

# Clinical Assessment of the Effectiveness of Three Different Controlled-release Drugs in the Management of Chronic Periodontitis: An *In vivo* Study

Mohammad Jalaluddin<sup>1</sup>, Shruti Shivakumar<sup>2</sup>, Sandeep S Arora<sup>3</sup>, Deesha Kumari<sup>4</sup>, Mahesh Jayachandran<sup>5</sup>, Rethi Gopakumar<sup>6</sup>, Thilla S Vinothkumar<sup>7</sup>

## ABSTRACT

**Aim:** The aim of the current research was to evaluate the efficiency of metronidazole gel, tetracycline fibers, and chlorhexidine chip agents in the treatment of chronic periodontitis.

**Materials and methods:** A total of 60 healthy patients free from systemic diseases and having chronic generalized periodontitis were chosen for the purpose of this study. The subjects thus included were subjected to phase I therapy consisting of scaling and root planning performed over two visits by a single clinician, following which oral hygiene advice was rendered. A week after phase I management, the subjects were called again and re-evaluated to verify the chosen criteria. Subjects who were thus elected based on the inclusion criteria were assigned at random to one of the three investigational groups as (20 subjects in each group) Group A: Metronidazole, Group B: Tetracycline fibers, Group C: Chlorhexidine Chip. The follow-up after 1 week was regarded as the baseline appointment. Documentation of the gingival index, plaque index as well as the periodontal pocket depth (PPD) during the baseline appointment, plus after 1 month and 3 months after baseline was done and subjected to statistical analysis.

**Results:** The highest reduction of the gingival index (GI) values was noted with the use of chlorhexidine chip ( $0.88 \pm 0.07$  and  $0.82 \pm 0.11$ ) in pursuit by tetracycline fibers ( $0.96 \pm 0.13$  and  $0.88 \pm 0.10$ ) plus the metronidazole investigational group ( $1.02 \pm 0.04$  and  $0.98 \pm 0.10$ ), respectively. Highest reduction of the PI values was noted with the use of tetracycline fibers ( $0.82 \pm 0.14$  and  $0.76 \pm 0.02$ ) in pursuit by chlorhexidine chip ( $0.88 \pm 0.18$  and  $0.94 \pm 0.06$ ) as well as metronidazole investigational group ( $1.18 \pm 1.08$  and  $1.06 \pm 0.21$ ), respectively. The greatest reduction in PPD from  $5.78 \pm 0.14$  to  $3.14 \pm 0.10$  was noted with use of tetracycline fibers.

**Conclusion:** The current research, amid its limitations arrived at a conclusion that although a thorough scaling as well as root planning (SRP) is efficient in managing consistent periodontal pockets, superior results can be attained by employing topically delivered metronidazole gel, tetracycline fibers as well as chlorhexidine chips as adjuncts to the management strategy employed.

**Clinical significance:** Multiple chemical substances may be utilized subgingivally as a management strategy to augment the efficiency of nonsurgical mechanical periodontal treatment. Topical drug delivery systems into the periodontal pocket show potential as a treatment strategy to attain superior clinical results when employed as an adjunctive form of therapy to the traditional nonsurgical periodontal management techniques. Rigorous research labors at this time, concentrate on evolution of novel techniques for efficient management.

**Keywords:** Chronic periodontitis, Controlled release drugs, Nonsurgical therapy, Scaling and root planning.

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<sup>1</sup>Department of Periodontics and Oral Implantology, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha, India

<sup>2</sup>Department of Pedodontics and Preventive Dentistry, JSS Dental College and Hospital, JSS Academy of Higher Education and Research (JSS AHER), Mysore, Karnataka, India

<sup>3</sup>Department of Oral and Maxillofacial Surgery, S. Nijalingappa Institute of Dental Sciences & Research, Kalburgi, Karnataka, India

<sup>4</sup>Department of Public Health Dentistry, AB Shetty Memorial Institute of Dental Sciences (ABSMIDS), NITTE (Deemed to be University), Mangalore, Karnataka, India

<sup>5</sup>Department of Periodontics, Noorul Islam College of Dental Sciences, Trivandrum, Kerala, India

