Original Article

"A Conservative Approach to Treat Chronic Periodontitis by Local Drug Delivery with Tetracycline Fibers and Metronidazole Gel"-A Clinical Study

G. Santhi, Y. S. H. S. Chakravarthy, G. Anusha, Nishanthoury Suryadevara, M. Madhusudan Rao, V. Mohan Krishna Reddy

Department of Periodontics, Lenora Institute of Dental Sciences, Rajamahendravaram, Andhra Pradesh, India.

Abstract

Background: The aim of the study was to evaluate and compare the efficacy of sub gingivally delivered metronidazole gel and tetracycline fibers when used as an adjunct to scaling and root planing (SRP) in the treatment of chronic periodontitis. **Materials and Methods:** This is a split mouth study design where three sites are selected from each patient and allocated into three treatment groups. Group 1 comprising Metronidazole gel + SRP, Group 2 Tetracycline fibers + SRP, and Group 3 SRP alone which is the control group. The clinical parameters such as Plaque index, Gingival index, Probing pocket depth (PPD), and Clinical attachment level (CAL) were recorded at baseline, 1st and 3rd months. **Results:** In this study, two groups Metronidazole + SRP group, Tetracycline + SRP group showed decrease in PPD and CAL gain from baseline to 3 months, but more statistically significant scores $P < 0.001$ were seen in tetracycline group. However, in SRP group this difference in PPD, CAL scores when compared to test groups was not significant. **Conclusion:** All the three treatment groups showed statistically significant changes in the clinical parameters from baseline to 3 months. Tetracycline fibers treated group showed better efficacy in terms of reduction in PPD and gain in CAL followed by metronidazole gel group and SRP alone group.

Keywords: Chronic periodontitis, Local drug delivery, Metronidazole gel, Tetracycline fibers.

Introduction

Periodontitis is defined as "An inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms (or) group of specific microorganisms resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, gingival recession (or) both."[1] Periodontitis, a disease involving supportive structures of the teeth prevails in all groups, ethnicities, races, and both genders.[2]

In periodontitis, the production of pro-inflammatory cytokines and tissue-degradative enzymes is initiated and advanced by oral bacterial infection, ultimately resulting in the destruction of periodontal tissue. The clinical signs of periodontitis are changes in the morphology of gingival tissues, bleeding on probing, as well as periodontal pocket formation. This pocket provides an ideal environment for the growth and proliferation of anaerobic pathogenic bacteria such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Bacteroides forsythus*. The microorganisms colonizing the subgingival are present the principal etiological factor in the development of the inflammation and tissue destruction occurring adjacent to bone. A thorough understanding of the etiopathogenesis of periodontal disease has provided the clinicians and researchers with a number of diagnostic tools and techniques, which has widened the treatment options.[3]

Conventionally, the mainstay of periodontal therapy included mechanical scaling and root planing (SRP). However, mechanical therapy alone may, at times fail to eliminate the pathogenic bacteria effectively, especially in inaccessible areas, leading to recurrence of the disease. Furthermore, mechanical debridement may not usually eradicate certain species such as *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, and *B. forsythus* and probably additional microbial taxa from the subgingival ecosystem due to the invasive potential of these

Access this article online

Website: www.jrad.co.in

DOI: https://doi.org/10.53064/jrad.2022.13.5.256

Address for correspondence: Dr. G. Santhi, Department of Periodontics, Lenora Institute of Dental Sciences, Rajamahendravaram, Andhra Pradesh, India.
Email: dhaliya2011@gmail.com

Received: Jul. 22, 2022; **Accepted:** Aug. 03, 2022; **Published:** Sep. 13, 2022

How to cite this article: Santhi G, Chakravarthy YSHS, Anusha G, Suryadevara N, Rao MM, Reddy VMK. "A Conservative Approach to Treat Chronic Periodontitis by Local Drug Delivery with Tetracycline Fibers and Metronidazole Gel"-A Clinical Study. J Res Adv Dent 2022;13(5):33-36.

