Article published online: 2021-11-01

ORIGINAL ARTICLE

Clinical efficacy of chlorhexidine chips and tetracycline fibers as an adjunct to non surgical periodontal therapy

Munishwar Singh, A. K. Shreehari, P. K. Garg, Sangeeta Singh

Division of Periodontology, Department of Dental Surgery, Armed Forces Medical College, Pune, Maharashtra, India

Address for correspondence:
Dr. Munishwar Singh,
Division of Periodontology,
Department of Dental Surgery,
Armed Forces Medical College,
Pune - 411 040, Maharashtra, India.
E-mail: msmalhi@yahoo.com

ABSTRACT

Context: Local drug delivery agents. **Aims:** To clinically evaluate the efficacy of Chlorhexidine chip (PerioCol™ CG) with Tetracycline fibers (Periodontal Plus AB™). **Settings and Design:** Randomized controlled, split mouth study design with an observation period of six months. **Materials and Methods:** Patients were allocated in 3 experimental treatment groups, Group A: SRP + CHX Chip, Group B: SRP + Tetracycline fibers, and Group C: SRP alone (control group). 420 bleeding sites in 35 patients (18 females and 17 males) with chronic periodontitis (5-8mm probing depth), were evaluated clinically for pocket probing depth (PD), Clinical Attachment level (CAL), and Bleeding on Probing (BoP). **Statistical Analysis:** *T*-test and CV. **Results:** All the treatment groups were found to be efficacious as demonstrated by improvement in PD, CAL, and BoP. In the short term, CHX group showed increased gain of CAL but on long term observation the Tetracycline fiber group showed better consistent clinical results in comparison to the other two groups. **Conclusions:** Group B (SRP + Tetracycline fibers) resulted in better optimum clinical results in comparison to the other two treatment groups.

Key words
Chlorhexidine chips, chronic periodontitis, local drug delivery, periodontal pocket, tetracycline fibers

INTRODUCTION

It has been well established that bacteria have a prominent role in periodontal disease. Though mechanical therapy (scaling and root planing [SRP]) has been the main stay of periodontal therapy but its efficacy is limited by biochemical considerations and physical impediments. Soon after SRP, the bacteria begin reattaching to the teeth forming a biofilm. Overtime, this biofilm becomes more pathogenic due to succession of bacteria. Antimicrobial agents (AMAs) may be used as an adjunct to reduce the bacterial challenge to the periodontium. Their controlled release directly into the periodontal pockets by chips, films, microspheres, gels, strips, monolithic devices, fibers, etc., is an effective therapeutic intervention. Goodson (1985) suggested that for a drug delivery system to be effective and clinically useful in periodontal therapy, it must be delivered to the base of the pocket, should achieve a minimal inhibitory concentration (MIC), and sustain the achieved concentration in the periodontal pocket for a sufficient period of time to be effective.[1] In addition, other considerations include the ease of placement, retention after placement, biodegradability of the agent, and acceptable cost.[2]

Access this article online	
Quick Response Code:	Website: www.ejgd.org
	DOI: 10.4103/2278-9626.134840

The most crucial factor determining the success and efficacy of a local drug delivery (LDD) agent is the length of time the microflora is exposed to the agent and the goal is to maintain effective concentrations of AMA at the site of action for longer periods, despite drug loss from crevicular fluid clearance. LDD agents can be divided into two classes according to the duration of medicament release: (1) Sustained release devices and (2) Controlled delivery devices. Sustained release formulations are designed to provide drug delivery for less than 24 hours. On the other hand, controlled delivery system should have a duration of drug release that exceeds one day.[3]

Chlorhexidine (CHX) is a broad-spectrum antimicrobial agent that at low concentrations causes damage to the cell membrane of microorganisms, while at higher concentrations is known to cause precipitation and coagulation of the proteins in the cytoplasm of exposed

microbes.[4] Various studies[5-9] have validated the efficacy of CHX chip, and it has been noticed that the average concentration of CHX in the gingival crevicular fluid remains greater than 125 mg/mL for eight days and is inhibitory to 99% of bacteria isolated from periodontal pockets.[10]

