ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 6, Issue – 3, June - 2023, Page No. : 493 – 504

2 % curcumin gel as an adjunct to scaling and root planning in periodontitis patient with type 2 diabetes.

[1]Dr. Grace Mary Joseph, Postgraduate Student, Department of Periodontics, A. J. Institute of Dental Sciences, Mangaluru, Karnataka.

[2]Dr. Parimala Kumar, Reader, Department of Periodontics, A. J. Institute of Dental Sciences, Mangaluru, Karnataka.

Corresponding Author: Dr. Grace Mary Joseph, Post graduate student, Department of periodontics, A.J Institute of Dental Sciences, Mangaluru, Karnataka.

Citation of this Article: Dr. Grace Mary Joseph, Dr. Parimala Kumar, "2 % curcumin gel as an adjunct to scaling and root planning in periodontitis patient with type 2 diabetes", IJDSIR- June - 2023, Volume – 6, Issue - 3, P. No. 493 – 504.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Periodontitis and diabetes exhibits a two-way relationship. Patients with diabetes have an increased prevalence and severity of periodontal disease. Il-6, a multifactorial cytokine is associated with pathogenesis of diabetes as well as play a very important role in inflammation and bone resorption associated with periodontitis. Curcumin is a herbal agent with multitude of uses and its anti-inflammatory property enhances the periodontal therapy. The present study is designed to estimate the efficacy of 2 %curcumin as an adjunct to scaling and root planning in periodontitis patients with diabetes by assessing the clinical parameters, saliva IL-6 levels and HbA1c levels.

Method: A clinical study was conducted in 40 periodontitis patients with diabetes (HbA1c < 9%) in the age group of 30-60 years. They were classified into two groups. Group 1: scaling and root planning and Group 2: Scaling and root planning with 2 % curcumin gel application on same day, 10th day and at end of three months. Clinical parameters (GI, PI, CAL and PPD), saliva IL-6 levels and HbA1c levels were estimated in both the groups at baseline and at end of three months. In group 2 clinical parameters were recorded on 10th day and at end of one month.

Results: Present study revealed that 2 % curcumin as an adjunct to scaling and root planning enhanced clinical parameters and improved HbA1c levels. IL-6 analysis revealed no statistically significant changes from baseline to end of 3 months in both the groups. The intra group assessment in group 2(SRP + curcumin) showed that, clinical parameters assessment was better at end of 10th day and end of 1 month.

Conclusion: Present study suggests that 2% Curcumin can be used as an adjunct to SRP among periodontitis patients with diabetes because of its anti-inflammatory property and saliva IL-6 can be used as a non-invasive tool for diagnosis of periodontitis and pre diabetes.

Keywords: Chronic Periodontitis, Type II Diabetes, IL-6, 2 % curcumin gel, HbA1c

Introduction

Periodontitis is a chronic inflammatory disease characterized by inflamed gingiva, bleeding on probing, increased probing pocket depth, clinical attachment loss, pus discharge, and resorption of alveolar bone. It is multifactorial in origin and is being affected by bacterial environmental, behavioural as well as systemic factors.[1] One of the most common primary etiologic reasons for periodontal disease is the pathogenic bacteria in the subgingival region.[2] Diabetes mellitus is a metabolic disorder characterized by hyperglycaemia due to defective secretion or activity of insulin[3] and is considered as a risk factor for periodontitis.[4] IL -6 is a multifactorial cytokine produced by a variety of cells and is secreted by macrophages in response to inflammation and is involved in recruitment and apoptosis of leukocyte and T-cell activation. IL-6 and its soluble receptor induce bone resorption, either by increasing the receptor activator of nuclear factor κ ligand (RANKL) or by directly inducing the formation of osteoclast recruitment and apoptosis of leukocyte and T-cell activation. Elevated levels of salivary IL-6 at the periodontally infected sites from diabetic patients prove the systemic influence of diabetes on periodontium.[5] Thus, by evaluating the salivary IL-6 level, the risk and severity of periodontitis in type 2 diabetic patients can be predicted. In the future, the salivary IL-6 levels can be used as an important biomarker for the diagnosis, prognosis, and to predict the treatment outcomes of periodontitis.

Conventional periodontal therapy aims at improving overall gingival health and prevent the progression of attachment loss. But at times in certain regions their still persists gingival inflammation and further loss of attachment in spite of adequate supportive therapy. Scaling and root planning along with local drug delivery reduces microbes and also improves the periodontal clinical parameters. Hence, administration of systemic or [2]local drug delivery enhances the periodontal treatment due to its site-specific nature.

