Medical Dental Prophylaxis of Endocarditis

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Antibiotics have long been the main reason for the increase in man's longevity. Since their discovery, man has tried to reduce the level of infection by treating with antibiotics. At the same time, prophylactic use has been suggested, although this is controversial. Their routine use is not recommended, and empirical treatments at non-therapeutic doses, and indiscriminately, should be avoided, because they may become dangerous and harmful, causing among other things, the prevalence of resistant microorganisms and the eventual potentiation of an increase in morbid states. Infectious endocarditis is a systemic pathology that can start with a bacteremia, which comes either from dental procedures or/and chronic processes that already existed. Its etiopathogeny consists of a combination of bacteremia and two other factors: Cardiac injury, which can be congenital or/and acquired, and a debilitated immunological system (patients who have transplanted organs, or those who have auto-immune diseases, such as pemphigus vulgaris, systemic lupus erythematosus). The main goal is to prevent or to fight against the transient bacteremia, reducing its intensity and duration, and also to kill the bacteria in at-risk patients. In this way, infectious endocarditis can be prevented; the dental surgeon plays an important role in the prevention of this condition, which joins medical and dental aspects. This can be done by antibiotic prophylaxis. The dentist needs to be acquainted with the medical protocols of the heart health societies.

Key Words: Endocarditis, prophylaxis.

Infectious endocarditis is an uncommon cardiopathy, with a high rate of morbidity, being fatal when not diagnosed and treated in time. Several causes have been indicated as predisposing and/or triggering agents, among them dental procedures. Nowadays the negative impact that buccal infection can have on systemic health is known to be due to the resultant bacteremia. This bacteremia is the entrance point for microorganisms or their products into the blood stream. However, there are other factors that contribute, such as: congenital cardiopathy, a deficient immune system and/or poor buccal hygiene.

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There are some ways of avoiding, or at least easing this impact. One of these ways would be antibiotic prophylaxis. The prophylactic use of antibiotics avoids its presurgical use, before the occurrence of bacteremia.

Antibiotic prophylaxis, however, has been controversial and polemic. We must not make antibiotics a panacea, thinking that they will solve the problem, and consequently forget about means of prevention, such as the maintenance of biosafety, which, when correctly used, can reduce the occurrence of contamination and infection. Correct preventive use of antibiotics demands great pharmacological knowledge of the drugs that will be used, because if correctly used these drugs will be effective, but if not, there can be a increase in the patient's morbid status, without any benefit.

In the specific case of infectious endocarditis, we find that there is a great deal of difficulty (even greater than

for other conditions) to choose the right preventive medicine, because there's a great range of etiological agents; there is also a possibility of an incorrect diagnosis, due to the similarity of other pathologies.

Several rules for the application of antimicrobial medicines have appeared over time, and they have been used according to the evolution of research in period. Nowadays, studies such as that of Wippel [1] show that the application of antimicrobial agents has definite rules and can be accomplished with precision.

The professional has to keep in mind that the prophylactic procedure does not redeem him of any kind of responsibility towards the patient and that endocarditis can appear despite the use of good prophylaxis. It is not possible to always foresee the infectious process.

The literature relates that most patients who were thought to have some kind of disease, either did not have it or were afraid of telling it to the professional, and omitted the information. Most of them do not know how dangerous their morbid status may be, nor are they aware of the consequences of this omission. The patient's cooperation is necessary for the success of the adopted propaedeutic; that is why the professional should always keep his patient abreast of what is happening, because, when the patient is included as "part of the team", he becomes co-responsible for the success of the treatment.

The interchange between health professionals and, at the same time, between professionals and patients, facilitating the desired interchange of information, creates a channel of communication that will make the choice of the best procedure and prophylactic medicine for the patient's condition possible.

Literature Review

The great frequency of infection after dental treatment, with infectious endocarditis being one of theses clinical conditions, associated with important morbidity and high lethality, is well known; Bear [2], Sonis [3], Passeri [4], Dajani [5], Durack [6] have indicated that antibiotics should be used to prevent post-dental procedure infections.

Endocarditis is an infectious process that affects the endocardium, not only in normal hearts, but also in those that may have some kind of disease that can come from a bacteremia in the buccal cavity [7]. This bacteremia occurs spontaneously way, in daily processes, such as chewing and brushing the teeth. It is therefore transitory, and rarely lasts more than 15 minutes [8]. The risk of this kind of bacteremia seems to depend on two points: the extension of the traumatism of the soft tissue and the degree of preexistent inflammatory disease [3]. The microorganisms take advantage of the break in the skin mucosal anatomic barriers to break into the deeper tissues and reach the blood stream and, by doing so, also get to more distant places in the organism [9]. Bacteremia may occur in any process that provokes bleeding. The bacteria transported by the blood can accommodate themselves in injured heart valves in the endocardium or in the endothelium, near congenital defects [10].

