Volume : 5 | Issue : 12 | December-2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 78.46

Original Research Paper

Comparative evaluation of Three Periodontal Local Antimicrobial Therapies in Persistent Periodontal Pockets: A Six month clinical study

Periodontology

KEYWORDS: - Antimicrobial therapy, Periodontal therapy, Periodontal disease

Dr. Sheekha Shah | MDS Periodontology & Implantology

ABSTRACT

Currently, several local antimicrobial delivery systems are available to periodontists. The aim of this 6 month follow-up parallel study was to evaluate the efficacy of three commercially available local delivery systems as adjuncts to scaling and root planing in the treatment of sites with persistent periodontal lesions. Although all 3 locally applied antimicrobial systems seem to offer some benefit over scaling and root planing alone, a treatment regimen of scaling and root planing plus tetracycline fiber placement gave the greatest reduction in probing depth over the 6 months after treatment.

The aim of periodontal treatment is to halt disease progression. Clinical trials indicate that meticulous scaling and root planing, in conjunction with a patient's proper plaque control, can arrest periodontitis[1-5], but this therapy occasionally fails and therefore adjunctive forms of therapy need to be considered. Local delivery of antibacterial agents into periodontal pockets has been extensively developed and investigated since the late 1970s[6-14], and many systems have been designed to maintain high levels of antimicrobial agents in the crevicular fluid with minimal systemic uptake[15-20]. Many clinical studies have been conducted to assess the value of these systems as adjuncts to root planing or as the sole treatment for untreated periodontal lesions[12-17]. If these systems are used as adjuncts to scaling and root planing, studies suggest that there is a slight advantage over scaling and root planing alone, although this difference has often been clinically minimal or statistically insignificant.

A recent review summarizes the substantial clinical data that exist on local delivery systems in periodontics and highlights the fact that multiple applications are frequently suggested which still fail to show significant benefits over controls[18]. Few studies have evaluated the effects of local drug delivery systems on sites that responded poorly or showed recurrence of disease after scaling and root planing[19,20]. Thus, we studied the comparative efficacy of 3 periodontal local delivery antimicrobial systems on sites with previously unsuccessful mechanical therapy. This report has a study data at baseline, 6 weeks, 3 months, and 6 months following therapy.

MATERIALS AND METHODS

Study Design

This was a parallel-design study. Patients with persistent pockets that did not respond favorably to scaling and root planing were randomized into 4 treatment groups. One group received scaling and root planing only, whereas the other 3 groups received scaling and root planing plus one of 3 antimicrobial systems adjunctively as described subsequently. Clinical parameters were recorded at baseline, 6 weeks, 3 months, and 6 months after the last treatment.

Subjects and Sites

The patients recruited for this study had been attending the Department of Periodontology, College of Dental Science and Research Centre, Ahmedabad for chronic periodontitis therapy. The mean age of these patients was 45±5.4 years; there were 50 patients total (30 females and 20 males). The distribution of these demographic variables was similar in that the range of age means for all 4 groups was between 44.3 and 46.3 years (P=0.90), and the sex ratio between the treatment groups was not significantly different.

Fifty subjects completed the full course of study and of the 5 subjects dropped out, 1 in the S group, 2 in the S+Min group, and 2 in the S+Met group. The participants had received quadrant scaling and root planing under local anesthetic, and despite mechanical treatment and good oral hygiene, still had deep pockets with bleeding on probing.

Inclusion criteria:

1. At least 4 non-adjacent teeth with probing depth ≥5 mm.
2. Bleeding on probing.

Exclusion criteria:

1. Sites with furcation involvement.
2. Systemic disease or a history of systemic antimicrobial therapy over the past 6 months.

Once consent was given, alginate impressions were taken and soft occlusal acrylic stents were fabricated for the measurement of attachment levels.

Clinical Measurements

At the baseline visit and at 6 weeks, 3 months, and 6 months after the last treatment.

