



International Journal of Current Research and Academic Review

ISSN: 2347-3215 (Online) ✨ Volume 5 ✨ Number 5 (May-2017)

Journal homepage: <http://www.ijcrar.com>



doi: <https://doi.org/10.20546/ijcrar.2017.505.013>

NSAIDS as Host Modulating Agent- A Review

Savitha Palanisamy^{1*} and Jaiganesh Ramamurthy²

¹Undergraduate student, Department of Periodontics, Saveetha University, Chennai, India

²Reader Department of Periodontics, Saveetha University, Chennai, India

*Corresponding author

Abstract

Host modulatory therapy is a treatment concept that aims to reduce tissue destruction and stabilize or even regenerate the periodontium by modifying or down regulating destructive aspects of host response and up regulating protective or regenerative responses by means of pharmacological agents. NSAIDS are effective in treating periodontal diseases in adjunct to the nonsurgical and surgical periodontal therapy. Various destructive enzymes and inflammatory mediators are involved in destruction. These are elevated in case of periodontal destruction. Host modulation aims at bringing these enzymes and mediators to normal level. The majority of periodontal breakdown is caused by host destructive enzymes like matrix metalloproteinases (MMPs) and inflammatory mediators (prostaglandins, interleukins) that occur as a part of inflammatory response. This review will highlight the role of NSAIDS as host modulating agent.

Article Info

Accepted: 28 March 2017

Available Online: 20 May 2017

Keywords

Host modulation, NSAIDS, Periodontal disease, non surgical and surgical periodontal therapy.

Introduction

Periodontitis is a chronic infectious inflammatory disease caused by microbes; however the presence of microbes is not enough for the cause of its complex nature of disease. Inflammation is the prime cause of periodontal disease. Host response to the invading bacteria plays a major role in the periodontal tissue loss. There is established evidence concluding that deficient host response increases periodontal tissue destruction (1).

The host modulation therapy is to restore the balance of pro-inflammatory or destructive mediators and anti-inflammatory or protective mediators to that seen in healthy individuals. Host Modulation Therapy (HMT) is a treatment concept that reduces tissue destruction and stabilizes or even regenerates inflammatory tissue by

modifying host response factors (2). It is a new treatment modality that has been incorporated into the dental therapeutics but it has not been well implemented in the dental practice due to the unavailability of the host modulatory agents (3).

Host modulation with chemotherapeutic agents or drugs is a promising new adjunctive therapeutic opportunity for management of periodontal diseases. The concept of host modulatory therapy was first introduced to dentistry by William and Golub et. al. and then expanded by many other researchers in the dental profession(4).

Pathogenesis of periodontitis

Plaque has been recognized as the primary etiologic agent for the development of periodontal disease, (5).

Periodontal pathogens present within the microbial biofilms initiate the periodontal disease by producing harmful by-products and enzymes that break down extracellular matrices and host cell membranes, in order to produce nutrients for their growth and possibly subsequent tissue invasion (6). This results in a host immune-inflammatory response in the periodontal tissues characterised by the production of inflammatory cytokines [e.g. interleukins (IL), prostanoids (e.g. prostaglandin E2)] and enzymes [including the matrix metalloproteinases (MMPs) (7). The level of these inflammatory mediators in the periodontal tissues is usually balanced by the anti-inflammatory cytokines and enzymes of the host immune system which ultimately functions to eliminate microbial pathogens and protect the host. However, an improper or exuberant immune response in certain individuals directly leads toward overproduction of destructive enzymes and inflammatory mediators (8). This immune-inflammatory response that develops in the periodontal tissues determines the susceptibility of individuals to periodontal disease. The variability in the host response also results from environmental and acquired risk factors which can accentuate the host inflammatory response and create an imbalance between the pro-inflammatory and anti-inflammatory activities in the periodontal tissues that result in the tissue destruction (9).

Host modulation therapy

The concept of host modulation is fairly new to the field of dentistry but is universally understood by most physicians who routinely apply the principles of host modulation to the no of chronic disorders. This concept to dentistry was introduced by Williams and Golub(5). Williams in 1990 concluded that, "There are compelling data from animal and human trials indicating that pharmacologic agents that modulate the host responses believed to be involved in the pathogenesis of periodontal destruction may be effective in slowing progression of periodontal disease (10). Various host modulatory therapies (HMT) have been developed or proposed to block pathways responsible for periodontal tissue breakdown.

It is a treatment concept that aims to reduce tissue destruction and stabilize or even regenerate the periodontium by modifying or down regulating destructive aspects of host response and up regulating protective or regenerative responses. The purpose of host modulatory therapy is to restore balance

between on the one hand, pro-inflammatory mediators and destructive enzymes and on the other hand anti-inflammatory mediators and enzyme inhibitors(11).

Host modulating agents

New strategies of managing periodontitis are to reduce bacterial load while simultaneously suppressing destructive host response. Host modulation with chemotherapeutics or drugs is an exciting new adjunctive therapeutic option for the management of periodontal diseases.

