Original Research Article

EVALUATION OF THE EFFECTIVENESS OF TWO LOCAL DRUG DELIVERY AGENTS IN THE MANAGEMENT OF CHRONIC PERIODONTITIS – A COMPARATIVE STUDY

Abstract

Background: The prime aim of periodontal therapy is the arrest of bacteria/host induced inflammation and to maintain healthy periodontium. Pathogenic organisms which are not mechanically accessible can be eliminated by antibacterial agents. Several local antimicrobial drug delivery agents have been developed with a view to maintain adequate levels of crevicular fluid at the target site and preventing systemic uptake. **Aim**: Tetracycline fibres (Periodontal plus AB) and curcumin gel (curenext) are two such drugs used as adjuncts to scaling and root planing in the treatment of chronic periodontitis. Comparative evaluation of the effectiveness of these two agents will be helpful in the selection of a particular type of treatment modality. **Methodology**: Eighty sites from 30 patients were selected for the study and were divided into two groups of 40 sites for tetracycline fibres and 40 sites for curcumin gel application as adjuncts to scaling and root planing in the treatment of chronic periodontitis. Clinical parameters such as gingival index, plaque index, oral hygiene index, probing pocket depth and gain in clinical attachment level were assessed in all the patients after 30 days and 90 days in both groups**. Results and discussion**: Study revealed that both tetracycline fibres and curcumin gel are effective agents as adjuncts to scaling and root planing in the treatment of chronic periodontitis. **Conclusion**: Though both tetracycline fibers and curcumin gel were found to be effective for the treatment of chronic periodontitis, tetracycline was found to be slightly more effective. This may be due to the property of substantivity exhibited by tetracycline.

Key words: Periodontitis, Local drug delivery, tetracycline fibers, curcumin gel

Introduction

"Chronic periodontitis is a multifactorial disease resulting from the formation of periodontal pocket and progressive loss of attachment. Periodontal pocket formation represents the pathologic sequele of microbial and inflammation mediated degradation of collagenous connective tissue and alveolar bone. Periodontal disorders include a spectrum of infections affecting the oral cavity, in which the chief etiology is dental plaque that causes inflammation in the tissues supporting the dentition" (1). Mechanical debridement may fail to eliminate the putative pathogens from the pockets completely because of the inaccessibility of the location of the organisms within the gingival tissue. Systemic administration of drugs leads to absorption into the blood stream and distribution throughout the body. According to Chatuuvedi et al (2012) local drug delivery mode is considered more beneficial in the control of localized periodontal

disease as adjunct to non-surgical periodontal therapy. Local drug delivery mode is considered more beneficial in the control of localized periodontal disease as adjunct to non-surgical periodontal therapy. Commonly used antimicrobial local drug delivery agents include Chlorhexidine- containing chip (Periochip), Doxycycline gel (Atridox), Minicycline microsperes (Arestin), ethylene or vinyl acetate copolymer fiber containing tetracycline and bioresorbable tetracycline fiber (Periodontal Plus AB). Curcumin Longa has been used as a therapeutic agent in ayurvedic medicine for years. A comparative study on the clinical effectiveness of a synthetic drug tetracycline fiber (which may have side effects) and an ayurvedic drug curcumin gel (supposed to have no side effects) is considered worthwhile.

Review of Literature

Several authors have found that effective treatment of periodontitis is the mechanical debridement to remove biofilm and calculus from the affected root surfaces followed by adjunct therapy by local delivery of drugs (3 – 7). The advantages of local drug delivery are:

1. Achieving high concentration of the drug at localized site (100 times as compared to systemic therapy)
2. Suitable for agents which cannot be given systemically (such as chlorhexidine)
3. No systemic side effects
4. Low chances of super-infection or drug resistance
5. Reduction in total drug usage, drug accumulation and frequency

The adjunctive use of local delivery of drugs may enhance the results in isolated periodontal pocket sites that do not respond to conventional therapy (8). Purucker et al., (1994) compared “the clinical response of local versus systemic treatment as adjuncts to scaling and root planing and observed that local delivery of tetracycline fibre and the systemic administration of amoxicillin/clavulinate given for 3 months after scaling and root planing produced similar clinical outcomes over the 9-month observation period”. Newman et al., (1994)in their evaluation study to “compare the efficacy of scaling and root planing (SRP) alone versus SRP plus adjunct therapy with tetracycline fibre observed that SRP plus adjunct therapy was more effective in the treatment of periodontitis”. Kinane et al., (1999) compared the effectiveness of three periodontal local antimicrobial therapies: scaling and root planing alone, in conjunction with 25% tetracycline, 2% minacycline gel or 20% metronidazole gel and observed that application of three locally applied antimicrobial systems offered benefits and also that tetracycline gave the best effect.

