www.djas.co.in
ISSN No-2321-1482

ORIGINAL ARTICLE

DJAS 3(III), 165-173, 2015

Dental JOURNAL
of Advance Studies

SURGICAL VS NONSURGICAL THERAPY ADJUNCTED WITH TETRACYCLINE LOCAL DRUG DELIVERY IN DIABETIC PATIENTS: A RANDOMIZED CLINICAL TRIAL

Aashutosh V. Karnik[1], Mala Dixit Baburaj[2]
[1]Assistant Professor, Department of Periodontics, Bharati Vidyapeeth Deemed University Dental College and Hospital, Mumbai, India
[2]Professor and Head, Department of Periodontics, Nair Hospital Dental College, Mumbai, India

ABSTRACT

Objectives: The present study was carried out to determine if non-surgical therapy adjuncted with local drug delivery of tetracycline fibers produces at least optimally comparable results as surgical therapy in non-insulin dependent diabetic individuals with moderate to severe periodontitis. **Method and Materials:** 80 sites with periodontal pockets measuring 5-8 mm in 40 controlled non-insulin dependent diabetes mellitus patients were treated with either tetracyclinelocal drug deliveryorflap surgery. Measurements of Probing pocket depth and Clinical attachment level at selected sites in each patient along with Plaque Index and Gingival Index were documented at baseline and after 4 weeks, 6 weeks, 9 weeks and 12 weeks post treatment. **Results:** Both non-surgical therapy adjuncted with local drug delivery and surgical therapy were found to be comparably effective in reduction of all parameters except Probing Pocket Depth, for which surgical therapy was statistically significantly more efficacious ($p<0.01$), though clinically the difference was insignificant. **Conclusions:** Within the limits of the study, non-surgical therapy adjuncted with local drug delivery of tetracycline fibers appears to be clinically as efficacious as surgical therapy and may be employed as the preferred therapy for treatment of deep pockets measuring 5-8 mm in controlled non-insulin dependent diabetes mellitus patients.

Keywords: Chronic Periodontitis, Local Anti-infective Agents, Non-insulin Dependent Diabetes Mellitus, Nonsurgical Periodontal Debridement, Tetracycline Hydrochloride

INTRODUCTION

Diabetes mellitus is a clinically and genetically heterogeneous group of metabolic disorders manifested by abnormally high levels of glucose in the blood. Diabetes mellitus and its interrelationship with periodontal disease has been a topic of intense research and scrutiny since a long time. The importance of this disorder to the dental team is evident from the estimate that a dental practice having an adult population of 2000 can expect to encounter 40 to 80 people with diabetes.[1]

Philips et al, in their review on clinical inertia in glycemic control, stated that data from the United States suggest that of the 65% of the patients diagnosed with diabetes, only 73% are prescribed pharmacologic therapy and only 33% of those thus treated achieve a HbA1C (Glycated Hemoglobin A1C) value of less than 7% by the American Diabetes Association (ADA) goal.[2] Rees, in a monograph, stated that the long term glycemic control of even the so called 'controlled' diabetics may not be very consistent by rigid standards, yet the patient's physician will provide medical clearance to perform periodontal therapy because the patient is likely to tolerate the procedure without undue difficulty. In this circumstance the Periodontist should

Corresponding Author:
Aashutosh V Karnik
E-mail:
karnikaashutosh@gmail.com
Received: 3rd August 2015
Accepted:2nd November 2015
Online: 11th January 2016

proceed with caution since inadequate diabetes mellitus control can adversely affect the severity of the periodontal disease response; the patient's wound healing capacity and the ability of the patient to withstand both emotional and physical stress. All these factors can result in a compromised clinical outcome. The clinician should insist that the patient achieve and sustain a highly effective level of oral physiotherapy, and in most instances a nonsurgical approach to periodontal therapy is preferred in individuals with diabetes mellitus, with or without the use of appropriate antibiotic therapy.[3]

Heitz-Mayfield, in a meta-analysis of three systematic review papers that reviewed all combined randomized controlled trials comparing scaling and root planing with open flap debridement, demonstrated that non-surgical therapy produces changes comparable to surgical therapy in clinical attachment level.[4]

Tetracycline fiber therapy has been shown to produce greater pocket depth reduction, attachment level gain and improvement in clinical response than and in addition to the effects that occur due to prophylaxis and improved home care.[5] Pavia, Nobile and Angelillo in a meta-analysis demonstrated a greater change in terms of probing depth and attachment level when data was pooled from studies in which tetracycline was administered as an adjunct to scaling and root planing. The meta-analysis concluded that results of various studies have documented that local delivery of tetracycline improves the clinical outcome of traditional treatment of scaling and root planing and should be considered particularly as an adjunct to it.[6]

The present study was carried out to determine if non-surgical therapy adjuncted with local drug delivery of tetracycline fibers produces at least optimally comparable results as surgical therapy in controlled non-insulin dependent diabetic individuals with moderate to severe periodontitis. These observations may point out if non-surgical therapy adjuncted with tetracycline local drug delivery may be used as the preferred form of therapy in lieu of flap surgery in treatment of deep pockets in diabetic individuals, considering the fact that their wound healing patterns and overall body biochemistry segregate them from other patients with periodontal disease.

