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RESEARCH ARTICLE

CLINICAL AND MICROBIOLOGICAL EVALUATION OF LOCALLY DELIVERED TETRACYCLINE AS AN ADJUNCT TO SCALING AND ROOT PLANING AND ITS COMPARISON TO SCALING AND ROOT PLANING IN PATIENTS WITH CHRONIC PERIODONTITIS

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ABSTRACT

Introduction: The accumulation of bacterial biofilm is the main etiological factor of periodontal disease. So scaling and root planing is the mainstay treatment of periodontal therapy. Apart from this, a number of antibiotics like tetracycline, metronidazole, ofloxacin, and chlorhexidine have also been shown to be effective in chronic periodontitis as measured by a decreased pocket depth, attachment level gain, reduction of bleeding on probing and reduction in periodontal pathogens.

Aim: The aim of the present study was to clinically and microbiologically evaluate the therapeutic efficacy of controlled release tetracycline fibres as an adjunct to scaling and root planing versus scaling and root planing in the treatment of chronic periodontitis.

Material and methods: A total of 25 patients with chronic periodontitis in the age group of 25 to 55 were selected and were randomly divided into test group and control group. The test group included was treated by scaling, root planing and placement of controlled release tetracycline fibers in the periodontal pocket. The control group was treated with only scaling and root planing. The clinical parameters measured were the plaque index and gingival index. The microbial analysis was done for assessment of A. actinomycetemcomitans, P.gingivalis and P.intermedia by anaerobic culture. The clinical measurements were measured at baseline, 30th, 60th, and 90th day while the microbial analysis was done at baseline and on the 90th day.

.**Results:** There was a significant improvement in the clinical parameters as evident from reduction in plaque index and gingival index ($p<0.001$). The microbial analysis showed significant reduction in prevalence of A.actinomycetemcomitans and P.intermedia though there was no significant reduction in number of P.gingivalis.

Conclusion: It can be concluded that tetracycline fibre therapy along with scaling and root planing is more effective than scaling and root planing alone in the treatment of chronic periodontitis.

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INTRODUCTION

It has been well established that periodontitis has a multifactorial etiology with primary etiological agents being pathogenic bacteria that reside in the subgingival area. The pathogenic bacteria that cause periodontitis are mainly gram negative, microaerophilic bacteria like Aggregatibacter actinomycetemcomitans (A.a), Porphyromonas gingivalis (P.g.) and Prevotella intermedia(P.i) (Haffajee, 1994 and Consensus report for Periodontal Disease, 1996). Due to the nature of bacterial etiology of periodontitis, various local and systemic antibacterial agents have been used to treat such diseases.

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The systemic delivery has got certain disadvantages like requirement of higher doses to achieve necessary concentration at the target site, organ toxicity and hypersensitivity reactions. This has led to the use of local drug delivery system with the chemotherapeutic agent being delivered to the base of the pocket, thus minimizing the impact of the agent on non-oral body site (Rams, 1999). The potential benefits gained by local drug delivery are improved patient compliance, improved drug access to the site of disease and lower drug dosage. The methods employed to convey antimicrobial agents into the periodontal pocket include mouth rinse, subgingival irrigation and controlled release of the drug (Goodson, 1979). The antimicrobial agents used as local drug delivery include tetracycline, metronidazole, minocycline, chlorhexidine etc (Finkleman, 1998). Many deficiencies in drug delivery for treatment of periodontal disease can be-remedied by the use of

controlled delivery devices placed directly into the periodontal pocket. Local administration of antibiotics has attracted the attention of many investigators and it was reasoned that, by placing a drug delivery device close to the site of disease activity, effective drug levels could be achieved much above the minimum inhibitory concentration of the pathogenic flora. They also could be maintained for prolonged periods using only a few milligrams of a potent antibiotic (Goodson, 1987 and Greenstein, 1998). Several intrapocket devices have been described including ethyl vinyl acetate ethyl cellulose films, white petrolatum carriers, collagen films, etc. Tetracycline as a local drug delivery system has been shown to be effective in the treatment of periodontal disease amongst all local delivery drug system as measured by a decreased pocket depth, attachment level gain, reduction of bleeding on probing and reduction in periodontal pathogens (Radvar, 1996; Kinane, 1999). In addition, tetracycline has also demonstrated substantivity in subgingival environment (Baker, 1983). The aim of this study was to clinically and microbiologically evaluate the therapeutic efficacy of controlled release tetracycline fibers as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