<sup>6</sup>Department of Conservative Dentistry and Endodontics, Noorul Islam College of Dental Sciences, Trivandrum, Kerala, India

<sup>7</sup>Department of Restorative Dental Sciences, College of Dentistry, Jazan University, Jazan, Saudi Arabia

**Corresponding Author:** Mohammad Jalaluddin, Department of Periodontics and Oral Implantology, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha, India, Phone: +91 9338131843, e-mail: drjalal1979@gmail.com

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## INTRODUCTION

An inflammatory disorder of the tissues sustaining the dentition is referred to as periodontitis. This disease is set off by particular microflora or collection of definite bacteria that cause a string of events that lead to annihilation of the periodontal tissues and development of periodontal pockets, receding gingivae or a mixture of the two. Thus, periodontitis is a periodontal disorder caused by multiple etiologies that is provoked by periodontal disease causing microbiota as well as influenced by parameters like developmental malformations of teeth, systemic causes that affect the tissues of the oral cavity, surrounding atmospheric conditions, and stress as well as social and economic causes.<sup>1</sup>

During the initial stages of this condition known as gingivitis, the inflammatory process is typically restricted to the gingiva although it eventually expands to involve the tissues deep inside as in periodontitis, causing swollen gingiva, bleeding plus bad odor. In the later stages of the disorder, the surrounding collagen of periodontal tissues is subjected to degeneration, along with resorption of the alveolar bone and migration of the gingival epithelium alongside the surface of the tooth leading to development of a periodontal pocket.<sup>2</sup>

Meticulous scaling as well as root planning (SRP) is necessary to avert the subgingival region from being recolonized by the periodontitis causing microorganisms. Nevertheless, mechanical treatment may be unsuccessful in causing elimination of disease-causing bacteria totally owing to their position in the gingivae or in places unapproachable to periodontal instrumentation.<sup>3,4</sup>

Topical management using antibacterial substances in types such as mouth washes, dentifrice, or gels may be effective in scheming supragingival plaque. The disadvantages of rinsing, irrigation and alike methods of drug assignment comprise swift clearance that causes insufficient contact to drug resulting in deficient clinical results.<sup>5</sup> Subgingival antimicrobial deliverance arrangement is an extensively employed method which not only use dissimilar antimicrobial substances, but also utilize diverse delivery systems that manipulate the quantity as well as maintains the quantity of available drugs over a period of time. Many clinical research studies have evaluated the values of different locally delivered antimicrobial administration either as monotherapy or along with the scaling and root planing in the treatment of chronic periodontitis. To our knowledge, the literature indicates that no study has been performed to compare and assess the clinical effectiveness of metronidazole gel, tetracycline fibers, and chlorhexidine chip in the management of chronic periodontitis. Therefore, the current research was performed to assess the efficiency of three different controlled-release medications as adjunct to scaling and root planing in the management of sites with persistent periodontal pockets.

## MATERIALS AND METHODS

### Selection of Study Population

A total of 60 participants who were free from systemic ailments and healthy, but with chronic generalized periodontitis were chosen from the patients attending the outpatient department of periodontics, Kalinga Institute of Dental Sciences, Bhubaneswar, India. Ethical approval was obtained and written consent was taken from all the participants. Subjects with less than 30% of the teeth affected, who had a constant periodontal pocket with depth of probing  $\leq 5$  mm as well as bleeding/suppurative upon probing were included in the study. Furcation involved teeth, those with aggressive periodontal

disease, utilizing antimicrobial treatment 2 months prior to inclusion in this research, chlorhexidine/tetracycline/metronidazole allergy, pregnant/lactating women, smokers, receipt of any form of periodontal management  $\leq 3$  months prior to the first visit were excluded from the study.

### Phase I Therapy

Patients included in this research were subjected to phase I treatment consisting of SRP in two appointments performed by one clinician (P6 Piezo electric scaler, and GraceyCurrettes, Hu Freidly®, Chicago, IL, USA), following which oral hygiene maintenance advice was rendered. A week after phase I management, the subjects were called again and re-evaluated to verify the chosen criteria. SRP in all individuals was done by one operator till the surface of the root was rendered smooth/tidy by the clinician.