Herbal drugs have long era of use and good patient tolerance as well as better public acceptance. Curcumin has been used extensively in ancient ayurvedic medicine since ages, as it is non-toxic and has a variety of therapeutic properties including anti-oxidant, analgesic, anti-inflammatory, anti-septic activity, and anti-carcinogenic activity.[6] Curcumin plays a very important role in the management of periodontal disease. One added advantage of curcumin is that it helps in decreasing the antibiotic resistance, by suppression of NF-κβ activation.[7]HbA1c is related to the mean blood glucose concentration over the past 1–3 months, and it is considered to be a standardized measurement used to estimate the effect of diabetes treatment. Studies have proved that periodontal treatment leads to reduction of HbA1c in diabetic patients with periodontitis with improvements in periodontal clinical parameters.[17]

In periodontitis patients, the production of proinflammatory cytokines such as IL -6 increases and these cytokines can influence the progression of periodontitis.[2] Interleukin 6 (IL-6) is critical parameter in periodontal research because of its effect in inflammation and has been related to the severity of periodontal disease and age.[8]Using saliva as a liquid media for evaluation has its unique advantages, including ease of handling and performing, compliance of patients and, in short, being a cost-effective tool for diagnosing.[9] Salivary IL-6 has been positively correlated with HbA1c in Type 2 Diabetes Mellitus.

The aim of the study was to compare the difference between two treatment modalities, with and without curcumin gel application as an adjunct to scaling and root planing among the diabetic population, by comparing their salivary IL -6 count & HbA1c levels.

Materials and method

A total number of 40 subjects aged 30-60 years, visiting the outpatient Department of Periodontology, A.J. Institute of Dental Sciences, Mangalore with diabetes and chronic localized periodontitis, were enrolled for this clinical study based on the inclusion and exclusion criteria as listed below. Single blinded trial was conducted to reduce bias.

Single blinded trial was conducted to reduce bias.

Inclusion criteria:

- Patients who were willing to participate in the study
- Subjects with Age group of 30 to 60years.
- Patients with chronic localized periodontitis.
- Patients with pockets measuring less than 5mm (4-5mm)
- Patients with type 2 diabetic mellitus
- Patients who were able to follow verbal or written instructions.
- **Exclusion criteria**

1. Patients with systemic disorders (Myocardial infarction, musculoskeletal diseases and trauma)
2. Patients with HbA1c levels > 9%
3. Patients under antibiotics, anticoagulants, steroids, hormonal therapy and also patients who underwent periodontal treatment in the past 6 months
4. Pregnant patients and lactating mothers.
5. Patients with habit of tobacco chewing, smoking, alcohol consumption
6. Patients with severe chronic periodontitis and Aggressive periodontitis
7. Patients with acute intraoral lesions assessment of Clinical Parameters:
   - Plaque Index (Silness&Loe ,1964)
   - Gingival Index (Loe&Silness, 1963)
   - Clinical attachment loss
   - Probing pocket depth by Williams graduated periodontal probe

Forty subjects satisfying the inclusion criteria were assigned into two groups based on lottery method.

Group I (n=20, control group): Scaling and Root Planning alone.

Group II (n=20, test group): Scaling and Root Planing + 2% curcumin

subgingival Gel application

Patients in both groups were first monitored for their HbA1c levels. In both the groups, at baseline the clinical parameters were recorded. After taking saliva sample, thorough Scaling and Root Planning were performed using ultrasonic scalers in both the groups. Following Patients of both groups were, put on meticulous oral hygiene regimen, and the oral hygiene maintenance were monitored throughout the study period.

Following Scaling and Root Planning, Group II will undergo 2% curcumin gel application on the same day followed by on the 10th day, end of first month. 0.5 - 1ml of 2 % curcumin gel which were deposited into the sulcus with the help of a 2ml blunt syringe. Standardized oral hygiene instructions were given, modified bass method of brushing demonstrated. The assessment of clinical parameters and the biochemical analysis were carried out before and after the treatment at baseline and at end of 3rd month.

Storage

The saliva samples were centrifuged at 3000rpm for 15minutes. The supernatants were taken for the biochemical analysis and was stored at -80◦c until use.

Salivary interleukin-6 analysis

Salivary concentration of IL-6 was determined by using Human ELISA kit

Glycosylated haemoglobin A measurement

HbA1c levels were analysed for the metabolic assessment in patients with diabetes and periodontitis. HbA1c was measured and expressed as percentages.

Normal range of HbA1c test was <6%. Patients with HbA1c levels less than 9% were taken for the study.

Results

Statistical analysis of the data was performed using SPSS 20.0. The continuous variables were presented as mean±SD. Pre post comparison of the outcome measures were done using paired t test. Comparison between the groups were performed using unpaired t test. A p value<0.05 was considered statistically significant.

Table 1: Showing pre post (3 months) comparison of Plaque Index in group 1(SRP) and Group 2(SRP+ 2 % Curcumin)

		Mean	N	Std. Deviation	Average difference	t value	p value
Group 1	Pre	1.800	20	0.448	0.025	0.960	0.349
	Post(3 months)	1.775	20	0.424			
Group 2	Pre	1.905	20	0.451	0.410	7.627	p<0.001
	Post(3 months)	1.495	20	0.417			

The table shows, In Group 1, pre plaque index score was 1.8±0.448 after 3 months it reduced to 1.775±0.424. The analysis showed an average difference of 0.025 which was not statistically significant with p>0.05.

Table 2: Showing pre post comparison of gingival index in Group 1 and Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Group 1	Pre	1.965	20	.3774	.2100	8.768	p<0.001
	Post(3 months)	1.755	20	.3634			
Group 2	Pre	2.095	20	.4199	.3600	7.712	p<0.001
	Post(3 months)	1.735	20	.3297			

The table shows, In Group 2, pre gingival index score was 2.095±0.4199 after 3 months it reduced to 1.735±0.329.The analysis showed an average difference of 0.36 which was statistically significant with p<0.001.