species into the gingival epithelial cells and sub epithelial connective tissues, and their high affinity for crevicular epithelium and dentinal tubules.[4]

As periodontal disease is caused by a number of bacterial species, nonspecific continuous plaque removal is not possible for prevention and therapy specific suppression of pathogenic bacteria. A valid alternative and antibiotic approaches are developed to regain and maintain periodontal health.[5] Systemic antibiotics may be used adjunct to the mechanical treatment of periodontitis and for cases with evidence of ongoing disease despite of the previous mechanical therapy. There are several drug side effects and toxicity with systemic antibiotics. Therefore, to override these short comings, local delivery of antibacterial agents into periodontal pockets have been extensively studied. The term local drug delivery is usually used to suggest more specific (or) targeted delivery of an agent in the desired site. Local drug delivery system provides several benefits (1) The drug can be delivered near the site of disease activity at a bactericidal concentration. (2) It can facilitate prolonged drug release.

Dr. Max Goodson 1979 championed and developed local delivery of therapeutic agents into a viable concept. This modem of drug delivery avoids most of the problems associated with systemic therapy, limiting the drug to its target site and hence achieving a much higher concentration.[3,4]

Materials and Methods

To evaluate and compare the efficacy of sub gingivally delivered metronidazole gel and tetracycline fibers when used as an adjunct to SRP in the treatment of chronic periodontitis. To compare the clinical effects of SRP + Metronidazole gel, Tetracycline fibers + SRP and SRP alone in the treatment of chronic periodontitis. The sample size of 25 patients was selected from patients who reported to our department. This is a split mouth study design where three sites are selected from each patient and allocated into 3 treatment groups. Group 1 comprising Metronidazole gel + SRP, Group 2 Tetracycline fibers + SRP, and Group 3 SRP alone which is the control group. Patients with good systemic health who had not undergone any surgical or nonsurgical periodontal therapy in the past 6 months, patients aged between 25 years and 60 years. Each patient had at least 3 teeth with probing pocket depth (PPD) of 5–8 mm in each quadrant. The selected patients did not take any local or systemic antibiotic therapy within the last 6 months before baseline examination.

Patients having history of allergy to tetracycline and metronidazole drugs. Patients with history of using anti-microbial drugs. Patients with habit of smoking. Pregnancy and lactating women. The clinical parameters of the patient were recorded at baseline, 1 month and 3 months. Periodontal status of the patient was recorded using following periodontal parameters. (1). Plaque Index (PI) (Silness J and Loe H 1964). (2). Gingival Index (GI) (Loe H and Silness J, 1963). (3). PPD The pocket was measured from gingival margin to the base of the pocket. (4). Clinical Attachment Level (CAL) The CAL was measured from fixed reference point using an acrylic stent.

Procedure

25 patients who met the inclusion and exclusion criteria were selected and informed regarding the purpose and use of the study. Clinical parameters such as PI, GI, pocket depth, and CAL were recorded. Metronidazole gel (2%) and tetracycline fibers (2 mg Tetracycline Hcl) were administered into the respective treatment sites after thorough SRP. In the control group only, SRP was performed. The clinical parameters were again recorded at 1st and 3rd months [Figure 1].

Statistical analysis

Wilcoxon-matched pairs test was used to compare PI scores, GI scores at baseline, 1 month and 3 months. Paired t test was used to compare the baseline, 1 month and 3 months PPD scores and CAL scores in three groups.