Consequently, bacteremia commonly occurs with the manipulation of infected tissues, and also in traumatic procedures, being eliminated by the defense mechanism of the host. But when the microorganisms reach the circulation in large enough numbers and remain there for appropriated time, the endocarditis may install itself [11].

So, the role of bacteremia in the aetiopathogeny of infectious endocarditis systemic disease, which involve medical and odontological aspects, is known and it can be prevented. The participation of the dental surgeon in this prevention is extremely important. The primordial goal is to avoid or fight against transient bacteremia in susceptible individuals [12].

Quintiliani & Maderazo [13], Amato Neto & Pasternak [14], and Fonseca [15] indicated that in the prescription of an antibiotic, the professional must take some factors into account, such as: the type of infection, the antimicrobial, the conditions of the host and the cost. The professional should also be informed about microbiology, and the bacterial pattern of susceptibility to the antibiotics in the oropharynx, as well as phamacokinetics, in order to select and prescribe the best medication.

Although, as indicated by Wippel [1] and Tong & Rothwell [16], the application of antibiotics in empirical

form, in non therapeutic doses and indiscriminately, should be avoided, since it has little or no scientific base in prophylactic odontology, becoming a dangerous and harmful act, causing among other effects the favoring of resistant bacteria, Sonis [3], Gonçalves [17] agreed that due to the great arsenal of antimicrobial drugs in use, as well as the great number of etiologic agents, in each specific case, the choice becomes very difficult, so the prevention of the infectious endocarditis becomes controversial and empirical.

While Lavelle [18] indicated a few studies that proved the effectiveness of the antibiotics in the prophylaxis of infectious endocarditis, Rahn [19] and Durack [6] showed that although we could not prevent transient bacteremia and that there was no evidence that antibiotics can effectively prevent infectious endocarditis in human beings, they found clear signs that antibiotic treatment could decrease bacteremia and that they could prevent infectious endocarditis in animals.

Santos & Marangoni [20] indicated that that the objective of prophylaxis in surgery is to minimize the quantity of pathogens at the injury, not aiming at prevention and post surgical complications distant from the operated area, even if related to the surgery or an associated bacteremia. However, though it is not the objective, prophylaxis can probably decrease the occurrence of these infections. Consequently, they agree with Sonis [3]: "although there isn't direct evidence that the prophylaxis with antibiotics is capable in the prevention of infectious endocarditis there's adequate evidence that it decreases the incidence of bacteremia."

Lavelle [18] mentioned that failures in prophylaxis have already been demonstrated and related them to an increase in the resistance to beta-lactam and also to other antibiotics. Roberts [21] alerted that not all the failures gave rise to infectious endocarditis. Soares [22] related the occurrence of cases of infectious endocarditis, even with etiological agents sensitive to the antibiotic that was used, while Howe [23] indicated that the parenteral regime can be counterproductive, causing failure in the prophylaxis, as the patients could deliberately omit information, in an attempt to avoid intravenous medicine.

Cortezzi & Ferreira [24], Venugopalan & Worthing [25], Abrahão [26] agreed that the recommendations for antibiotic coverage reflect the analysis of literature correct to this procedure, including *in vitro* data about the sensitivity of the pathogen, which probably causes infectious endocarditis, studies making use of experimental models in animals and retrospective analysis of cases of human endocarditis in terms of prophylactic antibiotic therapy and its apparent effectiveness.

Howe [23] advocated that the total prevention of infectious endocarditis, associated with dental procedures is an impossibility. Describing buccal infections, Cortezzi [27] and Willet & Crawford [28], reported that most of them are basically caused by anaerobic Gram-positive cocci and Gram-negative rods. So, penicillin, erythromycin, cephalosporin, tetracycline and clindamycin would be the drugs chosen.

In the case of infectious endocarditis, being one of the most serious systemic complications of mouth infections, authors like Zerbal [29], Quintiliani & Maderazo [13], Grinberg [12], Passeri [4], and Chibinski & Fraiz [30], based on protocols of several medical entities, proposed several medicines to be used, not only in treatment but also in prophylaxis. Besides penicillin, erythromycin (in its various formulations – estolate, stearate, ethylsuccinnate), the cephalosporins, clindamycin, vancomycin, gentamicin, kanamycin, azithromycin, clarithromycin, and streptomycin are part of this arsenal.