Table 3: Showing pre post comparison of Clinical attachment level in Group 1 and Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Group 1	Pre	4.0500	20	.75915	.5500	2.6040	p<0.05
	Post(3 months)	3.5000	20	.82717			
Group 2	Pre	4.0000	20	.56195	1.1500	6.9020	p<0.001
	Post(3months)	2.8500	20	.67082			

In Group 1, pre-Clinical attachment level score was 4.05±0.759 after 3 months it reduced to 3.5±0.827 with an average difference of 0.55 which was statistically significant with p<0.05.

In Group 2, pre-Clinical attachment level was 4.0±0.561 after 3 months it reduced to 2.85±0.670 with an average difference of 1,15 which was statistically significant with p<0.001.

Table 4: Showing pre post periodontal pocket depth comparison of in Group 1 and Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Group 1	Pre	4.850	20	.74516	.4500	2.6510	p<0.05
	Post(3 months)	4.400	20	.68056			
Group 2	Pre	4.850	20	.67082	1.10	7.6780	p<0.001
	Post(3months)	3.750	20	.63867			

In Group 1 pre periodontal pocket depth was 4.85±0.745 after 3 months it reduced to 4.4±0.680 with an average difference of 0.45 which was statistically significant with p<0.05.

In Group 2, pre periodontal pocket depth was 4.85±0.670 after 3 months it reduced to 3.75±0.638 with an average difference of 1.1 which was statistically significant with p<0.001.

Table 5: Showing pre post comparison of IL -6 scorein Group 1 and Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Group 1	Pre	18.6336	20	11.79962	.0990	.1970	0.846
	Post(3 months)	18.5337	20	12.90110			
Group 2	Pre	18.2493	20	10.85160	2.5160	1.7240	0.101
	Post(3months)	15.7327	20	9.71149			

The table shows, In Group 1, pre-IL -6 score was 18.63±11.79 after 3 months it reduced to 18.53±12.90.

The analysis showed an average difference of 0.99 which was not statistically significant with p>0.05

The table shows, In Group 2, pre-IL -6 score was 18.249±10.85 after 3 months it reduced to 15.73±9. 711.The analysis showed an average difference of 2.516 which was not statistically significant with p>0.05.

Table 6: Showing pre post comparison of glycosylated haemoglobin in Group 1 and Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Group 1	Pre	7.6	20	0.836	0.11	1.402	0.177
	Post(3 months)	7.49	20	.93690			
Group 2	Pre	7.63	20	.71545	.2300	3.9910	p<0.05
	Post(3months)	7.40	20	.68785			

The table shows, In Group 1, pre glycosylated haemoglobin was 7.6±0.836 after 3 months it reduced to 7.49±0.936. The analysis showed an average difference of 0.11 which was not statistically significant with p>0.05.

The table shows, In Group 2, pre glycosylated haemoglobin was 7.63±0.715 after 3 months it reduced to 7.4±0.687.The analysis showed an average difference of 0.23 which was statistically significant with p<0.05.

Table 7 : Showing pre post comparison of PI in Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Pre to 10 days	Pre	1.9050	20	.45128	.5850	9.1150	p<0.001
	Post(10days)	1.3200	20	.35034			
pre to 1month	Pre	1.9050	20	.45128	.4600	12.0360	p<0.001
	Post(1month)	1.4450	20	.37483			
Day10 to 1month	Post(10days)	1.3200	20	.35034	0.125	6.571	P<0.001
	Post(1month)	1.4450	20	.37483			
1month to 3 months	Post(1month)	1.4450	20	.37483	0.05	1.269	p>0.05
	Post (3months)	1.4950	20	.41735			

The table shows, In Group 2, pre plaque index score was 1.905±0.451 after 10 days it reduced to 1.32±0.35, increased to 1.445±0.374 on first month and 1.495±0.417 on third month. The average improvements from pre to10 days was 0.585,10 days to 1 month was 0.125 were statistically significant with p<0. 001.The comparison between 1month to 3 months was not statistically significant with p>0.05.

Table 8: Showing pre post comparison of gingival index in Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
Pre to 10 days	Pre	2.0950	20	.41987	0.525	16.232	p<0.001
	Post(10days)	1.5700	20	.36288			
pre to 1month	Pre	2.0950	20	.41987	0.435	17.114	P<0.001
	Post(1month)	1.660	20	0.381			
Day10 to 1month	Post(10days)	1.5700	20	.36288	0.090	5.107	P<0.001
	Post(1month)	1.660	20	0.381			
1month to 3 months	Post(1month)	1.660	20	0.381	0.075	1.543	p>0.05
	Post (3months)	1.7350	20	.32971			

The table shows, In Group 2, pre gingival index score was 2.095±0.419 after 10 days it reduced to 1.57±0.362, increased to 1.660±0.381 on first month and 1.735±0.329 on third month. The average improvements from pre to10 days was 0.525,10 days to 1 month was 0.435 and day10 to 1 month was 0.090 were statistically significant with p<0. 001.The comparison between 1month to 3 months was not statistically significant with p>0.05.