### Random Allocation of Study Subjects

The standardized investigator for documenting all the information in each investigational group was subjected to blinding to the different investigational research groups. Subjects who were chosen based on the inclusion criteria were assigned at random to one of the three investigational groups. Simple lottery technique was employed for randomization using various chits marked as A, B, and C and placed inside a box. For each subject, one chit was chosen at random and the participant was allocated to the particular group marked on the chit as A, B, or C (20 subjects in each group).

### Group A: Metronidazole [Elyzol (25% Metronidazole)]

The metronidazole gel was supplied with a flexible, blunt needle. This facilitates the application gel to subgingival area till the periodontal pocket base. Noticing the gel at the gingival margin of the tooth that was subject to treatment, confirmed ample quantity of drug delivery inside the periodontal pocket.

### Group B: Tetracycline fibers (Periodontal Plus AB™)

Tetracycline fibers (Periodontal Plus AB™) manufactured goods contain 25 mg pure fibrillar collagen comprising roughly 2 mg of consistently infused tetracycline hydrochloride in every single vial. Periodontal Plus AB™ fibers are presented in a box consisting four separately packaged as well as divisible sterile product vials. After the fibers were soaked, they were then placed into the pocket with the help of periodontal probe with gentle pressure. The fibers were completely inserted into the gingival sulcus, and the gingiva was carefully adapted to close the entrance of the gingival margin.

### Group C: Chlorhexidine Chip (PerioCol™-CG)

Subgingival insertion of chlorhexidine chip was performed by introduction of round ending of the chip by direct means within the base of the periodontal pocket. The chip was pushed in the apical direction to accomplish a subgingival resting at the bottom of the periodontal pocket.

### Evaluation of Clinical Parameters

At the outset, a thorough periodontal evaluation of the whole mouth was done and only those patients who satisfied the inclusion criteria were subject to SRP. The follow-up visit a week later was regarded as the baseline appointment (Figs 1 and 2). Plaque index/gingival index plus the periodontal pocket depth (PPD) were documented at this appointment. These parameters were then recorded again a month and 3 months later. Primary periodontal therapy comprised oral hygiene instructions for plaque control that

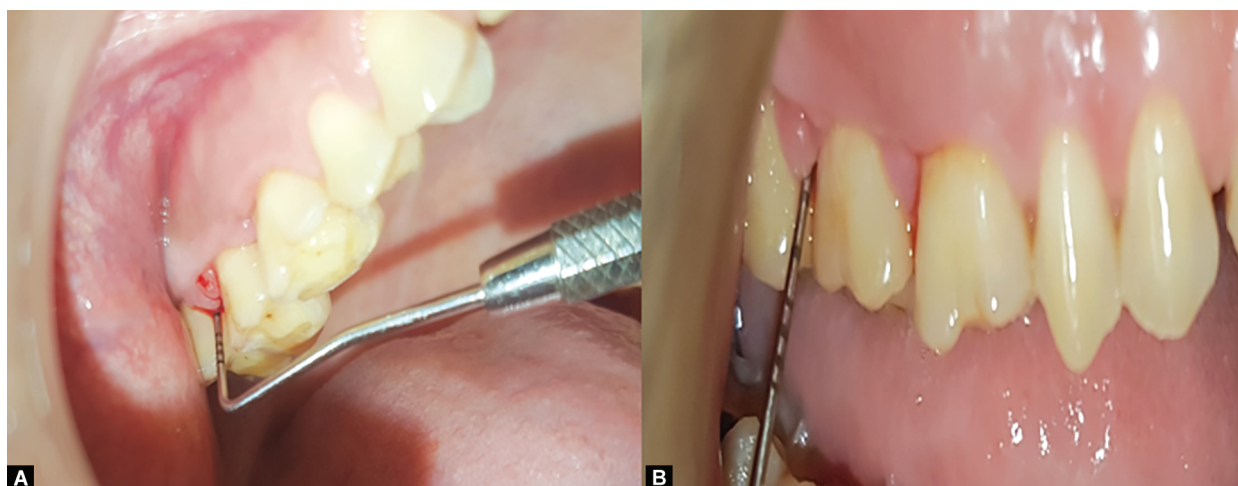


Fig. 1: Gingival index score changes in chlorhexidine chip group at 17 tooth region. (A) before treatment (B) after treatment