Clinical parameters:

1. Plaque index[22];
2. Modified Gingival Index[23];
3. Duplicate probing depth recordings using an electronic probe[24] with a controlled force of 20g; and duplicate attachment level recordings using the Florida Probe and occlusal stents.

Treatment Protocol

Each patient received one of the 4 treatments in this parallel-design trial. As described previously, for each patient, 4 sites with probing depths greater than 5mm which also bled on probing were treated.

These treatment regimens are given here:

1) scaling and root planing alone;

2) scaling and root planing plus application of 2% minocycline gel; the gel application was repeated 2 weeks and 4 weeks after the first application;

3) scaling and root planing plus application of 25% tetracycline ethylene vinyl acetate fibers; after 10 days the patient was recalled and the fibers were removed; and

4) scaling and root planing as described above plus application of 25% metronidazole gel. The application was repeated 7 days later.

At the first postoperative visit, patients were examined for any adverse signs or symptoms related to these treatments.

Statistical Analysis

For each treatment group, the baseline and 6-week, 3-month, and 6-month probing depth and attachment level data were subjected to a paired t test. The changes in probing depth and attachment level were subjected to general linear model (GLM). The Kruskal-Wallis test was used to compare the percentage of bleeding on probing sites between the groups. The plaque index and Modified Gingival Index data were analyzed by Wilcoxon's test for each treatment. Where there were significant differences, post-hoc comparisons were performed using multiple Mann-Whitney-U tests, and the significance level was corrected using the Bonferroni adjustment.

Volume : 5 | Issue : 12 | December-2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 78.46

RESULTS

In all 4 treatment groups, probing depth decreased significantly at all time points compared to baseline (Table 1). Mean reduction in probing depth at all time intervals throughout the 6 months of the trial was greatest in patients who received scaling plus tetracycline fiber treatment, followed by S+Min group, the S+Met group, and the S group. A primary analysis revealed no significant interaction between the covariate (baseline probing depth) and the treatment effect. Pair-wise comparisons revealed that probing depth reduction was significantly greater in the S+Tet group than scaling alone at all time points (P<0.008). There was also a significant improvement for scaling plus tetracycline fiber application over scaling and metronidazole at both 6 weeks and 3 months, although this did not remain significant at the 6-month time point.

Table 1: Probing Depth (Mean ± Standard Error of Mean)

Treatment group	Baseline	6 weeks	3 months	6 months
Scaling	5.480 ± 0.175	0.647 ± 0.118	0.873 ± 0.148	0.711 ± 0.188
Scaling + Minocycline gel	5.578 ± 0.162	0.911 ± 0.119	1.013 ± 0.143	1.102 ± 0.159
Scaling + Tetracycline fiber	5.402 ± 0.131	1.383 ±0.158	1.558 ± 0.152	1.380 ± 0.166
Scaling + Metronidazole gel	5.506 ± 0.147	0.834 ± 0.153	0.913 ± 0.206	0.929 ± 0.186

Table 2 shows the results of attachment level changes from an arbitrary reference point on theocclusal stents. All treatments resulted in a significant attachment gain compared to baseline. (P >0.12).

Table 2: Clinical Attachment Level Gain (Mean ± Standard Error of Mean)

Treatment group	Baseline	6 weeks (p=0.121)	3 months (p = 0.378)	6 months (p = 0.768)
Scaling	0.292 ± 0.075	0.547 ± 0.118	0.544 ± 0.148	0.537 ± 0.143
Scaling + Minocycline gel	0.325 ± 0.203	0.411 ± 0.195	0.417 ± 0.143	0.573 ± 0.109
Scaling + Tetracycline fiber	0.673 ± 0.096	0.729 ±0.115	0.728 ± 0.152	0.687 ± 0.136
Scaling + Metronidazole gel	0.404 ± 0.147	0.543 ± 0.163	0.543 ± 0.206	0.541 ± 0.214

