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Comparative evaluation of efficacy of tetracycline fibres and nanobiofusion gel as a local drug delivery agent in chronic periodontitis: A clinical study

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Abstract---Introduction: Local drug delivery agents (LDD) in the management of periodontitis has gained acceptance and popularity compared to systemic drugs for its decreased risk in development of resistant flora, opportunist infection and side effects. Tetracycline fibers and Nanobiofusion gel (NBF) are one such antimicrobial agents that have a wide spectrum of action. Objective: To evaluate the clinical efficacy of administering Tetracycline fibers and NBF gel as an adjunct to Scaling and root planning (SRP) in chronic periodontitis patients. Materials and methods: A total of 20 patients (40 sites) with

chronic periodontitis having probing pocket depth 5-7mm are selected and grouped into two groups. Group A in which sites are treated by SRP followed by sub gingival placement of NBF gel, where as in Group B the sites are treated by SRP followed by sub gingival placement of tetracycline fibers. Clinical evaluation of all parameters are taken at baseline, 2 weeks and 3months. Results: At the end of the 3 months Group 2 showed greater reduction in the pocket depth and also showed a significant gain in the CAL (2.0 mm) as compared to Group 1. Whereas PI and GI also showed significant improvements in both the groups. Conclusion: Tetracycline fibers as LDD agents are safe and effective adjuncts to SRP and produce significant clinical benefits compared to that of NBF gel.

Keywords---local drug delivery, tetracycline fibers, nanobiofusion gel.

Introduction

Periodontal pockets are densely populated with pathogens which are responsible for periodontal destruction. These pathogens may not always be accessible for mechanical detriment and require an adjunctive. Local drug delivery agents (LDD) when placed within the pocket come into direct contact with the micro-organisms and help in their elimination. periodontitis is a chronic inflammatory condition of, affecting the tooth supporting structures leading to destruction of the periodontium and bone resorption which ultimately leads to tooth loss. It is multifactorial in nature, influenced by local and systemic factors.

Although bacteria are the primary cause of periodontal disease, the interpretation of microbial pathogenic factors alone may not be sufficient to cause periodontitis. Periodontal pathogens produce harmful enzymes and by- products that break host cell membranes as well as extracellular matrices to produce nutrients for their growth. In doing so, they institute damage directly or indirectly by triggering host- mediated responses that lead to injury to the tissues. In a continual state of pathogenic infection extensive treatment is required. Therefore, clearance of the sub gingival infection and elimination of the periodontal pocket are considered a priority in the treatment of periodontitis. Administration of antimicrobial agents is a rapid and inexpensive method to augment mechanical periodontal debridement.

Local deliveries of antimicrobial agents into periodontal pockets have been broadly studied since 1979. This mode 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. Drug delivery systems are often classified according to the mechanism controlling drug release and are categorized into three: Solvent controlled matrix systems stationed on macromolecular matrix permeability to small molecules after matrix swelling into hydrated medium. Reservoir systems restrained by drug diffusion across a polymeric membrane. Chemically controlled systems where the rate of drug release is restrained by the rate and extent of erosion of the polymeric matrix and degradation of chemical bonds. For all these systems, the basic polymer can be of

natural origin such as collagen or proteins , semi- synthetic such as synthetic or cellulose derivatives, all of which must willingly degrade during use. Goodson et.al., in 1979 first proposed the concept of controlled delivery intreating periodontitis. The persuasiveness of this form of therapy is that, it reaches the base of periodontal pocket and is maintained for an sufficient time for the antimicrobial effect to occur. Various local drug delivery system for treating periodontitis are - Fibers, Film, Injectable systems, Gels, Strips and compacts, Vesicular systems, Micro particle system, Nanoparticle system etc [1].Tetracycline has an incredible ability to reduce microbial burden by its antimicrobial effect, prevents collagenase activity, and potentially inhibits bone loss. Local tetracycline therapy suggested more advantage with fibers compared to other devices [2].

Nano-Bio Fusion (NBF) gingival gel used in the study is a possessed scientifically formulated, bio adhesive antioxidant gel harvesting naturally occurring antioxidants for targeted action. It principally act based on the NBF technology which allows the ultrafine antioxidants to exceed the moist intraoral environment, enter the cells and rejuvenate, revitalize, support, protect, and optimize gum and soft oral tissue [3]. Thus, the present study has been attempted to evaluate the efficacy of administering tetracycline fibers and NBF gel as an adjunct to SRP in chronic periodontitis patients.