Tetracycline (TC) is a broad-spectrum polyketide antibiotic that binds to the 30S subunit of microbial ribosomes, thereby inhibiting protein synthesis and being active against both Gram-positive and Gram-negative bacteria. The delivery of TC has been promoted in several systems (powder, irrigation solution, gel, incorporated in nonresorbable fibers [dialysis tubing or ethylene–vinyl acetate monolithic fibres]).[11] Regrettably, majority of the studies have tested a single form of LDD system or systemic administration instead of comparing various forms of therapy. A thorough literature search revealed only 27 intra subject split mouth studies over the years, with most being conducted with metronidazole gel. To the best of our knowledge, only two split mouth studies between CHX chips and TC fibers exist.[12,13] One[12] is a case report while the other[13] is a single time administration of CHX and TC fibers with a follow up duration of only three months. As CHX and TC are the most commonly dispensed LDD agents, a split mouth study comparing their effect over a six-month period was planned, with administration of the agents twice during the study period.

MATERIALS AND METHODS

Thirty-five patients were selected amongst the patients attending the outpatient department. The subjects were ascertained to be in good general health without any systemic disease. The selected patients had not received antibiotics, steroids, or oral prophylaxis for at least six months prior to the start of the study. Forty-one patients (21 males and 20 females) age between 20-50 years having a set of 22 or more teeth, pocket probing depth of 5-8 mm, clinical attachment loss >3 mm at minimum six teeth, presence of bleeding on probing, and willingness to comply were included. They were free from any unusual oral lesions, any condition requiring premedication before dental treatment, non-allergic to TC or CHX, and without any prosthesis. After recruitment, all patients passed an etiotropic phase wherein supragingival scaling, polishing, and repeated oral hygiene instructions were imparted. This phase lasted till their full-mouth plaque score (FMPS) and full-mouth bleeding score (FMBS) were less 15% (four sites per tooth); thus, the patient qualified for baseline examination. Of the total of 41 subjects, six patients had to be excluded after enrolment while passing the etiotropic phase (two subjects: unsatisfactory oral hygiene performance; four subjects: intake of antibiotics for other medical reasons) [Figure 1].

Clinical measurements

Clinical parameters pocket probing depth (PD), Clinical Attachment level (CAL), and Bleeding on Probing (BoP) were measured at baseline, one, three, and six months after therapy at all the selected teeth. PD and gingival recession were measured at four sites per tooth to the nearest 0.2 mm by an automated periodontal probe (Florida Probe Corporation, Gainesville, FL, USA) equipped with a handpiece to detect the cementoenamel junction (CEJ) and a constant probing force of 0.2 N (Florida Probe with "PASHA" probe [Pressure-controlled, Automated, Standardised Handpiece]) was used [Figure 2]. PD was automatically measured as the distance from the probe tip inserted into the bottom of the periodontal pocket to the probe flange which was gently touching the gingival margin. Gingival recession was measured as the distance from the gingival margin to a reference point i.e. CEJ or a restoration margin, when appropriate after the probe flange had been drawn back to the reference point. CAL of each site was calculated as the sum of PD and recession. BoP was

