



# Impact of Non-Steroid Anti-Inflammatory Drugs and Antibiotics Upon Oral-Dental Health- A Literature Review



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## Abstract

The etiological traits, respectively the intensity of clinical manifestation of dental caries are influenced and coordinated predominantly not by the bacterial genotype of cariogenic microorganisms, but by their phenotypic features in the context of various environmental factors. According to the Global Burden of Disease report the point of issue of non-treated tooth decay lesions in permanent teeth is still actual in international scales. Non-steroid anti-inflammatory drugs are characterized with wide range of application in dental medicine practice. The implementation of these medicines is related to the process of suppression of arachidonic acid metabolism by cyclo-oxygenase pathway of reactions. The products of these metabolic interactions, namely prostaglandins, affect pain and induce the activity of osteoclasts during stages of active disorder of the periodontal apparatus. As an infectious disease the etiology of periodontitis is associated to the active participation of periodontal pathogens. Initiated as a bacterial disease, its course of progression is under the impact of common health traits, medium-related conditions, genetically- based characteristics. Lots of solid scientific literature sources ascertain that the efficient control of dental plaque and calculus, in condition of properly performed, adequate to the clinical state non-surgical and surgical periodontal procedures, ensures successful therapeutic approach in long perspective.

**Keywords:** Non-steroid anti-inflammatory drugs; Antibiotics; Oral-dental state; Caries; Periodontitis

**Abbreviations:** VPI: Visible Plaque Index; MBI: Marginal Bleeding Index; GI: Gingival Index; PD: Probing Depth; CAL: Clinical Attachment Loss; GR: Gingival Recession

## Introduction

The disease of tooth decay is characterized with considerable magnitude of distribution in international scales [1]. Concerning the specifics of epidemiology of caries, the incidence of this oral health disorder is most common in countries of the Middle East, Latin America, South Asia, and at lower rate in China [2-4].

Determined as a “complex” and “multifactorial” disease, tooth decay as a process of destruction of hard teeth tissues can be efficiently controlled and adequately managed by implementation of fundamental principles of primary, secondary and tertiary preventive cares [5-7]. The contemporary conception of dental caries is related to the process of de-mineralization of the non-organic ingredients of enamel, followed by decomposition of the organic substrate in condition of high acidity of the medium, caused by the metabolic activities of acidogenic and acidophilic microorganisms of *Streptococcus mutans* and *Streptococcus sobrinus* [8]. Bacteria of the species of *Lactobacillus acidophilus* take active participation in the carious process on later stages, related to chronic course of the disease.

On the other hand, the disturbance of the equilibrium of homeostasis into oral cavity provokes transformation of *Candida albicans*, as one of the representatives of the residual microflora, into opportunistic microorganisms. Researchers have taken cognizance of the potentials of *Candida albicans* for reinforcement of the cariogenic virulence of plaque biofilm [9,10].

The etiological traits, respectively the intensity of clinical manifestation of dental caries are influenced and coordinated predominantly not by the bacterial genotype of cariogenic microorganisms, but by their phenotypic features in the context of various environmental factors [11]. According to the Global Burden of Disease report the point of issue of non-treated tooth decay lesions in permanent teeth is still actual in international scales [12]. Studies carried out in the USA, Australia, Norway and Iceland eloquently outline the tendency of elevation in caries experience [13]. Profound population investigations performed in different periods of childhood ascertain that in young children the carious process affects mainly occlusal teeth surfaces, and during adolescence more vulnerable to caries attacks are the approximal

sites of teeth [14]. These interrelations of caries activity correspond to the necessity of implementation of a significant number of tools for the purposes of efficient preventive programs on individual and population level [15].