MATERIAL AND METHODS

The present case-control study was conducted at Pad.Dr.D.Y.Patil school of dentistry in Navi Mumbai. A total of 25 study participants were randomly selected using the following inclusion and exclusion criteria. The subjects were in the age range of 25-55 years(mean age 38.93±8.96) with chronic periodontitis patients having probing pocket depth ≥ 4mm or ≤7 mm and/or clinical attachment levels (CAL) > 4mm. Subjects excluded from the study were patients with systemic diseases that affect the periodontium, pregnant or lactating females, patients who received any anti-inflammatory drugs, antibiotics or corticosteroids within previous 3 months, patients with any allergy to tetracycline, smokers and patients who had undergone scaling and root planing (SRP) or sub-gingival instrumentation < 6 months before the baseline examination.[15,16] The nature of the study was explained to all the participants and written informed consent was obtained from each study participant. The study was approved from Institutional Ethical Committee and the procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration 1975, revised in 2000.

Site Selection Criteria

With the help of a pressure sensitive probe (Have Neous) full mouth probing was carried out and sites for local drug delivery applications were selected (Fig.1). Subjects selected were two non-adjacent sites with a periodontal pocket depth ≥ 4mm or ≤7 mm. A-total of 50 sites were included for the study and in each patient, two non-adjacent quadrants were divided into two sites i.e. Twenty five control sites (scaling and root planing) and test sites (scaling and root planing with local delivery of tetracycline fibers).Prior to scaling and root planing each selected site was subjected to assessment of plaque index (Silness, 1964) and gingival index (Loe, 1963). After recording clinical parameters of each site in selected patients, subgingival scaling and root planing was done.

Administration of Periodontal AB Plus

This product (Periodontal AB Plus, Advanced Biotech, Chennai, India) consists of 25 mg of pure fibrillar collagen containing approximately 2 mg. of evenly impregnated tetracycline hydrochloride. A few drops of sterile saline solution was added on fibers to wet it before the placement of fibers in the pocket.

Fig. 1. Preoperative clinical examination with help of pressure sensitive probe (Have Neous)

A small portion of the wet fibre was taken and placed at the prepared site and gently inserted into the pocket with periodontal probe (Fig.2). Gentle force was used so that the material fills the depths and curves of the pocket. The gingiva was subsequently adapted to close the entrance of the defect site and hand pressure was applied for just a few minutes to encourage haemostasis and a cyanoacrylate (Epiglu)® adhesive was used. All the sites were re-evaluated at 1 week for any reaction to fibers. Oral hygiene and clinical parameters were recorded at baseline, 15th, 30th, 60th and 90th days. Subgingival plaque sample was collected from control & test sites i.e. scaling and root planing plus tetracycline fibers quadrant on baseline and on the 90th day.

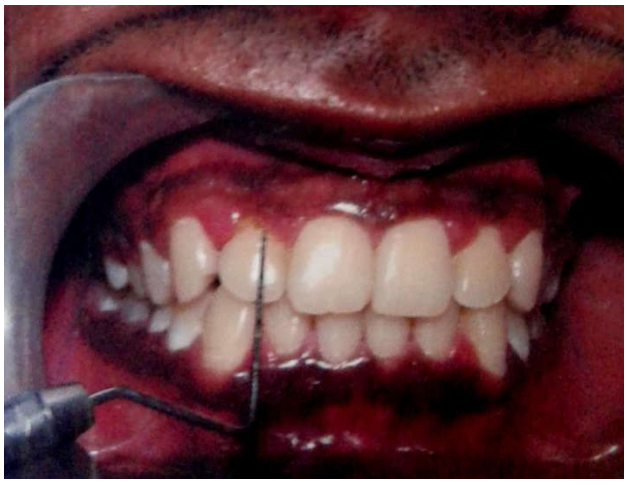


Fig. 2. Administration of controlled release tetracycline fibers (Periodontal AB plus)