Results

In this study, 14 subjects were males with mean age of (45.79) constitute about 56.00% and 11 were females with mean age of (40.09) and constitutes about 44.00%. There is significant reduction in the values of plaque and gingival scores from baseline, 1 month and 3rd month in all the patients. Comparison of baseline, 1 month and 3 months PPD in 3 groups (M+SRP, T+SRP, and SRP) by paired t test. In M+SRP group the baseline and 1 month, baseline and 3 months showed statistically significant difference in the PPD scores ($P = 0.0001$), whereas at 1st and 3 months scores did not show any statistically significant difference. In T+SRP group the difference in PPD scores between baseline and 1 month and between baseline and 3 months showed statistically significant difference, but at 1st month and 3rd month this difference was not significant. In SRP group, the difference in PPD scores from baseline

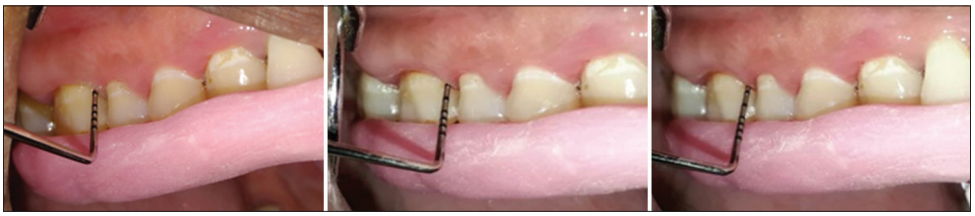

Figure 1: (i) Baseline probing pocket depth and Clinical Attachment Level (CAL), (ii) 1 month probing pocket depth and CAL, (iii) 3rd month probing pocket depth and CAL

to 1 month and from baseline to 3-month time period there is statistically significant difference, but between 1month and 3 month this difference was not statistically significant [Table 1]. Comparison of baseline, 1 month and 3 months CAL scores in three groups (M+SRP, T+SRP, and SRP) by paired *t*-test. In M+SRP group baseline and 1 month, baseline and 3 months showed statistically significant difference in CAL scores; however, the change from 1 month to 3 months is not statistically significant. In T+SRP group the difference in CAL scores between baseline and 1 month and between baseline and 3 months showed statistically significant difference but when compared between 1 month and 3 months, the difference was not significant. In SRP group the difference in the CAL scores between baseline and 1 month, baseline and 3 months showed statistically significant difference, but when compared between 1 month and 3 months the difference was not significant [Table 2].

Discussion

The scientific rationale for adding locally applied anti-infective agents to SRP is that certain broad-spectrum antimicrobial agents can theoretically reduce the number of subgingival bacteria left behind after SRP. Although mechanical removal or disruption of subgingival biofilms by SRP is usually an effective therapeutic approach for the treatment of chronic periodontitis, it does not sterilize the subgingival environment.[6]

Amongst the advantages of local drug delivery, most important is that it can attain 100 fold higher concentration of an antimicrobial agent in subgingival sites compared with a systemic drug regimen. It may employ antimicrobial agents not suitable for systemic administration, for example, broad spectrum antiseptic solutions. It reduces potential problems with patient compliance. It reduces systemic side effects. It reduces the risk of developing drug resistant microbial populations at non oral body sites.[7-9]

In this study, two groups metronidazole + SRP group, Tetracycline + SRP group showed decrease in PPD and CAL gain from baseline to 3 months, but more statistically significant scores $P < 0.001$ were seen in tetracycline group. However, in SRP group this difference in PPD, CAL scores when compared to test groups was not significant. This emphasizes the efficacy of metronidazole gel and tetracycline fibers as adjunct to SRP in reducing the periodontal parameters with more improvement seen within tetracycline group.