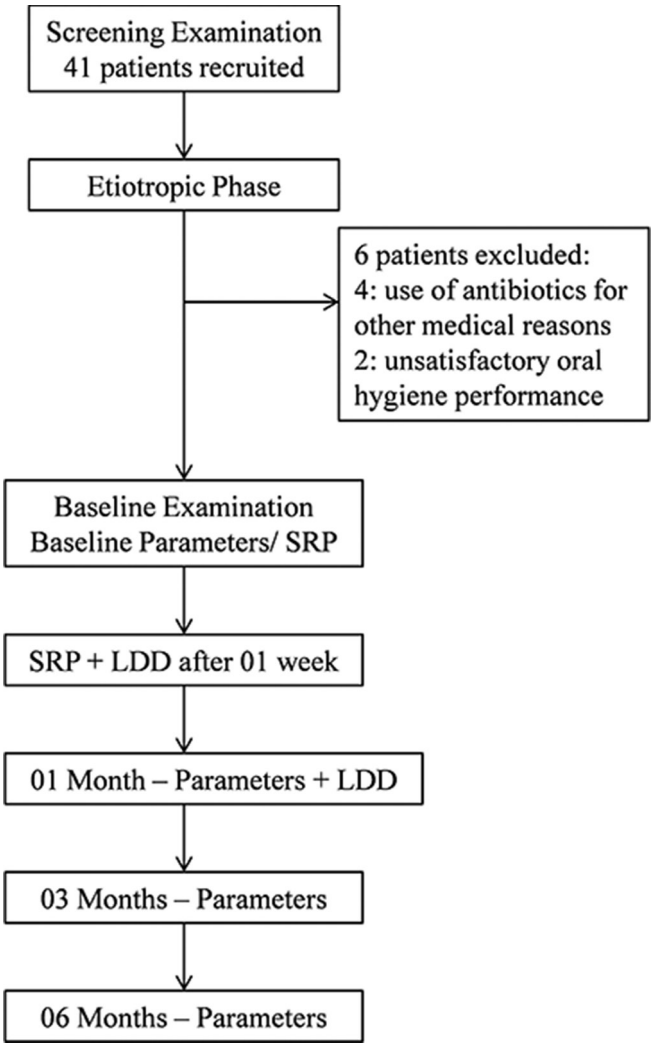

Figure 1: Study outline

recorded dichotomously as present or absent for each site after probing the respective quadrant.

Scaling/root planing

Following baseline examination, SRP was performed quadrant per quadrant under local anesthesia in four visits at all sites exhibiting a PD >5 mm. SRP was completed within one week. At the post-treatment control i.e. 1 week after conclusion of SRP, teeth were supragingivally scaled and polished, and oral hygiene instructions were reinforced. Subsequently, the patients were allocated either to the CHX chip group (Group A/Test), TC fiber group (Group B/Test), or only SRP group (Group C/control) by simple randomization to eliminate the bias in treatment assignment.

The chosen sites were isolated with cotton rolls, then air dried with dental unit's three-way syringe, and CHX chip was inserted into the dried periodontal pocket (baseline PD >5 mm) and gently pushed to the bottom of the periodontal pocket. The chip was adjusted to size with a scalpel if necessary and a maximum of two chips per tooth were dispensed. Similarly, the contralateral sites received TC fibers [Figures 3 and 4]. A periodontal pack was given after the placement of chips/fibers so that a higher local concentration of AMA was maintained for a longer duration of time.

Supportive periodontal therapy

All patients received routine Supportive periodontal therapy (SPT) consisting of clinical measurements, supragingival scaling, followed by polishing and provision of oral hygiene instructions at all control visits of one, three, and six months. Local anesthesia was delivered if demanded and root planing was performed at all BoP positive sites with a PD >5 mm and at sites exhibiting a PD >5 mm. After completion of one month SPT visit, repetition of insertion of the CHX chips and TC fibers in test sites with remaining PD >5 mm was done. One week before all SPT visits of one, three, and six months, supragingival scaling with polishing of all teeth and reinforcement of oral hygiene instructions were carried out so as to minimize the measurement errors due to newly formed calculus and avoid false-positive BoP results due to sole sulcular bleeding.

Data presentation and statistical analysis

The Florida probe's probing data was exported from the probe database to Excel (MS Excel 2007, Microsoft Corporation, Redmond, WA, USA) using an export software program (Data Downloader, Florida Probe Corporation, Gainesville, FL, USA). After adding other data, the entire database was imported into a statistical software program, locked, and analyzed (SPSS 17.0 for Windows, SPSS Inc., Chicago, IL, USA). Student's T-test was used for calculating the significance level and intragroup comparison. Coefficient of variation was used for intergroup comparison as well as to find the most precise procedure of all the three groups.

