Inflammatory and prooxidant markers in response to periodontal treatment - A case report

Ricardo Andreu1,2*, Sergio Santos-del-Riego2 and Francisco Payri3

1Dental Clinic, Paterna, Valencia, Spain
2Department of Physiotherapy Medicine and Biomedical Sciences, University of A Coruña, A Coruña, Spain
3CMT, Politechnic University of Valencia, Valencia Spain

Abstract

Background: The aim of this study is to determine the changes in serum levels of malondialdehyde, 8-hydroxy-2’-deoxyguanosine, hsCRP and fibrinogen as indicators of oxidative stress and inflammatory markers, in response to non-surgical periodontal treatment.

Case description: The patient, a 51-year-old male diagnosed with periodontitis was taken so as to be studied with a therapeutic objective, which should allow after three months the time of diagnosis and after non-surgical treatment. Topical doxycycline was used as adjunctive medication.

Conclusion: A significant reduction in both serum levels of pro-inflammatory markers and oxidative stress indicators is observed after periodontal treatment.

*Correspondence to: Ricardo Andreu, Dental Clinic, Paterna, Valencia, Spain, E-mail: r.andreu58@icloud.com

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Introduction

Inflammatory markers

Different studies like Beck et al. [1] and Gostman et al. [2], indicate that periodontitis produces bacteremia, which is manifested in an increase in proinflammatory markers, TNFα, IL-1, IL6 and hsCRP. Buhlin et al. [3], Gani et al. [4] and in 2010 Nakajima et al. [5] refers to periodontitis is associated with limited levels of markers such as hsCRP and IL-6. On the other hand, D’Aiuto et al. [6] and Behle et al. [7], observe a significant reduction in inflammatory markers after periodontal treatment; even of PAI-1, VCAM-1 and MMP-9.

Previous studies have also shown improvements in proinflammatory markers, IL-6 and αTNF in patients to whom topical doxycyclin is applied [8,9], which consequently shows inflammation modulating actions in its local application.

Prooxidant markers

The cells obtain energy through coupled oxidation-reduction (redox) reactions, during aerobic respiration. In this way, O₂ is responsible for the formation of the so-called reactive oxygen species or ROS, which are molecules of high reactivity by having a missing electron [10]. NADPH oxidase primarily, they are also important xanthine oxidase (XO) and decoupled endothelial nitric oxide synthase (eNOS) [10] which promote ROS production and are involved in the development of vascular damage.

Inflammatory periodontal lesions present an important infiltrate of monocytes and macrophages, which has the purpose of containing the infectious process [11-17]. These defensive mechanisms will become an aggression for the periodontal tissues as a consequence of the production of free radicals (FR).

On the other hand, the nuclear factor NFKβ, which is inactive in plasma due to the inhibitor IκB. The degradation of this subunit, which is very sensitive to ROS, allows the promotion of the expression of genes that lead to the inflammatory response, this is a link between prooxidant states and chronic inflammatory processes [18].

When the free radicals react with a fatty acids molecule of the cellular lipid membranes [19], malondialdehyde (MDA) is generated, which is an indicator of tissue damage [20]. Another molecule that is damaged by free radicals is DNA, as a consequence of the arrival of ROS inside the cell nucleus, the action of the radical OH⁻ is able to originate more than 20 modifications in the nitrogenuous bases. We can highlight 8-hydroxy-2’-deoxyguanosine (8-OHdG), which is produced as a result of the interaction with guanine. It can be used like a marker of oxidative damage [21-29].

Therefore, serum concentrations of MDA and 8-OH-dG are increased in patients with periodontal disease as an expression of increased oxidative stress in the etiology of the lesions and their quantification, consequently, it will allow us to assess the prooxidant state.

Case description

The patient diagnosed with periodontitis was taken to be studied 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.
Methodology

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, fibrinogen, MDA and 8-OH-dG in urine.

