Over the years, the circumstances of time — war times — showed the way to significant advances regarding principles to treat and prevent infections. Within a few years, the value and success of chemotherapy was entirely verified and the discovery of different antibacterial agents set the basis for using antibiotics in either therapeutic or prophylactic fashion.[7,8]

Contemporary Development

Since the late 1940s, when introduced, prophylactic antibiotic therapy, PAT, was overused, disproportionate, and imprecise, creating controversy about its effectiveness.[2,8,9] Many early studies showed no benefit, higher infection rate and emergence of microorganism-resistant infections related with such prophylaxis.[6,10-14]

The pathway to the understanding and subsequent establishment of actual prophylaxis principles did begin to be defined with the studies of Miles about the relationship of host defense mechanisms and bacterial lodgment.[15] It would get consolidated in the early 1960s with Burke's work. He described the decisive period during a bacterial invasion and demonstrated the importance of antibiotic administration timing in order to be prophylactically effective.[13-18] Burke's findings were later confirmed by other authors and in clinical practice.[19-44] These studies throw light on definitive and current principles to approach antibiotic prophylaxis in surgery, including oral surgery.

Concerned about identifying and treating patients at high risk of postoperative surgical wound infections, Altemeier was the first in suggesting some criteria for the prophylactic use of antibiotics and developed a classification of surgical wounds in relation to its degree of contamination. They were divided in four classes as: clean, clean-contaminated, contaminated, and dirty.[7,45,46] In 1964, the National Academy of Sciences-National Research Council Study (NRC) defined this classification. Clean-contaminated surgery was defined as a nonelective surgery that is otherwise a clean, controlled opening of a normally colonized body cavity; no significant spillage and/or minor break in sterile technique, reoperation via clean incision within seven days; blunt trauma, intact skin, negative exploration through intact skin.[4,6,47-50] Regarding the probability of predicting wound infection, this approach was very simple and practical, actually, it still continues to be useful, but unfortunately it depends only on one variable, which is the bacterial contamination.

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In 1977, Cruse and Foord in their large 10-year prospective study established the infection rate for each class (clean 1.5 percent, clean-contaminated 7.7 percent, contaminated 15.2 percent, and dirty 40 percent). Oral surgery procedures were not included in this interesting study.[49,51]

The understanding about surgical wound infections would progress. Probes concerning the importance of finding other risk variables conducted Ehrenkranz in 1981 to identify and correlate some patients' factors (remote infection, diabetes mellitus and/or operations lasting more than four hours) in clean operations with high risk of infection.[52] Similarly in 1985, Haley and colleagues in the study of the efficacy of nosocomial infection control, SENIC, identified three independent risk factors — operations on the abdomen or chest, operations lasting beyond two hours and patient clinical status (at least three medical diagnoses on discharge) — in addition to wound class, for postoperative wound infections. In this study the infection rate for each wound class was: clean 2.9 percent; clean-contaminated 3.9 percent; contaminated 8.5 percent; and dirty 12.6 percent.[53]

In 1991, after the work of Haley and colleagues, the National Nosocomial Infection Surveillance, NNIS, study reduced the four risk factors to three: wound class, length of the surgery and patients with American Society of Anesthesiologists, ASA, scores of III to V. In this study, infection rates were reported to be: clean 2.1 percent; clean-contaminated 3.3 percent; contaminated 6.4 percent; and dirty 7.1 percent.[54]

As in the Cruse and Foord study, neither the SENIC study nor NNIS included oral surgery procedures. These two assessments, SENIC and NNIS, showed to be appropriated as a guide for antibiotic prophylaxis since they do integrate the determinant factors — surgical wound class, presence of bacteria, procedure duration and host defenses — which are required for the development of an infection.[55-58]

However, neither SENIC scheme nor NNIS incorporate many other known risk factors affecting wound healing, which could be additional predictors of host susceptibility, like alcoholism, obesity, smoking, advanced age, tissue perfusion, glucose control, poor nutrition, corticosteroid use, medication, previous radiotherapy or chemotherapy and anemia that either may or may not be alterable before surgery.[50,59-81] Among others, all of these independent variables are frequently hard to check and to be adapted into a controllable risk scheme.