Curcumin (diferuloylmethane), the main bioactive component of turmeric, is reported to have anti-inflammatory (12-14), antioxidant (15 - 18), antiallergic, anticarcinogenic, antimutagenic, anticoagulant, antidiabetic, antibacterial, antiprotozoal, antifungal, antiviral, antiulcer,

hypotensive and hypocholesterolemic activities (19-20). Kudva et al., (2012) in a comparative study on "the adjunctive efficacy of turmeric, curcumin and traditional nonsurgical methods for treating periodontal pockets found that plaque index and gingival index showed significant improvement in curcumin treated group". Several authors have recommended the local delivery of curcumin as an adjunct therapy in the treatment of chronic periodontitis (22-24).

Materials and Methods

Thirty patients in the age group 30 – 55 years attending the Department of Periodontics, PSM College of Dental Science & Research with chronic periodontitis having periodontal pocket depths of 5 – 8 mm after scaling and root planing were selected for the study.

Selection criteria:

Inclusion Criteria: Patients in the age group 30 – 55 yrs with chronic periodontitis having periodontal pocket depths of 5 – 8 mm after scaling and root planning and who were willing to take part in the study were included.

Exclusion Criteria : Patients with medically compromised conditions, on antibiotics within 6 months prior to the study, who have undergone periodontal therapy in past 6 months, who were pregnant/lactating mothers and those reported to have any form of allergy to tetracycline or curcumin were excluded.

Sample size Calculation:

$$n = 2\left[\frac{(Z1+Z2)\times sd}{d}\right]^2$$

$$n = 2\left[\frac{(2.8)\times 0.81}{0.5}\right]^2$$

$$=41.15$$

$$\cong 40 \text{ in each group}$$

Z1= constant at 95% confidence interval Z2 = constant at 80% power

sd = standard deviation from parent article d = clinically significant difference

A total of 80 sites (40 sites for each group) were included for evaluating the effectiveness of curcumin gel and tetracycline fibers. The sites were grouped as follows:

Group A: Application of curcumin gel – 40 sites

Group B: Application of tetracycline fibers – 40 sites

Tetracycline fibres were soaked and placed into the pocket with the help of a tweezer and periodontal probe was used to insert into periodontal pocket with gentle pressure. Curcumin gel was applied directly from a disposable syringe into the pocket without traumatizing or

damaging the periodontal tissue. After insertion of the dug locally, the region was secured with Coe-pak™ (GC American Inc, USA.)

The clinical parameters: Plaque index, Oral hygiene index, Gingival index, Probing pocket depth, and Clinical attachment level were assessed using the techniques employed by Newman et al., (2002). Clinical parameters were assessed before starting the therapy and recorded as baseline values. All patients were refrained from chewing hard and sticky food, flossing on the treated side and not to disturb the area with tongue, finger or tooth pick. For the removal of coe-pak the participants were recalled after 1 week. Clinical parameters were reassessed at 30 days and 90 days and recorded.

Statistical analysis: Data obtained were analysed using IBM SPSS-23 software. Statistical comparisons were performed using students ”t” test.

Results

Gingival index: Mean gingival index showed significant decrease ($p<0.001$) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days. The results obtained are represented in Table 1.

Table 1: Gingival index values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis.

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	2.03 ±0.16	1.02 ±0.15*	1.02 ±0.15^{ns}
Tetracycline	40	2.15 ±0.18	1.04 ±0.14*	1.04 ±0.14^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent ‘t’ test was performed to calculate p value.

*Significant P <0.001., ns: Not significant

Oral hygiene index: Mean oral hygiene index values showed significant improvement ($p<0.001$) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated groups. The results are depicted in Table 2.

Table 2: Oral hygiene index values in curcumin gel and tetracycline fibres treated patients with chronic periodontitis.

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	1.08 ±0.27	0.08 ±0.01*	0.08 ±0.01^{ns}
Tetracycline	40	1.05 ±0.22	0.05 ±0.01*	0.05 ±0.01^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value.

*Significant P <0.001., ns: Not significant

Plaque index: Mean plaque index showed significant decrease (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated group. The results are given in Table 3.

Table 3: Plaque index values in curcumin gel and tetracycline fibres treated patients with chronic periodontitis.

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	1.98 ±0.36	0.98 ±0.15*	0.98 ±0.15^{ns}
Tetracycline	40	2.05 ±0.32	1.05 ±0.22*	1.05 ±0.22^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value.

* Significant P <0.001., ns: Not significant

Probing pocket length:

Mean probing pocket length showed significant improvement (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated groups. The results are depicted in Table 4.

Table 4: Probing pocket depth values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis.

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	5.10±0.30	4.28±0.51*	4.28±0.51^{ns}
Tetracycline	40	5.05 ±0.22	3.78±0.53*	3.73±0.55^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value.

*Significant P <0.001., ns: Not significant

Clinical attachment level: Mean clinical attachment level showed significant improvement ($p<0.001$) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated groups. The results are given in Table 5.