The second part will have an interventionist character, in which all patients will undergo a nonsurgical periodontal treatment, topical doxycycline will be applied in lesions ≥ 5 mm.

The third part will carry out a new periodontal study three months after having carried out the treatment, level of hsCRP, fibrinogen, MDA and 8-OH-dG, will be determined again.

Results

A 51-year-old male, non-smoker, with no relevant pathological history, diagnosed with periodontal disease. The cut-off point for PD ≥ 3 mm is the most commonly used in the literature and in this study the CAL value ≥ 3 mm is used to establish the diagnosis according to the 2018 AAP-EFP criteria [30].

Underwent non-surgical periodontal treatment; the treatment in a single session or “full mouth” with the use of antiseptics and/or topical antibiotics in our case, have amply demonstrated clinical benefits [31], with topical application of doxycycline in periodontal lesions ≥ 5 mm and prospective follow-up, determining both clinical and biochemical parameters at the baseline and three months after the end of the treatment.

Baseline values: Clinical parameters: PD (mm) 3.47; CAL (mm) 3.77; % PD 4 (mm) 59; % PD 6 (mm) 4.86; BOP % 27.27.

Biochemical parameters: hsCRP (mg/L) 0.28; Fibrinogen (mg/dL) 260; MDA (μmol/L) 1.1; 8-OH-dG (μg/g) 11.9.

Re-evaluation. Clinical parameters: PD (mm) 3.29; CAL (mm) 3.60; % PD 4 (mm) 51; % PD 6 (mm) 3.47; BOP% 18.75.

Biochemical parameters: hsCRP (mg/L) 0.18; Fibrinogen (mg/dL) 214; MDA (μmol/L) 0.7; 8-OH-dG (μg/g) 6.1.

Observed variation. Clinical parameters: PD (mm) -0.18; CAL (mm) -0.17; % PD 4 (mm) -8; % PD 6 (mm) -1.39; BOP% -8.52.

Biochemical parameters: hsCRP (mg/L) -0.1; Fibrinogen (mg/dL) -46; MDA (μmol/L) -0.4; 8-OH-dG (μg/g) -5.8.

Discussion

The values of all the clinical parameters studied improve with respect to those observed at baseline, highlighting the decrease in the BOP index of 8.52%. The determination of the BOP index, as an indicator of local inflammation, allows us, by contrasting it with the determinations of the biochemical parameters, to show its influence on the systemic inflammatory load and especially with the serum fibrinogen level [32].

A significant reduction in both serum levels of pro-inflammatory markers and oxidative stress indicators is observed after non-surgical periodontal treatment, especially fibrinogen in -46 (mg/dL) and of 8-OH-dG in -5.8 (μg/g).

Previous studies have also shown improvements in pro-inflammatory markers, IL-6, aTNF and oxidative stress [33,34] in patient receiving topical doxycyclin [35,36].

The application of topical doxycycline can contribute in this way by modulating actions of inflammation on its local application, as has been previously observed after its systemic administration at sub-therapeutic doses [37- 39].

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 pro-inflammatory and oxidative stress markers, among them fibrinogen stands out and that given the immunomodulatory properties of doxycycline, the final balance results in a decrease in the values of serum levels of the different markers.

In summary, more studies with prospective and longitudinal characteristics, of greater size and duration, are necessary in order to more accurately objectify the influence of periodontal disease with systemic inflammation and, as a consequence, its relationship especially with chronic pathologies.

Conclusion

As a general conclusion of the present study, it can be affirmed that, as a consequence of periodontal treatment, there is a generalized improvement in clinical variables, pro-inflammatory markers and systemic pro-oxidants, at least in the short term.

This represents an important benefit, as a result of the reduction of the inflammatory load and systemic oxidative stress, with the consequent benefits for general health, without forgetting the alteration of the affinity for the nitrogenous bases of the oxidation products of guanine and therefore its possible mutagenic character.

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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