METHOD AND MATERIALS

Study Design

The study was a parallel randomized trial carried out at Nair Hospital Dental College in Mumbai from 1st January, 2008 to 31st August, 2009. It was independently reviewed and approved by the human subjects ethics board of the institute and was conducted in accordance with the World Medical Association Declaration of Helsinki 1975, as revised in 2000. A total of 40 patients were selected for this study from the out-patient department and their informed written consent was taken prior to the study. Patients were selected using the following selection criteria: 1) Patients with controlled non-insulin dependent diabetes mellitus (random blood glucose 120-140 mg/dl); 2) Patients who had not taken antibiotics for the past 6 weeks; 3) Patients who had moderate to severe periodontitis with pockets between 5mm-8mm at minimum 2 sites measured after a minimum of 15 days after scaling and root planing. To minimize the surgical area, sites close to each other were preferred. The following patients were excluded from selection: 1) Patients who had significant systemic history other than diabetes mellitus; 2) Patients who gave history of allergy to tetracycline; 3) Pregnant patients, lactating mothers or females taking oral contraceptives; 4) Smokers; 5) Patients who were showing signs of oral candidiasis.

Patients were subjected to detailed case history, examination and counselling for maintenance of good oral hygiene, prior to nonsurgical periodontal

debridement. Modified Bass method was taught for toothbrushing and appropriate interdental cleansing aids were prescribed. The type of diabetes was established by using the following criteria: 1) Age of onset > 25 years; obesity; 2) Treatment primarily based on diet control, exercise and oral hypoglycemic agents with only occasional emergency use of supplementary insulinand; 3) Physician's consent.[1] Their glycemic control was established by using the following criteria: 1) Physician's consent; 2) Random blood glucose testing (120-140 mg/dl was considered acceptable).[8]

After enrollment, the investigatorsrandomly allocated the subjects into two groups: Group 'NS + LDD' (Non-Surgical therapy + Local Drug Delivery) and Group 'S' (Surgical therapy). Simple randomization was carried out by the investigators using the chit method, after writing NS+LDD and S on 20 chits each, folding the chits, putting them in a box and mixing them well. Two sites fulfilling the above mentioned criteria were identified in each patient and were named 'a' and 'b', to be monitored at the aforementioned time intervals. The deepest sites around the selected teeth were included in the study. The baseline readings of Probing Pocket Depth (PPD) and Clinical Attachment Level (CAL) were recorded with a UNC-15 Probe after a minimum of 15 days subsequent to scaling and root planing and were designated as 'a1' and 'b1'. The subsequent readings of PPD and CAL were designated as follows: 1) 'a2', 'b2' at 4 weeks; 2) 'a3', 'b3' at 6 weeks; 3) 'a4', 'b4' at 9 weeks; 4) 'a5', 'b5' at 12 weeks. Along with PPD and CAL, Plaque Index (PI)[9]and Gingival Index (GI)[10]were also measured post treatment at the same time intervals.

Intervention Groups

GROUP 'NS + LDD'

In Group 'NS + LDD', tetracycline resorbable fiber local drug delivery was done using Periodontal Plus AB® fibers. Periodontal Plus AB® fibers are made up of 25 mg of pure fibrillar collagen containing approximately 2 mg (1.7±0.25 mg) of evenly impregnated tetracycline hydrochloride that functions as a local anti-infective agent providing continuous release of tetracycline for a minimum of 10 days. These fibers release tetracycline at a rate of approximately 2 µg/mg-hr in the periodontal pocket with average concentration of 1500 µg/ml per site during the first 10 days' treatment period.

