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Role of curcumin as a subgingival irrigant: a pilot study

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Background: The objective of this study was to evaluate subgingival irrigation as an adjunctive therapy and compare curcumin irrigation with commonly used irrigant chlorhexidine (0.2%).
Study design: Selected periodontal sites were treated on day 0 (baseline) by a single episode of scaling and root planing. Subsequently selected sites were irrigated (triple irrigation regimen) with either saline (0.9%), chlorhexidine (0.2%), curcumin (1%) or served as non-irrigated control sites on day 0 (baseline) immediately following instrumentation. Triple irrigation regimen was repeated for the next 5 consecutive days and on days 15 and 21. Clinical parameters recorded were probing pocket depth (PPD), bleeding on probing (BOP), and redness for 200 sites in 20 patients with chronic periodontitis. BOP and redness were recorded as dichotomous variables for 6 consecutive days and on days 15, 21 and 42; PPD was recorded on baseline and days 15, 21 and 42.
Results: Irrigated sites had significant improvement on all parameters as compared with non-irrigated sites on days 2, 3, 4 and 5. Curcumin group showed significant reduction in BOP (100%) and redness (96%) when compared with chlorhexidine group and saline group on day 5. However, the difference between groups was not significant at the next recall visits. Mean PPD reduction was significantly greater for the curcumin group than all other groups on all post-treatment days.
Conclusion: Subgingival irrigation is a useful adjunct and 1% curcumin solution is able to cause better resolution of inflammatory signs (BOP and redness) and PPD reduction than chlorhexidine and saline irrigation as an adjunctive therapy. However, further studies are required to substantiate these findings.

■ Introduction

Conventional periodontal therapy can improve the overall gingival health and, in general, halt the progression of attachment loss. However, in some sites gingival inflammation persists or recurs and periodontal attachment loss progresses despite regular supportive therapy. This can be related to insufficient suppression or elimination of periodontopathic bacteria or even their penetration into the gingival connective tissue[1].

This led to the use of chemotherapeutic agents in periodontal therapy. At first these were systemically administered, but systemic side effects along with limited efficacy against periodontopathogens limited their use in periodontal therapy[2]. To reduce the side effects produced by systemically administered antimicrobials, local administration was seen as an alternative method, including sub-gingival irrigation and the use of gels, hollow fibres, acrylic strips, dialysis tubings and collagen preparations.

Although self-administration of chemotherapeutic agents is not difficult to master, it does rely on patient cooperation. Additionally, it may not be prudent to become overly dependent on irrigation for numerous chronic problem areas, because clinical evaluations should be made continuously to determine the need for therapy, to evaluate the results of treatment and to decide if re-treatment is needed. These considerations dictate the need for professional application of chemotherapeutic agents.

With a mouthwash or supragingival irrigation, it is not possible to predictably deliver an agent to the deeper parts of a pocket[3]. It has been reported that scaling and root planing (SRP), when combined with a local delivery system such as subgingival irrigation, reduces microbes and improves clinical parameters better than SRP alone[4]. Various subgingival irrigants have been studied, including chlorhexidine digluconate (CHX), stannous fluoride, tetracycline hydrochloride, hydrogen peroxide, and iodine, with variable clinical results. CHX has been the most widely researched antiseptic for local use. Studies with 0.2% CHX as subgingival irrigant as an adjunct to SRP have reported significant and sustained reductions of spirochetes and motile rods[5].

However, the use of synthetic compounds has certain disadvantages, for example with CHX the staining of teeth, alteration of taste sensation and mucosal allergy have been reported. Microorganisms have been known to develop resistance to antibiotics such as tetracycline-HCl when used in the long term. Due to these clinical drawbacks of synthetic agents, the relatively safe nature of herbal extracts has led to their use in various fields as an alternative. Use of herbal extracts with active ingredients such as *Salvia officinalis, Mentha piperita, Menthol, Matricaria, Chamomilla, Cemmiphora myrrha, Carum carvi, Eugenia caryophyllus* and *Echinacea purpura* as a formulation for subgingival irrigation was studied by Pistorius et al[6]. Significant improvement in gingival inflammation was reported compared with the control.

Research has shown that although bacteria are essential for periodontitis, most of the damage is caused by inflammatory mediators and free radicals[7–9]. Thus any agent that can target both bacteria and host inflammatory products would be highly beneficial in stopping the destruction associated with periodontitis.