Table 9: Showing pre post comparison of periodontal pocket depth and CAL in Group 2

		Mean	N	Std. Deviation	Average difference	t value	p value
periodontal pocket depth	Pre	4.85	20	0.6708	0.2	2.179	0.042
	Post(1month)	5.05	20	0.8255			
CAL	Pre	4.00	20	0.5619			
	Post(1month)	4.00	20	0.5619			

CAL remained same in pre and after 1 month whereas PPD significantly changed between pre and post 1 month with a average difference of 0.2 and p<0.05.

Table 10: Showing co parison between the groups

Group		N	Mean	Std. Deviation	t value	p value
Plaque index	Group 1	20	0.025	0.116	6.466	p<0.001
	Group 2	20	0.41	0.24		
Gingival index	Group 1	20	0.21	0.107	2.859	p<0.05
	Group 2	20	0.36	0.209		
CAL	Group 1	20	0.55	0.945	2.23	p<0.05
	Group 2	20	1.15	0.745		
periodontal pocket depth	Group 1	20	0.45	0.759	2.962	p<0.05
	Group 2	20	1.1	0.641		
Interleukin6	Group 1	20	0.1	2.266	1.564	0.126
	Group 2	20	2.517	6.528		
Glycosylated hemoglobin	Group 1	20	0.15	0.231	1.035	0.307
	Group 2	20	0.23	0.258		

The above table depicts the comparison of mean difference between pre to 3 months in Group 1 and

Group 2. Plaque index, Gingival index, CAL and periodontal pocket depth

Mean difference from pre to 3 months were significantly high in Group 2 as compared to Group 1. Interleukin6 and Glycosylated haemoglobin did not differ significantly between Group 1 and 2.

Discussion

Diabetes mellitus is a prevalent chronic disease in India. Type 2 diabetes is the most common type of diabetes in India, affecting approximately 90 to 95% of the people .[10] Studies have supported a two-way relation between diabetes and periodontal status.[11,12,13,14] Various studies have shown that with age severity of periodontitis increases proportionally with uncontrolled glycaemic status. Karjalainen and Knuuttila [15] had suggested that hyperglycaemia impairs overall cell function, as insulin is required for glucose to enter cells to provide a source of energy. It also decreases PMN cell chemotaxis, phagocytosis and intracellular killing of bacteria. The ability of glycosylated hemoglobin to carry oxygen would be impaired, thereby decreasing tissue oxygenation. Hyperglycemia induces blood flow abnormalities including increased blood viscosity, reduced erythrocyte deformability, and increased platelet aggregation, which further enhance tissue hypoxia. There was increased BOP, PPD, increased tooth mobility and greater loss of attachment as the individuals with diabetes are twice as likely to exhibit attachment loss. These factors result in increased periodontal destruction. Several meta-analyses have confirmed that effective periodontal therapy can result in reduced hba1c. Hence evaluation of glycaemic control plays a very important role in periodontitis.

Periodontitis and diabetes are chronic inflammatory diseases that increase inflammatory IL-6 levels which reflects in saliva. Periodontitis triggers systemic and local immune-inflammatory response by significantly increasing the expression of IL-6 which further contributes to bone loss by inducing bone resorption, either by increasing RANKL or by directly acting on osteoclast formation in periodontitis[16,17] .In DM patients, the chronic hyperglycemic state results in AGE formation and AGE-RAGE interaction induces the expression of proinflammatory cytokine IL-6 and the abnormal increase in the cytokine levels induced by AGE exacerbate the inflammatory response.

Curcumin, an age-old plant-derived polyphenol extracted from the rhizome of turmeric (Bisht et al., 2010)[18,19], has become popular in the last 50 years due to its multiple therapeutic functions. The mechanism of periodontal disease involves the production of several inflammatory mediators. Periodontal pathogens activate NF-κb, Janus kinase (JAK)/signal transducer, activator of transcription (STAT), mitogenactivated protein kinases (MAPK), and other signaling pathways and produce inflammatory cytokines such as IL-6, TNF-α and IL-1β to promote inflammation (Li et al., 2021)[18,20]. Curcumin, the active ingredient in turmeric, has various anti-inflammatory properties and may delay the disease process of periodontal disease in its initial stages. It has been shown to suppress the NF-κb pathway in human gingival fibroblasts in early stages and thus may inhibit P. gingivalis LPS-induced COX2 synthesis (Hu et al., 2013)[18,21,22] and the production of TNF-α, IL-8 and IL-6 by inhibiting NF-κb activation in mast cells (Kong et al., 2018)[23]. Additionally, curcumin could exert an anti-inflammatory effect by directly inhibiting the JAK/STAT signalling pathway and phosphorylation of p38 MAPK, thereby reducing the expression of inos, COX-2, monocyte chemoattractant protein-1 (MCP-1), and intercellular adhesionmolecule-1(ICAM-1) (Guimarães et al[24]2013, Boyle et al[80] 2015) to reduce the

inflammatory response. The decrease in periodontal pathogens and LPS in Gram-negative bacterial walls could inhibit innate and adaptive immune responses in periodontal tissues. This effect could also explain why curcumin could suppress the inflammatory process in periodontal tissue[10].