As the scientific literature has established *Streptococcus viridians* (alpha-hemolytic streptococci) and *Staphylococcus aureus*, as the most common etiological agents in infectious endocarditis of dental origin, from the upper respiratory tract and from the esophagus, it's against them that prophylaxis should be used. Initially, penicillin would be the drug chosen, however, Lopes [31], White [32,33], and Zerbal [29] have alerted about the existence of resistant staphylococcus strains. Fonseca [34] related that although penicillin continues to be active against streptococci, these were not staphylococci sensitive to natural (G and V) and semi-synthetic penicillin

(ampicillin/amoxicillin). While for the antistaphylococcal penicillins (oxacillin, methicillin) there are already reports about resistant sprains, as was already found for microorganisms resistant to cephalosporins, an alternative antibiotic group for people who are allergic to penicillin. Consequently, the staphylococci already are among the most serious therapeutic problems.

Nevertheless, the protocols of medical associations for the prevention of infectious endocarditis indicate since 1990 amoxacillin as the right drug to be taken because it's better absorbed by the gastrointestinal tract than its "mother", ampicillin, producing a higher and longer lasting serum level (6-14 hours). This direction is followed and suggested in the prophylaxis to be used by medicals by authors like Passeri [4], Zerbal [29], Abrahão [26], Andrade [35], and Chibinski & Fraiz [30].

According to Moore [36], when we talk about buccal infection, medicals have used erythromycin. Since its introduction in 1952, it has been the first alternative for people who are allergic to penicillin. However, in 1990 it was not included as the first drug to be chosen for this condition anymore because of the great number of side effects, such as gastrointestinal problems, cross reactions with other macrolides, medical interactions with anticoagulant drugs (Warfarin®), corticosteroids, cyclosporines, and also the fact that it includes a phamacokinetic which is complicated in its various formulations (estolate, stearate, ethylsuccinate) Fonseca [34], Zerbal [29], Andrade [35], and others share this opinion, even though others maintain the previous directives before 1990, such as Fourniol [37] and Murta [38].

Although Fonseca [34] emphasizes that one third of the patients who are allergic to penicillin are also allergic to cephalosporin and Howe [23] has indicated "the small risk of cross sensibility" between these two groups of antibiotics, Quintiliani & Maderazo [13] reported that although the chemical structures of penicillin and cephalosporins are similar, the cross reaction rate between the groups is low. A patient with a history of late reaction to penicillin, like skin eruptions, probably has less than 5% chance to have the same reaction with cephalosporin. Currently, there are no data that indicate greater cross reactions in individuals with a history of anaphylaxis or immediate reaction to penicillin. Henriques & Rosa [39], Abrahão [26] have mentioned Dajani [5] and Passeri [4] quoting Dajani [40], who alerted that when the use of antibiotic prophylaxis is necessary in allergic persons, cephazollin may be used if the allergic reaction is not of the immediate – hypersensitivity type. So, the use of this medicine is generally safe for a patient who has skin eruption caused by penicillin. But they agreed with Quintiliani & Maderazo [13] that with an adverse reaction to penicillin (urticaria, anaphylaxis, angioedema), it's sensible to pick a non beta-lactam drug if possible. Although clindamycin is the most quoted antibiotic in the protocols of prevention of infectious endocarditis, and it's recommended by authors like Passeri [4], Henriques & Rosa [39], Andrade [35], Moore [36], and Cortezzi & Albuquerque [41], as the best choice to the alternative antibiotic prophylaxis in dentistry and also for surgical procedures in the buccal cavity, due to the predominance of anaerobic bacteria, and the fact that it can be bactericidal or bacteriostatic, depending on the dose and it causes fewer gastrointestinal problems than erythromycin, Fonseca [34] and Wannamacher & Ferreira [42] alerted to the possible appearance of gastrointestinal troubles like diarrhea, colitis (which do not disappear even if you quit using the drug), and also a metallic taste.

In 1997, Dajani [5] ratified the alteration in the protocol of 1990 before mentioning clindamycin as an alternative prophylactic antibiotic for patients with hypersensitivity to penicillin, but they also suggest two late generation macrolides as an alternative. They are azythromycin and claritromycin, however both are hard on the patient.

Dajani [43] quoted by Andrade [44], proved, comparing doses of 2.0 g and 3.0 g, that the former resulted in adequate serum levels for many hours; the recommendation of a protocol mentioned by Dajani [40], quoted by Passeri [4], of 3.0 g amoxicillin given 1 hour before the intervention and a second dose of 1.5g given 6 hours after the first dose, remained up to 1997 when, Dajani [5], members of American Heart Association (AHA), modified the directives, indicating a single dose of 2.0 g of amoxicillin for adults, orally, 1 hour before the procedure (Table 1).