Curcuma longa is a spice that contains the polyphenol curcumin in its rhizome. Curcumin's reported properties include anti-inflammatory[10,11], anti-oxidant[12,13], anti-microbial[14] and wound healing properties[15–17]. The anti-inflammatory, anti-oxidant and anti-bacterial properties of curcumin are desirable assets, which validate its use in the treatment of periodontitis.

The present study was designed to evaluate subgingival irrigation as an adjunctive therapy and compare curcumin irrigation (1%) with the commonly used irrigant CHX (0.2%).

■ Study design

■ Subjects

A total of 20 volunteers who reported to the outpatient Department of Periodontics, King George's University of Dental Sciences, with complaints of swollen and bleeding gums were selected for this 6-week pilot study. Subjects included in this study were in good general health and met the following criteria:

- over 30 years old;
- non-smokers/users of tobacco;
- no periodontal therapy in the last 6 months;
- no antimicrobials for 1 month prior to study;
- at least 5 periodontal sites ≥ 4mm in single rooted teeth (either maxillary or mandibular);
- moderately/severely inflamed gingiva that bleed on probing.

Periodontal sites included in our study were selected from single rooted teeth only (either maxillary or mandibular).

Design

The study model comprised four groups: the first received SRP only (non-irrigated control group); the second group received SRP with curcumin irrigation subgingivally (CU group); the third group received SRP with subgingival irrigation by CHX (CHX group); and the fourth group received SRP with saline irrigation subgingivally (saline group). All subjects participating in the study received instruction regarding treatment and possible outcome.

Materials

Commercially available CHX mouthwash (0.2%) and sterile physiologic saline (0.9%) were used.

Curcumin solution (1%) was prepared from 1 mg of curcumin extract (Sigma Lab, USA) dissolved in 5 ml of ethanol, with the addition of 95 ml of glycerol.

Clinical parameters

The criteria used for clinical evaluation were:

- Probing pocket depth (PPD): measurements were recorded using PCP UNC-15 probe. Recordings were taken at baseline and days 15, 21 and 42.
- Bleeding on probing (BOP) and redness were recorded as dichotomous variables. Recordings were made daily from day 0 (baseline) to day 5 and then on days 15, 21 and 42 for both the variables. For BOP, the probe was gently inserted into pocket and the presence of bleeding after 10 seconds was recorded as a positive finding.

Each tooth was divided into six surfaces with three facial and three lingual surfaces. Each surface was recorded as an individual site.

Methodology

A total of 20 subjects and 200 sites that met all the inclusion criteria were selected for this 6-week pilot study. Sites were randomly divided among the four groups. When adjacent sites were used, these were included in the same group. Treatment groups were balanced as evenly as possible with respect to tooth type, tooth surface and initial probing depth.

All subjects were given oral hygiene instructions followed by supra- and sub-gingival debridement. Supragingival scaling was done using an ultrasonic instrument followed by meticulous root planing with area-specific curettes (Gracey curettes, Hu-Friedy). A single episode of SRP was performed for all groups on day 0 until the operator felt confident that the root surface was clean, immediately followed by subgingival irrigation with the assigned irrigant.

A 2 ml disposable syringe equipped with a blunted 25-gauge needle, which was bent along its shank at an angle of approximately 130° and marked at 3 mm, was used. The needle was inserted in the pocket until the mark was below the gingival margin for subgingival irrigation. Each site was irrigated with 1 ml of solution over 20 seconds. This procedure was repeated three times with intervals of 5 minutes, and performed daily for the next 5 days, except for non-irrigated sites.

Triple irrigation procedure without SRP was repeated on days 15 and 21. Recordings were continued until day 42. Results obtained were analysed statistically.

Statistical analysis

A total of 200 sites were randomly distributed, with 50 sites in each group. Three clinical parameters were analysed (PPD, BOP and redness). For analysing reduction in PPD compared with baseline value for all the groups, means and standard deviations were calculated for each point of time (days 0, 15, 21 and 42). Intra-group comparison to day 0 (baseline) was made with student paired *t* test. Inter-group comparison for reduction in PPD (mean ± SD) at each point of time was by student *t* test (unpaired).

Percentage reduction in sites with BOP and redness on at a given time was analysed using proportion tests. Inter-group comparison for percentage reduction in BOP and redness was also analysed by proportion tests of at different treatment days.