In the present study, Group 2 (SRP + CU) obtained significant reduction in PI, GI, PPD and CAL scores when compared with that of Group 1 (SRP). This result is in accordance with that of Anuradha et al[25,26] and Gottumukkala et al[25,27]. Moreover, a significant reduction in clinical parameters like GI, PPD and gain in clinical attachment level was noted in Group 1 (SRP). This can be explained by the fact that thorough good quality SRP has a greater impact on the clinical findings irrespective of the adjunctive treatment procedures.[45] The inter group plaque index scores did not show any significant difference in Group 1 when compared with that of Group 2, this was similar to the study conducted by Vinholis et al[21,84]. And Paolantonio et.al[21, 85,.] Hence in the present study, curcumin group was found to be effective in removing local factors when performed along with scaling and root planning.[30] The inter group comparison of PPD and CAL scores between the Group 1 and Group 2 showed statistically significant result with Curcumin Group 1t each interval. On intergroup comparison in both the groups, there was significant mean reduction in scores from baseline to end of 3 months in Group 2. These results are in accordance with the study done by Nandini et al[24,86] and Mizrak et al[24,87]. The trend for slightly greater reduction in pocket depth and gain in CAL by curcumin compared to Group 1 could be due to its ability to enhance wound healing by regeneration. This is in accordance with the in vivo experiment on rats and guinea pigs by Sidhu Singh et al[88].

On comparing the hba1c levels in both group, Group 2 (SRP + Curcumin) Showed statistically significant reduction. To authors knowledge, this is the first study on estimation of hba1c levels among diabetes patients with periodontitis with adjunctive application of 2 % curcumin along with SRP. In a study conducted by. Lova et.al[93], 2021 it was seen that oral administration of curcumin, could reduce the oxidative stress and enhance anti-oxidant status in hyperglycaemic periodontitis rats. According to Araújo et.al[55],2022 a study on application of anti-oxidants as local drug delivery improved hba1c levels among type 2 diabetes patients with periodontitis.[55] Hence this study has clinically and statistically proved the anti-oxidant property of curcumin.

In the present study, efficacy of curcumin gel was estimated by evaluation of clinical parameters on 10th, end of 1 month and 3rd month. The intragroup comparisons of PI, showed a considerable improvement in scores from baseline to 10th day to be 0.585 and from 10th day to 1 month to be 0.125, both of which were statistically significant. The comparison between 1month to 3 months was not statistically significant. According to Singh et.al[54,94], 2015, curcumin was found effective in reducing plaque for a short term (up to 14 days), which could be attributed to the antiplaque properties of curcumin as described in previous literature. The anti-microbial property exhibited by curcumin could more likely be due to its ability to inhibit bacterial lipopolysaccharide-induced cytokine expansion and bacterial quorum sensing systems (Kandwal et al., 2015)[95]. The reduction in the plaque scores could also possibly be attributed to curcumin's antibiofilm activity as curcumin inhibits production of biofilm and disperses the biofilm made by micro-organisms (Dave et al., 2018)[96]. Similar observation was noted in GI scores as

well. The reduction in gingival inflammation of curcumin topical gel may be attributed to curcumin's anti-inflammatory (Singh et al[94]., 2015) antibacterial and antioxidant properties of curcumin. It selectively inhibits the synthesis of prostaglandin E2 and thromboxane and not the synthesis of prostacyclin. This could lead to the conclusion that curcumin gel has its maximum antiplaque and anti-inflammatory properties for 14 days and hence requires frequent application.

Patients with periodontitis and diabetes have increased salivary IL-6 levels. Adjunctive use of curcumin along with periodontal therapy has resulted in statistically significant reduction in hba1c levels (Group 2). Hence this study has clinically and statistically proved the anti-oxidant property of curcumin

In the present study, efficacy of curcumin gel was estimated by evaluation of clinical parameters on 10th, end of 1 month and 3rd month. The intragroup comparisons of PI, showed a considerable improvement in scores from baseline to 10th day to be 0.585 and from 10th day to 1 month to be 0.125, both of which were statistically significant. According to Singh et.al[54,94], 2015, curcumin was found effective in reducing plaque for a short term (up to 14 days), which could be attributed to the antiplaque properties of curcumin as described in previous literature. The anti-microbial property exhibited by curcumin could more likely be due to its ability to inhibit bacterial lipopolysaccharide-induced cytokine expansion and bacterial quorum sensing systems (Kandwal et al., 2015)[95]. The reduction in the plaque scores could also possibly be attributed to curcumin's antibiofilm activity as curcumin inhibits production of biofilm and disperses the biofilm made by micro-organisms (Dave et al., 2018)[96]. Similar observation was noted in GI scores as well. The reduction in gingival inflammation of curcumin topical gel may be attributed to curcumin's anti-inflammatory (Singh et al[94]., 2015) antibacterial and antioxidant properties of curcumin. It selectively inhibits the synthesis of prostaglandin E2 and thromboxane and not the synthesis of prostacyclin. This could lead to the conclusion that curcumin gel has its maximum antiplaque and anti-inflammatory properties for 14 days and hence requires frequent application. The intergroup comparison of PPD and gain in CAL in Group 2(srp+ curcumin) showed that there was a slight increase in periodontal pocket depth (4.85-5.05) and no changes in CAL from baseline to 1 month. This is contradictory to the study conducted by Gottumukkala, et al, wherein there was significant reduction in PPD and gain in CAL at end of 1 month. But statistically significant reductions in PPD and gain in CAL were noted at the end of 3 months along with decrease in hba1c levels. The application of curcumin gel into periodontal pocket in patients with DM may be beneficial.