Table 1. Recommendations for prophylactic treatment for dental procedures to prevent infectious endocarditis

Situation	Antibiotic	Adults	Children*
Standard general prophylaxis	Amoxicillin (Amoxil® 500 mg)	2.0g, orally, 1 h before procedure	50mg/kg, orally, 1 h before procedure
Allergic to penicillin	Clindamycin (Dalacin® 300 mg)	600mg,orally, 1h before procedure	20mg/kg, orally, 1 h before procedure
	Cephalexin# Cefadroxil#	2.0g, orally, 1 h before procedure	50mg/kg, orally, 1 h before procedure
	Azithromycin (Zitromax® 500 mg) Clarithromycin	500mg, orally, 1 h before procedure	15mg/kg, orally, 1 h before procedure
Unable to take oral medications	Ampicillin	2,0g, IM/IV, 30 min before procedure	50mg/kg, IM/IV, 30 min before procedure
Allergic to penicillin and unable to take oral medications	Clindamicyn	600mg, IV, 30 min before procedure	20mg/kg, IV, 30 min before procedure
	Cefazolin#	1.0g, IM/IV, 30 min before procedure	25mg/kg, IM/IV, 30 min before procedure

* Total children's dose should not exceed adult dose.
# Cephalosporins should not be used in individuals with immediate-type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillin.
IM: intramuscularly. / IV: intravenously.
Source: Henriques & Rosa [39].

Sonis [3], Lopes [31], Bear [2], Howe [23], following the directives suggested by entities responsible for research about infectious endocarditis prevention, indicated, up to 1990, a parenteral application as preferred for the administration of antibiotics due to its superior effect on blood serum levels. Subsequently, the same entities have given little emphasis to the parenteral procedure, possibly because of logical and financial considerations, being used only under some alternative prophylactic regimes or under specific conditions, such as for patients who will undergo surgery under general anesthesia and are fasting and are unable to ingest or absorb oral medications. Consequently, authors like Peterson [45,46], Passeri [4], Andrade [35], Chibinski & Fraiz [30], started recommending more frequent use of oral administration.

Rahn [19] alerted that the prophylactic use of antibiotics can decrease the risk of infectious endocarditis, but it does not present bacteremia. This way, the addition of topical antiseptics to antibiotics has been used in an attempt to reduce the occurrence of bacteremia. Antiseptics, such as iodine compounds (glycerin iodide, PVP-I®), diluted oxygenated water, and chlorhexidine, have been efficient, and were indicated by authors such as Passeri [4], Zerbal [29], Abrahão [26], Roberts [21], and Chibinski & Fraiz [30], chlorhexidine being the first choice as an antiseptic. However, Roberts [21] agreed with Rahn [19] about the effectiveness of chlorhexidine in the reduction of dental bacteremia, when they showed low antibacterial activity of chlorhexidine compared to povidone-iodine®. So, both have chosen povidone-iodine®, and not chlorhexidine as the best antiseptic.

Roberts [21], Rahn [19], Zerbal [29] and Prado [9] alerted that treatment with topical antiseptics does not mean substituting prophylaxis by systemic antibiotics. They have a preventive effect, but they ca not do away with the bacteremia completely. They represent, together with the maintenance of a good buccal health, a complementary way to the resolution of events that can lead to infectious endocarditis.

Conclusion

"Prevention is the best remedy". Antibiotics may prevent infectious endocarditis , but they cannot avoid bacteremia. Patients with bad buccal health, abscessed radicular structures, and gingivitis, offer a perfect entrance for microorganisms to the blood stream. So, the maintenance of good buccal health should be emphasized to the maximum. The use of medicines may help; it does help! Although we cannot forget that many rules about this use are a result of *in vitro* experiments, they do not substitute security norms and are not the solution for everything either; on the contrary, they can create problems. Each one has a side effect; and needs to be prescribed by a professional, so that he can use them in the best way.

The prophylactic use of antibiotics in infectious endocarditis of dental origin is often valued as new concepts arise; that's why entities like the AHA (American Heart Association) and the BSAC (British Society of Antimicrobial Chemotherapy) are always going over their directives. The dental surgeon must keep abreast of these changes and know that these rules are only a guide, and his clinical judgment is sovereign, because he knows the patient and his necessities; he is the responsible professional.

The dental surgeon should be aware that total prevention, independent of what the infection is, does not exist. But he has the moral obligation of preventing serious complications in the treatment. The mouth is part of a system that interacts with itself. An anamnesis that values the patient will certainly assist the professional in the choice of the medicine that will stimulate the answers of the host at that moment, according to his systemic conditions.

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