

Research Article



Efficacy of Subgingivally Delivered Flurbiprofen and Chlorhexidine Chip in the Treatment of Chronic Periodontitis – A Randomized Controlled Clinical Trial

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ABSTRACT

Antimicrobial and pharmacologic agents delivered locally in the periodontal pocket modulate the host response and enhance the effect of non-surgical periodontal therapy. The aim of present randomized controlled clinical trial was to determine the efficacy of multiple applications of subgingivally delivered Flurbiprofen and Chlorhexidine chip in patients with chronic periodontitis. 50 patients suffering from chronic periodontitis were randomized into groups A and B. Following scaling and root planing, patients were treated by subgingivally delivered Flurbiprofen or chlorhexidine chip. The chips were re-inserted sub-gingival at weeks 1, 2, 3, 5 and 7 if PD > 5mm. Clinical parameters including Plaque index, Gingival index, Papillary Bleeding Index, Probing depth and Clinical attachment level were recorded at baseline, 1, 3 and 6 months. Data analysis was carried out using SPSS package (Ver 10.5). Both the therapeutic approaches led to significant reductions in PI, GI, PBI, probing depths and greater gain in CAL compared to baseline over a period of 6 months ($p < 0.001$). Difference in mean PD reduction and CAL gain from baseline to 6 months in between the groups was $0.36 \pm 0.333\text{mm}$ which was not statistically significant. The combination of SRP and subgingival delivery of flurbiprofen or chlorhexidine chip was more effective than SRP alone in improving the clinical parameters. Furthermore, frequent applications of CHX or FBP chips resulted in greater mean PD reduction and CAL gain than single application.

Keywords: Chronic Periodontitis, Scaling and root planing, Local drug delivery, Chlorhexidine, Flurbiprofen.

INTRODUCTION

The search for periodontal pathogens has been underway for more than a century, and continues even up today. It is now known that the biofilm microorganisms can actively maintain their three-dimensional structure and are the primary cause of periodontal disease.¹

With this, conventional mechanotherapy is definitely the gold standard for the reduction or at least suppression of the pathogenic periodontopathic species. But the adjunctive use of chemotherapy in the last few decades has made wonders in the field of periodontal therapy.

With the recognition of the adjunctive use of chemotherapeutics, the local delivery of antimicrobial agents directly to the periodontal pocket seems to be a promising approach for the treatment of periodontal disease, serving the primary goal of achieving and maintaining therapeutic levels of the drug in the periodontal pocket for a longer period of time.⁷ Recently, it has been observed that Non-steroidal anti-inflammatory drugs (NSAID) may alter the host inflammatory response and hence, the course of periodontal disease.

Flurbiprofen is one of the common NSAIDs and is a potent inhibitor of cyclo-oxygenase (COX), which is a key element of the arachidonic cascade.

It decreases inflammation and pain by inhibiting COX-1 and COX-2 enzymes, which then inhibits the production of prostaglandins and leukotrienes. It is found to be a potent anti-inflammatory agent showing a significant

decrease in bone loss. It has also been shown to suppress the inflammatory mediators such as thromboxane B2 and prostaglandin E2.² Agents with antimicrobial properties have been in demand for local delivery in periodontal pockets, of which, Chlorhexidine is considered the gold standard. Chlorhexidine was amongst the best of a range of bisbiguanides synthesized ad hoc by Davies in 1954.³ Inhibition of plaque formation by binding to anionic acid groups on salivary glycoproteins and interfering with the adsorption of salivary bacteria to teeth are the mechanisms which makes chlorhexidine perfect for its use. The property of substantivity, allowing it to be well retained in the oral cavity for a longer period of time, takes it one step ahead.

An array of devices have been developed for the local delivery of drug and are commonly used but the technology of formulation of a periodontal chip has an immense opportunity as a novel, controlled release device. When placed subgingivally in the periodontal pocket, it releases the drug over a period of 7 days at an effective and constant rate, killing 90% of the bacteria in the periodontal pocket.⁴

To the best of our knowledge, there have been a very few studies that have investigated the effects of multiple applications of periodontal chips containing flurbiprofen and chlorhexidine in patients with chronic periodontitis.