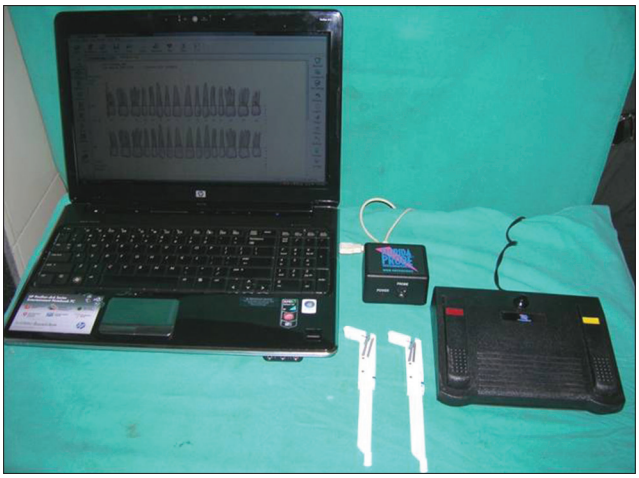

Figure 2: Florida probe

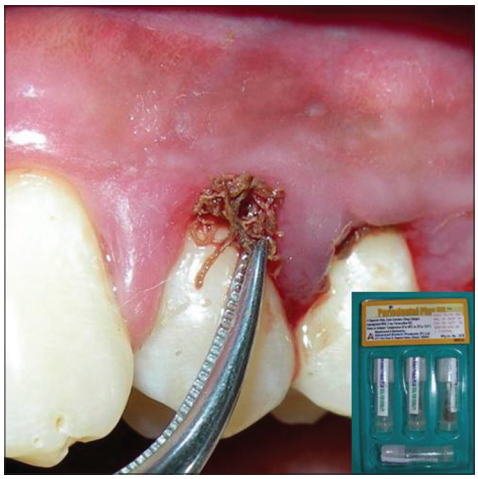

Figure 3: Insertion of tetracycline fibers

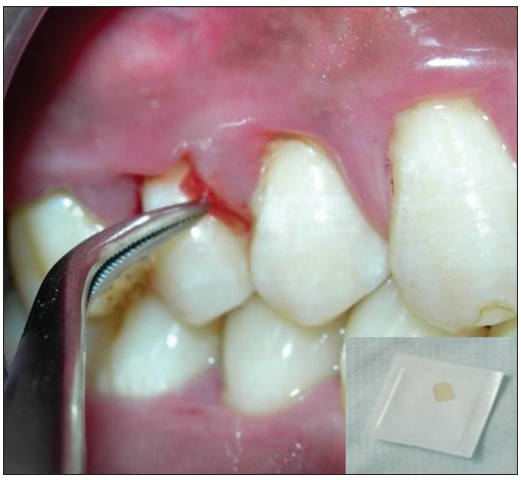

Figure 4: Insertion of chlorhexidine chips

RESULTS

Out of the total 41 selected patients, 35 patients (18 females and 17 males) in the median age of 36 years (range, 20-50 years) completed the total

duration of the study. Six subjects (four subjects: intake of antibiotics for other medical reasons and two subjects: unsatisfactory oral hygiene performance) dropped out. An average of seven CHX chips per patient (range, 6-10) were administered after SRP. At the SPT visit after one month, a significantly lower number of CHX chips were placed (3 chips per patient, range from 2-7, $P < 0.001$). Similarly, the amount of TC fibers placed in the periodontal pocket also decreased in the one month after SPT visit.

Full-mouth median values for clinical parameters

The changes in clinical parameters throughout the study period for full-mouth PD and CAL are shown in Tables 1-5. The same has also been depicted by histograms [Figures 5 and 6].

At one month, all three groups showed marked improvement in periodontal conditions as revealed by significant reductions of PD and CAL gain ($P < 0.001$).

After one and three months visit, a significant change was observed between the change in PD and CAL gain between all three groups. However, at that time, the change in CAL gain was significantly higher in the CHX group/Group A. It was observed that PD significantly increased again between three and six months, in group A, B, and C [Tables 1-3]. However, in comparison to baseline values, a significant difference was observed in all three groups at one, three, as well as six months.

Adverse events

Local adverse events occurred in the CHX group/Group A only. Eight patients (22.85%) complained about discomfort, pain, and soreness of gingival tissues after the insertion of CHX chips. Gingival swelling, redness, and gingival exudation were noted but disappeared after 3-7 days without therapeutic intervention. Symptomatic treatment consisted of prescription of an analgesic.

DISCUSSION

It is well established that the measures of outcome of periodontal therapy can estimate periodontal stability or future disease progression.[14] Higher proportions of increased deep PD sites indicate lack of periodontal stability and are considered to be the strongest predictor for future attachment loss.[15] Thus, the proportion of remaining deep sites is regularly used as an indicator for the requirement of additional periodontal surgery.[16] LDD agents help in decreasing the oral microbial load in the periodontal pocket, thus, resulting in better clinical parameters. The aim of this randomized controlled, split mouth study was to compare the clinical efficacy of SRP alone and SRP along with controlled delivery CHX chips (PerioCol™ CG) and TC fibers (Periodontal Plus AB™) as an adjunct to mechanotherapy in chronic periodontitis patients.