Table 3: Modified Gingival Index (MGI)

Treatment group	Baseline	6 weeks (p=0.121)	3 months (p = 0.378)	6 months (p = 0.768)
Scaling	2.292 ± 0.175	1.663 ± 0.118	1.558 ± 0.080	1.537 ± 0.153
Scaling + Minocycline gel	1.915 ± 0.103	1.298 ± 0.095	1.417 ± 0.132	1.500 ± 0.119
Scaling + Tetracycline fiber	2.171 ± 0.190	1.158 ±0.090	1.428 ± 0.112	1.373 ± 0.086
Scaling + Metronidazole gel	2.136 ± 0.117	1.496 ± 0.113	1.543 ± 0.096	1.541 ± 0.135
P value	0.440	0.062	0.0692	0.352

The Modified Gingival Index (MGI) scores decreased significantly after all treatments (Table 3). The bleeding on probing decreased in all treatment groups.

Table 4: Bleeding on Probing (Mean Percentage)

Treatment group	Baseline	6 weeks (p=0.121)	3 months (p = 0.378)	6 months (p = 0.768)
Scaling	92.37%	60.90%	55.75%	54.55%
Scaling + Minocycline gel	89.32%	52.38%	44.25%	52.09%
Scaling + Tetracycline fiber	91.54%	38.67%	32.15%	47.65%
Scaling + Metronidazole gel	88.58%	50.00%	47.90%	56.42%
P value	0.955	0.078	0.090	0.819

The greatest reduction occurred in the S+Tet group for the 6-week and 3-month visits, but these differences were not statistically significant when compared across all treatment groups (P=0.78 and P=0.90, respectively) (Table 4).

DISCUSSION

This study evaluated the clinical response to 3 locally delivered antimicrobials as adjuncts to scaling and root planing. The participants in this study had already been treated for chronic periodontal disease using quadrant scaling and root planing under local anesthesia and still had pockets ≥5 mm with bleeding on probing. At sites with persistent periodontal disease, despite previous mechanical therapy, adjunctive local antimicrobial treatment is effective.

Substantivity of an antimicrobial system implies the ability of that system to maintain adequate antimicrobial drug levels over a sufficient period of time. The sustained concentration of tetracycline at very high levels, greater than 1.6 mg/mL in the crevicular fluid over 10 days25, could explain the superiority of this treatment modality. To be effective, antimicrobials must reach their target site and be maintained there at sufficient concentrations long enough for their antimicrobial effect to occur26. The concentration required for efficacy is often estimated from the minimum inhibitory concentration (MIC)27. These biofilms will probably require a significantly higher concentration of antimicrobial to kill the bacteria given that Cargill et al.28 found that legionellae in biofilms were 135 times more resistant to iodination when compared to microorganisms growing in a non-organized or planktonic fashion, which disrupts the biofilm28-30.

A further factor in local drug delivery is that periodontal pockets are constantly flushed with inflammatory exudate. Goodson26 has estimated that the fluid in a 5mm pocket is replaced 40 times during one hour, which represents a very high clearance rate. Some drugs such as chlorhexidine can bind to the tissues of the periodontal pocket and can therefore establish a reservoir such that an equilibrium between the bound and free drug31.

The 3 drugs tested differ substantially in their delivery mechanisms. Langer and Peppas32 describe 2 classes of local delivery devices, sustained and controlled delivery devices. The minocycline and metronidazole systems provide sustained delivery, with exponential depletion of the drug reservoir within 24 hours33,34. The clinical improvement after mechanical treatment should be maintained at 3 monthly maintenance recalls. It may not be wise to use these systems more frequently than every 6 months because of the risk of creating an antimicrobial-resistant microflora.

