Original Article

Efficacy Of Commercially Available 10 Mg Curcumin Gel On Gingival Crevicular Fluid Periostin levels In In Chronic Periodontitis Patients

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Abstract

Inconsistency of the host in immunoinflammatory processes in the gingival and periodontal tissues in response to bacteria is thought to be the cause of periodontal disease pathogenesis.[1]The most common type of periodontitis is chronic periodontitis, which is characterized by a slowly growing inflammatory condition.[2]

In order to alleviate periodontal inflammation, a variety of treatment options such as nonsurgical and surgical therapy are available, depending on the severity of the disease.[3] The reduction or removal of periodontal pathogens, whether by nonsurgical or surgical therapy, as well as the patient's systemic status, patient compliance, and other factors, determine the success of periodontal therapy. Scaling and root planing (SRP) is the first nonsurgical procedure that has been compared to other therapies in terms of removing plaque and calculus supragingivally as well as subgingivally and thereby returning tissues to a healthy state.[4] Antibiotics, both local and systemic, can be administered in conjunction with SRP to treat chronic periodontitis. Because of its site specific nature and less adverse effects than antibiotics given systemically, chemotherapeutic drugs delivered locally through a syringe or irrigating devices into the pockets were effective against the flora located subgingivally.[3,5]

Despite of the progress in medical science, plants are still considered to be an important source of drugs worldwide & there is renewed interest coming in for use of various ayurvedic medicines & herbal products for dental health.[3]"Turmeric (common name for curcuma longa) is yellow, water insoluble pigment, an Indian spice derived from the rhizomes, a perennial member of the Zingiberaceae family".Curcumin (diferuloylmethane), bisdemothoxycurcumin, and demothoxycurcumin are active ingredients of turmeric, as with numerous volatile oils such as atlantone, turmerone, and zingiberone, as well as proteins, carbohydrates, and resins. Curcumin has anti-inflammatory, antioxidant, antibacterial, antiviral, anticarcinogenic, and anticarcinogenic properties.[5]

INTRODUCTION

The periodontium destruction causes as a result of the host immune response, which includes the production of pro-inflammatory cytokines like IL-1, IL-6, and TNF-α, proteases (matrix metalloproteinases [MMPs]), and prostanoids (e.g., prostaglandin E2, or PGE2), all of which increase alveolar bone resorption.[6]Curcumin inhibits the production of these inflammatory cytokines by modulating the activity of transcription factors and signalling pathways, particularly nuclear factor—B (NF-B), mitogen activated protein (MAP) kinases, and activating protein-1, and regulates the inflammatory response by suppressing the activity of lipoxygenae, cyclooxygenase-2, and inducible nitric oxide synthase enzymes (AP-1). As a result, inhibiting proinflammatory cytokines is aided by downregulation of these mechanisms. So, when delivered locally, curcumin, which can target both bacteria

and host inflammatory cells, can be a potential method in treating periodontitis by bypassing first pass metabolism and extending drug residency at the site of action.[7]

Thus in order to measure the efficacy of any locally administered drugs there must be improvement in both clinical and biochemical parameters so GCF, an inflammatory exudate where biomarkers can be identified helps in evaluating the inflammatory status of the periodontal tissues.[8]

Periostin (gene POSTN), a secreted adhesion molecule important for periodontal tissue integrity, is abundantly expressed in the PDL, where it plays an important role in wound healing and periodontal abnormalities, assisting in tissue maturation. It's a 90-kD protein that was first discovered in mice in 1993 and was given the name osteoblastic specific factor-2 before being renamed periostin due to its presence in the PDL and periosteum.[9]Fibroblasts secrete it, which can be found in numerous tissues, GCF, serum, and saliva. It works as a matricellular protein to activate cells by binding to their cell surface receptors, allowing them to carry out their biological responsibilities.[10] When exposed to Porphyromonasgingivalis lipopolysaccharide and TNF-α, which are prevalent in periodontitis and elevated in a healthy periodontal condition, its expression is downregulated in periodontal ligament fibroblasts.[11]So periostin acts as a marker for cell behaviour in matrix biomechanics and for reconstructive cellular matrix interactions in such situations, assisting in collagen formation, adhesion, cell migration, mechanical stress responses, and wound repair.[9]

Therefore, this study was done to evaluate and compare the efficacy of commercially available 10 mg Curcumin gel on Periostin level in GCF in treatment of chronic periodontitis with non surgical periodontal therapy.