Also, it should be noted that only one randomized clinical trial was found after a thorough search of the literature comparing the effects of these. In view of the aforementioned scenario, the aim of the study is to evaluate the effectiveness of multiple applications of



subgingivally delivered 2mg Flurbiprofen Chip compared with 2.5mg Chlorhexidine chip in the management of patients with chronic periodontitis.

MATERIALS AND METHODS

A total of 50 patients visiting to the out-patient Department of Periodontics, Faculty of dental sciences, M.S Ramaiah University of applied sciences, Bangalore who were diagnosed with chronic periodontitis were recruited into the study. The ethical clearance for this study was obtained from the ethical committee of the institution. Patients aged between 30 to 79 years, with a minimum of 10 natural teeth present, presence of at least two teeth with periodontal pockets 5–8 mm in depth, positive bleeding on probing in at least one site, radiographic evidence of alveolar bone loss and those who had not undergone any periodontal treatment in the previous 6 months were selected for the study. Patients with systemic antibiotic therapy or use of NSAIDs prior to study entry, those on medications known to result in gingival overgrowth, pregnant or lactating females, Type I or non-stable type II diabetics, smokers and those with known allergies to NSAIDs or Chlorhexidine were excluded. Selected patients were randomized using “allocation concealment” method in a double-blinded manner into Group A and Group B. Group A received Scaling and Root Planing [SRP] and sub-gingivally delivered flurbiprofen chip into the periodontal pocket and Group B received Scaling and Root Planing [SRP] and sub-gingivally delivered chlorhexidine chip into the periodontal pocket. The patients were educated about the disease and subject of the study and an informed consent was obtained. After one week of initial therapy in the patients who maintained oral hygiene, baseline clinical parameters were recorded. Subjects underwent scaling and root planing using ultrasonic scalers and periodontal curettes.

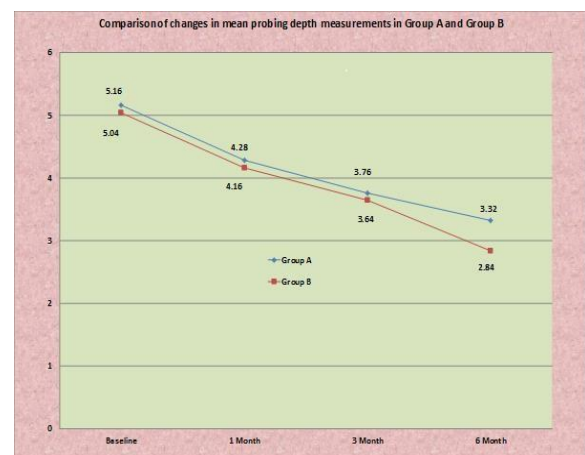
All the measurements were standardized using customized acrylic stents with grooves. The recordings were made using a UNC 15 probe (Hu-Friedy's). The treatment was performed by the clinician who was blinded of the type of chip placed. Experimental sites A and B with probing depth 5-8 mm were randomly assigned on the day of subgingival chip placement. The periodontal pocket was isolated and the chip was inserted into the periodontal pocket to its maximum depth. Patients were instructed not to perform any interdental hygiene for 1 week in the treated site.

At weeks 1, 2, 3, 5 and 7, the same type of chip were re-inserted if probing depth > 5mm persisted. Post treatment evaluation & follow up was done at 1, 3 and 6 months. Bleeding on Probing, Plaque Index, Gingival index, Probing pocket depth and Clinical Attachment level were recorded using UNC-15 probe.

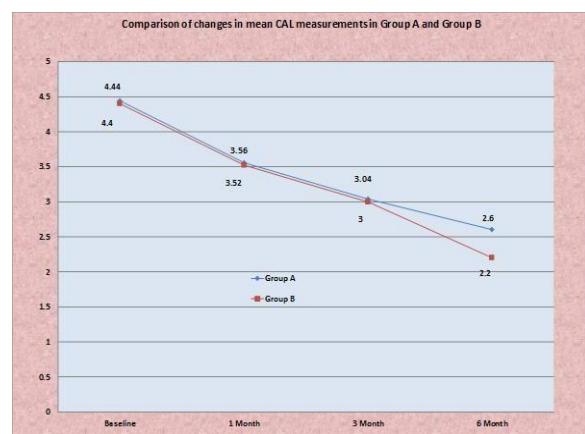
Statistical Analysis

The results were averaged for continuous data and number and percentage for dichotomous data are