Table 1: Group A: SRP+CHX Chips

Duration	Mean value (in mm)	Std. deviation	95% confidence interval		*P* value
			Lower	Upper	
At Baseline	6.94	0.998	1.794	2.434	0.000
At 1 month	4.83	0.923			
At 1 month	4.83	0.923	0.939	1.461	0.000
At 3 months	3.63	0.690			
At 3 months	3.63	0.690	−0.103	0.331	0.292
At 6 months	3.51	0.981			
At Baseline	6.94	0.998	3.018	3.839	0.000
At 6 months	3.51	0.981			

SRP – Scaling and root planing; CHX – Chlorhexidine

Table 2: Group B: SRP+Tetracycline fibers

Duration	Mean value (in mm)	Std. deviation	95% confidence interval		*P* value
			Lower	Upper	
At Baseline	6.71	0.987	1.983	2.417	0.000
At 1 month	4.51	0.919			
At 1 month	4.51	0.919	0.603	0.940	0.000
At 3 months	3.74	0.852			
At 3 months	3.74	0.852	0.082	0.375	0.003
At 6 months	3.51	0.781			
At Baseline	6.71	0.987	2.891	3.509	0.000
At 6 months	3.51	0.781			

SRP – Scaling and root planing

Table 3: Group C: SRP alone

Duration	Mean value (in mm)	Std. deviation	95% confidence interval		*P* value
			Lower	Upper	
At Baseline	7.09	0.951	1.140	1.546	0.000
At 1 month	5.74	0.980			
At 1 month	5.74	0.980	0.120	0.794	0.009
At 3 months	5.29	0.926			
At 3 months	5.29	0.926	−0.543	−0.028	0.031
At 6 months	5.57	1.092			
At Baseline	7.09	0.951	1.078	1.950	0.000
At 6 months	5.57	1.092			

SRP – Scaling and root planing

Table 4: Mean change in PD

	Group A	Group B	Group C
Mean	2.37	2.71	1.46
Std. deviation	1.374	1.045	1.221
CV	57.97	38.56	83.63

PD – Probing depth

Table 5: Mean change in CAL

	Group A	Group B	Group C
Mean	3.43	3.20	1.51
Std. deviation	1.195	0.901	1.269
CV	34.83	28.16	84.03

CAL – Clinical attachment level

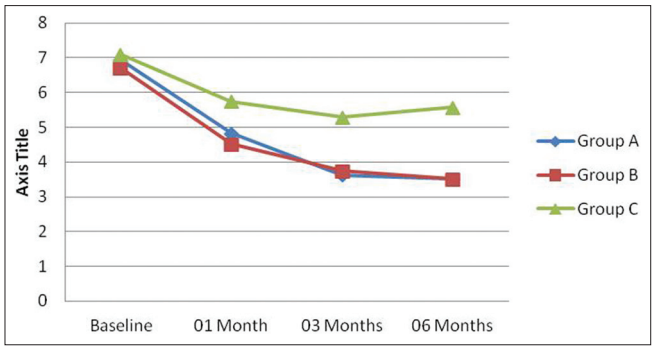

Figure 5: Probing depth

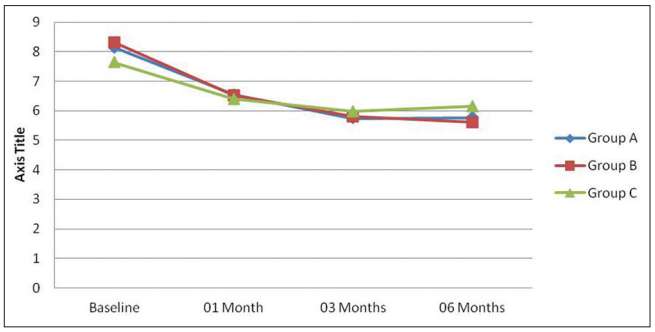

Figure 6: Clinical attachment level

PerioCol™ CG is a small rectangular orange-brown CHX chip (rounded at one end) for easy insertion into the periodontal pockets. Each chip is derived from a biodegradable matrix of type 1 fish collagen and contains approximately 2.5 mg of CHX gluconate (Eucare Pharmaceuticals, Chennai).

Periodontal Plus AB™ consists of four individual vials, with each vial containing 25 mg of pure fibrillar collagen containing approximately 2 mg of evenly impregnated TC hydrochloride (Advanced Biotech, Chennai).