Materials and Methods

A total of twenty human subjects with 40 sites comprising of both sexes aged 30-60 years, who came to the outpatient Department of Periodontology were selected. A design of this study was randomized, controlled, split-mouth study. The patients were explained about the treatment procedure and informed consent was obtained from them. (Both verbal and written). The study was approved by Institutional Review Board and Institutional Ethical Committee .

Sites selected for patients enrolled for the study were treated in a split-mouth pattern. Subjects to be included were in the:

- 1) Age group of 30-60 years;
- 2) Had not received any surgical or non-surgical periodontal therapy in the last six months;
- 3) The subjects must have at least 20 teeth in case of chronic periodontitis with probing pocket depth of 5-7mm on atleast one tooth per quadrant.

The patients were excluded from the study because of the following reasons:

- 1) Pregnancy;
- 2) History of taking antibiotics or using antibacterial mouth washes/rinses for the last 6 months;
- 3) Known hypersensitivity to Tetracycline;
- 4) Teeth with furcation involvement;
- 5) History of smoking, and drug or alcohol abuse.

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Clinical methods

A total of 20 patients i.e., 40 sites from the patients were selected and grouped into two groups.

Group A: - Sites will be treated by SRP followed by subgingival placement of NBF gel. (Figure 1)

Group B: - Sites will be treated by SRP followed by subgingival placement of tetracycline fibers. (Figure 2)

Treatment Procedure

All the patients were subjected to SRP at the baseline. An acrylic stent was customized for accurate measurement. Prior to SRP each selected site was subjected to assessment of the following parameters (Figure 3)

- (1) Plaque index (PI) (Sillness and Loe 1964);[4]
- (2) Gingival index (GI) (Loe and Sillness, 1963) [5]
- (3) Periodontal pocket depth (PPD),
- (4) Clinical attachment level (CAL).

After recording the clinical parameters, thorough SRP was performed on the sites selected for the study. In one site from the split mouth design commercially available NBF gel was placed and the other site was treated with Periodontal plus AB fibers. Sites selected for NBF gel: NBF gel was induced within the pocket depth with a needle(Figure4). The NBF gel was inserted in excess such that it overflowed the pocket. Sites selected for tetracycline fiber therapy : Fibers were soaked

in saline and placed within the depth of the periodontal pocket surrounding the tooth (Figure 5). Fibers were placed from depth to gingival margin.

To ensure prolonged retention of the adjunctive used a periodontal dressing (Coe Pak) was placed. Post operative instructions were given to the both groups. At each interval (Baseline, 2 weeks and 3 months), the clinical parameters were recorded. (Figure 6 and 7) Clinical parameters were assessed sequentially. The estimation of plaque was done on the basis of density of plaque at the gingival margin area of the sites using plaque index (Sillness and Loe 1964). Gingival index was recorded for 4 surfaces (dentofacial, facial, mesio-facial and lingual) of every tooth to be treated. Probing Pocket depth was measured with the help of UNC-15 probe and the distance between the base of the pocket and gingival margin was measured with the help of previously customized acrylic stent. As the resistance to further penetration was noticed, readings were recorded to the nearest millimeters. Clinical attachment level was measured from apical extent of stent to base of pocket minus distance from stent to CEJ.

Results

The data was analyzed using student paired t test for intergroup comparison and Wilcoxon signed rank test for intra group comparison. The mean value of clinical parameters of PI, GI, PPD and CAL, recorded from patients in both the groups are shown in table 1 and 2. The clinical parameters showed a significant reduction from Baseline to 3 months in both the groups. The intergroup comparison showed that the mean GI in the group A and group B at baseline were 2.26 and 2.15, respectively, which were not statistically significant, and after 2 weeks the mean values were 1.52 and 1.26 respectively which showed statistically significant results ($P = 0.006$) and at 3 months were 1.30 and 1.12 respectively, which showed statistically significant results ($P = 0.016$). The mean PI in the group A and group B at baseline were 2.48 and 2.42, respectively, which were not statistically significant, and after 2 weeks the mean values were 1.34 and 1.26 respectively which showed statistically significant results ($P = 0.001$) and at 3 months were 0.92 and 0.75 respectively, which showed statistically significant results ($P = 0.042$). The mean PPD in the group A and group B at baseline were 5.5 and 5.5, respectively, which were statistically non-significant, and after 2 weeks the mean values were 5.00 and 4.10 respectively which showed statistically significant results ($P = 0.000$) and at 3 months were 4.20 and 3.40 respectively, which showed statistically significant results ($P=0.001$). The mean CAL in the group A and group B at baseline were 5.20 and 5.40, respectively, which were not statistically significant, and after 2 weeks the mean values were 5.10 and 4.80 respectively, which showed statistically significant results ($P = 0.000$) and at 3 months were 4.30 and 3.40 respectively, which showed statistically significant results ($P=0.001$).

