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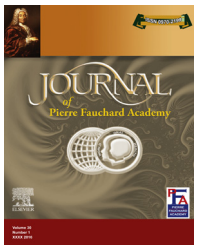

Clinical evaluation of thermoresponsive and mucoadhesive chitosanin situ gel containing Levofloxacin and Metronidazole in the treatment of periodontal pockets – A split-mouth, clinical study

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ABSTRACT

Objectives: Recently, mucoadhesive formulations have become popular as drug delivery for periodontal pocket and oral mucosa. The objective of this study was to evaluate the clinical efficacy of thermoresponsive and mucoadhesive chitosan in situ gel in treatment of chronic periodontitis.

Methods: Vehicle and medicated in situ gel containing Levofloxacin and Metronidazole was applied in ten systemically healthy subjects (20–50 yrs) with chronic periodontitis adjunctive to scaling and root planing (SRP) in comparison to SRP alone. Clinical parameters were plaque index (PI), gingival index (GI), and bleeding on probing (BoP), which were recorded at baseline and 15th, 30th, 60th, and 90th days, as well as probing pocket depth (PPD), clinical attachment level (CAL), and gingival recession (GR), which were recorded at baseline and 30th, 60th, and 90th days.

Results: The results suggested that changes in clinical parameters were significant from baseline for all groups on the 90th day. On the 90th day, PI was 0.7 ± 0.48, 0.4 ± 0.51, and 0.3 ± 0.48; GI was 0.6 ± 0.051, 0.5 ± 0.52, and 0.3 ± 0.48; BoP was 0.5 ± 0.52, 0.3 ± 0.48, and 0.2 ± 0.42; PPD reduction was 2.5 ± 0.52 mm, 3.4 ± 0.69 mm, and 4.6 ± 0.51 mm; CAL gain was 1.2 ± 0.42 mm, 2.6 ± 0.84 mm, and 3.8 ± 0.42 mm; and GR was 1.1 ± 0.73 mm, 1.0 ± 0.00 mm, and 0.5 ± 0.52 mm for SRP, vehicle, and medicated in situ gel groups, respectively. Reduction in PPD and gain in CAL was also significant after comparison between the treatment groups.

Conclusion: Vehicle and medicated in situ gel showed better clinical outcomes as compared to SRP alone, which could be attributed to the presence of chitosan that is not only effective in treatment of periodontitis but also acts as a good carrier to deliver drug into periodontal pockets.

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1. Introduction

A healthy periodontium is mandatory to prevent the loss of teeth as well as to minimize the risk of certain systemic diseases through periodontal infections. With the advancement in science and technology, evidences are there that periodontitis acts as a risk factor for the systemic diseases directly or indirectly.[1] Periodontitis is caused by a wide diversity of microorganisms including the gram +ve, gram −ve, facultative anaerobic, microaerophilic, obligate anaerobic, cocci, rods, and spirochetes. Antimicrobial therapy acts as an adjunct to the scaling and root planing (SRP) with the aim to inhibit the growth or kill the periodontopathic microorganisms in various situations like inapproachable sites such as invasion of bacteria into the dentin, cementum, alveolar bone, connective tissue, aggressive periodontitis, moderate-to-severe chronic periodontitis, refractory periodontitis, and periodontitis as a manifestation of systemic diseases. Periodontitis is a mixed infection; therefore, combination therapy is preferred over the single agent to eliminate the pathogens because a single agent fails to eliminate all pathogenic microorganisms from the deep periodontal pockets.[2–5]

Metronidazole (MZ), a nitroimidazole derivative, has been widely used for the treatment of periodontal disease and is the drug of choice because it has selective antibacterial efficacy against obligate anaerobes and exhibits good concentration in serum as well as in gingival crevicular fluid (GCF).[6–8] Levofloxacin (LVF), a fluroquinolone, is an active isomer of ofloxacin, which is active against both aerobic gram-positive and gram-negative organisms and facultative anaerobic bacteria.[9–11]