After completion of the etiotropic phase, all the selected patients exhibited low plaque levels at baseline and subsequent appointments indicative of good oral hygiene performance, successful re-motivation, and adherence to oral hygiene instructions in supportive periodontal care. Group A and B did not show any further significant changes in plaque levels after baseline and showed significantly less supragingival plaque even after six months. All the groups showed marked and significant improvements in PD, CAL, and BoP ($P < 0.001$) [Tables 1-3]. PD changes between Group A and B were comparable though PD reduction was higher in Group B [Table 4 and Figure 5]. CAL "gain" was comparable for both the groups, with Group A showing better results in comparison to Group B [Table 5 and Figure 6]. Though improvement of self-performed oral hygiene do have an effect on the parameters, it is unlikely to have caused significant change of PDs and CALs because improved oral hygiene alone only marginally affects the subgingival microflora.[17]

Although the maximum benefits of SRP with or without adjunctive antimicrobials are generally expected to occur within the first three months after treatment,[18,19] a continuous improvement in full-mouth PD over the whole observation period of six months was observed in group B. In contrast to Group A and B, PD increased and decreased CAL "gain" was statistically significant in Group C between three and six months [Table 3]. Intergroup comparison between Group A and B showed Group B to have a lower coefficient of variation, thus confirming this group to be more precise of all the groups [Tables 4 and 5] despite decreased CAL "gain" observed in the first month. The most intriguing finding from this study has been that CHX has shown to achieve a concentration of 125 mg/mL for eight days which is more than the concentration achieved by TC; however, decreased PD reduction and increased CAL "gain" was observed in comparison to TC group. The reason for the same could not be explained due to scant literature available on comparison of these agents. Group B faring better than Group A could be attributed to less tissue penetration of CHX. Tissue levels of CHX after chip insertion have not been reported, whereas subgingival placement of a TC-loaded fiber produces effective concentrations of TC within periodontal soft tissues.[20] It could also be attributed to TC's action of inhibiting collagenase activity, collagen degradation, and bone resorption as shown by Golub *et al.*[21] TC has shown to reach a concentration of 1590 μg/mL and is shown to be bactericidal to oral bacteria present on root surface.[22] Amazingly, despite the high concentration of TC present in the periodontal pocket, it does not have any adverse effect on the pocket epithelium.[23] Interestingly, a study by Purucker *et al.*[24] has shown TC fiber therapy and systemic amoxicillin and clavulanic acid to have a similar clinical outcomes, while another study[25] showed TC therapy to be as effective as SRP. Though the authors do not advocate it to be as equally efficacious as the gold standard i.e. SRP, it has shown promising results.

CONCLUSION

Both CHX chips and TC fibers are capable of delivering a high concentration of drug to the site of periodontal infection, though Group B (SRP + TC fibers) resulted in better optimum clinical results in comparison to the other two treatment groups. For the selection of appropriate local drug system, the clinician has to weigh the efficacy of the product, availability, ease of the use, and the cost factor. Although, LDD systems do not replace time tested periodontal therapies, they definitely prove to be a strategic interventional modality with an important place in the treatment of periodontal disease. LDD systems are an effective and simple nonsurgical method, offering the dentist an additional method to aid in the control of periodontal disease.

