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Effect Of Non-Surgical Periodontal Therapy On Levels Of Salivary MMP- 8 In Chronic Periodontitis Patients: Systematic Review

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Introduction

Chronic periodontitis is a condition that results in the loss of tooth-supporting connective tissue and alveolar bone and, if untreated, is a major cause of tooth loss in adults. [1] It is a prevalent condition, affecting 47.2% of the adult US population aged 30 years or older. [2] According to the Centre for Disease Control and Prevention and American Academy of Periodontology case definitions, the prevalence of moderate and severe periodontitis are estimated as 30.0% and 8.5%, respectively, among US adults. [1]

Periodontitis, when viewed from a histopathological perspective, is characterized by a complex interaction between periodontal bacteria and host inflammatory response which results in the release of pro-inflammatory cytokines which leads to the destruction of supporting periodontal structure and the alveolar bone.[3] One of the important host factors responsible for collagen destruction and extracellular matrix destruction is Matrix Metal loproteinases (MMP). Many MMP are studied over the years and the important ones are MMP -1, 8, 9, 13, and 14. [3]

Chronic Periodontitis presents in various forms and it's challenging for the clinicians to manage the varying extent and severity the disease presents. Treatment of Chronic periodontitis can range from Scaling and Root Planning (SRP) to SRP with adjunctive treatments to surgical interventions.[1] The options chosen however can vary and depend on the degree of Chronic Periodontitis. The effect of treatment of chronic Periodontitis is reflected in the improvement of clinical parameters and the Histological parameters.

When a Literature search was carried out we came across a few systematic reviews [4, 5] which showed that chronic periodontitis patients had increased levels of MMP8 levels. Thus we decided to go a step further and decided to see if non-surgical therapy brings about a reduction in the MMP8 Levels.

On literature search, it was noted that along with SRP procedure along with other adjunctive therapies were available which reduced the MMP 8 levels.

Thus the PICOS was designed accordingly.

Population- aged 18- to 58-year-old having chronic periodontitis.

Intervention – Scaling and root planning/ Scaling and root planning along with Adjuvant therapy.

Control- subjects with clinically healthy periodontium.

Outcome - Change in salivary MMP- 8 levels in chronic periodontitis patients.

Study design – Randomized control trial

Material and methods

Literature Search/Data Base Search

Extensive literature search was carried out using the following electronic databases, amending the search strategies Trial Register of the Cochrane Oral Health Group (to 18 December 2015),Cochrane Central Register of Controlled Trials (CENTRAL) (2015, Issue 11), MEDLINE via Ovid (1946 to 18 December 2015), EMBASE via Ovid (1980 to 18 December 2015), HINARI, Science Direct, Google Scholar, Ebsco host and Wiley.

Also, US National Institutes of Health Trials Register (http:// clinicaltrials.gov) (to 18 December 2015) and Clinical Trial Registry-India were used as search engines. Free ones have been downloaded directly by the URLs generated from the database. The restricted group has been downloaded by the institutional access of the KAU library.

Search Strategy

The Mesh terms used were “Matrix Metal loproteinases 8” “Chronic Periodontitis” “Non-Surgical Periodontal therapy” “Scaling and Root Planning”. The Boolean operators used were “AND” and “OR”.

We placed no restrictions on the language and no time frame restriction of the publication was used for searching the electronic databases. Where only a relevant title without a listed abstract was available, a full copy of the article was assessed for inclusion. The references of included articles were checked for additional studies suitable for inclusion. The articles were assessed by two independent authors. Reference lists were checked to identify any other articles that might provide information relevant to the research question.

67 records were obtained from various search engines, of which after assessment, 27 duplicates were removed, of which 40 were screened and 25 full-text articles which were not available as full text were excluded. 15 full articles were assessed for eligibility. 04 studies were excluded as they don’t meet the inclusion criteria. Finally, 11 articles were included for the synthesis of the systematic review. **(Details in the PRISMA flow chart).**

Inclusion & Exclusion Criteria

The inclusion and exclusion criteria as mentioned in Table 1.

Inclusion Criteria
• Patients aged 18-58 years • Studies which studied MMP-8 levels by either Saliva, GCF samples • Study having a control group • Randomised Controlled Trails
Exclusion Criteria • Study having Patients above 58 years • Study having Medically compromised patients like Diabetes, Hypertension, Cardiac History • Studies that assessed MMP 8 levels in Aggressive Periodontitis • Studies that assessed MMP 8 levels in Juvenile Periodontitis

Article review

Two independent authors reviewed the articles. Only articles that complied with the inclusion criteria were reviewed further. Full copies of articles were reviewed independently by two reviewers (add reviewers initial) for compliance with the exclusion criteria. Those articles that assessed MMP 8 levels by any of the sample fluid be it Saliva, GCF or blood were included. Also all the studies which used ELISA method or any other method for MMP8 levels were included.

Data Extraction

A systematic data extraction sheet was constructed. The details included were Author, Year of publication, Country where study was carried out, Sample size, Fluid which was collected, Study group, Control group, Methodology, Duration of study and results of the study.

Results

Data Summary of Included study

Totally 11 articles were included in the study. 1 study used Plasma as sample to assess the MMP8 levels, saliva was used as medium in 3 studies and majority of studies i.e. 7 studies used Gingival Crevicular fluid (GCF).

