Local drug delivery with an experimental bioadhesive drug as an adjunct to scaling and root planing in chronic periodontitis – An experimental study

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Abstract
Introduction: The first line of treatment for chronic periodontitis has always been phase 1 therapy with scaling and root planing with oral hygiene reinforcement. Mechanical debridement may fail to eliminate pathogenic flora because of their location in areas inaccessible to periodontal instruments. Antimicrobial agents may work as adjuncts to mechanical therapy.
Materials and Methods: This study was designed as a case control study carried out on 30 patients suffering from chronic periodontitis. Two contralateral sites with moderate deep pockets in the each patient were chosen and the teeth were divided into two groups. Group A sites got scaling and root planing alone while group B sites got an adjunctive antimicrobial experimental bioadhesive drug containing tetracycline, serratiopeptidase and bactase enzyme. Recall visits were scheduled at 30 and 90 days. General linear model showed decrease in gingival and periodontal indices which was statistically significantly greater in the experimental drug group.
Conclusion: Local drug delivery with the experimental bioadhesive drug is an effective nonsurgical method for use as an adjunct to mechanical debridement.

Keywords: Mechanical therapy, Tetracycline, Local drug delivery.

Introduction
It has been long recognized that bacterial plaque and their biologically active products have been implicated as the primary etiological agents of periodontal disease. Treatment of periodontal disease is routinely based on mechanical debridement of the tooth surface, and appropriate and meticulous maintenance of oral hygiene. However, comprehensive mechanical debridement of sites with deep periodontal pockets is difficult to accomplish. Mechanical therapy alone may fail to eliminate pathogenic flora because of their location within the gingival and dental tissues or in other areas inaccessible to periodontal instruments.[1] As an adjunctive approach, administration of local or systemic antibiotics is used because of the microbial etiology of periodontitis.[2,3] It also aids in pocket elimination with non-surgical pocket therapy where surgery is contra-indicated. With systemic antibiotics, to obtain an effective concentration in the periodontal pocket, repeated intakes over a long period are required.[4] Furthermore, there is risk of inducing bacterial resistance. With systemic tetracycline administration, a dose of 250 mg produces a transient peak concentration in gingival fluid of 5 to 14 μg/ml.5 Local administration of antimicrobial drugs directly into the pocket has been suggested as a means of bypassing systemic complications and targeting localized areas of periodontal destruction. Local drug delivery limits the drug to its target site with little or no systemic uptake hence, lessening the risk of side effects. The local concentration achieved can be much higher than is possible via the systemic route. Some agents used presently include tetracycline, metronidazole, minocycline, doxycycline, chlorhexidine. Amongst these agents, tetracycline and its derivatives remains the most extensively used antibiotic. It is a primarily bacteriostatic broad spectrum antimicrobial with anticollagenase and antiinflammatory actions. It inhibits bone resorption and has the ability to promote attachment of fibroblasts to root surface. Tetracyclines are substantive (3-21 days) on root surfaces, potent, not toxic at prescribed dosages, and after local drug delivery have been detected at 1 to 20 μm within the epithelial tissue.[5] Serratiopeptidase is a proteolytic enzyme and exhibits anti-inflammatory action. Besides reducing inflammation, it also has the ability to block the release of pain-producing amines from the inflamed tissues. It also increases the permeability of the crevicular membrane allowing increased drug penetration in the connective tissue. It has also been shown to inhibit biofilm formation on prosthetic devices and increase antibiotic availability.[6] Bactase is a blend of naturally available enzymes that inhibits and reduces bacterial growth. It attacks the cell wall of bacteria depriving them of oxygen and iron required for their survival and multiplication. It also helps in reducing plaque and inflammation. Bactase contains 7 major components: lysozyme, glucoxidase, amylase, papain, amyloglucosidase, peptizyme and lactoferrin.[7] The three constituents are synergistic to each other and may provide more beneficial effect compared to individual components. Thus, an effort is made to combine these 3 constituents into one, which is expected to be stable, biologically acceptable, play a dual role as an anti-inflammatory and antimicrobial agent, bioadhesive, provide a high bacteriocidal concentration in GCF.

Materials and Methods
Materials
The experimental drug has been devised in a powder form, which is a pluronic polymer coated liquid crystalline precursor form, which is bioadhesive in nature, and is converted into gel when it comes in contact with the

contents of a periodontal pocket and the crevicular fluid. The powder has been shown to be a sustained delivery system, releasing therapeutic concentrations of the drug over a period of 30 hours.