REFERENCES

1. Goodson JM. Controlled drug delivery: A new means of treatment of dental diseases. Compend Contin Educ Dent 1985;6:27-32,35-36.
2. Greenstein G, Polson A. The role of local drug delivery in management of periodontal disease: A comprehensive review. J Periodontol 1998;69:507-20.
3. Greenstein G, Tonetti M. The role of controlled drug delivery for periodontitis. The Research, Science and Therapy Committee of the American Academy of Periodontology. J Periodontol 2000;71:125-40.
4. Rath SK, Singh M. Comparative clinical and microbiological efficacy of mouthwashes containing 0.2% and 0.12% chlorhexidine. Dent Res J 2013;10:364-9.
5. Soskolne WA, Heasman PA, Stabholz A, Smart GJ, Palmer M, Flashner M, *et al.* Sustained local delivery of chlorhexidine in the treatment of periodontitis: A multi-center study. J Periodontol 1997;68:32-8.
6. Daneshmand N, Jorgensen MG, Nowzari H, Morrison JL. Slots J. Initial effect of controlled release chlorhexidine on subgingival microorganisms. J Periodontal Res 2002;37:375-9.
7. Jeffcoat MK, Bray KS, Ciancio SG, Dentino AR, Fine DH, Gordon JM, *et al.* Adjunctive use of a subgingival controlled-release chlorhexidine chip reduces probing depth and improves attachment level compared with scaling and root planning alone. J Periodontol 1998;69:989-97.
8. Azmak N, Atilla G, Luoto H, Sorsa T. The effect of subgingival controlled-release delivery of chlorhexidine chip on clinical parameters and matrix metalloproteinase-8 levels in gingival crevicular fluid. J Periodontol 2002;73:608-15.
9. Grisi DC, Salvador SL, Figueiredo LC, Souza SL, Novaes AB, Grisi MF. Effect of a controlled release chlorhexidine chip on clinical and microbiological parameters of periodontal syndrome. J Clin Periodontol 2002;29:875-81.
10. In: Dumitrescu, AL. editor. Chemotherapeutic Agents. Antibiotics And Antiseptics in Periodontal Therapy. 1st ed. Springer; 2010. p. 213.
11. Quirynen M, Teughels W, De Soete M, van Steenberghe D. Topical antiseptics and antibiotics in the initial therapy of chronic adult periodontitis: Microbiological aspects. Periodontol 2000 2002;28:72-90.
12. Verma E, Belludi SA, Banthia R. Local drug delivery with chlorhexidine chip and tetracycline fibers as an adjunct to mechanical therapy in isolated periodontal pockets – A case report. Int J Clin Dent 2011;4:383-84.
13. Srivastava R, Verma PK, Tandon P, Kumar R, Gupta KK, Srivastava A. Chlorhexidine chip and tetracycline fibers as adjunct to scaling and root planing – A clinical study. Braz J Oral Sci 2009;8:201-5.
14. Renvert S, Persson GR. A systematic review on the use of residual probing depth, bleeding on probing and furcation status following initial periodontal therapy to predict further attachment and tooth loss. J Clin Periodontol 2002;29:82-9.
15. Badersten A, Nilveus R, Egelberg J. Scores of plaque, bleeding, suppuration and probing depth to predict probing attachment loss. 5 years of observation following nonsurgical periodontal therapy. J Clin Periodontol 1990;17:102-7.
16. Loesche WJ, Schmidt E, Smith BA, Morrison EC, Caffesse R, Hujoel P. Effects of metronidazole on periodontal treatment needs. J Periodontol 1991;62:247-57.
17. Loos B, Claffey N, Crigger M. Effects of oral hygiene measures on clinical and microbiological parameters of periodontal disease. J Clin Periodontol 1988;15:211-6.
18. Badersten A, Nilveus R, Egelberg J. Effect of nonsurgical periodontal therapy. II. Severely advanced periodontitis. J Clin Periodont 1984;11:63-76.
19. Berglundh T, Krok L, Liljenberg B, Westfelt E, Serino G, Lindhe J. The use of metronidazole and amoxicillin in the treatment of advanced periodontal disease. A prospective, controlled clinical trial. J Clin Periodont 1998;25:354-62.
20. Ciancio SG, Cobb CM, Leung M. Tissue concentration and localization of tetracycline following site-specific tetracycline fiber therapy. J Periodont 1992;63:849-53.
21. Golub LM, Ramamurthy N, McNamara TF, Gomes B, Wolff M, Casino A, *et al.* Tetracyclines inhibit tissue collagenase activity. J Periodontal Res 1984;19:651-5.
22. Morrison SL, Cobb CM, Kazakos GM, Killoy WJ. Root surface characteristics associated with subgingival placement of monolithic tetracycline-impregnated fibers. J Periodontol 1992;63:137-43.
23. Kazakos GM, Cobb CM, Morrison SL, Barker BF, Killoy WJ. Gingival response to subgingival placement of monolithic tetracycline-impregnated fibers: Microscopic observations. Int J Periodontics Restorative Dent 1993;13:150-71.
24. Purucker P, Mertes H, Goodson JM, Bernimoulin JP. Local versus systemic adjunctive antibiotic therapy in 28 patients with generalized aggressive periodontitis. J Periodontol 2001;72:1241-5.
25. Drisko CL, Cobb CM, Killoy WJ, Michalowicz BS, Pihlstrom BL, Lowenguth RA, *et al.* Evaluation of periodontal treatments using controlled-release tetracycline fibers: Clinical response. J Periodontol 1995;66:692-9.

How to cite this article: Singh M, Shreehari AK, Garg PK, Singh S. Clinical efficacy of chlorhexidine chips and tetracycline fibers as an adjunct to non surgical periodontal therapy. Eur J Gen Dent 2014;3:134-9.

Source of Support: Nil, **Conflict of Interest:** None declared.