Bioavailability of drug in GCF, which is administered systemically, is low and requires a higher dose for it to be effective and is associated with inherent side effects. Direct application of drug into the periodontal pocket increases the bioavailability of drug, but its concentration is rapidly reduced due to constant GCF flow and it is estimated that GCF is 40 times replaced in a hour.[12] Local drug delivery is known as site-specific therapy and subgingival application of drug needs a vehicle and a limiting agent, which increase the substantivity of the drug for prolonged action. The ideal requisite for the local drug delivery should be biocompatible, biodegradable, mucoadhesive, nonallergenic, and release of the drug in a controlled manner.

Chitosan is a natural mucoadhesive polysaccharide obtained from the deacetylation of exoskeleton of crustaceans, e.g. shrimps, crabs, and lobsters. Chitosan is the material of choice as a controlled drug delivery vehicle in biomedical application because it can be formulated into various forms like film, gel, beads, sponges, microparticle, nanoparticle, solutions, fiber, and membranes, and it is also known for its various biological properties: mucoadhesive, biocompatible, biodegradable, antibacterial, wound healing, nontoxic, economical, and widely distributed in nature.[13,14]

Subgingival delivery can be done in film, fiber, injectable gel, in situ gel, strips, microparticle, and nanoparticle form. In our previous study, chitosan-based film cross-linked with gluteraldehyde having LVF, and MZ was formulated with solvent casting method that exhibited sustained release up to 7 days, good antibacterial activity, and decreased clinical parameters in subjects with periodontitis.[15] In situ gel has the property to change in its physical state from sol to gel at the inserted site and does not come back due to its semisolid nature. The objective of this study was to evaluate the clinical efficacy of thermoresponsive, and mucoadhesive chitosan in situ gel in the treatment of chronic periodontitis.

2. Materials and methods

This study was a randomized, split-mouth and vehicle-controlled study. This was approved from the Institute Ethical Committee of Banaras Hindu University, Varanasi, India. Before starting the study, a written informed consent was obtained from each subject after explaining about the nature of the study. In this study, the treatment was provided by one investigator, and the all measurements were recorded by another investigator who was blinded to the treatment given.

2.1. *Study design*

This clinical study was performed in Faculty of Dental Sciences, IMS, BHU, Varanasi, Uttar Pradesh, India. 10 volunteer subjects with chronic periodontitis (20–50 yrs) of either sex were recruited from the outpatient department. The subjects were examined for a sign of chronic periodontal disease, based on inclusion and exclusion criteria. The inclusion criteria were as follows: (1) good general health and free from systemic disease; (2) subjects suffering from chronic periodontitis with pocket depth ≥5 mm (Figs. 1a, 2a and 3a) and having bleeding on probing (BoP) from base of the pocket; (3)

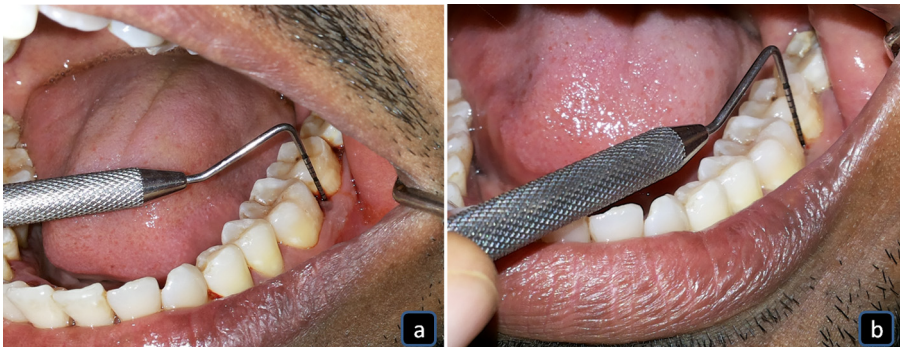

Fig. 1 – (a) Preoperative and (b) postoperative periodontal pocket depth in the scaling and root planing group.

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