Methods

Clinical evaluation: A total of 30 subjects comprising of both the sexes and diagnosed as suffering from chronic localized or generalized periodontitis, above 21 years of age were considered for the present study from the outpatient of department of Periodontology. Selection criteria included subjects diagnosed as suffering from chronic periodontitis with pocket depth of 5mm to 8mm in at least 2 non adjacent sites in different quadrants of the mouth with at least 20 remaining teeth. Exclusion criteria included subjects with a history of systemic antibiotic usage in the past 3 months, oral prophylaxis in the last 6 months and history of allergy to any components of the drug or periodontal dressing. Pregnant and lactating mothers, and mobile teeth in the selected region were also excluded. Study Protocol: A special proforma was designed for the present study so as to have a systematic and methodical recording of all the observations and information. The relevant data comprising of details of the chief complaint, preliminary history, brushing habits etc. were recorded in the special proforma. Clinical examination was done in a dental chair, under standard conditions of light, using a mouth mirror, explorer, William's graduated periodontal probe and tweezer and assessment of clinical parameters was carried out. Selected sites were randomly divided into control sites and experimental sites, which were treated by using split mouth design. Control sites: 30 sites were treated by scaling and root planing alone. Experimental sites: 30 sites were treated with scaling and root planing followed by placement of the experimental material in the periodontal pocket. Recording of clinical and microbiologicalparameters:

The parameters that were recorded include

1. Plaque index (Turesky-Gilmore-Glickman modification of the Quigley-Hein, 1970)
2. Gingival index (Loe and Silness, 1963)
3. Sulcus Bleeding index (Muhlemann and Son, 1971)
4. Probing Pocket depth measurement using William's graduated probe using acrylic stent
5. Relative distance between base of pocket and fixed reference point on the stent for assessing clinical attachment gain or loss
6. Microbiological study of collected plaque sample for spirochetes under dark field microscopy.

The above clinical and microbiological parameters were recorded on 0 day, 1 month and 90 days.

Clinical Protocol

Periodontal Therapy: The clinical and microbiological parameters were assessed at the baseline at selected sites followed by thorough scaling and root planing. On completion of scaling and root planing, control sites were covered with Coe-Pak. After SRP, the experimental site was completely dried using air syringe and then the site was isolated with cotton rolls to prevent contamination from saliva. The powder is carried to the periodontal pocket, and inserted till the pocket depth with the curette. The powder converts into gel form immediately on adhering to the contents of the pocket, and can be easily manipulated in the pocket using gentle finger pressure. The pocket opening was covered with Coepak to retain the material in the pocket as well as to prevent the ingress of oral fluids. Patient was instructed not to brush in the area where periodontal dressing is placed, not to chew hard or sticky food, not to floss on the treated site, not to probe the area with tongue, finger or tooth pick and to report immediately, if the material or pack is dislodged before the scheduled recall visit or if discomfort, burning sensation or any other allergic reaction occurs. Subjects were recalled after 7 days for removal of the periodontal dressing, for oral hygiene maintenance instructions and recording of subjective and objective criteria. Recall visits were again scheduled after 1 month and 45 days of placement of local experimental drug for measuring the clinical parameters, microbiological study and for assessment of subjective and objective criteria as per the study design.

Statistical Analysis

Post treatment changes from baseline to different time intervals in various clinical parameters were analyzed by paired t-test (Intragroup). Intergroup comparisons of post-treatment changes were analyzed by unpaired t-test. p-value <0.05 was considered as significant difference.

Results and Discussion

In the present study, statistically significant reduction in mean plaque index, gingival index, sulcus bleeding index, probing pocket depth and also statistically significant gain in clinical attachment in both the groups from the baseline was observed. Significant reduction in the percentage of spirochete count was observed for both the groups when compared to the baseline. Statistically significant reduction in gingival index, sulcus bleeding index, probing pocket depth and also statistically significant gain in clinical attachment were observed in experimental sites when compared to the control sites. Significant reduction in the percentage of spirochete count and was observed in the experimental group when compared to the control group. In the present study, acceptability of the experimental material by all the subjects was observed in terms of taste and comfort. Good biological acceptability was seen as no evidence of burning sensation, dryness/soreness, ulcer formation and staining of teeth. It is clear from the results of present study that this combination along with scaling and root planing is effective in removing the local irritants, reducing gingival inflammation, reducing pocket depth and also results in gain in clinical attachment. The results are consistent with those achieved by Heijl et al 19918, Kinane et al 19999. The percentage reduction in spirochetes is similar to that achieved in study of Maze et al 199510 and Lindhe et al 197911 It can be concluded that the

experimental local drug delivery system containing tetracycline hydrochloride, serratiopeptidase and bactase can be effectively used as an adjunct to scaling and root planing and is more effective than scaling and root planing alone in the treatment of periodontal pockets To elucidate the use of this local drug delivery system in future, a long term study carried out on a large sample of subjects is required. Also, in addition to darkfield analysis, culture methods for microbiological analysis of individual periodonto pathogens should be carried out. An attempt is required to find out the efficacy of the experimental material in comparison to the marketed local drug delivery system.