Non-steroid anti-inflammatory drugs are characterized with wide range of application in dental medicine practice. The implementation of these medicines is related to the process of suppression of arachidonic acid metabolism by cyclo-oxygenase pathway of reactions [16]. The products of these metabolic interactions, namely prostaglandins, affect pain and induce the activity of osteoclasts during stages of active disorder of the periodontal apparatus. After the stage of periodontal surgery, ibuprofen gives impact upon pain sensitivity, diminishing the concentration of PGE<sub>2</sub> in gingival tissues by more than 95% [17]. In condition of a randomized, placebo-controlled clinical trial the implementation of flurbiprofen for a definite period of 18 months has resulted in considerable arrest of the intensity of periodontal bone loss among people suffering from severe chronic periodontitis. There has been established a tendency of reduction of the volume of fibroblasts in inflamed gingival connective tissue [18]. Simultaneously, TNF- $\alpha$  serves the role of an essential mediator of the inflammatory response by its potentials for initiating synthesis and release of prostaglandin and matrix metalloproteinase by fibroblasts [19]. Researchers confirm that TNF- $\alpha$  considerably elevates the rate of transportation of naproxen by gingival fibroblasts [20]. Gingival fibroblasts are also characterized by the capacity for accumulation of tetracyclines and fluoroquinolones [21]. These functionality-related traits of fibroblasts in gingiva lead to increased concentrations of systemically administered doxycycline and ciprofloxacin into gingival connective tissue and crevicular fluid compared to blood serum [22]. Very important to be accentuated on the fact that in terms of inflammation gingival tissue is oversaturated with fibroblasts. Therefore, non-steroid anti-inflammatory drugs concentration by fibroblasts can be up-regulated by TNF- $\alpha$  [16].

The purpose of the study is to investigate the impact of non-steroid anti-inflammatory drugs and antibiotics upon oral-dental health based on a profound scientific literature review. A variety of researches has been perused and analyzed.

### Results and Discussion

The etiology of caries is related to the significant role of the factors of cariogenic microorganisms, fermentable carbohydrates, quality and quantity traits of enamel, time, properties of saliva [23-25]. Although researchers are aware of the potentials of different causative factors and principles of the pathophysiology of that disorder with destructive effect upon hard teeth tissues, it has not been eradicated yet [26]. Sugar-containing foods and drinks are among the most dangerous predisposing indicators for initiation and progression of this behavioral disease with infectious nature [27-30].

Sucrose included as a constituent in pediatric medications

[27,31] leads to decrease on the level of pH of medicine formulation [26,32-34] and viscosity of fluid in consistency medication [30,35]. Consequently, the processes of de-mineralization, decomposition of protein compounds, respectively, cavity formation go by progressive stages [36]. Pediatricians have the main task to modulate children's and parents' attitude towards their common and oral-dental health [37]. Namely specialists at the scope of Pediatrics are expected to investigate thoroughly the interrelations between tooth decay and antibiotics' application in the different periods of childhood. Scientists from different parts of the world have accentuated on the statement that pediatricians are inclined to neglect the correlation between application of antibiotics and enhanced risk of caries, based on the ingredients of fermentable carbohydrates into medicines of antibiotics [38-40]. Approximately  $\frac{1}{4}$  of the pediatricians who took part in the study considered antibiotics as deleterious agents causing defects to teeth tissues. Only  $\frac{1}{5}$ th of all the participants recommended children to perform strict oral hygiene procedures after each oral intake of antibiotics. Researchers establish that negligence of parents towards regular individual and professional oral health cares, especially lack of motivation for maintenance of proper hygiene level, results in significantly increased distribution of clinical cases of Early Childhood Caries [41,42].

Taking into consideration the contemporary tendency of high speed of distribution of tooth decay among children who consume various medication, including antibiotics, researchers accentuate on the definite necessity of enriching the knowledge of pediatricians about medicines' constituents of fermentable carbohydrates as one of the main factors for caries [43]. Namely pediatricians have the responsibility to direct the attention of children and their parents towards the significance of regular and strict age-related complex individual oral hygiene cares as an obligatory prerequisite for proper oral-dental health [44].

Early childhood caries is evaluated as one of the most common chronic health disorders in children [45,46]. This disease has been established to be five times more common than asthma. If not treated adequately, ECC can act as a predisposing factor for malnutrition, handicaps in speech and disturbances of the normal, physiologically based individual development. As a noxa affecting not only teeth tissues, but giving impact upon the body, ECC can provide favorable conditions for initiation and progression of cardiovascular disorders, premature birth, diabetes.