Various HMT have been developed to block or modify the pathways of periodontitis (2).

Inhibition of matrix metalloproteinase (MMPs): This is achieved by chemically modified tetracyclines (CMTs)

Inhibition of arachidonic acid metabolite: Through NSAIDs

COX-1inhibitors:Indomethacin, Flurbiprofen, Naproxen.

COX-2 inhibitors: Rofecoxib.

COX and LOX inhibitors: Triclosan, Topical ketoprofen.

LOX inhibitors: Lipoxins.

Modulation of bone metabolism

Bisphosphonates

Hormone replacement therapy (HRT)

Calcium supplementation.

Regulation of immune and inflammatory response:

Suppressing pro-inflammatory cytokines: IL1 and TNF- α receptor antagonist.

Nitric oxide inhibition.

Generation of protective antibodies through vaccination.

Infusion/ supplementary anti-inflammatory cytokines: IL-4 and IL-10.(12)

Non steroidal anti inflammatory drugs

Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) have been used to treat pain of acute or chronic inflammation. They are effective in inhibition of prostaglandin synthesis. They limit the progression of periodontitis through their ability to reduce inflammation and bone resorption. A pathway involved in periodontal disease pathogenesis involves

the synthesis and release of prostaglandins and other arachidonic acid metabolites within periodontal tissues. Both bacterial and host factors initiate tissue damage (13). This damage allows phospholipids in plasma membranes of cells to become available for action by phospholipase A2 and thereby results in production of free arachidonic acid (AA) (14).

Mechanism of action

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the formation of prostaglandins, including PGE₂, which is produced by neutrophils, macrophages, fibroblasts, and gingival epithelial cells in response to the presence of lipopolysaccharide (LPS). PGE₂ has been observed to be increased in periodontal disease compared with the level in healthy patients. PGE₂ also inhibits fibroblast function and has inhibitory effects on the immune response. NSAIDs inhibit prostaglandins and thus reduce tissue inflammation.

NSAIDs inhibit the PG synthesis by inhibiting the enzyme cyclooxygenase. Aspirin is an irreversible inhibitor of COX (by acetylation) while the others are reversible competitive COX inhibitors. There are two forms of cyclooxygenase viz., COX1 and COX-2 (15). COX-1 is found in most of the normal cells (constitutive

and is involved in maintaining tissue homeostasis. COX-2 is induced in the inflammatory cells by cytokines and other mediators of inflammation. This COX-2 catalyses the synthesis of prostanoids which are the mediators of inflammation. Most NSAIDs inhibit both COX-1 and COX-2 while some newer agents like celecoxib and rofecoxib selectively inhibit only COX-2 (16).

Inhibition of arachidonic acid metabolite

Arachidonic acid can be metabolised via the cyclooxygenase (CO) or lipoxygenase (LO) pathways. The final products of the CO pathway include prostaglandins, prostacyclin, and thromboxane.(17) Elevated levels of PGE₂ and other AA metabolites have been reported in gingival crevicular fluid (GCF) and periodontal tissues in patients exhibiting gingivitis, periodontitis, and periimplantitis (18). Mean crevicular PGE₂ concentrations are also significantly elevated in patients who exhibit disease progression compared to periodontally stable individuals. One proposed approach to modulate the host response is inhibition of enzymes responsible for the release of these destructive products. NSAIDs currently under investigation are Flurbiprofen, Naproxen, Meclofenamate and Ketorolac.(19).

Studies – NSAIDS as host modulating agents

STUDIES	MODE OF INTERCEPTION	RESULTS
Yen <i>et al.</i> (2008)	SRP+ celecoxib (COX – 2 inhibitors) 200mg for 6 months	Celecoxib had effective adjunct to SRP to reduce progressive attachment loss in patient with chronic periodontitis.
Kotsakis GA <i>et al.</i> (2011)	Aspirin < 162 mg/ day	This low dose aspirin had no effect on periodontal treatment with chronic periodontitis.
Azoubel <i>et al.</i> (2008)	SRP + etoricoxib 120 mg/ day for 7 days	Etoricoxib did not produce any clinical improvement but reduced PGE ₂ levels in GCF that could be related to improve in bone conditions.
Zeren <i>et al.</i> (2006)	SRP+ Ibuprofen 800 mg/ day for 2 weeks	Adjunctive use of Ibuprofen demonstrated no beneficial effect on the outcome of periodontal treatment for chronic periodontitis.

Adverse Effects

Anti-inflammatory doses are usually associated with adverse effects especially when used over a long period.

GI tract Nausea, epigastric distress, vomiting, erosive gastritis, peptic ulcer, increased occult blood loss in stools are common.(20).

Allergic reactions are not common and may be manifested as rashes, urticaria, photo sensitivity,

rhinorrhoea, angio-oedema and asthma especially in those with a history of allergies.(21)

Pregnancy and infancy: NSAIDs when taken at term delays the onset of labour due to inhibition of PG synthesis (PGs play an important role in the initiation of labour).It can also increase postpartum bleeding due to inhibition of platelet aggregation.