Table 5: Clinical attachment level values in curcumin gel and tetracycline fibres treated patients with chronic periodontitis.

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	2.03 $\pm$0.16	1.02 $\pm$0.15*	1.02 $\pm$0.15^{ns}
Tetracycline	40	2.15 $\pm$0.18	1.04 $\pm$0.14*	1.04 $\pm$0.14^{ns}

Values are expressed as mean $\pm$ SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value.

*Significant P <0.001., ns: Not significant

Discussion

"Periodontitis is a biofilm associated disease and are difficult to treat with antibiotics unless biofilm is disrupted mechanically. Chronic periodontitis develops as a result of host-bacterial interaction in which the pathogens produce harmful byproducts that initiate host immune inflammatory responses leading to the breakdown of extracellular matrices and bone resorption, creating bone defects eventually leading to tooth loss" (27). "It is characterized by the presence of gingival inflammation, periodontal pocket formation, clinical attachment loss and development of osseous deformities around the affected teeth. Scaling and root planning (SRP) in conjunction with antibacterial agents were administered either systemically or locally" (28). However, systemic administration has been found to be associated with side effects and local delivery of drugs was found more beneficial (28,29). "SRP with adjunctive chlorhexidine chips showed better clinical outcomes than SRP alone for the management of periodontal pockets in patients with chronic periodontitis" (30,31).

In this study, effort has been made to compare the effectiveness of two commercially available local delivery agents – curcumin gel (curenext - an ayurvedic drug) and tetracycline fibres (Periodontal plus AB - an allopathic drug) in treating chronic periodontitis. Kataria et al., (2015) applied "tetracycline fibers as an adjunct to scaling and root planing and found it to be very effective in reducing gingival and periodontal inflammation". "A Tetracycline-Serratiopeptidase- a combination gel of tetracycline and serratiopeptidase was investigated" by Maheshwari et al., (2006) and observed that the formulation had shown statistically significant results along with mechanical debridement. Sachdeva and Agarwal (2011) made "tetracycline in the form of a modified collagen matrix and used along with scaling and root planing. They concluded that there was significant probing pocket depth reduction and

gain in clinical attachment for the SRP plus tetracycline group compared to SRP alone".

Newman (2015) reported that "adjunctive curcumin showed better improvement in the reduction of gingival inflammation and bleeding. The mechanism of periodontal disease involves the production of several inflammatory mediators. Periodontal pathogens activate NF-κB, Janus kinase (JAK) signal transducer, activator of transcription (STAT), mitogen-activated protein kinases (MAPK), and other signaling pathways and produce inflammatory cytokines such as IL-6, TNF-α and IL-1β to promote inflammation" (37). "Curcumin, the active ingredient in turmeric, has various anti-inflammatory properties and may delay the disease process of periodontal disease in its initial stages. It has been shown to suppress the NF-κB pathway in human gingival fibroblasts in early stages and thus may inhibit *P. gingivalis* LPS-induced COX-2 synthesis" (38) and "the production of TNF-α, IL-8 and IL-6 by inhibiting NF-κB activation in mast cells" (39). "Additionally, curcumin could exert an anti-inflammatory effect by directly inhibiting the JAK/STAT signaling pathway and phosphorylation of p38 MAPK, thereby reducing the expression of iNOS, COX-2, monocyte chemoattractant protein-1 (MCP-1), and intercellular adhesion molecule-1(ICAM-1) to reduce the inflammatory response" (40,41).

In the present study statistically significant improvements were observed in all the clinical parameters (oral hygiene index, gingival index, plaque index, probing pocket depth and clinical attachment level) measured at 30 days compared to the values at baseline level, the response being slightly better in the case of tetracycline treated group. No difference was observed when the values at 90 days were compared with those at 30 days. The findings were in agreement with earlier studies (23,27,28).

In this study microbial evaluation was not carried out. Long term studies with a large sample size are required to further assess the clinical efficacy of both local delivery dugs.

Conclusion

Though scaling and root planing (SRP) alone is efficient in managing chronic periodontitis, superior results can be obtained by employing topically delivered tetracycline fibres and curcumun gel. It may be concluded that tetracycline fibres (PeriodontalPlus AB) and curcumin gel (Curenext) can be used as adjuncts to scaling and root planing in the treatment of chronic periodontitis. Application of both agents showed significant beneficial effects, but tetracycline showed slightly better effect. The more beneficial effect of tetracycline may be due to the property of substantivity exhibited by this drug. Curcumin being an ayurvedic drug with little or no side effects can be an excellent alternative to tetracycline in treatment of chronic periodontitis.

ETHICAL APPROVAL:

Ethical clearance was obtained for the study from the Institutional ethics committee (No.17/Ethics/PSMCDSR/2018 dt. 04/12/2018).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

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