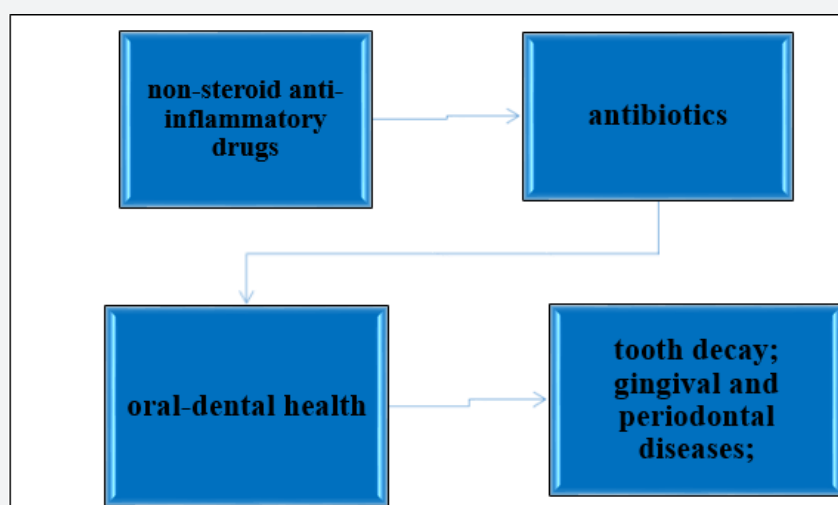
As an infectious disease the etiology of periodontitis is associated to the active participation of periodontal pathogens [47,48]. Initiated as a bacterial disease, its course of progression is under the impact of common health traits, medium-related conditions, genetically- based characteristics [49-51]. Lots of solid scientific literature sources ascertain that the efficient control of dental plaque and calculus, in condition of properly performed, adequate to the clinical state non-surgical and surgical periodontal procedures, ensures successful therapeutic approach in long perspective [52-54].

Simultaneously, there are patients who have not been favorably influenced by conventional periodontal therapy [55]. Others demonstrate high susceptibility to the infectious pathogenic mechanism of that destructive disorder of the supportive apparatus [56]. Profound researches confirm that individual immunity system specifics determine the rate of progression, respectively the degree of aggravation of clinical manifestation of periodontitis [57,58].

Regarding the pathogenic mechanisms of morphological and functional disintegration of periodontal tissue complexes, it must be accentuated on the key role of arachidonic acid metabolites. Their production is coordinated by the enzyme of cyclooxygenase.

Namely nonsteroidal anti-inflammatory drugs (NSAIDs) are responsible for the pharmacologically related inhibition of the biocatalyst of cyclooxygenase, respectively synthesis of metabolic compounds of arachidonic acid. The last induce and sustain the intensity of the process of secretion and release of matrix metalloproteinase and osteoclasts [59].

On one hand, nonsteroidal anti-inflammatory drugs provide an explicit effect of host modulation in terms of inflammatory process. On the other hand, there has been established an enhancement of the rate of host modulation when combined to a cause-related periodontal therapy [60-62] (Figure 1).



**Figure 1:** Interrelations between anti-inflammatory medicines and oral health.

Thorough investigations are devoted to the deteriorative impact of non-steroidal anti-inflammatory drugs upon oral mucosa and gastrointestinal mucosa [63]. And the potentials of NSAIDs to disturb the process of proper and optimal restoration of the gingival tissue after series of procedures of non-surgical periodontal therapy must be carefully explored. Simultaneously, in the context of two scientific literature reviews has been accentuated on the positive effects of nonsteroidal anti-inflammatory drugs upon the pathological processes of inflammation of gingival tissue and aggravation of periodontitis by the means of decrease of the intensity of alveolar bone resorption [64,65]. These adverse results are probably associated to the considerable bone protection effect of nonsteroidal anti-inflammatory drugs [66]. Waite et al. [67] and Feldman et al. [68] organized and carried out two retrospective investigations with the definite purpose to assess the specifics of incidence and distribution of periodontal diseases in condition of non-steroid anti-inflammatory drugs application.