The sites receiving fiber therapy were carefully isolated using cotton rolls. Tetracycline impregnated collagen fibers were taken in a dappen dish and moistened with sterile normal saline (Figure 1a) and gently packed in the periodontal pockets. The fibers were inserted in the deepest sites and successive layers were placed till all subgingival areas were completely

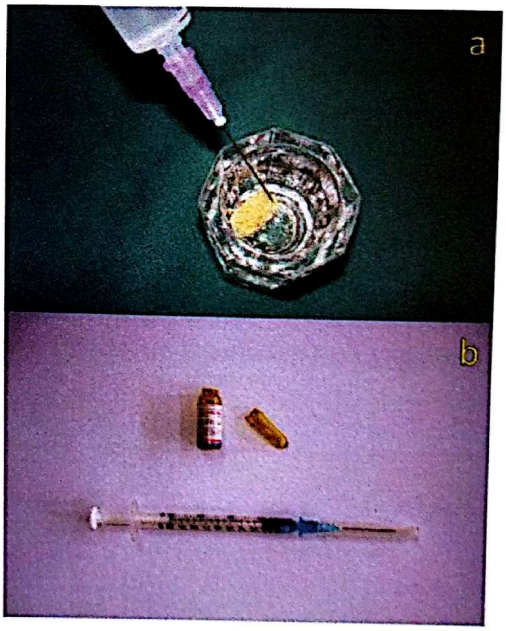

Figure 1: (a) Golden-yellow tetracycline resorbable fibers being moistened with sterile saline in a sterile dappen dish; (b) Blue colored cyanoacrylate tissue adhesive withdrawn from sterile ampoule into a syringe

filled to the gingiva margin. The back of a Universal Curette (U 4R/4L) was used to insert fibers in the periodontal pockets.

To retain the fibers in the pocket a thin layer of tissue adhesive, Amcrylate, was used to seal the gingival sulcus. Amcrylate is sterile tissue adhesive (Iso amyl 2-cyanoacrylate) in the form of a monomer that polymerizes on contact with moisture and solidifies within less than 5-10 seconds. The Amcrylate glass ampoule was cut and the Amcrylate solution was drawn into the syringe provided along with the Amcrylate uni-pack (Figure 1b). Amcrylate was applied in a thin layer and the excess was removed with dry swab immediately.

Patients were given following instructions till the time cyanoacrylate adhesive was not removed:1) Do not brush or floss the treated area; 2) Do not eat hard or crunchy foods; 3) Do not chew gum or sticky foods; 4)Avoid touching the treated area with tongue or fingers; 4) Report back if the adhesive dressing falls out before 7 days; 5) Although some mild to moderate sensitivity is normal after treatment with Periodontal Plus AB fibers, report back promptly if pain, swelling or other problems occur.

Approximately 4 days following the placement of tetracycline fibers, the patients were checked for fiber retention and any adverse soft tissue reaction. If the fibers were dislodged or lost, they were replaced. Cyanoacrylate adhesive was removed after 10 days of application. There was no need to remove the fibers as they were bio-resorbable.

GROUP 'S'

Patients in this group were subjected to Modified Flap Operation (Kirkland Flap) in selected sites. Anesthesia was achieved by infiltrations and/or nerve blocks using Inj. 2 % Lignocaine Hydrochloride with 1: 100, 000 Epinephrine. Kirkalnd sulcular incisions were made andfull thickness mucoperiosteal flaps were reflected taking care to minimize the extent of surgical area.

Thorough debridement was carried out to remove granulation tissue and any residual subgingival calculus. Root planing was carried out using curettes. The pocket lining was trimmed from within using scissors. The area was flushed with saline and sutured using 4 – 0 black braided silk. Periodontal dressing was placed using Coe-Pak.

The patients were given routine post-surgical instructions. They were prescribed Tab. Diclofenac potassium 50 mg B.D. for 3 days and Mouthwash Chlorhexidine 0.20 % B.D. for 7 days. The dressing was removed after 7 days and the patients were asked to gradually resume function and oral hygiene practices in the operated sites.

STATISTICALANALYSIS

The null hypothesis was that the NS + LDD and the S Group had statistically significant differences in mean values of PPD, CAL, PI and GI. After clinical observations, the data was collected and subjected to statistical analysis. Unpaired t Test was used to compare values within the groups.One way ANOVA was used for comparing the changes in PPD and CALbetween the two groups.For comparing the changes in PI and GI, Mann–Whitney U test was used. IBM SPSS 22 was used for the statistical analysis.

RESULTS

Of the 40 originally selected patients (24 males and 16 females), 3 dropped out of the NS + LDD Group while one was not considered for the study as the oral hygiene levels were unacceptable. 4 patients dropped out of the S Group, thus bringing the total to 32 patients, 16 in Group NS + LDD and 16 in Group S. The total number of sites monitored was 64 (Baseline data in Table 1). Figure 2 provides CONSORT Flow Diagram for the study.

