Clinical Sciences Research and Reports

Research Article ISSN: 2516-709X

Effects of topical doxycycline on inflammatory markers in periodontal disease

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Abstract

Periodontal disease is an infectious and inflammatory process of the supporting structures of the teeth, the result of the interaction between infection by pathogenic bacteria and the host's immune response. In periodontitis patients, compared to those with good periodontal health, there appears to be an increased risk of some systemic diseases in general and coronary artery disease in particular. It is not evident that this association is causal and, therefore, could be considered an independent factor for the development of cardiovascular diseases.

Introduction

Effects of topical doxycycline

Almost all microorganisms related to periodontal disease are sensitive to tetracyclines, because of this we use doxycycline, which is a second-generation semi-synthetic derivative, as an adjunct to periodontal treatment [1-4].

The literature shows heterogeneous results, thus, there are studies that show the effect of tetracyclines, especially second-generation ones, on the improvement of both clinical and biochemical parameters [5-8]. According to this line of thinking, there are studies that use slow release microspheres of minocycline or fibers with tetracycline [9-10]. Therefore, there are important differences in the short-term, but not in the long-term, and others that do not show differences regarding to scraping and root planning [11-14]. The heterogeneity of the results could be explained because of the short-term execution of the studies, almost all of them are considered three months. It has been suggested, in some studies that can obtain results even with statistical significance, that it would require a longer-term monitoring study execution, between 6 and 12 months or the repetition of doses throughout the treatment to optimize the response [15-16].

Inflammatory markers in periodontal disease

The existence at the moment of an extensive bibliography about periodontal disease, as a potential risk factor for various organs and systems, has given rise to some authors such as Steven Offenbacher in 1996, who proposed a new discipline, the "Periodontal Medicine". This sale refers to the specialty that aims to study the relationship between periodontal pathologies and systemic diseases [17]. Saikku et al. [18] published the first articles, in which the link between bacterial infections and coronary heart disease is highlighted; also in 1995 Patel et al. [19] links chronic viral infections by Cytomegalovirus and Herpesvirus. Periodontal disease and arteriosclerotic processes appear related in the works of Mattila et al. [20], Beck et al. [21] and in 2007 by Gostman et al. [22], which indicate that periodontitis produces bacteremia, which is manifested in an increase in proinflammatory markers, TNFα, IL-1, IL6 and hsCRP. Buhlin et al. [23], Gani et al. [24] and in 2010 Nakajima et al. [25] which refers to periodontitis is associated with limited levels of markers such as hsCRP and IL-6. Yoshii et al. [26] indicate that these levels do not precede periodontitis, but rise with it. D´Aiuto et al. [27], Behle et al. [28], observe a significant reduction in inflammatory markers after periodontal treatment; even of PAI-1, VCAM-1 and MMP-9. On the other hand, in 2001 Ridker et al. [29] study hsCRP as a predictor of cardiovascular risk and Tonetti et al. [30] demonstrates an improvement in endothelial dysfunction after periodontal treatment. All these studies and investigations can be interpreted as a link between periodontal disease and arteriosclerosis cardiovascular pathology.

Material and methods

Study population

A cross section of patients diagnosed with periodontitis was taken so as to be studied in a clinical trial with a therapeutic objective, which should allow after three months, evidence of the effectiveness of periodontal treatment. Topical doxycycline was applied as an adjuvant in order to optimize the results and achieve the objectives set; the work is structured in three parts.

The first part will have analytical purposes and will consist of a periodontal study, which will be performed at the time of diagnosis, as well as a blood test to determine the serum level of hsCRP and fibrinogen. The second part will have an interventionist character, in which all patients will undergo a non-surgical periodontal treatment, topical doxycycline will be applied in lesions ≥ 5 mm.

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Key words: *periodontal disease, periodontitis, inflammatory markers, topical doxycycline*

Received: May 15, 2020; **Accepted:** June 15, 2020; **Published:** June 19, 2020

The third part will carry out a new periodontal study three months after having carried out the treatment, and the blood level of hsCRP and fibrinogen will be determined again.

Selection criteria

Inclusion criteria: patients with a Probing Depth > 3 mm in at least one probing site in two or more teeth, and/or loss of interproximal clinical insertion ≥ 3 mm as criteria to diagnose the process as chronic periodontitis according to criteria of the AAP-EFP 2018 [31].

Exclusion criteria were: less than fourteen teeth, aggressive periodontitis, infectious or other inflammatory diseases, periodontal treatment in the last 6 months or antibiotics in the last 3 months, treatment with systemic anti-inflammatory drugs (NSAIDs), pregnancy or lactation, secondary obesity (hypothyroidism, Cushing's syndrome), or any medical condition requiring antibiotic treatment before the dental intervention

Results and discussion

Previous studies have also shown improvements in proinflammatory markers, IL-6 and αTNF in patients to whom topical doxycyclin is applied [32-33], which consequently shows inflammation modulating actions in its local application, as previously observed after systemic administration at subtherapeutic doses [34-36].

The biochemical reevaluation shows, after three months, after non-surgical periodontal treatment and according to the Brunner-Langer non-parametric model, as fundamental findings, the reduction of serum fibrinogen levels in the group treated with doxycycline 364.5 ± 93.2 versus 347.0 ± 100.8 ($p = 0.077$), while in the control group the serum levels increased 314.8 ± 63.7 versus 320.4 ± 65.1 ($p = 0.305$). Plasma fibrinogen levels show, in our study, a positive correlation with the BOP index of probing bleeding at the limit of significance ($p = 0.051$), as an expression of the impact of local inflammation on the systemic inflammatory load. In the present study, our results can be interpreted by the presence of a residual inflammatory load, a result of the aggression caused by periodontal treatment, which would lead to an increase in acute phase reactants, including fibrinogen, and given the immunomodulatory properties of doxycycline, the final balance results in a decrease in the values of serum levels. On the other hand, in the present study, the levels of hsCRP remain unchanged 0.25 ± 0.22 versus 0.22 ± 0.22 ($p = 0.478$), in the group treated with doxycycline, in line with other studies, which neither showed changes [37-39].

Conclusion

As a general conclusion of the present study, it can be stated that the effects on systemic proinflammatory markers remain undetermined at least in the short term. More studies with prospective and longitudinal characteristics, of greater size and duration, are necessary, in order to objectify with more precision the influence of periodontal disease with systemic inflammation and, consequently, its relationship with cardiovascular pathology. Moreover, treatment with doxycycline does not seem to have benefits on the improvement of serum levels of CRPus. Finally, and as a contribution to the present study, there is a decrease in serum fibrinogen levels after non-surgical periodontal treatment with the use of doxycycline as an adjuvant medication. This implies an important benefit, as a result of the reduction of the peaks of systemic inflammation, caused because of the periodontal treatment.

Consent

As per international standard, patient's consent has been collected and preserved by the authors.

Ethical approval

As per international standard, written ethical approval has been collected and preserved by the author (s).

Competing interests

Authors have declared that no competing interests exist.

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