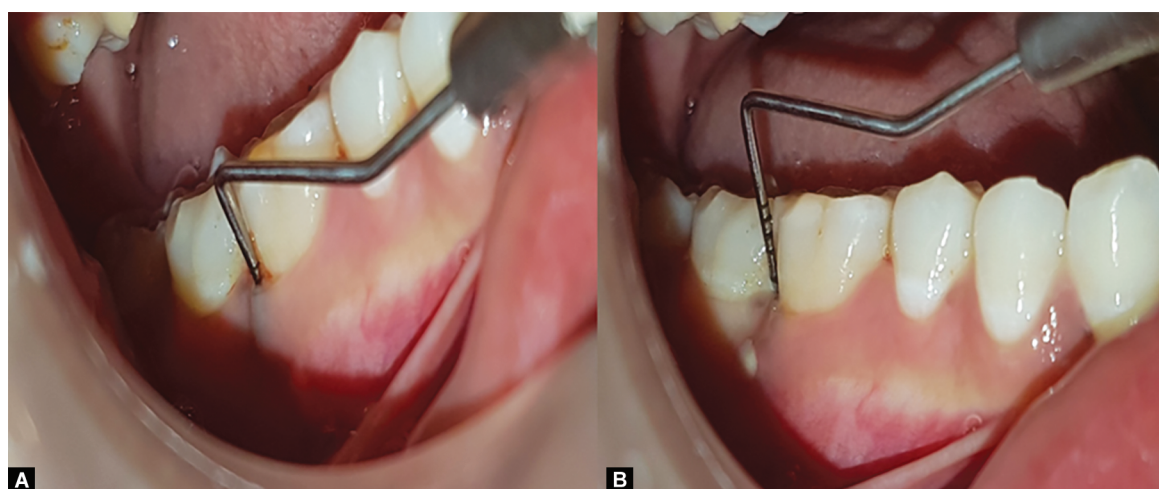


Fig. 2: Periodontal pocket depth index score changes in tetracycline fibers group at 46 tooth region. (A) before treatment (B) after treatment

could be done by the subjects on their own (like inter dental tooth brushing as well as flossing). Additionally, the subjects were also motivated toward the same.

### Statistical Analysis

SPSS version 20.0 software was employed in performing the statistical assessment. The average result obtained was then documented for every factor studied. Values were delineated as mean  $\pm$  SD. ANOVA test was utilized for comparative assessment amid the various time gaps employed. *Post hoc* test was used for comparative assessments amid the groups. A total of 95% was the confidence level of the research with a "p" value  $<0.05$  being significant. Every clinical factor was assessed at baseline, 1 month and 3 months after the baseline appointment.

### RESULTS

Table 1 depicts the mean gingival index (GI) score at the baseline visit, at 1 month and at 3 months. In the baseline visit, the GI value was  $1.46 \pm 0.09$  for metronidazole,  $1.42 \pm 0.06$  for tetracycline fibers as well as  $1.37 \pm 0.27$  for the chlorhexidine chip. Following 1 and 3 months, highest reduction of the GI values was noted with the use of chlorhexidine chip ( $0.88 \pm 0.07$  and  $0.82 \pm 0.11$ ) in pursuit by tetracycline fibers ( $0.96 \pm 0.13$  and  $0.88 \pm 0.10$ ) plus the metronidazole investigational group ( $1.02 \pm 0.04$  and  $0.98 \pm 0.10$ ),

respectively at the multiple intervals studied, the investigational groups showed differences that were statistically significant.

The mean plaque index (PI) at the baseline visit, at 1 month and at 3 months is depicted in Table 2. In the baseline visit, the PI value was  $1.32 \pm 0.19$  for metronidazole,  $1.32 \pm 0.16$  for tetracycline fibers as well as  $1.28 \pm 0.10$  for the chlorhexidine chip. Following 1 and 3 months, highest reduction of the PI values was noted with the use of tetracycline fibers ( $0.82 \pm 0.14$  and  $0.76 \pm 0.02$ ) in pursuit by chlorhexidine chip ( $0.88 \pm 0.18$  and  $0.94 \pm 0.06$ ) as well as metronidazole investigational group ( $1.18 \pm 1.08$  and  $1.06 \pm 0.21$ ), respectively. At the multiple intervals studied, the metronidazole group showed no differences that were statistically significant.