Table 1: Mean comparison of clinical parameters between both the groups at Baseline (Before Treatment)

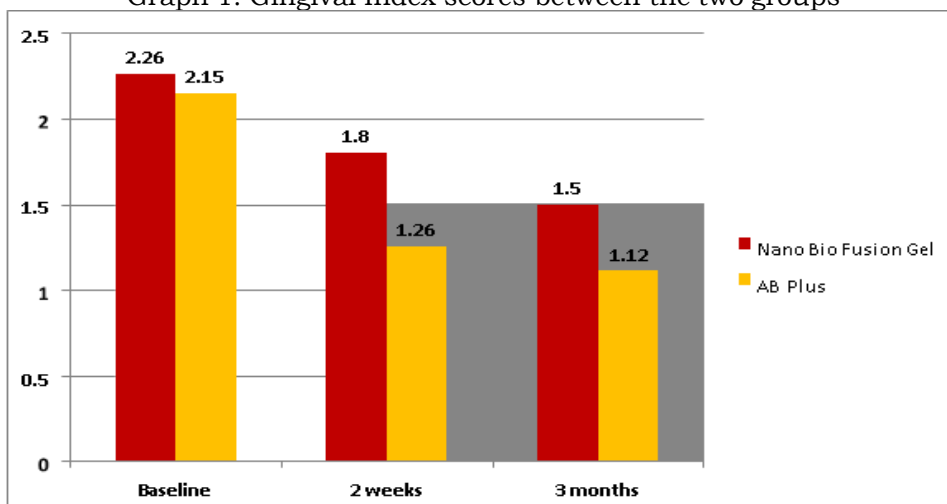
Independent Samples T Test							
	Group	N	Mean	Std.	Std.	Mean Difference	T

				Deviation	ErrorMean		Test
GingivalIndex	Nano Bio Fusion Gel	20	2.2600	.20656	.06532	0.11000	T = 1.435
	AB	20	2.1500	.12693	.04014		p = 0.168NS
	Plus						
Plaqueindex	Nano Bio Fusion Gel	20	2.4800	.10328	.03266	0.6000	T = 0.781
	AB	20	2.4200	.17512	.05538		p = 0.363NS
	Plus						
NS*: Not significant; Statistically significant at 5% level of significance (P<0.05)							
ProbingDepth	Nano Bio Fusion Gel	20	5.5000	.52705	.16667	0.0000	T = 0.000
	AB	20	5.5000	.52705	.16667		p = 1.000NS
	Plus						
CAL	NanoBio Fusion Gel	20	5.2000	.63246	.20000	0.2000	T = 0.671
	AB	20	5.4000	.69921	.22111		p = 0.511NS
	Plus						
CAL: clinical attachment level; Statistically significant at 5% level of significance (P<0.05)							

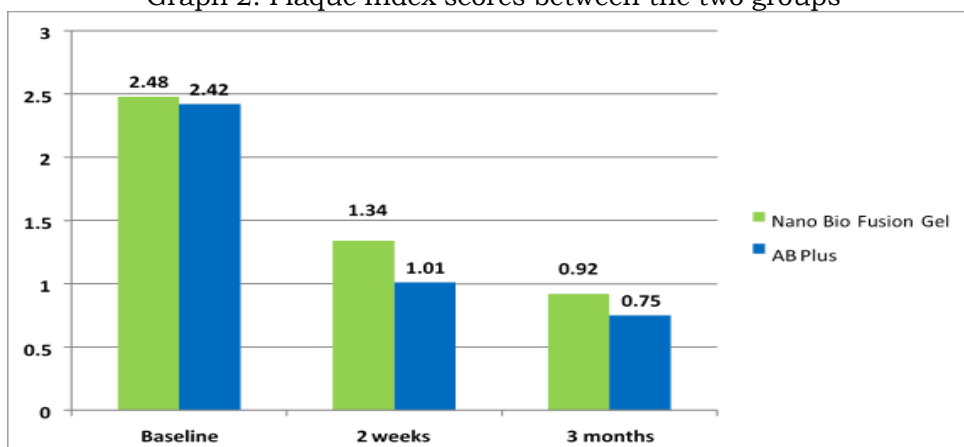
Table 2: Mean comparison of clinical parameters between both the groups at 2 Weeks (After Treatment)

