


Use of doxycycline in the treatment of periodontal diseases: a brief review

Uso da doxiciclina no tratamento de doenças periodontais: uma breve revisão

Uso de doxiciclina en el tratamiento de enfermedades periodontales: una breve revisión

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ABSTRACT

For a long time, it was considered a challenge to find a drug capable to act directly in the periodontal pockets without causing adverse effects innerent to its constant use. In what it seems, recent advances in the area of periodontal pharmacology managed to achieve said results with safety thanks to several studies in the area, be that with cientific articles or by the oversight of regulatory agencies such as the FDA. The doxycycline can be used in its antimicrobial form, subantimicrobial and of controlled release, each one of the mechanisms capable of causing a positive effect in periodontal treatment depending on how it is used and if used correctly where it is indicated. It is just a matter of time until this advances in periodontal pharmacology come to all continents and to all general clinicians and periodontists that have the interest in aquairing the correct knowledge on how to use them.

KEYWORDS: Doxycycline. Periodontal diseases. Anti-bacterial agents.

RESUMO

Por um longo tempo foi considerado um desafio encontrar um fármaco que pudesse agir diretamente nas bolsas periodontais sem que o mesmo cause os efeitos adversos inerentes ao seu uso constante. Ao que parece os avanços atuais na área da farmacologia periodontal conseguiram atingir tais resultados com segurança devido a inúmeros estudos na área seja por artigos científicos ou seja pela fiscalização de órgãos reguladores como a FDA. A doxiciclina pode ser usada na sua forma antimicrobiana, subantimicrobiana e de liberação local controlada, cada um dos meios tem o potencial de causar um efeito positivo no tratamento periodontal dependendo de como for usado e se usado corretamente onde é indicado. É apenas uma questão de tempo até que esses avanços na farmacologia periodontal cheguem até todos os continentes e a todos os clínicos gerais e periodontistas que tenham o interesse em adquirir o conhecimento correto de como usá-los.

PALAVRAS-CHAVE: Doxiciclina. Doenças periodontais. Antibacterianos.

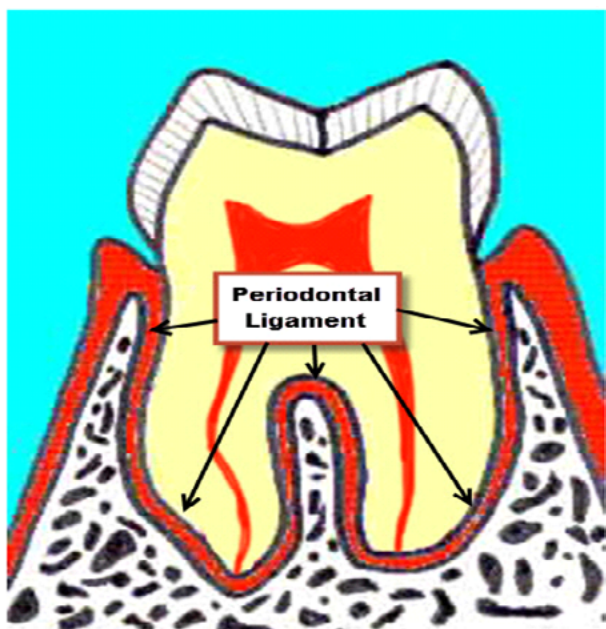
RESUMEN

Durante mucho tiempo se consideró un desafío encontrar un fármaco que pudiera actuar directamente sobre las bolsas periodontales sin provocar los efectos adversos inherentes a su uso constante. Parece que los avances actuales en el área de la farmacología periodontal han logrado alcanzar tales resultados de manera segura gracias a numerosos estudios en el área, ya sea a través de artículos científicos o mediante la supervisión de organismos reguladores como la FDA. La doxiciclina se puede usar en sus formas antimicrobiana, subantimicrobiana y de liberación local controlada, cada una de las cuales tiene el potencial de tener un efecto positivo en el tratamiento periodontal dependiendo de cómo se usa y si se usa correctamente donde está indicado. Es sólo cuestión de tiempo que estos avances en farmacología periodontal lleguen a todos los continentes y a todos los médicos generales y periodoncistas que estén interesados en adquirir los conocimientos correctos sobre cómo utilizarlos.

PALABRAS CLAVE: Doxiciclina. Enfermedades periodontales. Antibacterianos.

INTRODUCTION

Periodontal diseases require the presence of bacterial plaque to initiate the process of tissue injury to the periodontal ligament, but the immunologic response of the host is equally important¹⁻². The focus is no longer just on the bacterial plaque and has moved closer to the host's ability to fight the infection without causing an exaggerated inflammatory response with potential damage to the tissues that make up the periodontal ligament and the surrounding alveolar bone (Figure 1).



Fonte: <http://www.paulweberdds.com/learning-center/the-soft-tissues-of-the-tooth/the-periodontal-attachment/the-periodontal-ligament>

Figure 1 - Drawing showing shape simplified periodontal ligament.