On intra group comparison of IL -6 levels among Group 1 and Group 2, there was no statistically significant difference seen in between baseline and at the end of 3 months. This was in accordance to a study conducted by Aziz et.al[97], 2018, wherein scaling and root planning was effective in improving clinical parameters but, the extent of improvement of serum IL-6 was lower in diabetic patients than those in the non-diabetic patients and these can be attributed to their health status. Salivary IL-6 is in direct propotion with glycaemic status. Patients with periodontitis and diabetes have increased salivary IL-6 levels. Adjunctive use of curcumin along with periodontal therapy has resulted in statistically significant reduction in hba1c levels (Group 2).

Application of 2 % curcumin oral gel post SRP improved periodontal clinical parameters in patients with Type 2 Diabetes mellitus and also improved their

glycaemic status.[21]. The level of salivary IL-6 can be considered as a non-invasive biomarker in the diagnosis of diabetes and periodontal disease.[60]

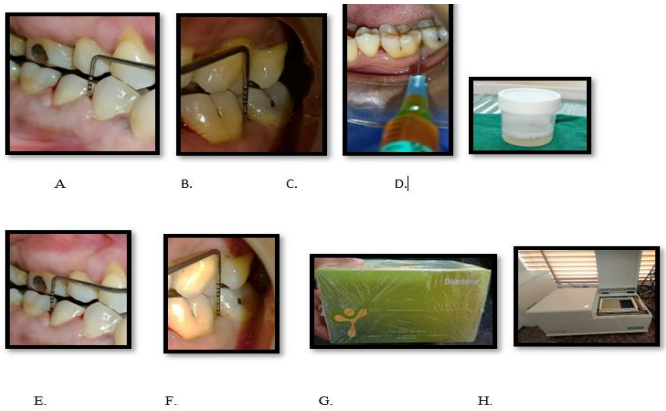
Limitations of the study

1. Most of the chosen patients were not on regular medication regime for diabetes.
2. Curcumin has a sustainable activity of 14 days following which there was a decline in its activity.

This could influence the clinical parameters at the end of 1st and 3rd month

Conclusion

From the present study it can be concluded that anti-inflammatory property of 2% curcumin gel resulted in glycaemic status (hba1c) improvement among type 2 diabetic patients with periodontitis. Curcumin as an adjunct to SRP was effective in ameliorating periodontal clinical parameters as well. Salivary IL-6 can be used as a non-invasive, reliable and cost-effective diagnostic tool for diagnosis of prediabetic patients with periodontitis.



A. Preoperative (group 1) B. Preoperative (group 2; curcumin) C. 2 % curcumin gel placed

D. Saliva samples collected E. Post-operative 3 months group 1

F. Post operative group 2 (curcumin) G. ELISA kit h. ELISA reader

References

1. Balaji A, Chandrasekaran SC, Subramanium D, Fernz AB. Salivary Interleukin-6-A pioneering marker for correlating diabetes and chronic periodontitis: A comparative study. Indian J Dent Res.*2017;28(2):133.*
2. Lubis P, Nasution R, Ilyas S, Ervina I, Primasari A. Effectiveness of 1% curcumin gel subgingival application on interleukin-6 levels in chronic periodontitis patients. Int J Appl Dent Sci. 2020;6(3):513-6.
3. Matthews DC. The relationship between diabetes and periodontal disease. **J** Can Dent Assoc. 2002 ;68(3):161-4.
4. Costa PP, Trevisan GL, Macedo GO, Palioto DB, Souza SL, Grisi MF, Novaes Jr AB, Taba Jr M. Salivary interleukin-6, matrix metalloproteinase-8, and osteoprotegerin in patients with periodontitis and diabetes. J. Periodontol. 2010;81(3):384-91.
5. Stathopoulou PG, Buduneli N, Kinane DF. Systemic biomarkers for periodontitis. Current oral health reports. 2015; 2:218-26.
6. Chainani- Wu N. Safety and anti-- inflammatory activity of curcumin: A component of turmeric (Curcuma longa). J Altern Complement Med 2003; 9:161-8
7. Baldwinas. Control of on cogenesis and cancer therapy resistance by the transcription factor NF-kappa B.J Clin Invest 2001;107:241-6.
8. Matu NK, Stephen L, Lalloo R. Prevalence and severity of periodontal disease: type 2 diabetics versus non-diabetics: scientific. S. Afr. Dent. J. 2009;64(2):64-8.
9. Wang X, Han X, Guo X, Luo X, Wang D. The effect of periodontal treatment on hemoglobin a1c levels of diabetic patients: a systematic review and meta-analysis. Plos One.2014 ;9(9):108412.
10. Shaikh UR, Shirahatti RV. Assessment of the effects of scaling and root planing on blood glucose

levels in type II diabetes patients: A pilot study. J. Int. Clin. Dent. Res. Organ. 2010 ;2(1):20.