Results

The percentage reduction in sites on given treatment days with visible signs of inflammation (BOP and redness) for all the treatment groups are shown in Tables 1 and 2, and inter-group comparisons for both these dichotomous variables are shown in Tables 3

Table 1 Percentage reduction in sites with BOP for different groups.

Days	CHX group		CU group		Control group		Saline group	
	n	% change	n	% change	n	% change	n	% change
Base line (0)	50	0	50	0	50	0	50	0
1	50	0	50	0	50	0	50	0
2	42	16*	38	24*	49	2	43	14*
3	29	42*	18	64*	39	22*	30	40*
4	14	72*	6	88*	26	48*	16	68*
5	4	92*	0	100*	14	72*	8	84*
15	0	100*	0	100*	0	100	0	100*
21	0	100*	0	100*	2	96	1	98*
42	2	96*	1	98*	4	92	2	96*

n, number of sites with BOP
% change, percentage reduction as compared with baseline
**p < 0.05 (change from baseline)*

Table 2 Percentage reduction in sites with redness for different groups.

Days	CHX group		CU group		Control group		Saline group	
	n	% change	n	% change	n	% change	n	% change
Base line (0)	50	0	50	0	50	0	50	0
1	50	0	50	0	50	0	50	0
2	48	4	43	16*	50	0	47	6
3	36	28*	22	56*	46	16*	39	22*
4	27	46*	10	80*	37	26*	27	46*
5	14	72*	2	96*	24	52*	16	68*
15	0	100*	0	100*	0	100*	0	100*
21	0	100*	0	100*	0	100*	0	100*
42	0	100*	0	100*	0	100*	0	100*

n, number of sites with BOP
% change, percentage reduction as compared with baseline
**p < 0.05 (change from baseline)*

and 4. The mean probing depths and standard deviation for all the groups on different treatment days are shown in Table 5. Inter-group comparison for reductions in mean PPD is shown in Table 6.

From Tables 1, 2 and 5 it was noted that all the treatment modalities including non-irrigated controls were successful in treating periodontal pockets as seen by reduction in bleeding scores, redness and mean pocket depth. There was a trend for significantly greater reduction in bleeding scores and redness for irrigated sites compared with non-irrigated controls, in the first 6 post-treatment days. However, on days 15, 21 and 42 the difference between irrigated sites and non-irrigated controls was not statistically significant.

Curcumin-irrigated sites (CU group) demonstrated significant resolution of inflammatory signs (BOP and redness) at an earlier stage (i.e. day 3 for BOP and day 2 for redness) than for the CHX and saline groups. There was 92% reduction in sites with BOP and 72% reduction in sites with redness in the CHX group, 80% reduction in sites with BOP and 72% reduction in sites with redness in saline group on day 5, compared with 100% reduction in BOP and 96% reduction in sites with redness on day 5 in the CU group. From baseline to recall at day 15, all

Table 3 Intergroup comparison for reduction in sites with BOP.

Day	Control vs CHX	Control vs CU	Control vs Saline	CU vs CHX	CU vs Saline	CHX vs Saline
2	*	*	*	NS	NS	NS
3	*	*	NS	*	*	NS
4	*	*	*	*	*	NS
5	*	*	NS	*	*	NS

**p < 0.05 (difference between groups is significant)*
NS, not significant

Table 4 Inter-group comparison for reduction in sites with redness.

Day	Control vs CHX	Control vs CU	Control vs Saline	CU vs CHX	CU vs Saline	CHX vs Saline
2	*	NS	NS	NS	NS	NS
3	*	*	*	*	*	NS
4	*	*	*	*	*	NS
5	*	*	NS	*	*	NS

**p < 0.05 (difference between groups is significant)*
NS, not significant

Table 5 Mean PPD reduction on different treatment days in different groups.