Following initial treatment, there is typically a marked pocket reduction with shrinkage occurring as inflammation reduces. It

should be noted that at the 6-month visit, more than half the sites in this group still showed bleeding on probing and a mean probing depth of 4.8 mm. The members of the tetracycline group of drugs, such as those included in the fiber and minocycline gel formulations, have a potential role in reducing matrix metalloproteinase activity35. All 3 locally applied antimicrobial systems offer some benefit over scaling and root planing alone. A treatment regimen of scaling and root planing plus tetracycline fiber placement showed the greatest reduction in probing depths for the previously persistent periodontal lesions in the 6 months following treatment.

CONCLUSION

Although all 3 locally applied antimicrobial systems seem to offer some benefit over scaling and root planing alone, a treatment regimen of scaling and root planing plus tetracycline fiber placement gave the greatest reduction in probing depth over the 6 months after treatment.

REFERENCES

1. Ramfjord S, Caffesse R, Morrison E, et al. Four modalities of periodontal treatment compared over 5 years. J Clin Periodontol 1987; 14:445-452.
2. Hill RW, Ramfjord SP, Morrison EC, et al. Four types of periodontal treatment compared over two years. J Periodontol 1981; 52:655-662.
3. Kaldahl WB, Kalkwarf KL, Patil KD, Dyer JK, Bates RE Jr. Evaluation of four modalities of periodontal therapy: Mean probing depth, probing attachment levels and recession changes. J Periodontol 1988; 59:783-793.
4. Isidor F, Karring T. Long-term effect of surgical and nonsurgical periodontal treatment. A 5 year clinical study. J Periodont Res 1986; 21:462-472.
5. Badersten A, Nilvéus R, Egelberg J. Four-year observations of periodontal therapy. J Clin Periodontol 1987; 14:438-444.
6. Goodson JM, Haffajee AD, Socransky SS. Periodontal therapy by local delivery of tetracycline. J Clin Periodontol 1979; 6:83-92.
7. Addy M, Rawle L, Handley R, Newman HN, Coventry JF. The development and in vitro evaluation of acrylic strips and dialysis tubings for local drug delivery. J Periodontol 1982; 53:693-699.
8. Friedman M, Golomb G. New sustained release dosage form of chlorhexidine for dental use. I. Development and kinetics of release. J Periodont Res 1982; 17:323-328. 9. Goodson JM, Holborow D, Dunn RL, Hogan PE, Dunham S. Monolithic tetracycline-containing fibers for controlled delivery to periodontal pockets. J Periodontol 1983; 54:575-579.
10. Minabe M, Uematsu A, Nishijima K, et al. Application of a local drug delivery system to periodontal therapy. I. Development of collagen preparations with immobilized tetracycline. J Periodontol 1989; 60:113-117.
11. Norling T, Landing P, Engström S, Larsson K, Krog N, Nissen SS. Formulation of a drug delivery system based on a mixture of monoglycerides and triglycerides for use in the treatment of periodontal disease. J Clin Periodontol 1992; 19:687-692.
12. Lindhe J, Heijl L, Goodson JM, Socransky S. Local tetracycline delivery using hollow fiber devices in periodontal therapy. J Clin Periodontol 1979; 6:141-149.
13. Ainamo J, Lie T, Ellingsen BH, et al. Clinical responses to subgingival application of a metronidazole 25% gel compared to the effect of subgingival scaling in adult periodontitis. J Clin Periodontol 1992; 19:723-729.
14. van Steenberghe D, Bercy P, Kohl J, et al. Subgingival minocycline hydrochloride ointment in moderate to severe chronic adult periodontitis: A randomized, double-blind, vehicle controlled, multicenter study. J Periodontol 1993; 64:637-644.