11. Cortelli JR, Pinheiro RM, Costa FD, Aquino DR, Raslan SA, Cortelli SC. Salivary and microbiological parameters of chronic periodontitis subjects with and without type 2 diabetes mellitus: a case-control study. Revista de Odontologia da UNESP. 2014; 43:196-202.
12. Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M, Knowler WC, et al. non-insulin dependent diabetes mellitus and alveolar bone loss progression over 2 years. J Periodontol. 1998; 69: 76-83.
13. Soskolne WA, Klinger A. The relationship between periodontal diseases and diabetes: an overview. Ann Periodontol. 2001; 6:91-8.
14. Lakschevitz F, Aboodi G, Tenenbaum H, Glogauer M. Diabetes and periodontal diseases: interplay and links. Curr Diabetes Rev. 2011; 7: 433-9.
15. Karjalainen KM, Knuuttila ML. The onset of diabetes and poor metabolic control increases gingival bleeding in children and adolescents with insulin dependent diabetes mellitus. J Clin Periodontal 1996; 23:1060-7.
16. Balaji A, Chandrasekaran S C, Subramanium D, Fernz A B. Salivary Interleukin-6 - A pioneering marker for correlating diabetes and chronic periodontitis: A comparative study.Indian J Dent Res 2017;28:133-137
17. Mihara M, Moriya Y, Kishimoto T, Ohsugi Y. Interleukin-6 (IL-6) induces the proliferation of synovial fibroblastic cells in the presence of soluble IL-6 receptor. Br J Rheumatol 1995; 34:321-5.
18. Araújo EG, Oliveira DM, Martins CC, Stefani CM. Efficacy of Antioxidant Supplementation to Non-Surgical Periodontal Therapy on Metabolic Control in Type 2 Diabetes Patients: A Network Meta-Analysis. Antioxidants. 2022 ;11(4):621
19. Bisht, S., Mizuma, M., Feldmann, G., Ottenhof, N. A., Hong, S. M., Pramanik, D., et al. (2010). Systemic Administration of Polymeric Nanoparticle-Encapsulated Curcumin (nanocurc) Blocks Tumor Growth and Metastases in Preclinical Models of Pancreatic Cancer. Mol. Cancer Ther. 2010;9 (8):2255–2264.
20. Li, Y., Jiao, J., Qi, Y., Yu, W., Yang, S., Zhang, J., et al. (2021). Curcumin: A Review of Experimental Studies and Mechanisms Related to Periodontitis Treatment. J. Periodontal Res. 2021;56 (5): 837–847.
21. Hu, P., Huang, P., and Chen, M. W. (2013). Curcumin Attenuates Cyclooxygenase-2 Expression via Inhibition of the NF-Kb Pathway in Lipopolysaccharide-Stimulated Human Gingival Fibroblasts. Cell Biol Int 2013;37 (5): 443–448.
22. Kong, R., Kang, O. H., Seo, Y. S., Zhou, T., Kim, S. A., Shin, D. W., et al. (2018). Mapks and NF-κb P-athway I-nhibitory E-ffect of B-isdemethoxycurcumin on P-horbol-12-myristate-13-acetate and A23187-induced I-nflammation in H-uman M-ast C-ells. Mol. Med. Rep.2018; 17 (1):630–635.
23. Guimarães, M. R., Leite, F. R., Spolidorio, L. C., Kirkwood, K. L., and Rossa, C., Jr. (2013). Curcumin Abrogates LPS-Induced Pro-inflammatory Cytokines in RAW 264.7 Macrophages. Evidence for Novel Mechanisms Involving SOCS-1, -3 and P38 MAPK. Arch. Oral Biol. 2013;58 (10),
24. Boyle, D. L., Soma, K., Hodge, J., Kavanaugh, A., Mandel, D., Mease, P., et al. (2015). The JAK Inhibitor Tofacitinib Suppresses Synovial JAK1-

STAT Signalling in Rheumatoid Arthritis. Ann. Rheum. Dis. 2015;74 (6):1311–1316.