Materials and Method

The present study was conducted in Department of Periodontology, ManavRachna Dental College, Faridabadand approved by the institutional ethics committee via ethical number CTRI/2020/11/028821.The study enrolled 45 patients (90 sites) taking the dropouts into consideration in which 4 patients failed to maintain the follow up visit and aged between 30-50 years with ≥20 teeth remaining of both sexes with chronic periodontitis exhibiting probing pocket depth of 4-6 mm and clinical attachment loss of ≤ 5mm in atleast 2 sites present bilaterally in posterior teeth in a single arch (maxillary/mandibular) adjacent teeth were included.Patients with a history of oral prophylaxis in past 3 months, intake of antibiotics, antioxidants and antibacterial mouth wash in last 3 months, pregnant and lactating mothers, use of any form of tobacco and any systemic disease were excluded from the study. Following the Covid-19 standard operating procedures patients were informed about the study duration and the benefits in detail and a written informed consent was obtained from all the patients willing to participate in the study. It is a randomized split mouth study design and the computer randomization method was used to randomize the sites into test group i.e, scaling and root planing (SRP) along with adjunctive use of commercially available10 mg Curcumin gel as local drug in the periodontal pocket and control groupi.e, scaling and root planing (SRP) alone.For standardization of the clinical parameters acrylic stents were made and GCF samples were collectedfrom the selected sites with the help of calibrated capillary micropipettes and stored in Eppendorf tube at -80^{o} C for estimation of periostin levels for each patient at baseline and 3 month using ELISA (Sandwich-ELISA principle)and clinical parameters were recorded which included PI (Turesky-Gilmore-Glickman modification of the Quigley and Hein plaque index,1970)[12], SBI (Muhlemann H.R and Son.S,1971)[13], PPD(Using UNC-15probe) and CAL (using UNC-15probe) at baseline, 1month and 3 months. After data collection all the participants selected in the present study received supragingival scaling and the selected sites underwent SRP and in thetest group the sites received commercially available 10mg Curcumin gel (curenext®) which was loaded in 2 ml syringe with an intrasulcular applicator tip**(**figure 1**)**.It was isolated using cotton rolls before placement, gel from syringe was applied in the site directly with an intrasulcular applicator tip and then withdrawn, while continuing to extrude the material, till the superior portion of the pocket.Coe-Pak™ was used to cover the pocket so as to prevent the ingress of oral fluids as well as to allow the retention of the material within the pocket **(**figure 2).Oral hygiene instructions were given and there was no dietary restrictions at baseline, 1 and 3 month visits. Patients were instructed not to use any chemotherapeutic agents or any oral irrigation devices during the study period. Patients were recalled on the 7th day for the removal of the periodontal dressing and at 1 and 3 months.

Statistical Analysis

The data were collected, tabulated in a Microsoft excel sheet and subjected to statistical analysis using Statistical Package for social sciences software (SPSS version 22.0 for windows; SPSS inc, Chicago, USA). Means and standard deviations were calculated for each group and were further assessed for statistical significance using parametric tests i.e. Paired t-test and Student t-test. The level of significance was set at $p < 0.05$.

RESULTS

On intragroup comparison, changes were statistically significant ($p = 0.001$), with reduction in plaque scores from baseline to 3 months in both the group. The changes in sulcular bleeding index were statistically significant ($p = 0.001$) at all the time intervals. For mean pocket probing depth and clinical attachment levels at different time interval inboth the groups there was statistically significant difference found. (Table 1).

On intergroup comparison, the plaque index scores and sulcus bleeding index of control and test group when compared it was found to be statistically not significant between the groups.At all-time intervals, there was a statistically significant difference between the probing pocket depths of both groups except from 1 to 3 months.Similarly for clinical attachment levels of both groups showed statistically significant differences at all-time intervals except from 1 to 3 months and the p value was p=0.550 from 1 to 3 months (Table 2).

On intragroup comparison, at baseline periostin levels was not significant (p=0.823) for both the groups.After 3 months follow up periostin levels increased to 6.764 ± 0.966 in control group and 8.654±1.32 in test group (Table 3). On intergroup comparison, the mean change of periostin levels from baseline to 3 months was 0.830±0.538 in control group and -2.675±0.975 in test group and were statistically significant (Table 4).

DISCUSSION

Curcumin(diferuloylmethane), is a natural drug that has recently acquired favour for treating periodontal disease in various concentrations.[3]It is turmeric's main yellow bioactive component, has been shown to exhibit a wide range of biological actions, hinting that it could be used as a subgingival drug. According to safety studies, both turmeric and curcumin are well tolerated at very high levels without producing any harm. [3,14]

The multifunctional protein periostin (POSTN) has been linked to a variety of tissue repair and regeneration processes. After being secreted, periostin displays a preference for attaching to molecules like tenascin-C, collagen, and BMP-1. This property improves tissue strength by assisting in the development of the extracellular matrix. Periostin is the most specific of the proteins expressed in the periodontal ligament.[15]

The clinical parameters in our study showed improvements in both the test and the control groups, and the results showed statistically significant changes. On intragroup comparison the reduction in PI was due to good oral hygiene maintenance by patients throughout the study period as oral hygiene instructions were reinforced at each visit. Results were similar to the study by Bhatia et al and Ravishankar PL et al that showed reduction in PI values from baseline to 3 months [3,16]and for SBI similarly in accordance with Behal R et al where reduction in bleeding from baseline to 45 days was observed thus SRP is effective in removing the local irritants and also in reduction of the periodontopathogens.[17]