In some researches has been accentuated on the effect of NSAID upon indicative parameters with definite clinical significance, namely VPI - Visible Plaque Index (Ainamo & Bay), MBI Marginal bleeding index (Cowell et al.), GI - Gingival index [50] PD - Probing depth, CAL - Clinical attachment loss, GR - Gingival recession. No interrelations have been confirmed between the period

of implementation of non-steroid anti-inflammatory therapy and clinical attachment loss, accentuating on the statement that prolonged application of these remedies does not have the potential for additive effects on the state of periodontal apparatus. Authors ascertained that proper administration of non-steroid anti-inflammatory drugs leads to suppression of the process and degree of inflammation of the gingival tissue, reduction of the values of probing depth, restoration of clinical attachment, overcoming para-clinical findings of radiographic visualized loss of alveolar bone [67,68].

In conclusion it is accentuated on the definite impact of non-steroid anti-inflammatory drugs and antibiotics on the oral-dental health, respectively intensity of initiation and progression of tooth decay, gingival and periodontal diseases.

### References

1. Anu V, Harshamol S, Helena T, Hannah PD, Gokila R, et al. (2018) Paediatricians cognizance about the deleterious effect of antibiotics and dental caries - a preliminary study. *Int J Pharm Sci & Res* 9(2): 708-711.
2. Yadav K, Prakash S (2017) Dental Caries: A Microbiological Approach. *J Clin Infect Dis Pract* 2: 118.
3. Yadav K, Prakash S (2017) Dental Caries: A Review. *Asian J of Biomed and Pharmaceutical Sci* 6: 1-7.

4. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, et al. (2012) Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 380(9859): 2163-2196.
5. Philip N, Suneja B, Walsh LJ (2018) Ecological Approaches to Dental Caries Prevention: Paradigm Shift or Shibboleth? *Caries Res* 52(1-2): 153-165.
6. Yu SM, Bellamy HA, Kogan MD, Dunbar JL, Schwalberg RH, et al. (2002) Factors that influence receipt of recommended preventive pediatric health and dental care. *Pediatrics* 110(6): e73.
7. Fejerskov O (2004) Changing paradigms in concepts on dental caries: consequences for oral health care. *Caries Res* 38(3): 182-191.
8. Philip M, Michael LH, Rogers DW, Melanie W (2016) *Marsh and Martin's Oral Microbiology*. (6<sup>th</sup> edn), p. 272.
9. Koo H, Bowen WH (2014) *Candida albicans* and *Streptococcus mutans*: a potential synergistic alliance to cause virulent tooth decay in children. *Future Microbiol* 9(12): 1295-1297.
10. Takahashi N, Nyvad B (2008) Caries ecology revisited: microbial dynamics and the caries process. *Caries Res* 42(6): 409-418.
11. Takahashi N, Nyvad B (2011) The role of bacteria in the caries process: ecological perspectives. *J Dent Res* 90(3): 294-303.
12. Kassebaum NJ, Smith AGC, Bernabé E, Fleming TD, Reynolds AE, et al. Global, Regional, and National Prevalence, Incidence, and Disability-Adjusted Life Years for Oral Conditions for 195 Countries, 1990-2015: A Systematic Analysis for the Global Burden of Diseases, Injuries, and Risk Factors. GBD 2015 Oral Health Collaborators. *J Dent Res* 96(4): 380-387.
13. Haugejorden O, Birkeland JM (2005) Analysis of the ups and downs of caries experience among Norwegian children aged five years between 1997 and 2003. *Acta Odontol Scand* 63(2): 115-122.
14. Burnham KP, Anderson DR (2002) *Model Selection and Inference. A Practical Information-Theoretic Approach*. (2<sup>nd</sup> edn), Springer-Verlag, New York, USA.
15. ten Cate O (2009) Why the ethics of medical education research differs from that of medical research. *Med Educ* 43: 608-610.
16. Zavarella MM, Gbemi O, Walters JD (2006) Accumulation of Non-steroidal Anti-inflammatory Drugs by Gingival Fibroblasts. *J Dent Res* 85(5): 452-456.
17. O'Brien TP, Roszkowski MT, Wolff LF, Hinrichs JE, Hargreaves KM (1996) Effect of a non-steroidal anti-inflammatory drug on tissue levels of immunoreactive prostaglandin E<sub>2</sub>, immunoreactive leukotriene, and pain after periodontal surgery. *J Periodontol* 67(12): 1307-1316.
18. Lindhe J, Karring T, Araujo M (2003) Anatomy of the periodontium. In: Lindhe J, Karring T, et al. (Eds.), *Clinical periodontology and implant dentistry*. Oxford: Blackwell Munksgaard, UK, pp. 3-49.
19. Birkedal-Hansen H (1993) Role of cytokines and inflammatory mediators in tissue destruction. *J Periodontol Res* 28(6 Pt 2): 500-510.
20. Walters JD, Nakkula RJ, Maney P (2005) Modulation of gingival fibroblast minocycline accumulation by biological mediators. *J Dent Res* 84(4): 320-323.
21. Yang Q, Nakkula RJ, Walters JD (2002) Accumulation of ciprofloxacin and minocycline by cultured human gingival fibroblasts. *J Dent Res* 81: 836-840.
22. Lavda M, Clausnitzer CE, Walters JD (2004) Distribution of systemic ciprofloxacin and doxycycline to gingiva and gingival crevicular fluid. *J Periodontol* 75(12): 1663-1667.
23. Selwitz RH, Ismail AL, Pitts NB (2007) Dental Caries. *Lancet* 369(9555): 51-59.