In 1992 the Centers for Disease Control and Prevention established some guidelines, described a classification of surgical infections and standardized some definitions. The term surgical wound infection was changed for surgical site infection, SSI, to include superficial, deep wound, and organ space infections, such as those arising from bone. Besides making the distinction between an infection of a surgical incision and one of a traumatic wound, this will allow more effective surveillance, prevention and control of SSI.[82]

Subsequently in 1999, the CDC Hospital Infection Control Practices Advisory Committee published a set of recommendations for the prevention of SSI. Specific guidelines regarding preoperative antimicrobial prophylaxis are included.[83]

Principles: State of the Art

Five evidence-based basic principles must be accurately understood and followed to warrant PAT effectiveness. The first and most essential principle of PAT is to understand the difference between "to prevent" and "to treat." The purpose of prophylactic antibiotics is to help prevent infections, while therapeutic antibiotics actually treat ongoing infections. Perhaps the local chaotic state of antibiotic use arises in the misconception of this elementary statement, since many practitioners in the clinical scenario deliberately, and wrongly, insist on approaching every situation through a "therapeutic" perspective.

The surgical procedure should have an increased risk of infection.[2] This second principle is in relation with the variables that have proven to be reliable predictors of SSI risk, the intrinsic degree of microbial contamination of the surgical site, duration of the operation and markers for host susceptibility, so that it implicates using an agent for operations or classes of operations in which its use has been shown to reduce SSI rates based on evidence from clinical trials or for those operations where incisional or organ/space SSI would have a catastrophic outcome.[83]

TRYING TO ALWAYS apply a PAT scheme in oral surgery by approaching the "expected" SSI rates based only on wound class is inaccurate.

Oral surgery has been classified as class 2. For this type of surgery current literature suggests an estimated infection rate of 5 percent to 15 percent, but this percentage is far from being a realistic cipher expected for procedures that involve practicing intraoral wounds.[1-5,84] It actually represents the erroneous and simplistic extrapolation of some results, the majority arising from trials which include different procedures from other surgical specialties. It is not a correct reasoning, from any standpoint, to assume an appendectomy, hysterectomy, cholecystectomy, or nephrectomy resemble multiple exodontias, impacted third molars, dental implants, or dentoalveolar surgery. Therefore, trying to always apply a PAT scheme in oral surgery by approaching the "expected" SSI rates based only on wound class is inaccurate.

Another variable that has been associated with SSI risk and postoperative morbidity is the length of operation.[51,53,54,85-87] A prolonged operative time (longer than either two hours or the approximate 75th percentile of the duration of the "specific" procedure being performed) has an increased risk of infection because it augments the likelihood of normal wound contamination, what could lead up to bacterial dissemination inside and from the surgical wound. Although this correlation has been found to be positive, specifically in the oral and maxillofacial field, it has not been verified so far.

Unfortunately, the surgical schemes and scenarios applied as evidence for this have been also completely different. Besides, T times for oral surgery procedures have not been established. After how long can a particular oral surgery procedure be designated as prolonged? Possessing this evidence-based information as reference would be of great asset to our professional community, in which myriad of practitioners (general, residents, and specialists) perform oral surgery. However, the surgical exposition time and transient bacteraemia provoked by intraoral invasive procedures could play a key role in this aspect, given that the occurrence of bacteraemia increases with the duration of operation, and there appears to be a direct relationship between its incidence and magnitude and the extent of underlying oral inflammation and infection.[88,89] This conceptualization would be of relevancy depending on which hands are holding "the knife."

A large longitudinal, prospective and controlled surveillance trial to determine the actual incidence of SSI (percent) in oral and maxillofacial surgery commonly performed operative procedures, ranging from "minor" dental to "major" head and neck surgery, regarding both former variables is mandatory.

