LOCAL DELIVERY OF ATRIDOX (DOXYCYCLINE GEL) AS ADJUNCTIVE IN MANAGEMENT OF CHRONIC PERIODONTITIS

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ABSTRACT

Treatment of chronic periodontitis affected patients is based on measures for reduction/eradication of periodontal pathogens and alteration of the systemic and local host susceptibility. This study aimed at evaluation the effects of topical application of Atridox (Doxycycline gel) in management of chronic periodontitis.

Subjects and Methods: This study was carried out on 15 patients(aged 25-55) with chronic periodontitis. They were received scaling and root planning(SRP) alone in one side and SRP plus Atridox (Doxycycline gel) in other side.

Each individual was subjected to the following measurements:
1. Evaluation of the clinical parameters pre and post treatment to detect the outcome of the treatment modality.
2. Dental plaque samples initially and at 3,6,9 and 12 months were obtained for microbiological evaluation.

Results:
1. Atridox (Doxycycline gel) delivered locally into periodontal diseased sites reduced all subgingival bacteria.
2. Both treatment modality led to a highly statistically significant reduction in microbiological counts as well as clinical parameters applied. No clinical relevant side effects were observed.

Key words: Local delivery antimicrobial agents / Medical periodontal therapy / ATRIDOX gel.

INTRODUCTION

Periodontal disease is a general term encompassing several pathological conditions such as chronic periodontitis, aggressive periodontitis, and necrotizing periodontitis. The clinical signs of periodontitis include changes in morphology of gingival tissues such as oedema, redness, reduction in consistency, and bleeding upon probing as well as loss of attachment with periodontal pocket formation (1).
Mechanical debridement is essential in removing hard accumulations on the roots, through subgingival scaling and root planning, but it is time-consuming, unpleasant for the patients, and technically difficult to perform (2). Studies have shown that subgingival debridement in periodontitis patients was followed by profound shifts in the composition of the subgingival microflora which is comparable with the microflora found in healthy sites. However, these changes are transient, especially in residual deep sites (probing pocket depth ≥6mm) after periodontal therapy. Re-colonization of the subgingival area by motile rods and spirochetes may occur within 2-8 weeks, which seems to be dependent on level of oral hygiene, efficacy of the subgingival debridement and residual probing pocket depth (3).

Chemotherapy may be directed at subgingival plaque, using antimicrobials, or at the host response using anti-inflammatory agents. Antimicrobials can be locally or systemically delivered; however in most cases antimicrobial chemotherapy should be considered adjunctive to mechanical debridement. The advantages of local and systemic chemotherapy must be balanced against the disadvantages and potential side effects of the agents (4). Local therapy provides much higher drug concentrations at the diseased site with lower total doses than systemic treatment doses. This minimizes the occurrence of systemic side effects and bacterial resistance. While the removal of all bacterial deposits in pockets deeper than 4mm is a difficult task, studies have shown that it was possible to obtain a measurable clinical effect by maintaining antibacterial activity in the periodontal pocket for approximately 1 week (5).

The tetracyclines (tetracycline hydrochloride, doxycycline, minocycline) are broad spectrum antibiotics that affect anaerobes and facultative organisms. They are bacteriostatic for many pathogens at concentrations found in the gingival crevicular fluid after systemic administration (3 to 6 µg/ml) (6). However, local delivery of these agents provides high concentrations that are bactericidal. Disadvantage of using tetracyclines are their ability to kill microorganisms associated with health as well as pathogens. Thus, local application of tetracyclines has been associated with minimal adverse side effects. Nevertheless, it was noted that12% of the normal flora were resistant to tetracycline (7), and often individuals with a history of taking this drug demonstrate increased drug resistance (8). Tetracyclines are substantive, potent, not toxic at prescribed dosages and after local delivery have been detected at 1 to 20 µm within the epithelial tissues (9,10).

Doxycycline is a broad-spectrum antibiotic synthetically derived from oxytetracycline. It is bacteriostatic, inhibiting bacterial protein synthesis due to disruption of transfer RNA and messenger RNA at ribosomal sites. In vitro studies has shown that P. gingivalis, P. intermedia, C. rectus, and F. nucleatum, which are associated with periodontal disease, are susceptible to doxycycline at concentrations ≤ 6.0µg/ml (11,12). It has been reported that scaling and root planning added to adjunctive subantimicrobial dose doxycycline resulted in mean attachment gains that significantly exceeded those achieved in placebo groups (13).

SUBJECTS AND METHODS

A-Patient Characteristics and grouping

Fifteen(15) patients(females =7 & males=8) with moderate to severe chronic (adult) periodontitis were selected for this study applying the split mouth technique. None of the patients had any history of antimicrobial therapy for the last 6 months, and no periodontal treatment prior to initiation of the present study. They were subjected for scaling and root planning, and one side of the oral cavity, received topical application of Atridox (Doxycycl-
bine gel) which contains two syringe mixing. Syringe A contain 450 mg of Atrigel Delivery system and syringe B contains doxycycline hyclate which equivalent to 250 mg doxycycline applied one time initially and at 3, 6, 9, and 12 months.

B-Clinical Examination

Five clinical parameters were recorded at baseline and at 3, 6, 9, and 12 months after treatments, they are:

- Gingival Index (GI) \(^\text{(14)}\).
- Plaque Index (PLI) \(^\text{(15)}\).
- Probing pocket depth and level of attachments \(^\text{(16)}\).
- Periodontal Index (PI) \(^\text{(17)}\).