24. Colak H, Dulgergil CT, Dalli M, Hamidi MM (2013) Early Childhood Caries Update: A Review of Causes, Diagnosis and Treatments. *J Nat Sci Biol Med* 4(1): 29-38.
25. Girish Babu KL, Doddamani GM, Kumaraswamy Naik LR (2017) Knowledge, attitude, and practice of pediatricians regarding pediatric liquid medicaments. *Eur J Dent* 11(1): 106-110.
26. Sunitha S, Prashanth GM, Shanmukhappa, Chandu GN, Subba Reddy VV (2009) An analysis of concentration of sucrose, endogenous pH, and alteration in the plaque pH on consumption of commonly used liquid pediatric medicines. *J Indian Soc Pedod Prev Dent* 27(1): 44-48.
27. Newbrun E (1969) Sucrose the Arch Criminal of Dental Caries. *ASDC J Dent Child* 36(4): 239-248
28. Díaz-Garrido N, Lozano C and Giacaman RA (2016) Frequency of sucrose exposure on the cariogenicity of a biofilm caries model. *Eur J Dent* 10(3): 345-350.
29. Anu V, Kumar MS, Kumar PM, Babu AS (2011) Sweet Score and Dental Caries Experience of 12-13 Year Old School Children in Chennai. *Journal of Indian Association of Public Health Dentistry* 9(5): 305-308.
30. Touger-Decker R, van Loveren C (2003) Sugars and dental caries. *Am J Clin Nutr* 78(4): 881S- 892S.
31. Gupta P, Gupta N, Pawar AP, Birajdar SS, Natt AS, et al. (2013) Role of Sugar and Sugar Substitutes in Dental Caries: A Review. *ISRN Dentistry* 2013: 519421.
32. Bigeard L (2000) The role of medication and sugars in pediatric dental patients. *Dent Clin North Am* 44(3): 443-456.
33. Saeed S, Bshara N, Trak J, Mahmoud G (2015) Effect of dietary combinations on plaque pH recovery after the intake of pediatric liquid analgesics. *European journal of dentistry* 9(3): 340-345.
34. Naik LK, Babu KG, Doddamani GM (2017) Changes in the dental plaque pH due to pediatric liquid medicaments. *Journal of International Oral Health* 9(2): 60-64.
35. Passos IA, Sampaio FC, Martinez CR, Freitas CH (2010) Sucrose Concentration and pH In Liquid Oral Paediatric Medicines of Long Term Use after Children. *Rev Panam Salud Publica* 27(2): 132-137.
36. Valinoti AC, da Costa Jr LC, Farah A, de Sousa VP, Fonseca-Gonçalves A, et al. (2016) Are Pediatric Antibiotic Formulations Potentials Risk Factors for Dental Caries and Dental Erosion? *Open Dent J* 10: 420-430.
37. Angelova S, Targova-Dimitrova T, Damyanova D, Bliznakova D (2017) Correlation between Behavioral and Clinical Factors for Tooth Decay in Children with Pyelonephritis. The 5th Human and Social Sciences at the Common Conference - HASSACC 2017 held during September 25-29, Humanities - Past, Nowadays and Future. Slovak Republic, p. 121-124. ISBN: 978-80-554-1374-7; eISSN: 2453-6075; cdISSN: 1339-522X.
38. da Silva Pierro VS, Barcelos R, Maia LC, da Silva AN (2004) Pediatrician's perception about the use of antibiotics and dental caries - a preliminary Study. *J Public Health Dent* 64(4): 244-248.
39. Bawazir OA, Alsuwayt B, Alqahtani W, Al-Dhafiri A, Al-Shamrani M (2014) Knowledge, attitude and practice of pediatricians and pharmacists in Riyadh City toward the use of sugar free medications. *J Contemp Dent Pract* 15(6): 755-760.
40. Folayan MO, Bankole OO, Osaguona A, Fatusi O, Oyedele T, et al. (2012) A survey of knowledge, opinion and practice of dentists, pharmacists and parents in Nigeria towards the use of sugar-free medication. *Eur J Paediatr Dent* 13(2): 136-142.
41. De Menezes VP, Cavalcanti G, Mora C, Garcia AFG, Leal RB (2010) Paediatric Medicine and Their Relationship to Dental Caries. *Brazilian Journal of Pharmaceutical Sciences* 46(1): 157-164.