Microbiological examination and analysis

A pool of subgingival plaque sample was collected from the selected quadrant with the deepest probing depth with sterile curette and assayed for the presence of A.a, P.g, and P.i by anaerobic culture i.e. from control and test sites. At baseline and on 90th day subgingival plaque sample was collected from both the groups. The samples were transferred to cotton tips of sterile swab of amies transport medium immediately. Both

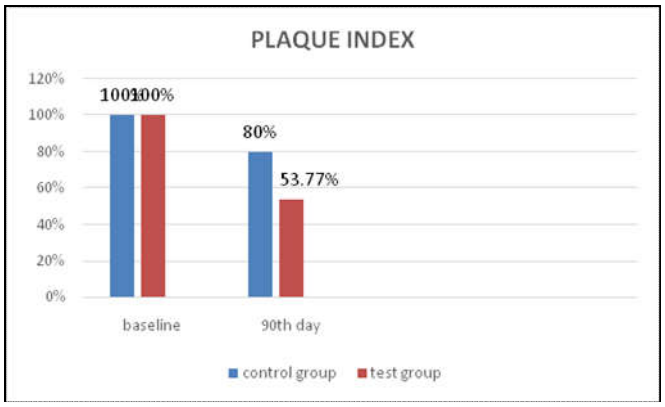
control and test samples were subjected to isolation and anaerobic blood agar plates independently on two sets (Fig.3). While primary inoculations were being done on blood agar, primary smears were also prepared for all the samples in order to know the morphology and predominance of bacterial flora. One set of sample was incubated in Mclntosch and Filde's anaerobic jar and the other set in CO_2 enriched candle jar. Anaerobic conditions within the jar were maintained using palladium catalyst and Gas-pak systems Anaerogen (EOS laboratories, Mumbai) by generating environment having CO2 and H2 coupled with displacement of oxygen.. Anaerobic conditions were verified using Lucas indicator comprising of Methylene blue. The anaerobic jars were kept in incubators at 37°C for 48 hours. Then the growth of bacteria was subjected to identification and characterization, subjected to microscopy and biochemical tests.The material collected from the patient was also inoculated in sterile brain heart infusion broth. All specimens were sent to microbiology department of K. J. Somaiya Medical College (Mumbai, India) and were processed within 2 hours of collection. The results were averaged out for each parameter and were depicted as mean ± SD. For comparisons between different time intervals paired t-test were used and independent samples were used for intergroup comparisons at different time intervals. The confidence level of the study was kept at 95% and hence a 'p' value <0.05 was considered as significant. Paired t test and student's t test were used to establish the difference between baseline, 30thday, 60th day and 90th day values using SPSS for Windows (Statistical Presentation System Software, 1999, SPSS Inc, New York version 10.0).

Fig. 3. Blood Agar

RESULTS

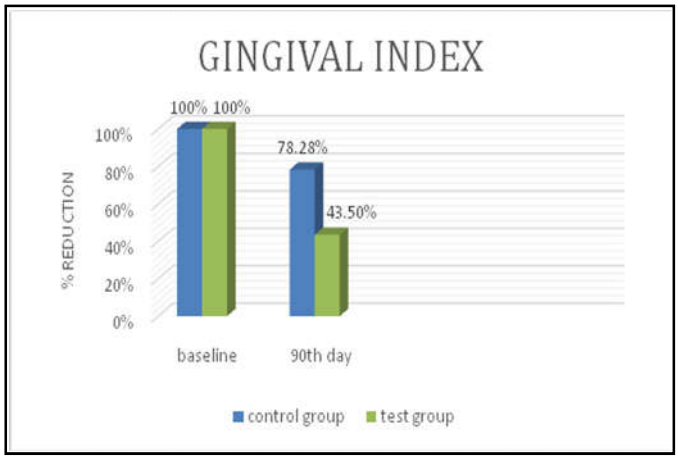
The recording of all the clinical parameters was done at baseline and after 30 days, 60 days and 90 days.

The mean reduction of plaque index scores in the control group, was 20 % from 0 - 90th day which was statistically significant (p<0.001) (Graph1). In the test group, the mean reduction of plaque score from 0 - 90th day was 46.23% which was also statistically significant (p<0.001) (Graph 1). The mean reduction in plaque scores between control group and test Group was highly significant.