For a long time, there has been a search for an effective antibiotic drug to treat periodontal diseases, whether chronic or aggressive. From penicillin's to lincosamides have already been tested, several options of non-steroidal anti-inflammatory drugs (NSAIDs) with or without antibiotic coverage have also been tested with varying degrees of success. The recent search is for a drug that can modulate the host's immune response, causing less tissue destruction. The present study will focus on doxycycline, an antibiotic from the tetracycline family with a broad-spectrum

bacteriostatic effect and which has shown interesting results if used in the treatment of periodontal diseases and the most interesting thing is that tetracyclines are the only known antibiotic that reaches concentrations in gingival fluid greater than in blood, around two to ten times more³⁻⁷.

The present literature review aims to review several articles that address the use of doxycycline to combat periodontal diseases and clearly expose its effectiveness in modulating the host's inflammatory response in addition to being just an antibiotic substance.

LITERATURE REVIEW

Doxycycline

Doxycycline is an antibiotic from the tetracycline family with bacteriostatic action in its 100 mg tablet form against a wide range of gram negative and gram-positive bacteria, in addition to sub antimicrobial doses (DDS) of 20 mg causing an anti-collagenolytic and reducing response of inflammatory action in the periodontal pocket, consequently reducing the tissue and bone destruction that occurs in these locations^{4,8-20} it can also be used directly in deep periodontal pockets in the form of 10% doxycycline hyclate. Therefore, the clinician can choose a dose of 100 mg to cause an antibacterial effect, a dose of 20 mg to cause a modulating effect on the host, in addition to being able to introduce doxycycline directly into the periodontal pocket, which requires a very careful evaluation. care of the patient before opting for a treatment option, which may even be a combination of drugs. Periodontal disease acts not only due to the bacterial presence, but also due to the individual's inflammatory response, which can be severe or controlled. Many patients present with an abnormal presence of dental calculus and progress to localized gingivitis in contaminated sites. However, in certain hosts, just the presence of a small amount of plaque is enough to cause a highly destructive inflammatory response to the periodontium. of support. In addition to the systemic and sub antimicrobial options, doxycycline is also available in its slow-release form known as doxycycline hyclate 10%. The hyclate acts

directly on the periodontal pockets, slowly releasing its contents over a period of several days, which will be discussed later.

Doxycycline in 100 mg Antibiotic Dose

Doxycycline in an antibiotic dose of 100 mg is commonly used in periodontics to treat acute and chronic periodontal diseases due to its broad spectrum of antibacterial action. It is usually administered in a loading dose of two 100mg tablets on the first day followed by 1 tablet of 100mg for another 13 days. In a study carried out by Llambés et al, several type 1 diabetic patients in a group with moderate to severe periodontitis were treated with doxycycline 100 mg, 1 capsule per day for 21 days after scaling and root planning and had a reduction in periodontal indices from 64 sites to 21 and bleeding on probing from 65 sites to 27, which was higher than with scraping alone without doxycycline. In another study in type 2 diabetic patients who received scaling and root planning plus doxycycline 100 mg for 14 days, HbA1c (glycated hemoglobin) levels were reduced, in addition to causing a decrease in *porphyromonas gingivalis* to undetectable levels in these patients 3 months after treatment. systemic treatment¹⁷, in addition, the use of doxycycline at an antibiotic dose has also been associated with a decrease in post-scraping probing depth and a decrease or absence of *porphyromonas gingivalis*¹⁷⁻¹⁸.

Doxycycline in 20 mg Subantimicrobial Dose

Doxycycline can be used to treat periodontal diseases in its 20 mg sub antimicrobial form, better known as Periostat™, so that two or one tablet is administered once a day for periods ranging from 3, 9 and up to 24 months⁷, however the drug is not yet sold in Brazil and is the only drug approved by the Food and Drugs Agency (FDA) for use in the treatment of periodontal diseases²⁰.

There has long been a search for a drug that can reduce the effects of collagenase on the periodontal ligament and its consequent destruction. The host's own inflammatory reaction can be extremely harmful if exerted in an uncontrolled manner, doxycycline in a sub antimicrobial dose (DDS) of 20mg has anti-collagenase, anti-matrix metalloproteinase and cytokine regulation effects^{8,10,19-20}, these anti-inflammatory mechanisms of doxycycline cause a reduction in the aggressiveness

of the host's immune response. There are cases of individuals with little plaque and an exacerbated and highly destructive response in the protective and supporting periodontium. In these cases, a sub antimicrobial dose is interesting to modulate the inflammatory response to a less aggressive level. In one study, groups of diabetic patients treated with doxycycline and scaling versus placebo were analyzed and reductions in glycated hemoglobin (HbA1c) levels were found in patients treated with doxycycline and scraping and no significant difference in the placebo groups¹³. Another study of type 2 diabetic patient with periodontal disease found a decrease in HbA1c levels in patients treated with DDS after scaling versus little or no difference in patients treated with doxycycline 100 mg and in the group placebo¹⁴. It is important to highlight, however, that there are studies showing that the use of doxycycline did not show any difference in HbA1c levels in patients with moderate to severe periodontitis after scaling and root planing¹⁵, which demonstrates a need for more studies on the theme.