Data of Excluded Studies

Based on the exclusion criteria 4 studies were excluded because of the following reasons. 2 Studies were done on Aggressive Periodontitis patients, 1 Study was done on Juvenile Periodontitis patients and 1 study was done in systemically compromised (Diabetic) Patients.

Discussion

MMP-8 and its Fluid Sources

MMP s are proteolytic enzymes that belong to the zinc protease superfamily involved in the physiological degradation of extracellular matrix proteins and basement membranes, and they are often categorized into several groups. A significant source of MMP-8 (neutrophil-type MMP-8) in humans is degranulation triggered by neutrophils, but MMP-8 (mesenchymal cell-type MMP-8) is

additionally de-nova expressed and secreted in small amounts by non-PMN-lineage cells like epithelial cells, smooth muscle cells, fibroblasts, macrophages, and endothelial cells.[5]

MMP-8 which is one of the important members of the MMPs family and belongs to the collagenous group exhibits a novel ability to decompose type I and III collagen which are found within the periodontal ligament. Therefore, it will be hypothesized that MMP-8 acts as a biomarker in periodontitis. [6]

The main source of oral salivary collagenase is PMNs that enter the mouth through the gingival sulcus. GCF levels of MMPs in patients with periodontitis were also studied in terms of their diagnostic and prognostic values.[7]

7 studies out of the 11 studies included used GCF because the sample to assess the MMP8 levels. 9 studies used the ELISA test to analyse the fluid and one study by Kinane DF[8] used monoclonal antibodies and the other study by Pozo[9] used Western blotting.

MMP8 and Scaling and Root Planning (SRP)

Smiley C J et al.[1] in their article discusses strong evidence-based recommendations that SRP helps in reducing the MMP 8 levels yet the Clinical Parameters of the diseases such as Bleeding on Probing, Probing depth, loss of attachment reduced over time. The author also recommends that along with SRP adjuvant therapies may be combined to assist bring the disease in check. [1]

In the current systematic review, 11 studies are included within which 4 studies compare the extent of reduction of MMP-8 levels after scaling and root planning only. Other 7 studies together with SRP other adjuvant therapy was used. 3 studies - Sub microbial Dose of Doxycycline was used as an adjuvant; 1 study - hyperbaric oxygen therapy was used; 1 study - Probiotic Mouthwash was used and last 1 study- used Ozonized Oil as an adjuvant.

The 4 studies which showed that SRP reduced MMP-8 levels were Kinane DF et al.[8], Pozo P et al.[9], Marcaccini AM et al [10], Sexton W M et al.[11] All of them compared MMP-8 levels after the Scaling and Root Planning (SRP) procedure between healthy patients and patients with periodontitis.

Adjuvants used along with SRP

Three studies Choi DH et al, [12]Tuter G et al, [13]Emingil G et al.[14] used sub antimicrobial dose of Doxy cycline as an adjuvant together with SRP procedure. In all three studies, it was observed that MMP 8 levels reduced much further when used along with adjuvants than SRP alone. Doxy cycline is one of the tetracycline derivatives that are known for its effectiveness in antibiotic applications. It is widely used because of its effectiveness in suppressing periodontopathic microorganism and has been used widely as an adjunct to periodontal therapeutic agents.[12]

Kanagaraj SS et al [15] used probiotic product merchandise was a combination of BIFILAC-lozenges, which had the following composition contains Lactobacillus sporogenous 100 Million, Streptococcus faecalis T-110 JP C 6 0 million, Clostridium butyrium TO- A4 million, and Bacillus mesenteric TO-A JPC 2 million. [15]

Nardi NP [16] used Ozonized olive oil as an adjuvant and both groups showed statistically significant differences. Ozone has analgesic and anti-inflammatory actions and is thought to act by a different

mechanism of action: The suggested mechanisms are (1) Decreased production of inflammatory products and (2) Inactivation of metabolic products that mediate pain by oxidation and by improving the vascular supply that ends up in increased oxygen availability to tissue and better rate of toxic product elimination. It further improves tissue regeneration and quickens wound healing. Moreover, ozone is a negatively charged ion, thus it rebalances the acidic environment in infection. [16]

Soranta N.P [17] used Hyperbaric Oxygen therapy (HBOT) together with traditional SRP was used. It was seen that the reduction in MMP 8 levels was statistically significant when SRP was combined with HBOT than SRP used alone. Hyperbaric oxygen therapy is a therapy method where one inhales 100% pure oxygen in a high-pressure room of more than 1 ATA (Absolute Atmosphere). Chen T and his colleague's (2002) study showed that HBOT increased oxygen distribution at the bottom of the periodontal pocket, it could inhibit the growth of anaerobic bacteria and also allowed ischemic tissue to receive adequate oxygen intake for rapid recovery of cellular metabolism.[18]

Hendiani I et.al [19] used mangos teen peel extract which is an herbal extract. It was administered within the pocket depth and examined after 15 days. This was one such study that didn't show a statistically significant difference compared to SRP alone.

Conclusion

The reduction in GCF MMP-8 levels following therapy indicates that MMP-8 is one molecule that may eventually prove useful as an indicator of current disease status and possibly as a predictor of future disease. The fact that simple Scaling and Root Planning (SRP) can reduce an important marker of inflammation is incredible. The use of simple adjuvants further proves to be a better option than SRP alone. Today there are many adjuvants available that can provide synergistic to SRP in reduction of periodontal inflammation. However, more clinical trials need to be carried out which helps us decide which of the adjuvants are better.

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