Day	CHX group		CU group		Control group		Saline group	
	PPD (mean ± SD)	Change (mean ± SD)	PPD (mean ± SD)	Change (mean ± SD)	PPD (mean ± SD)	Change (mean ± SD)	PPD (mean ± SD)	Change (mean ± SD)
0	6.52 ± 0.71	–	6.52 ± 0.71	–	6.83 ± 0.83	–	6.52 ± 0.71	–
15	4.20 ± 0.41	2.32 ± 0.40*	3.56 ± 0.71	2.96 ± 0.48*	4.61 ± 0.66	2.22 ± 0.39*	4.22 ± 0.76	2.30 ± 0.56*
21	4.04 ± 0.20	2.48 ± 0.60*	3.40 ± 0.65	3.12 ± 0.40*	4.48 ± 0.67	2.35 ± 0.78*	4.14 ± 0.86	2.38 ± 0.63*
42	3.92 ± 0.28	2.60 ± 0.42*	3.36 ± 0.70	3.16 ± 0.56*	4.48 ± 0.67	2.22 ± 0.78*	3.98 ± 0.87	2.54 ± 0.37*

**p < 0.05 (change from baseline)*
NS, not significant

the groups had similar improvements (100% reduction) in BOP as well as redness, which was consistent only for redness as observed on day 21.

Changes in PPD compared with baseline (Table 5) for all the groups were significant on all the noted treatment days. Reduction in mean pocket depth on days 15, 21 and 42 was better for irrigated sites than for non-irrigated control, but the difference was statistically significant only for curcumin-irrigated sites (Tables 5 and 6). The difference in mean PPD reduction on any given day was statistically significant for CU group (Table 6) compared with CHX and saline-irrigated sites.

On the last day (day 42) of recall, recurrence in 4% of sites of CHX and saline groups was seen for BOP, in 8% of sites of non-irrigated sites, whereas only 2% recurrence was noted in the CU group. This change was not statistically significant (Table 1). No trend for recurrence was noted for redness in any of the groups (Table 2).

■ Discussion

The objective of this study was to evaluate subgingival irrigation as an adjunctive therapy and compare

Table 6 Inter-group comparison for mean PPD reduction.

Day	Control vs CHX	Control vs CU	Control vs Saline	CU vs CHX	CU vs Saline	CHX vs Saline
15	NS	*	NS	*	*	NS
21	NS	*	NS	*	*	NS
42	*	*	*	*	*	NS

**p < 0.05 (difference between groups is significant)*
NS, not significant

curcumin irrigation with the commonly used irrigant CHX (0.2%). Non-irrigated sites and saline irrigated sites were kept as control groups. There was a trend for significantly greater reduction in bleeding scores and redness for irrigated sites compared with non-irrigated controls, for the first six post-treatment days. It can be hypothesised that flushing pockets with subgingival irrigants was effective, because motile forms tend to lie free on the surfaces of plaque masses, thus facilitating their removal.

A clinical study with similar design could not be found for comparison. In general, results for the CHX group are in agreement with studies by Westling and Tynelius-Bratthall[18] and Fine et al[19], who reported improved results for reducing signs of inflammation, particularly BOP, using 0.2% CHX as a subgingival irrigant.

Statistically significant improvement in the CU group compared with the CHX-irrigated and saline-irrigated groups was seen on days 2, 3, 4 and 5 for BOP and redness as markers of inflammation. This difference did not persist as the recall period increased between days 15, 21 and 42. The healing response after root debridement is dependent on the degree of pre-existing inflammation and trauma induced to sulcular epithelium. In the present study, meticulous debridement was done with Gracey curettes to avoid trauma to soft tissues. Better results obtained by curcumin irrigation can be attributed to its anti-inflammatory, anti-oxidant properties, in resolving inflammation at an earlier stage than CHX, which acts as an anti-bacterial only. Curcumin acts similarly to aspirin and aspirin-like anti-inflammatory drugs in diminishing inflammatory mediators of arachidonic acid metabolism[10]. Curcumin has an advantage over aspirin, as it selectively inhibits synthesis of prostaglandin E_2 and thromboxane while not affecting synthesis of prostacyclin. Curcumin, by virtue of its anti-inflammatory property, reduces inflammatory mediators and causes shrinkage by reducing inflammatory oedema and vascular engorgement of connective tissues. It also promotes migration of fibroblasts in the wound bed and results in reduction of vascularisation by bringing about fibrosis of connective tissue. It enhances wound healing by causing an increase in fibronectin and transforming growth factor β transcription[15]. Due to the diverse range of actions, curcumin-treated sites show faster resolution of inflammatory signs and greater reduction in probing depth than other treated sites.

The trend for slightly greater reduction in PPD by curcumin could be due to its ability to enhance wound healing. Gopinath et al[20] showed that curcumin incorporated in collagen, which acts as supportive matrix for slow release, increases wound reduction and enhances cellular proliferation.

The present study provides a rationale for the local application of curcumin as a subgingival irrigant, as a feasible and productive approach to supplementing mechanical debridement.