Independent Samples T Test							
	Group	N	Mean	Std. Deviation	Std. Error Mean	Mean Difference	T Test
Gingival Index	Nano Bio Fusion Gel	20	1.5200	.15492	.04899	0.2600	T = 3.133 p = 0.006
	AB Plus	20	1.2600	.21187	.06700		
Plaque index	Nano Bio Fusion Gel	20	1.3400	.16465	.05207	0.3300	T = 3.999 p = 0.001
	AB Plus	20	1.0100	.20248	.06403		
Probing Depth	Nano Bio Fusion	20	5.0000	.47140	.14907	0.9000	T = 5.014 p = 0.000

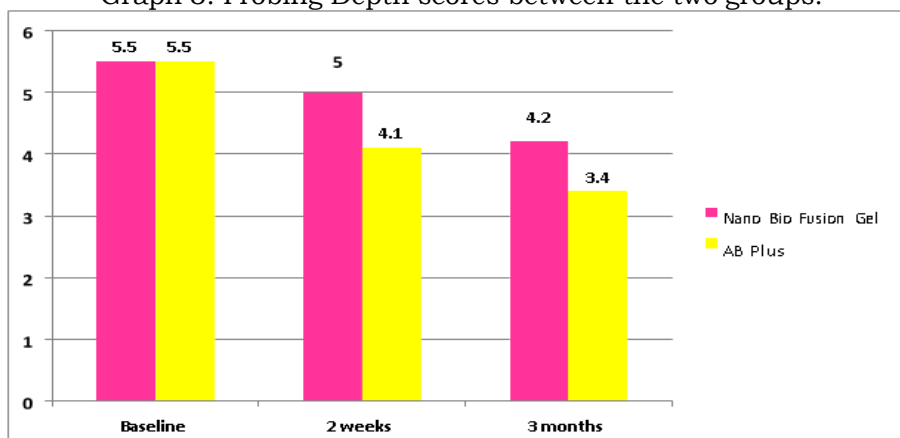
Graph 1: Gingival Index scores between the two groups



Graph 2: Plaque Index scores between the two groups



Graph 3: Probing Depth scores between the two groups:



Graph 4: CAL scores between the two groups

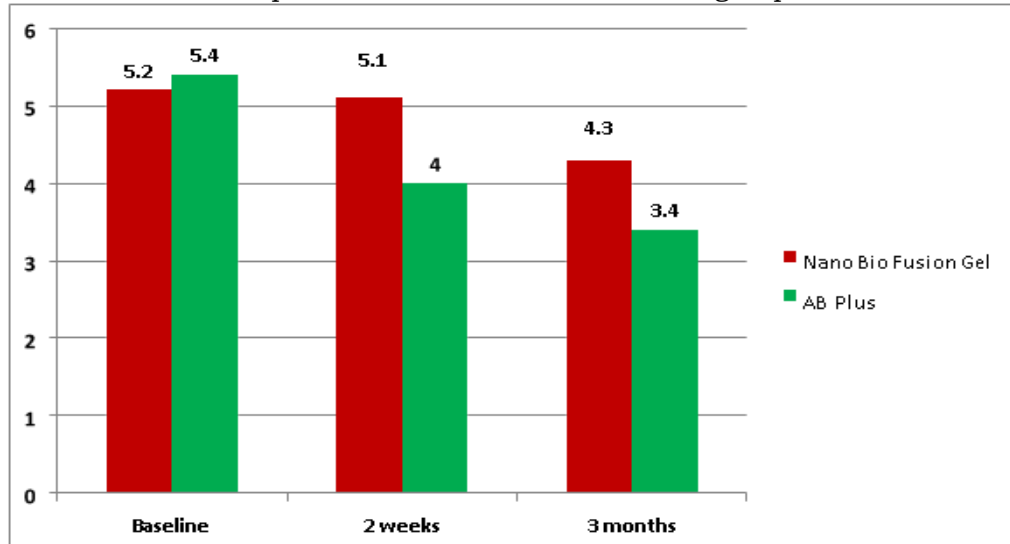


Fig 1: Nanobiofusion Gel



Fig 2: Periodontal Plus AB Fibres



Fig 3: Probing Depth At Baseline In NBF gel group



Fig 3: Probing Depth At Baseline In AB Plus Group



Fig 4: Application Of NBF Gel



Fig:5 – Application Of Ab Plus



Fig:7: Probing Depth At 14 Days



Fig:7: Probing Depth at 3 Months

Discussion

Periodontitis, initiated by bacteria, frequently appears in localized areas in the patient's oral cavity. These altered localized areas impart themselves well to treatment using an antimicrobial agent. Antimicrobial agents may be used systemically or can be applied directly to the pocket [6]. In order to obtain an effective concentration of the antimicrobial drug in the periodontal pocket after

systemic administration, repeated in takes over a prolonged period of time may be required which may lead to adverse effects such as development of resistant strains and superimposed infections preclude the use of these agents as the sole treatment modality [7]. The main objective of the periodontal therapy is to reduce or eliminate the periodontal pocket, which can be carried out by non-surgical or surgical methods.