A decrease in the mean score of PPD from  $5.92 \pm 0.17$  at the baseline visit to  $3.46 \pm 0.19$  after 3 months was noticed with use of metronidazole. Similarly, a decrease in mean scores of PPD from  $5.78 \pm 0.14$  to  $3.14 \pm 0.10$  was noticed with the use of tetracycline fibers. Chlorhexidine chips reduced these values from  $5.74 \pm 0.19$  to  $3.92 \pm 0.07$ . Table 3 shows statistically significant differences at different time periods with respect to the PPD for all the investigational groups.

The inference of the present study indicates that along with the scaling and root planing tetracycline fibers showed better results compared to metronidazole gel and chlorhexidine chip in the treatment of persistent pockets.

**Table 1:** Assessment of mean gingival index (GI) value at baseline, 1st month and 3rd month

Clinical parameter	Groups	Duration	Mean $\pm$ standard deviation	F value	p-value
Gingival index (GI)	Group A: Metronidazole	Baseline	1.46 $\pm$ 0.09	5.314	0.001
		1st month	1.02 $\pm$ 0.04		
		3rd month	0.98 $\pm$ 0.10		
	Group B: Tetracycline fibers	Baseline	1.42 $\pm$ 0.06	5.231	0.001
		1st month	0.96 $\pm$ 0.13		
		3rd month	0.88 $\pm$ 0.10		
	Group C: Chlorhexidine Chip	Baseline	1.37 $\pm$ 0.27	6.146	0.001
		1st month	0.88 $\pm$ 0.07		
		3rd month	0.82 $\pm$ 0.11		

**Table 2:** Assessment of mean plaque index (PI) value at baseline, 1st month and 3rd month

Clinical parameter	Groups	Duration	Mean $\pm$ standard deviation	F value	p-value
Plaque index (PI)	Group A: Metronidazole	Baseline	1.32 $\pm$ 0.19	7.306	0.18
		1st month	1.18 $\pm$ 1.08		
		3rd month	1.06 $\pm$ 0.21		
	Group B: Tetracycline fibers	Baseline	1.32 $\pm$ 0.16	5.489	0.001
		1st month	0.82 $\pm$ 0.14		
		3rd month	0.76 $\pm$ 0.02		
	Group C: Chlorhexidine Chip	Baseline	1.28 $\pm$ 0.10	6.128	0.001
		1st month	0.88 $\pm$ 0.18		
		3rd month	0.94 $\pm$ 0.06		

## DISCUSSION

Periodontal disorders include a spectrum of infections affecting the oral cavity, in which the chief etiology is dental plaque that causes inflammation in the tissues supporting the dentition. Both forms of management including surgical/nonsurgical seek to eliminate the etiology and the deleterious effects it causes to the periodontium. Mechanical process of SRP is a key nonsurgical management strategy. Topical deposition of antimicrobial substances is highly popular as it causes greater quantities of drug at the proposed area of action employing a smaller dose, along with lower side-effects

**Table 3:** Assessment of mean periodontal pocket depth (PPD) values at baseline, 1st month and 3rd month

Clinical parameter	Groups	Duration	Mean $\pm$ standard deviation	F value	p-value
Periodontal pocket depth (PPD)	Group A: Metronidazole	Baseline	5.92 $\pm$ 0.17	9.148	0.001
		1st month	4.02 $\pm$ 0.02		
		3rd month	3.46 $\pm$ 0.19		
	Group B: Tetracycline fibers	Baseline	5.78 $\pm$ 0.14	9.217	0.001
		1st month	3.96 $\pm$ 0.04		
		3rd month	3.14 $\pm$ 0.10		
	Group C: Chlorhexidine Chip	Baseline	5.74 $\pm$ 0.19	8.159	0.001
		1st month	4.58 $\pm$ 0.01		
		3rd month	3.92 $\pm$ 0.07		

that occur when the same drug is administered systemically. A local manner of delivering the medication renders a direct entry into the blood stream *via* the jugular vein by surpassing the first pass metabolism in the liver thereby resulting in greater bioavailability.<sup>6</sup>

The factors studied clinically were documented at the baseline visit, after a month and 3 months. Three-month tenure was selected as the action of local medications within the periodontal pocket sustain for 11 weeks following delivery. Additionally, the characteristic recall appointment in periodontally affected patients following therapy is 3 months. This is in harmony with the research by Jeffcoat MK et al.<sup>7</sup> Local drug deposition decreases probing depth plus causes enhancement of attachment level in comparison to SRP.