Furthermore, the present findings suggest that subgingival irrigation may play a role in the management of chronic periodontitis by reducing gingivitis as measured using BOP and visual assessment of redness as indicators of gingival health. The present study was a short-term clinical trial, which showed curcumin irrigation was superior in restoring gingival health. Further studies are required to ascertain whether the effect on periodontitis sites is clinically and statistically significant over longer period of time.

■ Conclusions

Pistorius et al[6] suggested use of herbal formulation with variety of active ingredients as an adjunctive procedure to reduce gingival inflammation. In this investigation, we introduced another herbal formulation

(curcumin, 1%) as an irrigant to reduce inflammatory gingival signs (BOP and redness) and promote better healing with reduced residual pocket depth, and demonstrated its superior efficacy. Further studies are required to substantiate these findings.

■ References

1. Saglie R, Newman MG, Carranza FA Jr, Pattison GL. Bacterial invasion of gingiva in advanced periodontitis in humans. 1982;53:217–222.
2. Weinstein et al. Antimicrobial agents. The pharmacological basis of therapeutics. Edn 5. New York: MacMillan, 1975.
3. Pitcher G, Newman H, Strahan J. Access to subgingival plaque by disclosing agents using mouthrinsing and direct irrigation. J Clin Periodontol 1980;7:300–308.
4. Greenstein G. Effects of subgingival irrigation on periodontal status. J Periodontol 1987;58:827–836.
5. Lander PE . The antimicrobial and clinical effects of a single subgingival irrigation of chlorhexidine in advanced periodontal lesions. J Clin Periodontol 1986;13:74–80.
6. Pistorius A, Willershausen B, Steinmeier EM, Kreislert M. Efficacy of subgingival irrigation using herbal extracts on gingival inflammation. J Periodontol 2003;74:616–662.
7. Page R. The role of inflammatory mediators in the pathogenesis of periodontal disease. J Periodont Res 1991;26:230–242.
8. Yoshimura A, Hara Y, Kaneko T, Kato I. Secretion of IL-1 beta, TNF-alpha, IL-8 and IL-1ra by human polymorphonuclear leukocytes in response to lipopolysaccharides from periodontopathic bacteria. J Periodontal Res 1997;32: 279–286.
9. Graves DT. The potential role of chemokines of inflammatory cytokines in periodontal disease progression. Clin Infect Dis 1999;28:482.
10. Sajithal GB, Chithra P, Chandrakasan G. Biochem Pharmacol 1998;55:1955–1962.
11. Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of tumeric. J Altern Complement Med 2003;9:161–168.
12. Ramsewak RS, DeWitt DL, Nair MG. Cytotoxicity, antioxidant and anti-inflammatory activities of curcumins I-III from *Curcuma longa*. Phytomedicine 2000;7:303–308.
13. Osawa T, Sugiyama Y, Inayoshi M, Kawakishi S. Antioxidative activity of the tetrahydrocurcuminoids. Biosci Biotechnol Biochem 1995;59:1609–1612.
14. Singh R, Chandra R, Bose M, Luthra PM. Antibacterial activity of *Curcuma longa* rhizome extract on pathogenic bacteria. Curr Sci 2002;83:737–740.
15. Sidhu GS, Singh AK. Enhancement of wound healing by curcumin in animals. Wound Repair Regen 1998;6:167–177.
16. Ozaki K, Kawata Y, Amano S, Hanazawa S. Stimulatory effect of curcumin on osteoclast apoptosis. Biochem Pharmacol 2000;59:1577–1581.
17. Phan TT, See P, Lee ST, Chan SY. Protective effects of curcumin against oxidative damage on skin cells in vitro: its implication for wound healing. J Trauma 2001;51:927–931.
18. Westling M, Tynelius-Bratthall G. Microbiological and clinical short-term effects of repeated intracrevicular chlorhexidine rinsings. J Periodontal Res 1984;19:202–209.
19. Fine JB, Harper DS, Gordon JM, Hovliaras CA, Charles CH. Short-term microbiological and clinical effects of subgingival irrigation with an antimicrobial mouthrinse. J Periodontol 1994;65:30–36.
20. Gopinath D, Ahmed MR, Gomathi K, Chitra K, Sehgal PK, Jayakumar R. Dermal wound healing processes with curcumin incorporated collagen films. Biomaterials 2004;25: 1911–1917.