The present study results are in accordance with Bhatia et al, Anitha V et al and Arslan R et al where controls and tests showed significant reduction in PPD at the end of one month. [16,18,19]Also there were statistically significant changes seen in CAL. This is because of the anti-inflammatory and wound healing capacity of curcumin which was used as an adjunct to SRP and thus promoting the migration of fibroblasts in wound bed and thus resulting in reduction of vascularization of connective tissue. The findings were in accordance to a study by Agarwal E et al and Dave DH et al where changes in CAL for both groups was significant at all the time intervals except between 1 -3 months and 1-2 months respectively.[14,20]

On intergroup comparison, the changes were not significant for PI and SBI observed at different time intervals. This was similar to the study by Sharma A, Agrawal E et al and Bhatia M et al where no significant differences

was found in PI and SBI scores at any point of interval and can be attributed to the reason that it was a spilt mouth study design, good patient compliance and improved gingival status due to resolution of inflammation after SRP for both groups. .[16,20,21]

A study by NagasriM et al, Ravishankar PL et al, Dave DH et al and Bhatia M et al there was decrease in the PPDand gain in CAL when compared to control group at different time intervals. This could be due to elimination of pathogenic bacteria because of the beneficial effects of SRP along with adjunctive use of curcumin.[3,5,14,16]Curcumin gel that was used as a local drug delivery at the selected sites had added benefits, by suppression of the activation of nuclear factor-kappa B, downregulation of the expression of the cell proliferation, metastatic gene products and antiapoptotic and has various biologic properties and thus T-cells, B-cells, macrophages, neutrophils, natural killer cells, and dendritic cells are among the immune cell types that have their proliferation and cellular responses modulated.It induces re-epithelialization and stimulates epithelial cell migration to the wound area by boosting the localization of transforming growth factor-1.[3] But there was no significant changes seen for PPD and CAL when both groups were compared between 1-3 months which can be due to the initial healing which completes at 1 month after SRP and re-epithelization at 7 days, good oral hygiene in both groups and the release of the drug is for initial 24 hours, therefore the gel had proved to be beneficial in better reduction of PPD and gain in CAL but further the effect was not seen. This finding is in accordance to a study by Bhatia M et al where in-vitro release of curcumin gel that is assessed by UV spectrophotometry showed 16.30% release of curcumin in 24 hours and at the end of the 7th day the drug release was found to be 69.44%.[16] So it can be said that the changes remained sameand similar changes were seen in Nagasri M et al.because of the earlier re-epithelialization and increased levels of transforming growth factor-β1.[5]

The periostin levels on intragroup comparison showed statistically significant increase in periostin levels at the end of 3 months when compared to baseline. This could be in relation to thorough SRP that led to decrease in bacterial load, leading to reduction to inflammatory mediators thus enhancing the expression of periostin. In contrast periostin levels were found to be lower in the chronic periodontitis patients as there was increase in bacteria and its byproducts.[15] The TNF-α (inflammatory mediator) it strongly inhibit the periostin expression in fibroblasts and PDL cells thus impeding normal periodontium functions.

Our study results are similar to study by Aral CA et al and Balli UM et al who found that there was a negative relationship between GCF periostin levels and clinical parameters whereas a positive correlation was observed between salivary periostin levels and the results were statistically significant.[10,22]On intergroup comparison it was seen that the test group showed more significant increase in periostin levels compared to controls. The study results can be due to the use of curcumin as a local drug delivery agent in the test site, Curcuma longa which is a yellow, water-insoluble pigment extracted from the root of turmeric has Curcuminoids which possess wide range of biologic activities and targets many molecules and receptors.[3]

So as it is seen that SRP was beneficial for both the groups but when curcumin gel was used as an adjunct it showed profound effect on treatment of chronic periodontitis and also helped in improving the levels of periostin which helps in increasing fibroblastic activity.

LIMITATIONS

The study duration should have been longer for a clear judgment and better evaluation of the results and in addition no microbiological analysis was donewhich would have been beneficial in detecting the efficacy of local drug delivery. Also the radiographic analysis was not done and larger sample size would have yielded better results. So studies involving larger sample size and longitudinal studies is recommended to further evaluate the efficacy of 10 mg curcumin gel on clinical parameters and periostin levels.

CONCLUSION

Within the limitations of the study it was concluded that commercially available 10 mg curcumin gel as an adjunct to SRP is effective in the treatment of chronic periodontitis. The role of curcumin on change in periostin levels can open up new horizon in biomarker to ascertain the initial periodontal disease activity.

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SELF FUNDING

Conflict of Interest

There is no conflict of interest.

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Figure 1

Figure 2

Legends

Figure1: Placement of 10 mg curcumin gel (Curenext®)

Figure 2: Placement of Coe-Pak ™