Hepatotoxicity can also occur when high doses of NSAIDs are used over a long period. Plasma levels of liver enzymes are raised.(22)

Contraindications

Peptic ulcer, liver diseases, bleeding tendencies and viral fever in children contraindicate the use of aspirin/salicylate.

Pregnancy - Aspirin should be avoided in pregnancy because it can cause premature closure of the ductus arteriosus in the foetus. Treatment with NSAIDs should be stopped one week before any surgery because of the risk of bleeding due to anti-platelet effect.(23)

Conclusion

Host response modulation by therapeutic agents should not be considered a stand-alone procedure. Non-steroidal anti-inflammatory drugs inhibit arachidonic acid (AA) metabolites slow alveolar bone loss and this approach may be an adjunct to conventional mechanical treatment. Since NSAIDs are lipophilic and are well absorbed into gingival tissues, its topical application and has its effect in periodontal treatment for chronic periodontitis.

References

1. Kritika Jangid, Jaiganesh Ramamurthy, Varghese Mathew, and ND Jayakumar, Anti- Cytokine Therapy in Periodontitis, RJPBCS 6(1):376,2015.
2. ShaluBathla, Host Modulatory Therapy, In Periodontics Revisited, 1st Edition, 292-295, 2011.
3. Maria Emanuel Ryan and Phillip M. Preshaw, Host Modulation, In Carranza's Clinical Periodontology, 10th Edition, 275-282, 2007.
4. Genco R, Kornman K, Williams R, Offenbacher S, Zambon J, Ishikawa I, *et al.* Consensus report periodontal diseases: pathogenesis and microbial factors. Ann Periodontol. 1(1):926-32, 1996.
5. Haffajee AD, Socransky SS. Microbial etiologic agents of destructive periodontal diseases. Periodontol 2000. 1994;5:78-111.
6. Kirkwood KL, Cirelli JA, Rogers JE, Giannobile WV. Novel host response therapeutic approaches to treat periodontal diseases. Periodontol 2000.
7. Preshaw PM. Host response modulation in periodontics. Periodontol 2000. 2008;48:92-110.
8. Ryan ME, Preshaw PM. Host Modulation. In: Newman MG, Takei HH, Klolleold PR, Carranza FA, editors. Carranza's Clinical Periodontology. 11th ed. India: Saunders; 2012. pp. 275-280.
9. Souza JA, Rossa C, Jr, Garlet GP, Nogueira AV, Cirelli JA. Modulation of host cell signaling pathways as a therapeutic approach in periodontal disease. J Appl Oral Sci. 2012;20:128-38.
10. Williams RC. Periodontal disease. New England Journal of Medicine. 1990;322(6):373-82.
11. Oringer R. Modulation of the host response in periodontal therapy. Journal of Periodontology. 2002; 73(4):460-70.
12. Albandar JM. Global risk factors and risk indicators for periodontal diseases. Periodontology 2000, 29(1):177-206. 2002
13. Howell TH, Williams RC. Nonsteroidal antiinflammatory drugs as inhibitors of periodontal disease progression. Critical Reviews in Oral Biology & Medicine. 1993;4(2):177-96.
14. Kirkwood KL, Cirelli JA, Rogers JE, Giannobile WV. Novel host response therapeutic approaches to treat periodontal diseases. Periodontology 2000. 2007;43(1):294-315.
15. Ryan ME. Non-surgical approaches for the treatment of periodontal diseases. Dent Clin N Am 2005; 49:611-36.
16. Preshaw PM. Host response modulation in periodontics. Periodontol 2000 2008; 48:92-110.
17. Offenbaceer S, Odle B, Dyke T. The use of crevicular fluid prostaglandin E2 levels as a predictor of periodontal attachment loss. Journal of periodontal research. 1986;21(2):101-12
18. Albandar JM. Global risk factors and risk indicators for periodontal diseases. Periodontology 2000, 29(1):177-206. 2002
19. Howell TH, Williams RC. Nonsteroidalantiinflammatory drugs as inhibitors of periodontal disease progression. Critical Reviews in Oral Biology & Medicine, 4(2):177-196, 1993.
20. Venes D, editor. Taber's medical dictionary. Philadelphia: F.A. Davis Company; 2009.
21. Tatakis DN, Kumar PS. Etiology and pathogenesis of periodontal diseases. Dent Clin N Am 2005; 49:491-516.
22. Van Dyke, T E. The management of inflammation in periodontal disease. J Periodontol 2008; 79:1601-8.
23. Albandar JM. Global risk factors and risk indicators for periodontal diseases. Periodontology 2000, 29(1):177-206. 2002

How to cite this article:

Savitha Palanisamy and Jaiganesh Ramamurthy. 2017. NSAIDS as Host Modulating Agent-A Review. *Int.J.Curr.Res.Aca.Rev.* 5(5), 97-100. doi: <https://doi.org/10.20546/ijcrar.2017.505.013>