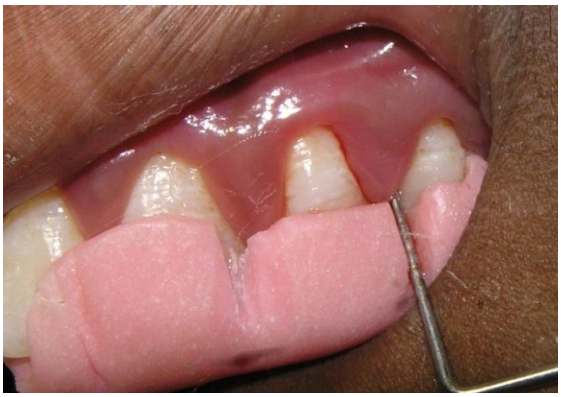

Fig. 1: Pocket measurement with a standardised acrylic stent

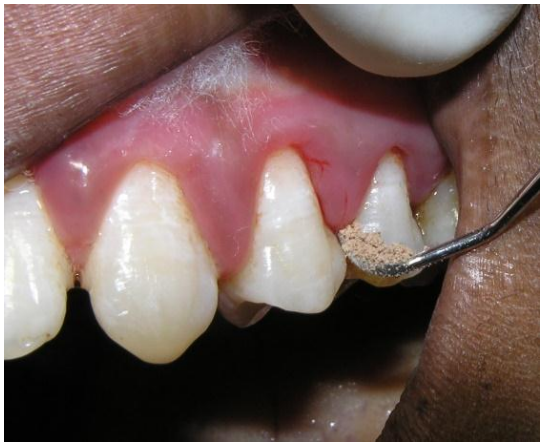

Fig. 2: Drug carried to pocket on a curette

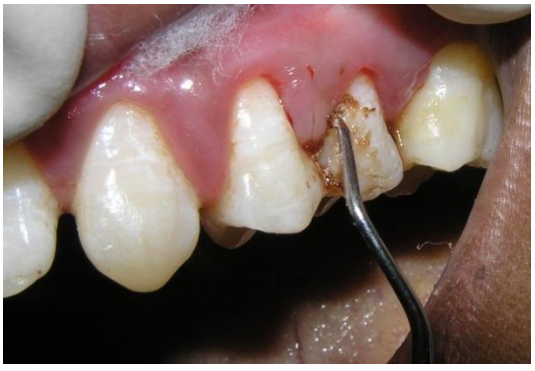

Fig. 3: Insertion and stabilisation of drug inside pocket

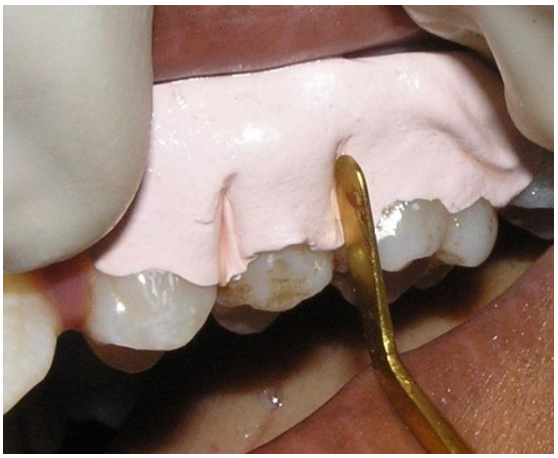

Fig. 4: Application of Coe-pack

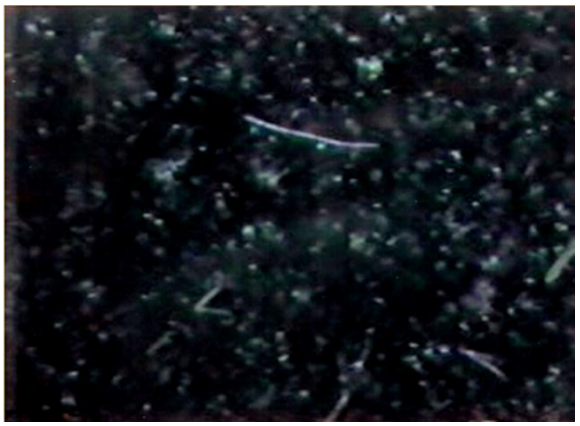

Fig. 5: Dark field microscopy showing spirochetes at baseline

Fig. 6: Dark field microscopy showing spirochetes at 30 days

Table 1: Showing reduction in plaque index, gingival index and sulcus bleeding index scores at 30 and 90 days

Days	Mean plaque index reduction		Mean gingival index reduction		Mean SBI reduction	
	Cont	Exp	Cont	Exp	Cont	Exp
0-30 days	1.20	1.25	0.57	1.01	1.16	1.66
0-90 days	1.55	1.62	0.97	1.78	1.48	2.18

Table 2: Showing reduction in Mean attachment gain, mean ppd and mean percentage of spirochetes at 30 and 90 days

Days	Mean attachment gain		Mean probing pocket depth reduction		Mean % reduction of spirochetes	
	Cont	Exp	Cont	Exp	Cont	Exp
0-30 days	0.90	1.23	0.95	1.45	48.63	68.89
0-45 days	1.20	1.31	1.42	1.70	53.70	74.55

Conclusion

The experimental local drug delivery system containing tetracycline, serratiopeptidase and bactase may be a useful adjunct to reduce pocket depth and gingival inflammation in chronic periodontitis cases. It may also be useful in cases where inflammation persists inspite of thorough local debridement.

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