presented as Table and Figure. Normality Assumption was checked by using Shapiro Wilk's test. The Shapiro Wilk's test showed that data was not normal, so non parametric analysis was carried out. Kruskal Wallies test is used when the sample data fail to fulfill the requirements of an analysis of variance. Unlike the parametric t-test, Mann-Whitney non-parametric test makes no assumptions about the distribution of the data. The student-t test was used to determine statistical difference between groups in the parameters measured. In all the above tests, the “p” value of less than 0.05 was accepted as indicating statistical significance. Statistical Package for Social Science (SPSS) package (Ver 10.5) was used for data analysis.



Graph 1



Graph 2

RESULTS

No statistically significant differences were observed in the mean age and gender distribution in both the groups at baseline. The mean age of patients in group A was 43.8 years while in group B was 40.8 years ($p > 0.05$). Both the experimental groups showed improvements in PI scores at 6 months follow up visit when compared to baseline levels but the improvements were statistically significant in group B ($p < 0.001$). Mean GI score reduction was not significant in both the groups at 3 months but both the experimental groups showed statistically significant improvements in GI scores at 6 months follow up visit when compared to baseline levels. However, the

improvements were highly statistically significant in group B ($p < 0.001$) as compared to group A ($p = 0.014$). Statistical significant differences were seen in the values of plaque and gingival index in between the groups at 6 months ($p=0.002$). Mean PBI score reduction was statistically significant in both the groups at 6 months follow up visit when compared to baseline levels. However the improvements were highly statistically significant in group B ($p < 0.001$). Statistical significant differences were seen in the values of PBI in between the groups at 6 months ($p < 0.001$).

At baseline, there were no statistical significant differences between the probing depths at probing sites. Both the treatment groups showed highly significant

changes in PPD and CAL from baseline to 3 months and 6 months. ($p < 0.001$). Mean probing depth reductions from baseline to 6 months were 1.840 ± 0.624 for experimental group A and 2.200 ± 0.957 for group B.

When the comparison was made between the groups, no statistically significant differences were seen in the values of PD and CAL at 1, 3 and 6 months in between the groups. (Graph 1, 2) Also, there were no statistically significant differences in the change of the values of PD and CAL from baseline to 1 month ($p=1.000$), 3 months ($p=1.000$) and 6 months ($p=0.122$) (Table 1, 2). When the comparison was made between the groups, no statistically significant differences were seen in the values of GM at 1, 3 and 6 months ($p=0.634$).

Table 1: Comparison of changes in Pocket depth measurements from baseline between Group A and Group B

	Group	N	Mean	SD	Min	Max	't' value	'p' value
1 Month - BL	Group A	25	-0.880	0.332	-1	0	0.00	1.00
	Group B	25	-0.880	0.332	-1	0		
3 Month - BL	Group A	25	-1.400	0.500	-2	-1	0.00	1.00
	Group B	25	-1.400	0.577	-3	-1		
6 Month - BL	Group A	25	-1.840	0.624	-3	-1	2.480	0.122
	Group B	25	-2.200	0.957	-4	-1		

Table 2: Comparison of changes in CAL measurements from baseline between Group A and Group B

	Group	N	Mean	SD	Min	Max	't' value	'p' value
1 Month - BL	Group A	25	-0.880	0.332	-1	0	0.00	1.00
	Group B	25	-0.880	0.332	-1	0		
3 Month - BL	Group A	25	-1.400	0.500	-2	-1	0.00	1.00
	Group B	25	-1.400	0.577	-3	-1		
6 Month - BL	Group A	25	-1.840	0.624	-3	-1	2.480	0.122
	Group B	25	-2.200	0.957	-4	-1		

DISCUSSION

With newer periodontal pathogens being discovered and newer hypothesis been put forward, there cannot be a cook-book for the treatment of periodontal disease. Mechanical therapy is usually the first mode of therapy recommended and is considered the gold standard till date. However, the temporary effect of subgingival scaling and root planning and its inability to eradicate all periodontal pathogens demands an era of change.^{5,6}

Site specific and therapeutic levels of the drug achieved at the site of infection by locally delivered antimicrobials have proven to be more convenient, effective and easy-to-use as compared to systemic antibiotics.