15. Goodson JM, Cugini MA, Kent RL, et al. Multicenter evaluation of tetracycline fiber therapy: II. Clinical response. J Periodont Res 1991; 26:371-379.
16. Heijl L, Dahlen G, Sundin Y, Goodson JM. Tetracycline loaded monolithic fibers: A four quadrant comparative study of efficacy in periodontal therapy. J Clin Periodontol 1991; 18:111 116.
17. Minabe M, Takeuchi K, Nishimura T, Hori T, Umemoto T. Therapeutic effects of combined treatment using tetracycline-immobilized collagen film and root planing in periodontal furcation pockets. J Clin Periodontol 1991;18:287-290.
18. Tonetti M. The topical use of antibiotics in periodontal pockets. European Workshop in Periodontology II. Quintessence 1997; 78-109.
19. Stabholtz A, Soskolne WA, Friedman M, Sela MN. The use of sustained release delivery of chlorhexidine for the maintenance of periodontal pockets: 2-year clinical trial. J Periodontol 1991; 62:429-433.
20. Newman MG, Kornman KS, Doherty FM. A 6-month multi-center evaluation of adjunctive tetracycline fiber therapy used in conjunction with scaling and root planing in maintenance patients: Clinical results. J Periodontol 1994; 65:685-691.
21. Radvar M, Pourtaghi N, Kinane DF. Comparison of 3 periodontal local antibiotic therapies in persistent periodontal pockets. J Pe riodontol 1996; 67: 860-865.
22. Silness J, Löe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 1964; 22:112-135.
23. Lobene RR, Weatherford T, Ross NM, Lamm RA, Menaker L. A modified gingival index for use in clinical trials. Clin Prevent Dent 1986; 8:3-6.
24. Gibbs CH, Hirschfeld JW, Lee JG, et al. Description and clinical evaluation of a new computerized periodontal probe—the Florida Probe. J Clin Periodontol 1988; 15:137-144.
25. Tonetti M, Cugini MA, Goodson JM. Zero-order delivery with periodontal placement of tetracycline-loaded ethylene vinyl acetate fibers. J Periodont Res 1990; 25:243-249.
26. Goodson J. Pharmacokinetic principles controlling efficacy of oral therapy. J Dent Res 1989; 68: 1625-1632.
27. Walker CB, Pappas JD, Tyler KZ, Cohen S, Gordon JM. Antibiotic susceptibilities of periodontal bacteria. In vitro susceptibilities to eight antimicrobial agents.J Periodontol 1985; 56:67-74.
28. Cargill KL, Pyle BH, Sauer RL, McFeters GA. Effects of culture conditions and biofilm formation on the iodine susceptibility of Legionella pneumophilia. Can J Microbiol 1992;38:423-429.
29. Vorachit M, Lam K, Jayanetra P, Costerton J. Resistance of Psuedomonas psuedomallei growing on a biofilm on silastic discs to ceftazamide and co-trimoxazole. Antimicrob Agents Chemother 1993;37:2000-2002.
30. Wright TL, Ellen RP, Lacroix J-M, Sinnadurai S, Mittelman MW. Effects of metronidazole Por phyromonas gingivalis biofilms. J Periodont Res 1997;32:473-477.
31. Bonesvoll P, Gjermo P. A comparison between chlorhexidine and some quaternary ammonium compounds with regard to retention, salivary concentration and plaque-inhibiting effect in the human mouth rinses. Arch Oral Biol 1978; 23: 289-294.
32. Langer R, Peppas N. Present and future applications of biomaterials in controlled drug delivery systems. Biomaterials 1981; 2:201-214.
33. Satomi A, Uraguchi R, Noguchi T, Ishikawa I, Tamaru H, Kitamura M. Minocycline HCl concentration in periodontal pockets after administration of LS 007. J Japan Periodont Assoc 1987; 937-943.
34. Stoltze K. Elimination of Elyzol 25% dental gel matrix from periodontal pockets. J Clin Periodontol 1995;22:185-188.
35. Pourtaghi N, Radvar M, Kinane DF. The effect of subgingival antimicrobial therapy on the levels of stromelysin and tissue inhibitor of metalloproteinases in gingival crevicular fluid. J Periodontol 1996; 67: 866-8