Tetracycline is known for its antibacterial actions and also due to number of additional properties that have been recently identified. These include collagenase inhibition, anti-inflammatory actions, and inhibition of bone resorption. Tetracycline-HCl is a bacteriostatic agent that inhibits bacterial protein synthesis and, as such, requires a significantly longer exposure time for bacterial damage than, for example, metronidazole or CHX. It however, has the ability to bind to the hard tissue walls of pockets to establish a drug reservoir.[10,11]

Among the various locally delivered chemotherapeutic agents' metronidazole, a member of nitroimidazole class of antibiotics has bactericidal action against anaerobes, such as *Prevotela intermedia*, *Porphyromonas gingivalis*, *Tannerella forsythia*, Fusobacterium species, and spirochetes such as *Treponema denticola* and *Treponema vincentii*, which are generally believed to be the main pathogens associated with periodontitis. Griffiths *et al*. 2000. The combination therapy of subgingival scaling and metronidazole gel was superior to the conventional treatment of subgingival scaling alone (SRP),

Table 1: Comparison of baseline, 1 month and 3 months probing pocket depth scores in three groups (Metronidazole gel+SRP, Tetracycline fibers+SRP, SRP) by paired *t*-test

Groups	Time	Mean	SD	Mean Diff.	SD Diff.	% Of change	Paired t	*P*-value
Metronidazole gel+SRP	Baseline	5.75	0.57	1.13	0.42	19.69	13.3805	0.0001*
	1 month	4.62	0.57					
	Baseline	5.75	0.57	1.28	0.46	22.27	13.9937	0.0001*
	3 months	4.47	0.49					
	1 month	4.62	0.57	0.15	0.28	3.21	2.6423	0.143
	3 months	4.47	0.49					
Tetracycline fibers+SRP	Baseline	5.71	0.46	2.03	0.40	35.57	25.2870	0.0001*
	1 month	3.68	0.50					
	Baseline	5.71	0.46	2.08	0.44	36.41	23.8071	0.0001*
	3 months	3.63	0.48					
	1 month	3.68	0.50	0.05	0.19	1.30	1.2965	0.2071
	3 months	3.63	0.48					
SRP	Baseline	5.74	0.50	1.02	0.31	17.83	16.4478	0.0001*
	1 month	4.72	0.43					
	Baseline	5.74	0.50	1.00	0.29	17.41	16.9842	0.0001*
	3 months	4.74	0.41					
	1 month	4.72	0.43	-0.02	0.10	–0.51	–1.1862	0.2471
	3 months	4.74	0.41					

*P<0.05, SRP: Scaling and root planing

Table 2: Comparison of baseline, 1 month and 3 months clinical attachment levels scores in three groups (Metronidazole gel+SRP, Tetracycline fibers+SRP, SRP) by paired t test

Groups	Time	Mean	SD	Mean Diff.	SD Diff.	% of change	Paired t	*P*-value
Metronidazole gel+SRP	Baseline	7.87	0.92	1.62	0.68	20.54	11.9384	0.0001*
	1 month	6.25	0.80					
	Baseline	7.87	0.92	1.75	0.63	22.22	13.8608	0.0001*
	3 months	6.12	0.77					
	1 month	6.25	0.80	0.13	0.28	2.11	2.3744	0.259
	3 months	6.12	0.77					
Tetracycline fibers+SRP	Baseline	7.91	0.81	3.53	0.70	44.59	25.3400	0.0001*
	1 month	4.38	0.64					
	Baseline	7.91	0.81	3.58	0.68	45.25	26.2263	0.0001*
	3 months	4.33	0.58					
	1 month	4.38	0.64	0.05	0.18	1.19	1.4219	0.1679
	3 months	4.33	0.58					
SRP	Baseline	7.78	0.78	1.61	0.54	20.67	14.8677	0.0001*
	1 month	6.17	0.79					
	Baseline	7.78	0.78	1.56	0.56	20.00	13.7877	0.0001*
	3 months	6.22	0.79					
	1 month	6.17	0.79	–0.05	0.12	–0.84	–2.1768	0.396
	3 months	6.22	0.79					