Mean Probing Pocket Depth (PPD) scores for Group NS + LDD at baseline, 4 weeks, 6 weeks, 9 weeks and 12 weeks post treatment were 5.75 ± 0.61,

Table 1: Baseline Data of Group NS+LDD and Group S

Number	Group NS+LDD						Group S					
	PPD in millimeters		CAL in millimeters		PI	GI	PPD in millimeters		CAL in millimeters		PI	GI
	Site 'a'	Site 'b'	Site 'a'	Site 'b'			Site 'a'	Site 'b'	Site 'a'	Site 'b'		
1	5	5	6	6	1.23	1.21	6	5	6	5	0.81	1.12
2	6	5	6	5	1.13	1.25	5	6	5	7	1.13	1.52
3	5	6	6	7	0.93	1.34	5	5	5	5	1.49	1.48
4	5	6	6	7	0.95	1.32	6	6	6	6	1.15	1.21
5	6	5	6	5	1.23	1.24	5	6	5	6	0.84	1.25
6	5	6	6	5	0.73	1.37	7	8	7	8	0.65	1.17
7	7	6	7	6	0.81	1.93	5	5	6	5	0.89	1.11
8	5	7	6	8	1.42	1.58	7	7	7	7	1.28	1.27
9	6	6	6	6	0.86	1.35	5	6	5	6	1.19	1.43
10	6	5	7	6	1.74	1.67	6	6	6	6	1.43	1.53
11	6	5	6	5	1.36	1.28	7	8	7	8	0.64	1.25
12	5	7	5	7	0.99	1.38	6	6	6	6	1.32	1.13
13	6	5	6	5	0.72	1.21	5	5	5	5	0.64	1.26
14	7	8	7	8	1.27	1.33	6	5	6	5	0.89	1.25
15	6	6	6	6	0.91	1.24	5	6	5	6	1.45	1.21
16	5	5	7	5	0.83	1.27	5	5	5	5	0.93	1.04

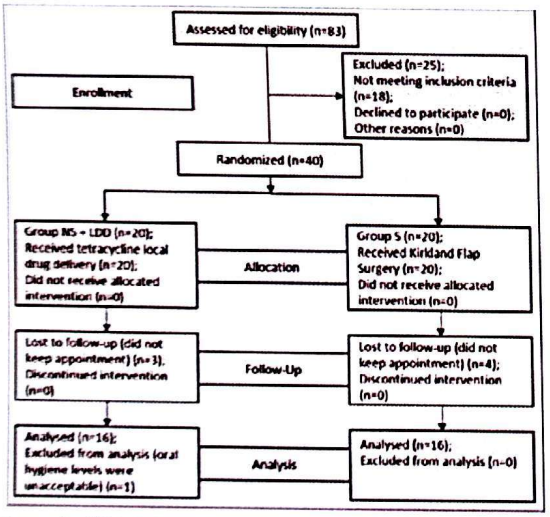

Figure 2: CONSORT Flow Diagram of the progress through enrolment, intervention allocation, follow-up and analysis of a parallel-randomized trial of two groups

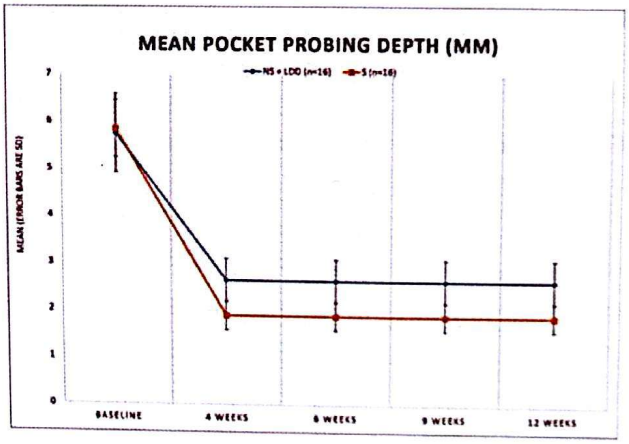

Figure 3: Mean PPD across Group NS+LDD and Group S

2.66 ± 0.30, 2.66 ± 0.30, 2.66 ± 0.30 and 2.66 ± 0.30 respectively. In Group S, the mean PPD measurement at baseline, 4 weeks, 6 weeks, 9 weeks and 12 weeks post treatment were 5.84 ± 0.83, 1.91 ± 0.46, 1.91 ± 0.46, 1.91 ± 0.46 and 1.91 ± 0.46 respectively. Figure 3 describes the changes in mean PPD over the course of the study at both sites in both groups. In both groups at both sites, statistically significant difference was found in PPD values between baseline and 4 weeks ($p < 0.01$). No statistically significant difference was found between 4 to 6 weeks, 6 to 9 weeks and 9 to 12 weeks in both sites ($p > 0.05$). On comparing changes inmean scores of PPD between the two groups using one way ANOVA, except for the baseline, there was a statistically significant difference between Group NS + LDD and Group S (F ratio significantly more than 1) (Figure 4).