In this research, greatest decrease of PI values was noted with tetracycline fibers group in pursuit by chlorhexidine chip/metronidazole use. Although, on the whole the PI values were lower than the baseline value. This is in accordance with the research performed by Shubhra Vaish et al.<sup>8</sup> They concluded that the supragingival plaque underwent noteworthy reduction from baseline in every investigational group owing to complete oral supragingival/subgingival scaling. PI values were sustained at a small level all through the research phase, implicating appropriate oral hygiene preservation by all patients providing a triumphant inspiration in supportive periodontal therapy.

Heasman et al.,<sup>9</sup> Shantipriya Reddy et al.<sup>10</sup> noted that all participants included in their research depicted a considerably enhanced GI/PI following therapy with maintenance of the outcomes during the entire research tenure. The enhancement in GI/PI somewhat differed amid the groups. Every participant was allowed entry into the research on an intention to treat basis along with performing SRP at the baseline appointment for all teeth. Elaborate oral hygiene directives were rendered to all patients that were reinforced in each follow-up visit.

Tetracycline depicted a significant reduction in the PPD in the current study. Similar decrease in PPD was documented by Friesen et al.<sup>11</sup> and Perinetti et al.<sup>12</sup> This decrease could be achieved owing to augmented gingival health as a result of reduced edema of the gingival margin along with enhanced collagen quantity, which

caused reduction in penetration of the tissue on probing. However, Drisko et al.<sup>13</sup> did not notice any such differences in their research.

Tetracyclines are better than other antibiotics as they are capable of adhering to both cementum as well as soft tissues. Also, tetracycline is the sole antibiotic that can attain greater level of GCF concentration vs serum level. Tetracycline causes inhibition of collagenase action, collagen break down as well as bone resorption. Tetracyclines have proven efficiency against gram-positive/gram-negative anaerobic microorganisms linked with chronic periodontitis in adults. They apply antimicrobial outcomes by restraining protein production.<sup>14</sup>

In this research, the PPD decrease was superior in metronidazole group vs chlorhexidine chip group. An increased inflammatory response was demonstrated by Mohamed Haris PM et al.<sup>15</sup> in the gingival connective tissues that lies right below the junctional epithelium, resulting in a decreased concentration of subgingival bacteria. Griffiths et al.<sup>16</sup> demonstrated a drastically decreased PPD following therapy with metronidazole gel which is in agreement with the outcomes of our research.

PPD is a frequently employed diagnostic means for evaluating annihilation of periodontal tissues and is a significant clinical indicator for diagnosis and prognosis of periodontal pathosis/therapy.<sup>17</sup> Lili Ma and Xiuchun Diao<sup>18</sup> documented a statistically significant differences in PPD decrease amid the investigational groups at 1 month (MD 0.63), 3 month (MD 0.69), as well as 6 month (MD 0.75) intervals with consequences in favor of regions managed with CHX chip and SRP.

The limitations of the current research are low sample size, lack of microbiological assessment, and biochemical examination. The possible side/adverse effects of subgingival insertion such as allergy, gingival erythema, pain, discomfort, periodontal abscess formation were not evaluated. The observation period in the present study was not long enough. So additional longitudinal research is needed in bigger samples for greater periods of time to assess the result of such local drug delivery medications in management of periodontal pathosis.

## CONCLUSION

The current research, amid its limitations arrived at a conclusion that although a thorough SRP is efficient in managing consistent periodontal pockets, superior results can be attained by employing topically delivered metronidazole gel, tetracycline fibers as well as chlorhexidine chips as adjuncts to the management strategy employed.

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