C-Microbiologic Investigations

a. Sampling: Bacterial samples were obtained using standardized method for microbiological evaluation one time before and then post-operatively at intervals of 3, 6, 9, and 12 months. using sterile curettes which inserted gently into the pocket, then held in position for 10 seconds. The samples were transferred into sterile Broth media for proper and suitable culturing technique.

b. Culturing: Each specimen was cultured on 2 blood agar plates; one incubated aerobically at 37°C for 24 hours and the other anaerobically for 48 hours. Selective media used were blood agar with kanamycin and vancomycin for Bacterioids; and blood agar with neomycin for Fusobacteria, and placed in a candle jar containing 10% CO\(_2\) for 48 hours. Colonies on anaerobic blood agar plates which showed Gram-negative short Fusiform to filamentous shapes were presumptively identified as Bacteroids or Fusobacteria.

Statistical Analysis

Data obtained from clinical, microbiologic evaluations were analyzed by one-way analysis of variance test (ANOVA) to draw the significance.
RESULTS

Fifteen subjects were included in the present study, and completed the 12 month study period. The age range of subjects was (30-55) years with mean age of 40.06±7.04. Following the completion of the designed treatment, measurements of clinical parameters were recorded at 3, 6, 9, and 12 months intervals in the side treated with scaling and root planning plus Atridox (Doxycycline gel) and the side treated with scaling and root planning alone. Gingival Index, Plaque index, Periodontal pocket depth, clinical attachment level and Periodontal index showed improvement in both treated sides after 3, 6, 9, and 12 months intervals, when compared to the baseline data. There were slight differences in all clinical parameters in the side treated with scaling and root planning plus Atridox (Doxycycline gel) after 12 months when compared to the side treated with scaling and root planning alone.

The table of microbiological evaluation summarizes the microbial evaluation for topical application of ATRIDOX gel in management of chronic periodontitis, there were significant differences in anaerobic bacterial counts on blood agar at 9 month compared to pretreatment and at 12 month compared to 6 month (P<0.05), and there were highly significant differences in anaerobic bacterial counts at 12 month compared to pretreatment in the side treated with scaling and root planning alone.

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Microbiological Evaluation

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Chi-square test:

a, c, d (Anaerobes) P < 0.05 compared to baseline and 3 month, 6 month findings and a, ed (Aerobes) compared to baseline, 3 month, 6 month finding.

b, f (Anaerobes) P < 0.01 compared to the baseline, 3 month findings and b, c (Aerobes) compared to baseline and 3 months findings.

A = ATRIDOX.
with scaling and root planning plus ATRIDOX gel (P<0.01). In the side treated with scaling and root planning alone there were significant differences found at 3 month compared to the pretreatment and at 6,9 month compared to 3 month (P<0.05).

In the same table there were significant differences in aerobic bacterial counts on blood agar at 9 month compared to pretreatment and at 12 month compared to at 6 month (P<0.05). There were highly significant differences in aerobic bacterial counts at 12 month compared to 3and 6 month (P<0.01 & P<0.001) in the side treated with scaling and root planning plus ATRIDOX gel.

In the side treated with scaling and root planning alone there were significant differences in aerobic bacterial counts at 3 month compared to pretreatment and at 9 and 12 month compared to 3 month ( P<0.05).

The comparison between anaerobic and aerobic bacterial counts on blood agar at 3,6,9, and 12 month intervals from the side treated with scaling and root planning plus CHLO-SITE gel compared to the side treated with scaling and root planning alone, a significant difference was found (P<0.05).

**DISCUSSION**

The proper treatment of periodontal disease involves altering the periodontopathic bacteria situated deeply in the periodontal pockets, to remove the primary agents responsible for initiation of the disease process in an attempt to allow tissues to heal, and inflammation to resolve. Mechanical removal of agents, by scaling and root planning, is a vital step and effective, but some disease forms, however, continue to progress and may needs adjunctive therapy with effective antibiotic therapy (18).

It is generally agreed that, the success of periodontal therapy depends on the reduction of the periodontal pathogens in the subgingival area. Studies have shown that subgingival debridement in periodontitis patients is followed by profound shifts in the composition of the subgingival microflora which is comparable with the microflora found in healthy sites. However, these changes are transient, especially in residual deep sites (probing pocket depth ≥ 6mm) after periodontal therapy(3). Recolonization of the subgingival area by microflora seems to be dependent on the level of the oral hygiene of the patient, the efficacy of subgingival debridement and the residual probing pocket depth (3). The adjunctive use of antimicrobial agents to non-surgical therapy seems to provide additional effects (19).

Nine-month controlled clinical trails showed that subgingival application of the a resorbable doxycycline (ATRIDOX gel) results in significant pocket depth reduction of 1.33 and 0.8mm attachment gain. The magnitude of change was equivalent to that achieved by scaling and root planning in these 9 month studies (20). In the present study the subgingival application of ATRIDOX gel showed reduction in periodontal pocket depth of 3.15±0.54 and attachment gain 1.15±0.54 compared to the baseline 5.87±0.37 and 3.87±0.37 in the treated side with ATRIDOX gel plus scaling and root planning. A statistically significant difference for clinical parameters in the present study were found at 3, 6, 9, and 12 months when compared to the base line in the side treated with scaling and root planning plus ATRIDOX gel and the side treated with scaling and root planning alone. A similar finding was reported previously (21).

It should be emphasized that, the samples of this study were collected from the deep pockets in the side treated with scaling and root planning plus ATRIDOX gel and the side treated with scaling and root planning alone at baseline, 3, 6, 9, and 12 months during therapy. There were statistically differences found in microbiological results when compared between the side treated with scaling and root planning plus ATRIDOX gel and the side treated with scaling and root planning alone. Such finding is differed than findings of Preshaw et al (13).
REFERENCES