The other variable proven to be a

dependable predictor of SSI risk is host susceptibility. Besides surgical or environmental factors, host susceptibility can also be influenced by significant local and systemic factors which can compromise the host defense mechanisms response.[4,21,50,60,83,84,90,91] Under regular physiological and immunological conditions, PAT would not be necessary, except when the procedure per se entails some evidence-based risk, because a patient's immune system is able to deal with the surgical site microbial contamination and the high transient bacteraemia elicited by the invasive procedure.[88,92,93]

In susceptible or at-risk patients who present a significant underlying medical condition affecting their host defense status, such as immunocompromising situations/disease or metabolic disorders, PAT should always be considered, not only in oral surgery but also in class I or clean surgical procedures. Such being the case, the clinicians' rational judgment is decisive to avoid a ruinous outcome.

Select the correct antibiotic for the surgical procedure.[2] This principle emphasizes using an agent that is safe, inexpensive, and bactericidal with an in vitro spectrum that covers the most probable intraoperative contaminants for the operation.[83]

In spite of the more than 300 to 700 species of microorganisms coexisting in the healthy human oral cavity, when performing intraoral surgical procedures the most commonly encountered and likely infecting pathogens are primarily facultative streptococci (e.g., *viridians* group species, such as *S. mutans, S. salivarius, S. anginosus, S. sanguinis* and *S. mitis*), anaerobic gram-positive cocci (e.g., *peptostreptococci* species) and anaerobic gram-negative rods (e.g., *prevotella* and *porphyromonas* species, *fusobacterium* species).[94,95] Therefore, any PAT attempt should be aimed toward this limited group of potential endogenous pathogens and be based on their susceptibility to specific antibiotics. The agents that fulfill aforementioned requirements and still considered to be effective and suitable for this purpose are penicillins.

In spite of some evidence that indicates a tendency of bacteria to become more resistant to penicillins, globally marked differences in resistance levels do exist. By inducing and synthesizing inactivating and neutralizing enzymes, these agents, either alone or combined with a ß-lactamase inhibitor, continue to be the first choice in oral surgery.[96,97-117] In cases of true penicillin allergic patients clindamycin is the best alternative.[118-120]

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Antibiotic level and administration.[2] This principle implies to time the initial dose of antibiotic so that a high, bactericidal concentration of the drug is established in serum and tissues by the time the mucosa is incised.[41,83]

Beyond selecting the antibiotic, there are other important choices to take care about. These are, how much and when should it be administered?

To guarantee the success of PAT, the chosen agent should be given minimum at twice the therapeutic dose, so that levels in plasma and tissues are sufficiently high and available during the incision, the whole intraoperative and early postoperative periods to prevent contamination of the surgical site.

On the other hand, timing of initial administration is crucial.[16,41,121] To achieve the maximum effectiveness, the antibiotic must be administered parenterally within 30 minutes before the incision. Oral administration is also a valid and effective regimen. In this instance, it must be given one hour before the intervention.[122-125] Both of these preoperative schemes are optimal, therefore there is no rationale for beginning administration of PAT more than one hour preoperative so neither the day nor night before. Intraoperative and postoperative administrations are suboptimal and not good at all, hence they cannot be advisable in elective surgery.

Use the shortest effective antibiotic exposure.[2] This principle relates to maintain therapeutic levels of the antibiotic in both serum and tissues throughout the operation and until, at most, a few hours after the incision is closed in the operating room.[43,83,126] It encloses the question, for how long should PAT be administered?