42. Nirmala SV, Popuri VD, Chilamakuri S, Nuvvula S, Veluru S, et al. (2015) Oral Health Concerns with Sweetened Medicaments- Paediatricians acuity. *J Int Soc Prev Community Dent* 5(1): 35-39.
43. Angelova S, Targova T, Panov VI, Bliznakova D, Andreeva R (2017) Epidemiology of Tooth Decay in Children with Pyelonephritis. - The 5th Virtual Multidisciplinary Conference, December 9-16, Other medical sciences, p. 179-182. eISSN: 2453-7144; cdromISSN: 1339-5572; ISBN: 978-80-554-1407-2.
44. Hussein AS, Abu-Hassan MI, Schroth RJ, Ghanim AM (2013) Parent's Perception on the Importance of Their Children's First Dental Visit (a Cross-Sectional Pilot Study in Malaysia). *Journal of Oral and Dental Research* 1(1): 17-25.
45. FitzGerald LZ, Gulvartian N, Ramos-Gomez FJ, Prestwich B (2017) A Sociobiological Model of Early Childhood Caries: The Role of Allostatic Load. *Pediatr Dent Care* 2: 138.
46. Featherstone JD (2008) Dental caries: A dynamic disease process. *Aust Dent J* 53(3): 286-291.
47. Dae-Young K, In-Woo C, Hyun-Seung S, Hyeong-Sik A, Hyun-Jung K, et al. (2017) Effects of host modulation by nonsteroidal anti-inflammatory drugs on periodontal disease: a systematic review and meta-analysis. *J Dent Rehabil Appl Sci* 33(1): 7-18.
48. (1996) Consensus report. Periodontal diseases: pathogenesis and microbial factors. *Ann Periodontol* 1(1): 926-932.
49. Havemose-Poulsen A, Sørensen LK, Bendtzen K, Holmstrup P (2007) Polymorphisms within the IL-1 gene cluster: effects on cytokine profiles in peripheral blood and whole blood cell cultures of patients with aggressive periodontitis, juvenile idiopathic arthritis, and rheumatoid arthritis. *J Periodontol* 78(3): 475-492.
50. Løe H (1993) Periodontal disease. The sixth complication of diabetes mellitus. *Diabetes Care* 16(1): 329-334.
51. Tomar SL, Asma S (2000) Smoking-attributable periodontitis in the United States: findings from NHANES III. National Health and Nutrition Examination Survey. *J Periodontol* 71(5): 743-751.
52. Cobb CM (2002) Clinical significance of non-surgical periodontal therapy: an evidence-based perspective of scaling and root planing. *J Clin Periodontol* 29(Suppl 2): 22-32.
53. Targova T, Angelova S, St. Peev, Bliznakova D (2017) Non-surgical periodontal therapy in systemically healthy patients with chronic periodontitis- Issues of the Council of Scientists- Varna. *Series of Medicine and Ecology* 22(2): 25-29. ISSN: 1310-6031.
54. Angelova S, Targova-Dimitrova T, Damyanova D, Bliznakova D (2016) Distribution and Prevention of Periodontal Diseases in Children. *Varna Medical Forum*, 5(2): 159-163. Medical University of Varna, Bulgaria; ISSN: 1314-8338.
55. Haffajee AD, Socransky SS, Ebersole JL (1985) Survival analysis of periodontal sites before and after periodontal therapy. *J Clin Periodontol* 12(7): 553-567.
56. Giannobile WV, Braun TM, Caplis AK, Doucette-Stamm L, Duff GW, et al. (2013) Patient stratification for preventive care in dentistry. *J Dent Res* 92(8): 694-701.
57. Kornman KS, Page RC, Tonetti MS (1997) The host response to the microbial challenge in periodontitis: assembling the players. *Periodontol* 2000 14: 33-53.
58. Page RC (1991) The role of inflammatory mediators in the pathogenesis of periodontal disease. *J Periodontol Res* 26(3 Pt 2): 230-242.
59. Offenbacher S, Odle BM, Van Dyke TE (1986) The use of crevicular fluid prostaglandin E2 levels as a predictor of periodontal attachment loss. *J Periodontol Res* 21(2): 101-112.
60. Caton JG, Ciancio SG, Blieden TM, Bradshaw M, Crout RJ, et al. (2000) Treatment with subantimicrobial dose doxycycline improves the efficacy of scaling and root planing in patients with adult periodontitis. *J Periodontol* 71(4): 521-532.
61. Preshaw PM, Hefti AF, Novak MJ, Michalowicz BS, Pihlstrom BL, et al. (2004) Subantimicrobial dose doxycycline enhances the efficacy of scaling and root planing in chronic periodontitis: a multicenter trial. *J Periodontol* 75(8): 1068-1076.
62. Reddy MS, Geurs NC, Gunsolley JC (2003) Periodontal host modulation with antiproteinase, anti-inflammatory, and bone-sparing agents. A systematic review. *Ann Periodontol* 8(1): 12-37.
63. Slomiany BL, Slomiany A (2001) Nonsteroidal anti-inflammatory drugs impair oral mucosal repair by eliciting disturbances in endothelin-converting enzyme-1 and constitutive nitric oxide synthase. *J Physiol Pharmacol* 52(1): 81-92.
64. Salvi GE, Lang NP (2005) Host response modulation in the management of periodontal diseases. *J Clin Periodontol* 32(6): 108-129.
65. Salvi GE, Lang NP (2005) The effects of non-steroidal anti-inflammatory drugs (selective and non-selective) on the treatment of periodontal diseases. *Curr Pharm Des* 11(14): 1757-1769.
66. Juliano C, Francisco W, Mustafa GM, Cassiano KR (2016) The effect of inflammatory response modulator agents on gingivitis and periodontitis. *RGO Rev Gaúch Odontol* 64(3): 312-319.
67. Waite IM, Saxton CA, Young A, Wagg BJ, Corbett M (1981) The periodontal status of subjects receiving non-steroidal anti-inflammatory drugs. *J Periodontol Res* 16(1): 100-108.
68. Feldman RS, Szeto B, Chauncey HH, Goldhaber P (1983) Non-steroidal anti-inflammatory drugs in the reduction of human alveolar bone loss. *J Clin Periodontol* 10(2): 131-136.



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