Graph 1. Mean reduction of plaque index scores in test and control group from baseline to 90th day

The mean reduction in gingival index scores from 0 - 90tn day was 21.72% for control group and was highly significant (p<0.001) while in the test group the gingival index scores from 0 – 90 th day was 56.55% and was highly significant (p<0.001) (Graph 2) The mean reduction in gingival index scores between control Group and test Group was highly significant.

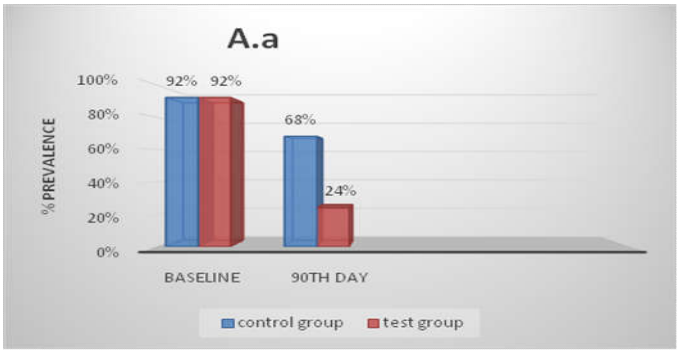


Graph 2. Mean reduction of gingival index scores in test and control group from baseline to 90th day

Aggregatibacter Actinomycetemcomitans

At baseline 23 subjects (92%) showed presence of the organism and on 90th day only 17 subjects were positive in the control group. It reduced to 68% of subjects at follow up on 90th day. The percentage of reduction seen was 24%, which was significant (P<0.05).

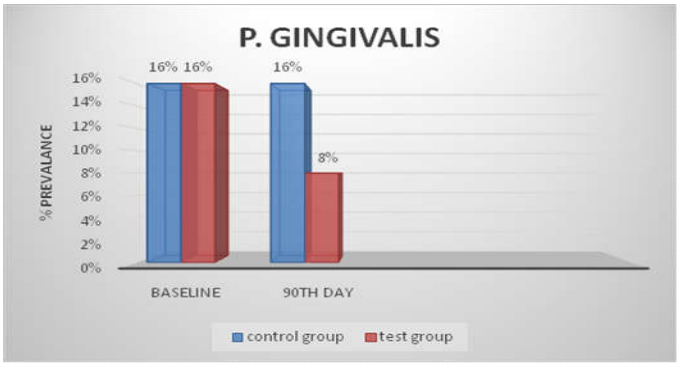
While in test Group at baseline 23 subjects showed presence of A.a and at follow up on 90th day only 6 subjects (24%) were positive. The percentage of reduction seen was 68%, which was highly significant (P<0.01) (Graph 3)



Graph 3. Percentage reduction in A. actinomycetemcomitans

P. Gingivalis

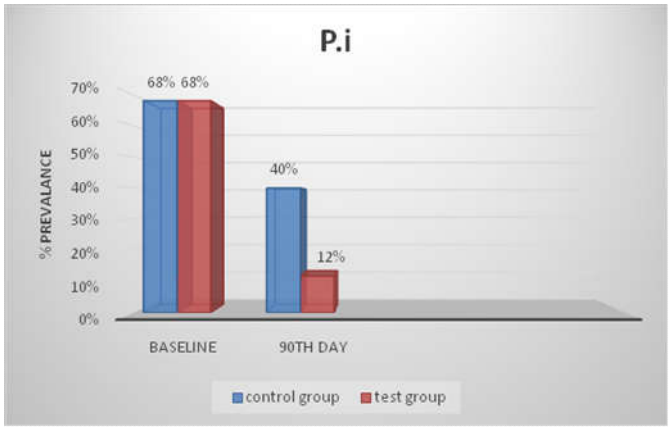
At baseline 4 subjects (16%) showed presence of the organism in control group and at the follow up on 90th day 4 subjects still showed presence of P.g in the control group. Thus at the baseline and on 90th day no reduction was seen in the no. of subjects positive for P.g. In the test group, 4 subjects showed presence of P.g and at follow up on 90th day 2 subjects were positive. Thus, at baseline while 16% of subjects of test Group harboured presence of P.g, it reduced to 8% of subjects being positive at the follow up on 90th day. (Graph 5)



Graph 4: Percentage reduction in P.gingivalis

P. Intermedia

At baseline 17 subjects (68%) showed presence of the organism and at the follow up on 90th day only 10 subjects (40%) were positive in control group.