*P<0.05, SRP: Scaling and root planing

and these differences were maintained for 9 months.[12] In the present study, metronidazole gel group showed statistically significant reduction in PPD from baseline (5.75) to 1st month (4.62) and 3rd month (4.47). Similarly gain in CAL is seen from baseline (7.87) to 1st month (6.25) and 3rd month (6.12). In spite of its bactericidal action especially on anaerobic bacteria metronidazole gel showed less efficiency in reducing periodontal parameters than tetracycline fibers this may be due to, Metronidazole does not have substantivity beyond 24 h, the application needed to be repeated at 7 days, to maintain effective levels for periopathogens, and to produce additional benefit of the drug for remaining microbes. Metronidazole follows first order kinetics, that is, gel provides increased drug concentration for 24 h after which it subsequently decreases rapidly at a rate directly proportional to their pocket concentration.[7]

Conventional SRP in conjunction with plaque control results in an alteration of the subgingival environment that is sufficient, in most instances, to improve periodontal health and to arrest further loss of attachment. The use of site-specific antimicrobial agents as local drug delivery focuses on elimination of periodontopathic bacteria which results in resolution of periodontitis which is considered as a site-specific disease.[13]

Summary and Conclusion

All the three treatment groups showed statistically significant changes in the clinical parameters from baseline to 3 months. Tetracycline fibers treated group showed better efficacy in terms of reduction in PPD and gain in CAL followed by metronidazole gel group and SRP alone group. The local drug delivery of drugs reduces the side effects of systemic usage of antibiotics and aids as a conservative approach to treat chronic periodontitis.

References

1. Newman MG, Carranza FA, Takei H, Klokkevold PR. Carranza's Clinical Periodontology. 10th ed. St. Louis: Elsevier; 2006.
2. Pragati S, Ashok S, Kuldeep S. Recent advances in periodontal drug delivery systems. Int J Drug Deliv 2009;1:1-14.
3. Elavarasu S, Suthanthiran TK, Naveen D. Statins. A new era in local drug delivery. J Pharm Bioallied Sci 2012;4:S248-51.
4. Singh S, Roy S, Chumber SK. Evaluation of two local drug delivery systems as adjuncts to mechanotherapy as compared to mechanotherapy alone in management of chronic periodontitis: A clinical, microbiological and molecular study. J Indian Soc Periodontol 2009;13:126-32.
5. Rams TE, Slots J. Local delivery of antimicrobial agents in the periodontal pocket. Periodontol 2000 1996;10:139-59.
6. Kalsi R, Vandana KL, Prakash S. Effect of local drug delivery in chronic periodontitis patients: A meta-analysis. J Indian Soc Periodontol 2011;15:304-9.
7. Pandit N, Dahiya R, Gupta R, Bali D, Kathuria A. Comparative evaluation of locally delivered minocycline and metronidazole in the treatment of periodontitis. Contemp Clin Dent 2013;4:48-53.
8. Goodson JM, Hogan PE, Dunham SL. Clinical responses following periodontal treatment by local drug delivery. J Periodontol 1985;56:81-7.
9. Lindhe J, Heijl L, Goodson JM, Socransky SS. Local tetracycline delivery using hollow fiber devices in periodontal therapy. J Clin Periodontol 1979;6:141-9.
10. Sachdeva S, Agarwal V. Evaluation of commercially available biodegradable tetracycline fiber therapy in chronic periodontitis. J Indian Soc Periodontol 2011;15:130-34.
11. Srivastava R, Verma PK, Tandon P, Kumar RM, Gupta KK, Srivastava A. Chlorhexidine chip and tetracycline fibers as adjunct to scaling and root planning-a clinical study. Braz J Oral Sci 2009;8:201-5.
12. Griffiths GS, Smart GJ, Bulman JS, Weiss G, Schrowder J, Newman HN. Comparison of clinical outcomes following treatment of chronic adult periodontitis with subgingival scaling or subgingival scaling plus metronidazole gel. J Clin Periodontol 2000;27:910-7.
13. Aimetti M, Romano F, Torta I, Cirillo D, Caposio P, Romagnoli R. Debridement and local application of tetracycline-loaded fibres in the management of persistent periodontitis: Results after 12 months. J Clin Periodontol 2004;31:166-72.