25. Shahzad, M., Millhouse, E., Culshaw, S., Edwards, C. A., Ramage, G., and Combet, E. (2015). Selected Dietary (Poly)phenols Inhibit Periodontal Pathogen Growth and Biofilm Formation. Food Funct. 2015;6 (3): 719–729
26. Shaikh UR, Shirahatti RV. Assessment of the effects of scaling and root planing on blood glucose levels in type II diabetes patients: A pilot study. J. Int. Clin. Dent. Res. Organ. 2010 ;2(1):20.
27. Shivanand P, Vandana KV, Vandana KL, Prakash S. Evaluation of Curcumin 10 mg (Curenext®) as Local Drug Delivery Adjunct in the Treatment of Chronic Periodontitis: A Clinical Trial. CODS J Dent 2016;8(2):59-63
28. Anuradha BR, Bai YD, Sailaja S, Sudhakar J, Priyanka M, Deepika V. Evaluation of anti-inflammatory effects of curcumin gel as an adjunct to scaling and root planing: a clinical study. J Int Oral Health 2015 ;7(7):90-93.
29. Gottumukkala SN, Sudarshan S, Mantena SR. Comparative evaluation of the efficacy of two controlled release devices: chlorhexidine chips and indigenous curcumin-based collagen as local drug delivery systems. Contemp Clin Dent 2014 ;5(2):175-181
30. Siddharth M, Singh P, Gupta R, et al. Comparative Evaluation of Subgingivally Delivered 2% Curcumin and 0.2% Chlorhexidine Gel Adjunctive to Scaling and Root Planing in Chronic Periodontitis. J Contemp Dent Pract 2020;21(5):494–499
31. Gottumukkala SN, Koneru S, Mannem S, Mandalapu N. Effectiveness of sub gingival irrigation of an indigenous 1% curcumin solution on clinical and microbiological parameters in chronic periodontitis patients: A pilot randomized clinical trial. Contemp. Clin. Dent. 2013 ;4(2):186
32. Vinholisah, Figueiredo LC, Marcantonio Júnior E, Marcantonio RA, Salvador SL, Goissis G. Sub gingival utilization of a 1% chlorhexidine collagen gel for the treatment of periodontal pockets. A clinical and microbiological study. Braz Dent J 2001; 12:209-13.
33. Paolantonio M, D' Ercole S, Pilloni A, D' Archivio D, Lisanti L, Graziani F, et al. Clinical, microbiologic, and biochemical effects of sub gingival administration of a Xanthan- based chlorhexidine gel in the treatment of periodontitis: A randomized multicenter trial. J Periodontol 2009; 80:1479-92.
34. Bhatia M, Urolagin SS, Pentyala KB, Urolagin SB, Menaka KB, Bhoi S. Novel therapeutic approach for the treatment of periodontitis by curcumin. J. Clin. Diagnostic Res:JCDR. 2014 ;8(12):65.
35. (86) Nandini N, Vidya D, Komal A. Comparative evaluation of 1% Curcumin solution and 0.2% Chlorhexidine irrigation as an adjunct to scaling and root planing in management of chronic periodontitis: A clinico-microbiological study. 2012;14(03).
36. Mizrak T, Guncu GN, Caglayan F, Balci TA, Aktar GS, Ipek F.Effect of a controlledrelease chlorhexidine chip on clinical and microbiological parameters and prostaglandin e2levels in gingival crevicular fluid. J Periodontol. 2006;77(3):437-43
37. Sidhu GS, Singh AK, Thaloor D, Banaudha KK, Patnaik GK, Srimal RC, et al. Enhancement of wound healing by curcumin in animals. Wound Repair Regen. 1998;6(2):167-77
38. Iova GM, Calniceanu H, Popa A, Szuhanek CA, Marcu O, Ciavoi G, Scrobota I. The antioxidant

effect of curcumin and rutin on oxidative stress biomarkers in experimentally induced periodontitis in hyperglycemic Wistar rats. Molecules. 2021;26(5):1332.

39. Araújo EG, Oliveira DM, Martins CC, Stefani CM. Efficacy of Antioxidant Supplementation to Non-Surgical Periodontal Therapy on Metabolic Control in Type 2 Diabetes Patients: A Network Meta-Analysis. Antioxidants. 2022 ;11(4):621
40. Terby S, Shereef M, Ramanarayanan V, Balakrishnan B. The effect of curcumin as an adjunct in the treatment of chronic periodontitis: A systematic review and meta-analysis. Saudi Dent J. 2021 ;33(7):375-85.
41. Singh, V., Pathak, A.K., Pal, M., Sareen, S., Goel, K., 2015. Comparative evaluation of topical application of turmeric gel and 0.2% chlorhexidine gluconate gel in prevention of gingivitis. Natl. J. Maxillofac. Surg. 2015;6: 67–71.
42. Kandwal, A., Mamgain, R.K., Mamgain, P., 2015. Comparative evaluation of turmeric gel with 2% chlorhexidine gluconate gel for treatment of plaque induced gingivitis: a randomized controlled clinical trial. Ayu .2015;36:145–150.
43. Dave, deepakharish, Patel, Phoram, Shah, Monali, Dadawala, sarvagnamayank, Saraiya, Kevin, Sant, ankitvilas, 2018. Comparative evaluation of efficacy of oral curcumin gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis. Adv. Hum. Biol. 2018;8 (2): 79.
44. Aziz AS, Kalekar M, Suryakar AN, Kale R, Benjamin T, Dikshit M. Pre-and Post-Treatment Effectiveness of SRP on Levels of IL-6, IL-10, and CRP in Chronic Periodontitis Patients with and without Diabetes. Am J Biochem. 2018;8(1):1-6.
45. Oliver RC, Tervonen T. Diabetes - A risk factor for periodontitis in adults? J Periodontal 1994; 65:530-8.
46. Asl Aminabadi N, Erfanparast L, Sohrabi A, Ghertasi Oskouei S, Naghili A. The Impact of Virtual Reality Distraction on Pain and Anxiety during Dental Treatment in 4–6-Year-Old Children: a Randomized Controlled Clinical Trial. J Dent Res Dent Clin Dent Prospects. 2012 Fall;6(4):117-24.
47. Murphy, Nancy. (1997, May). A multisensory vs. Conventional approach to teaching spelling. Unpublished master's thesis, Kean College, New Jersey, USA. (Eric Document Reproduction Service No. ED 405 564)