It is well understood and established today that PAT should finish when the last suture is placed to close the incision. Extending antibiotic administration beyond 24 hours or longer after surgery is neither necessary nor prudent. First, this conduct does not have impact on the infection risk, and second, it confers additional risks without any benefits.[127] Of great concern when routinely prescribing improperly a therapeutic modality of antibiotics, supposedly as prophylaxis, are the likelihood of an adverse medication reaction and the widespread emergence of resistant organisms.[126,128,129]

In short procedures, a single dose or one shot of antibiotic preoperatively are enough to set proper serum and tissue concentrations before contamination occurs. During long operations or when its duration exceeds the expected time, an extra intraoperative dose should be given. The timing of an additional dose of any antibiotic depends on its pharmacokinetics, for penicillins, specifically in its half-life.[96]

A supplementary principle, added by Laskin, would emphasize not to rely solely on PAT to prevent postoperative SSI.[130]

The value and effectiveness of PAT has been widely proven. Besides this stratagem, there are, among others, two critical factors influencing prevention and reduction of postoperative SSI, which are: aseptic operation technique and proper soft and hard tissue handling. Sources of alarm are those practitioners who, in many dental office settings with a limited bacterial control environment and are unskilled, want to compensate the deficiencies in both the aseptic-antiseptic ritual and proper surgical technique by prescribing antibiotics. The utopical idea of the more one gives antibiotics the more one protects the patient sounds very attractive, but it is unwise and mistaken.

Outpatient Oral Surgery Procedures

Hundreds of oral surgical procedures on an outpatient basis are performed every day in our local community. Uncomplicated tooth extractions and dentoalveolar surgery are among the most frequently practiced.

A great subject of controversy has to do with impacted third molar surgery. Some authors claim routine PAT is effective and of some benefit, while others do not recommend it. These two contrasting positions are well represented in current literature.[131-140] However, with regard to the available evidence, the lack of consensus can be partially explained. First, by the fact that in some clinical trials, unreliable outcome variables, such as alveolar osteitis, pain, swelling, trismus, and clinical recovery, have been used by mistake as indicators of SSI.[141-154] Second, antibiotics are frequently given after surgery as a prophylactic measure against SSI.[155-158] These reasons do imply methodological limitations and violation of PAT principle No. 4.

Dentoalveolar procedures, including third molar surgery, have both a so very low infection rate and rarely severe adverse consequences.[131,132,159] Therefore, in healthy patients, any PAT is not required. In those cases where PAT needs to be considered,

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because of a patient's comorbidities or pre-existing conditions, a single, high preoperative dose should be given.[157,159]

Another controversial issue has to do with the use of PAT when practicing dental implants placement surgery. Viewed in this light, some studies have tried to elucidate the relationship between antibiotics and implant survival/failures instead of true SSI.[3,160,161] Many do share similarities as to the matter of their study design weaknesses, once again by virtue of the methodological limitations or because they deviate from PAT principles.[162,163]

Anyway, results vary and coming to a consensus has been a tough sell.[164] Nevertheless, the current evidence neither recommend nor advise against the use of PAT to prevent SSI when placing dental implants.[165] Thereby, a sound clinical judgment is paramount and the recommendation would be to adhere strictly to PAT principles whenever patients present formerly mentioned risk factors.

Other procedures involving incisions within the oral cavity with manipulation of either soft or hard tissues, as well as those requiring either only or combined transoral and extraoral approaches — orthognathic, reconstructive and trauma surgery — must be subject to application of PAT principles.

Facing up to Future Challenges

Apparently, everything points to the fact that there is a lack of knowledge among most clinicians concerning prophylactic antibiotics prescription. The common belief and iterative idea "The more antibiotics I give to my patient, the more I protect them" is at the present unjustifiable. We are contributing to magnify day by day, the existing chaotic state around these agents by ignoring the current evidence and adopting this harmful behavior, which has poor scientific basis.

Notwithstanding, they are a wonderful and life-saving tool and causes of great concern to all because of the widespread overuse, must be the adverse consequences — the superinfections and the development of resistant strains they are producing.[166-168]

Down the years, the motivation to use this practice has been unclear. Long-standing habit and tradition have played key roles. Whatever it is, we have in each of our hands the obligation of changing this mindset from now on. The evidence and facilities for are available to undertake such mission. ■■■■

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