Twenty years ago, Goodson et.al., (1979) first proposed the concept of “controlled delivery of antibiotics” in treatment of periodontitis. In 2014, Malathi et.al., concluded from their study that locally delivered antimicrobial agents are administered to prevent plaque accumulation and to disinfect the root surface and adjacent periodontal tissues [8]. They are designed to enhance the healing following periodontal therapy. The present study which is aimed to compare the efficacy of NBF gel and tetracycline fibers as an adjunct to conventional therapy in patients with chronic periodontitis strongly recommends the use of tetracycline fibers as an adjunct to conventional therapy in patients suffering from gingival and periodontal disease.

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 [9]. The substantivity of tetracycline have proved to be effective against gram-positive and gram-negative anaerobic microflora associated with chronic periodontitis. They apply their antimicrobial effect by inhibiting protein synthesis. The improvement in GI and PI in the group I can be attributed to the antibacterial activity, effect on collagen breakdown and substantivity of tetracycline when delivered as LDD. It is available in vials containing 25 mg fibrillar collagen impregnated with 2mg tetracycline hydrochloride. Application of this fiber abolishes the need of a second appointment for fiber removal as a result of it biodegrades within the pocket.

The sites in group I were treated with collagen impregnated tetracycline fibers which was found to be advantageous in improving the periodontal status. NBF gel is a high functional nanobiofusion gel containing propolis, nano vitamin C, E and herb extract. The nano complex nature renders direct penetration and absorption when applied on oral tissue and stays on the tissue as bioactive protective film. It acts like a local delivery agent which when placed in the gingiva reduces the microbial load naturally leading to an improvement in the signs of gingivitis and periodontitis.

Till date there are no studies reported in literature where the efficacy of NBF gel and Tetracycline fibers have been compared as Local drug delivery (LDD) in a split mouth design. In various studies performed by Singh N et.al., Chatterjee A and Debarnath [10-12] on NBF gel which enhanced clinical outcomes and decreased disease progression. Tetracycline (TC) has shown to reach a concentration of 1590 µg/mL and is shown to be bactericidal to oral bacteria present on root surface [13]. Amazingly, despite the high concentration of TC within the pocket it does no harm to the pocket epithelium. present in the periodontal pocket [14]. However, a study by Purucker [15] has shown TC fiber therapy against systemic amoxicillin and clavulanic acid to be as effective as tetracycline fibers applied

locally while another study by Drisco CL et.al., [16] showed SRP alone to be as effective a TC fiber.

The reduction in probing pocket depth from baseline to three months in both groups is consistent with the study conducted by Vandekerckhove, Kinane and Gonçalves [17-19]. Current study was in accordance with Vandekerckhove et.al., where analyzed data from all sites indicated significant decrease in probing pocket depth. A significant gain in clinical attachment level was also accomplished from baseline to three months in both the treated sites ($P < 0.001$), differences observed in present study were similar to that of Goodson, Minabe, Newman, and Radvar [20-23]. Minabe found gain of clinical attachment level of around 2 mm and suggested that the local application of antibiotic using local drug delivery in combination with root debridement may contribute to gain in clinical attachment level. [21]

Conclusions

The advent of local drug delivery systems has proven to be a beneficial treatment in conjunction with scaling and root planning but not as a monotherapy. In this study the additional advantages of tetracycline therapy and ease of its use it proves a resource to maintain enhanced periodontal health. However further multicentric studies are advocated to prove the efficacy of NBF gel as LDD.

Limitations of the study

Firstly, due to the limited sample size, it is difficult to generalize the results and secondly analysis of microbiological and radiographic parameters are recommended for supporting the findings. Clinical Relevance Of The Study: Provides evidence that tetracycline fibers as locally delivered agents are safe and effective in comparison to NBF gel. Tetracycline fibers have a longer substantivity than NBF gel as NBF gel tends to flush away from the Sulcus.

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