The 20 mg DDS has been studied against periodontal diseases for over 20 years and it was initially feared that there would be bacterial resistance to even a low dose of doxycycline, however this is not what some studies have shown, carried out a study with 171 patients in a group for 3, 6 and 9 months in which they concluded that the bacterial flora did not develop resistance to the sub antimicrobial dose, the same data are corroborated by a review. It is important to highlight that short treatments using DDS, for at least 3 months, tend to have positive effects on the periodontium for much longer periods after the end of the treatment, which can last up to 9 months²¹⁻²⁵. It is known that periodontal disease causes an often exacerbated production and response of matrix metalloproteinases, better known as MMPs, which mainly degrade type 1 collagen, the most common in gingival tissues, in addition to also causing bone degradation this is very interesting for immunomodulating this response, consequently causing less damage to the supporting periodontal soft tissues^{7,11-12,14}. It has already been found in studies that short-term therapy with DDS, even though it reduces the amount of collagenase in the gingival fluid, tends to have a regression of the disease as soon as the drug is stopped during treatment, but in treatments lasting 3 months or more, it maintains a much larger window of disease freedom⁷. Studies carried out in patients with periodontitis without risk factors proved

that scaling and root planning plus the use of DDS achieved improvements in clinical attachment levels and subgingival pocket depth compared to placebo or control groups^{11,20-21,23}.

Doxycycline Hyclate

The use of a drug that can act locally in deep pockets and that has substantiality in the biological space in the form of slow release has been discussed for a long time, only recently significant advances have been made in the area, such as doxycycline hyclate (Atridox™) which can be inserted in the form of a gel in deep pockets and sealed in the region of the interdental papillae with surgical cement, the operating time in the pocket is around 7 days, the gel is biodegradable and does not need to be removed⁷. Doxycycline hyclate 10% is a drug for local use and slow release in the form of a gel, two syringes are attached and then mixed for 100 cycles, the drug must then be introduced directly into the deep pockets and then sealed with surgical cement. Doxycycline hyclate has the benefit of being easy to apply, in addition to not causing an imbalance in the buccal bacteria flora¹⁶. Carried out a study on smoker patients to evaluate the microbiological impact of doxycycline hyclate 10% Atridox™ applied locally in deep periodontal pockets of 5 mm or more and concluded that the group treated with periodontal scaling plus doxycycline hyclate 10% had lower numbers of *porphyromonas gingivalis* and *tannerella forsythensis*, but not *aggregatibacter actinomycetemcomitans*.

DISCUSSION

Nowadays, the pharmacological possibilities regarding the management of periodontal patients continue to increase, new discoveries are made and new medications are tested, all with the aim of improving and facilitating the treatment of both periodontitis and gingivitis. There is the possibility of using either doxycycline 100 mg when a more robust antibacterial action is desired, or DDS plus doxycycline hyclate 10% when you have a chronic problem. Scaling

and root planning treatments plus supplementation with one or more of these 3 drugs have demonstrated very satisfactory results in terms of reducing probing depth.

The use of drugs for the treatment of periodontal diseases must always be preceded by a good anamnesis and a good clinical examination to verify whether there is really a need for this type of auxiliary therapy. The indiscriminate use of drugs can lead to adverse reactions that can be harmful to the patient and can even interfere with treatment. One of the problems of our century is the excessive consumption of drugs by an increasing portion of the population, something that can be avoided by a correct assessment by health professionals of the real needs of those in their care.

It is also worth remembering that there is still no type of drug that can treat periodontal diseases alone, the need for scaling and root planning prior to pharmacotherapy is still the gold standard in the treatment of periodontitis and gingivitis. The search for a "miracle" drug that can act on the periodontal ligament, avoiding the often-painful process of scaling, has been researched for a long time, but nothing can overcome mechanical debridement and root planning as the main mechanism for removing bacteria and promote disorganization of the subgingival bacterial biofilm.

CONCLUSION

The use of drugs such as doxycycline in the treatment of periodontal diseases is gaining more and more space. It is safe as long as the basic principles of its use are followed. Remembering that scaling and root planing are still the gold standard in the treatment of plaque-related periodontal pathologies as the main etiological factor and drugs are only auxiliary tools for mechanical debridement.

It is likely that in the future periodontics will be permanently associated with the use of drugs as adjuncts in periodontal treatment with supra and subgingival scaling, increasingly encouraging results are found in articles and research which demonstrates the exciting possibility of new treatment options for a

of health problems that, according to an estimate by the World Health Organization, affect more than 90% of the world's population.

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