Graph 5. Percentage reduction in P.intermedia

The percentage of reduction seen was 28% which was significant (P<0.05). While in Test Group at baseline 17 subjects showed presence of p.i and at the follow up on 90th day only 2 subjects were positive. Thus at baseline 68% of subjects of Test Group showed presence of P.i and it reduced to 8% of subjects positive at the follow up on 90th day. The percentage of reduction seen was 60% which was highly significant (Graph 5).

DISCUSSION

The treatment of periodontal disease involves altering the periodontopathic bacteria in the periodontal pocket, to eliminate the etiological agents responsible for initiation of the disease process in an attempt to allow tissues to heal, and resolution of inflammation. Scaling and root planing, is a vital step and effective, but some disease forms, however, continue to progress and may need adjunctive therapy with effective antibiotic therapy (Russell, 1956). Studies have shown that subgingival debridement in periodontitis patients are followed by profound shifts in the composition of the subgingival microflora which is comparable with the microflora found in healthy sites (Rhemerv, 2006). In the present study, the clinical and microbiological efficacy of collagen impregnated tetracycline fibers as an adjunct to scaling and root planing was evaluated. The results of the present study showed that there was considerable reduction of plaque index and gingival index scores in both control and test groups This was consistent with the findings of Slots J (Slots, 1979). This improvement from 0 - 90th day following scaling and root planing may be due to adequate maintenance of oral hygiene of the patient. Various methods were used for collection of subgingival plaque. Sample could be collected by sterile paper points, barbed broach and curette. With the use of paper points and barbed broach there are chances of contamination of subgingival organisms and some superficial bacteria can also contaminate the sample. Collection of subgingival specimens with a sterile curette will garner approximately 100 million bacteria (Greenstein, 1985). In present study curette i.e. Gracey no. 1-2 for anterior and no. 13-14 for posterior teeth were used for subgingival sampling. The World Workshop on Clinical Periodontics (1996) described A.actinomycetemcomitans, P.gingivalis and T.forsythia. as relevant microorganisms associated with periodontal breakdown (Zambon, 1996 and Haffajee, 1999). Therefore the microbiological assessment of some of these putative periopathogens was carried out in the present study. There was an appreciable reduction in no of A.a, P.i but not in the no of P.g. The results are consistent with findings of studies where they found significant reduction of all subgingival microbial species including P. gingivalis, P.intermedia, and A.actinomycetemcomitans (Goodson, 1995; Sadaf, 2012 and Aimetti, 2004). Sbordone L et al in contrast concluded that the most prevalent anaerobic rods after 60 days of scaling and root planing therapy were P. gingivalis and f. nucleatum (Sbordone, 1990). However, detection of low numbers of P.gingivalis precluded statistically significant differences in the present study. The local drug delivery agent used was bioresorbable form of tetracycline in the present study. It biodegrades within 7 days, so there is no need of second appointment. Tetracyclines are superior to other antibiotics as they are the only class of antibiotics which has the ability for retention to the tooth cementum and soft tissues and can achieve higher levels of gingival fluid concentrations than serum levels (Rapley, 1992). Tetracycline has also been shown to inhibit collagenase activity, collagen degradation and bone resorption (Golub, 1985). Administration of an antibiotic directly into the periodontal pocket provides various

advantages. Apart from bypassing first pass metabolism, systemic side effects and maintaining higher concentration at the diseased site, development of resistance to antibiotics, when administered locally, has also not yet been observed for periopathogens. A meta-analysis and systematic review extracted from ten relevant articles showed a significant improvement in periodontal parameters such as clinical attachment levels, probing pocket depths, and sulcular bleeding index in favor of tetracycline as local drug delivery compared to placebo (Nadig, 2016). The main limitation of the study was that the probing depths and clinical attachment levels were not assessed The duration of the study was limited to ninety days, but as the findings are encouraging the need for a long term study to evaluate the true value of local delivery of tetracycline fibres.

Conclusion

It can be concluded that tetracycline fibre therapy along with scaling and root planing is more effective than scaling and root planing alone. However, further long term studies should be undertaken to obtain more clinical evidence for regular use of this material on clinical parameter for a larger sample.

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