The present study evaluating the efficacy of frequent applications of subgingivally delivered Flurbiprofen and Chlorhexidine Chip in patients with chronic periodontitis has shown a significant improvement in clinical

parameters at the end of 1, 3 and 6 months. Each subject demonstrated good oral hygiene and generally healthy gingival condition throughout the study. The flurbiprofen and chlorhexidine group showed statistically significant improvements in PI and GI scores at 6 months follow up visits when compared to baseline levels. Similar changes in gingival status have been reported using 1% w/w flurbiprofen toothpaste⁸ 0.3% flurbiprofen controlled release gel⁹⁻¹¹ and chlorhexidine chip¹²⁻¹⁶ in other studies. However, these changes in plaque and gingival scores could be the result of rigorous oral hygiene maintenance regime and regular follow-up visits by the patients throughout the study period.

Both the experimental groups showed statistically significant improvements in PBI scores at 6 months follow up visit when compared to baseline levels. However, the improvements were highly statistically significant in group B as compared to group A. The reduction in the bleeding



scores represents significant reduction in bacterial load and gingival inflammation in these sites. This is in agreement to another study by Gonzales¹⁷ where in the mean percentage of bleeding sites decreased from 95% to 35% after 10 days and to 42% after 28 days of placement of CHX chip. Goodson¹⁸ found significant reduction in red-complex bacteria after local delivery of antimicrobials. The greater reduction in bleeding scores observed in the present study is likely due to the frequent applications of chips and their effect on the microbial flora along with inflammatory response due to flurbiprofen.

Both the treatment groups showed highly significant changes in PPD and CAL from baseline to 3 months and 6 months. Single application of CHX chip by Heasman¹⁹ resulted in mean PD reduction of 0.55 – 0.78 mm after 3 and 6 months. But, frequent applications of these chips along with SRP at baseline resulted in a mean PD reduction of around 2 mm at the end of 6 months in this study. Thus, it lead to a reduction in a greater number of sites initially targeted for surgical therapy along with reduction in time and cost of the treatment. But, Grisi¹² and Daneshmand²⁰ reported that there were no statistically significant differences with SRP and adjunctive use of CHX in clinical parameters at the end of 9 months. This might be due to their longer follow up periods.

Mean CAL gain in the present study was 1.8 - 2.2 mm. These results exceed those by Machtei in a study²¹ after 8 weeks when using repeated local application of FBP and CHX chips. The greater CAL gain in the present study can also be attributed to the greater increased concentration of the drug caused by the multiple applications of the chips. It has been demonstrated that PGE2 and TXB2 levels decreased and remained relatively constant from day 29 to day 50 with flurbiprofen administration in a study by Abramson.²² Similar results were confirmed by various authors^{20,21,23-26} where there were significant improvements in the values of CAL after administration of FBP and CHX chips. When the comparison was made between the groups, no statistically significant differences were seen in the values of PD and CAL at 1, 3 and 6 months in between the groups. This is in agreement with the study done by Machtei.²¹

In the current study, both the experimental groups showed non-significant changes in gingival margin values when compared to baseline at 6 months post treatment. This observation suggests that both FBP and CHX do not mechanically interfere with the healing process. However, Grisi¹² in a study reported mechanical trauma with the use of CHX chip leading to an increased gingival recession.

Hence, within the limitations of the study, there was a significant improvement in all the clinical parameters in both the groups after a period of 6 months. These findings suggest that if both the chips are used consecutively or simultaneously, it might result in even

greater anti-bacterial and anti-inflammatory effect by the drugs.

CONCLUSION

Periodontal therapy can definitely be benefitted from the adjunctive subgingival administration of flurbiprofen and chlorhexidine chips.

Furthermore, frequent applications of CHX or FBP chips may result in a greater probing depth reduction than obtained with a single application. However, it should be noted that mechanical periodontal therapy is of utmost importance for the reduction of periodontopathic microorganisms. Further research is needed to evaluate the long term clinical advantage of this adjunctive therapy in the treatment of chronic periodontitis.

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