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Clinical efficacy of subgingivally delivered 0.5% controlled release clarithromycin gel in the management of chronic periodontitis

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ABSTRACT

Background: Main indication of adjunctive use of local antimicrobials lie around situations where the outcome of non-surgical mechanical treatment results in limited number of residual pockets. Purpose of this investigation was to evaluate clinical effect of subgingival application of 0.5% clarithromycin gel adjunctive to scaling and root planing (SRP) in management of localized chronic periodontitis.

Materials and method: Thirty sites in patients with chronic periodontitis were categorized randomly into two treatment groups: Scaling and Root Planing (SRP) plus 0.5% clarithromycin gel and SRP only. Clinical evaluation was undertaken using gingival index of Loe and Silness and plaque was assessed using the Turesky et al modification of Quigley Hein Index at baseline, 15 days and 1 month. Pocket probing depth and clinical attachment level were also measured using customized acrylic stents.

Result: Both therapies resulted in significant clinical improvements. Gingival index, probing depth and relative attachment level showed significantly better reduction in CLM group than in the control group. Plaque index also reduced in both the groups but the difference was not statistically significant between the groups.

Conclusion: Although both treatment strategies seem to benefit patients, the adjunctive use of 0.5% clarithromycin showed significant results with respect to clinical parameters.

1. Introduction

Periodontal disease is a general term which encompasses several pathological conditions affecting the tooth supporting structures. It includes conditions such as chronic periodontitis, aggressive periodontitis, systemic disease-associated periodontitis and necrotizing periodontitis.[1] It has been well-established that periodontal disease is the result of a local bacterial infection with a pathogenic microflora within the periodontal pocket. The microflora found in periodontitis is complex and composed mainly of gram negative anaerobic bacteria.[2] Moreover; studies have shown that the various clinical forms of periodontitis are associated with different microbiota.[3]

Traditional therapies for periodontal disease have included mechanical debridement to disrupt the subgingival flora and provide clean, smooth and biologically compatible root

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surfaces. Unfortunately, in some instances, the complex anatomy of the root and the contours of the lesion may hamper the treatment and prevent sufficient reduction of the bacterial load to make the tooth surface biologically acceptable. In addition, control of supragingival plaque is essential in order to prevent recolonization of the subgingival area by periodontal pathogens.[4] Poor supragingival and subgingival debridement and inadequate home care regimen leads to reestablishment of a pathogenic subgingival microflora and an associated rebound in the disease may occur in local sites.[5]

Anti-infective therapy, which combines both mechanical therapy and chemotherapeutic approaches to minimize bacteria, may be more effective in these cases.[6] Chemotherapeutic agents include systemic antibiotics, topical application of antiseptics and sustained release local drug delivery systems. However, systemic antimicrobials pose more side effects when compared to local chemotherapeutic approaches.[7]

Goodson, Haffajee and Socransky, in 1979,[8] first proposed the concept of controlled local drug delivery in the treatment of periodontitis. Local delivery of chemotherapeutic agents into the pockets, via syringe or irrigating device aims at targeting an anti-infective agent at the infection site and sustaining its localized concentration at the effective levels for a sufficient time, while concurrently evoking minimal or no side effects.

Controlled drug delivery is one which delivers the drug at a predetermined rate, for a predetermined period of time.[9] Many antimicrobials can be used in local drug delivery forms as Tetracycline fibers, Metronidazole, Minocycline ointment and chlorhexidine chip and doxycycline hyclate in bioabsorbable polymer. Penicillin and tetracycline derivatives have good efficacy, but the growing phenomenon of bacterial resistance and the induction of hypersensitivity reactions represent a serious limit to the use of these drugs.[10]

Another antibiotic that can be used as an adjunct to periodontal therapy is clarithromycin. Clarithromycin (CLM) is a macrolide antibiotic that inhibits protein synthesis by binding to the 23S ribosomal RNA in the 50S subunit of the bacterial ribosome. It possesses a broad antimicrobial spectrum, favorable tissue distribution, and a low incidence of adverse side effects.[11] Unlike many antibiotics, CLM readily penetrates cells to gain access to intracellular pathogens. It is highly effective against *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* and exhibits good activity against *Eikenella corrodens*, Prevotella sp., Fusobacteria, and other anaerobic and facultative pathogens.[12]

Recently, Pradeep et al (2011)[13] demonstrated that systemic utilization of CLM in combination with Scaling and Root planing (SRP) improved the efficacy of non-surgical periodontal therapy in reducing probing depth, improving clinical attachment level and in lessening microbial loads.

Thus, the present study was designed to investigate the clinical efficacy of subgingivally delivered 0.5% controlled release clarithromycin gel in the management of chronic periodontitis.

2. Materials and method

This double masked, randomized clinical trial was conducted in Department of Periodontology and Oral Implantology, I.T.S Dental College, Muradnagar, Ghaziabad. Ethical committee approval was obtained. All subjects were verbally informed and written informed consent was taken for participation in the study. One examiner recorded all indices.

2.1. Selection of subjects

Patients (15 in each group) in the age group of 25–40 years were selected from the Out-patient Department of Periodontology and Oral Implantology, I.T.S. Centre for Dental Studies and Research, Muradnagar, Ghaziabad, UP. A total of 30 patients suffering from chronic periodontitis were recruited and were allocated randomly into two groups.

Test group included the patients in which 0.5% CLM gel was placed along with SRP. In the control group, only SRP was done.

2.2. Inclusion criteria

- Patients were over the age of 25 years.
- Patients with at least one site with pocket probing depth (PD) 4–6 mm in posterior teeth were selected.

2.3. Exclusion criteria

- Allergy to macrolide antibiotics.
- Patients who were suffering from any known systemic diseases or immunocompromised.
- Patients who had received any surgical or non-surgical therapy 6 months prior to the start of the study.
- Patients who had received any antibiotic therapy in the last 6 months.
- Tobacco users and alcoholics were excluded.
- Pregnant and lactating females were also not included in the study.

2.4. Preparation of clarithromycin gel

The CLM gel was prepared as described by Shah et al.[14] The gel was prepared at Guru Nanak Institute of Pharmacy, Ibrahimpatnam, Hyderabad. Accurately weighed amount of poly lactic-co-glycolic acid (PLGA) was placed in glass vial and the required amounts of biocompatible solvents were added. The vial was heated to 60° and agitated using a mechanical shaker to obtain a clear solution. Weighed amount of CLM was added to the above polymer solution and dissolved completely to obtain homogeneous phase of polymer, solvent, and drug.

The formulation constituents for CLM *in situ* gel were N-methyl-2-pyrrolidinone as the biocompatible solvent and PLGA copolymer in a ratio of 75:25 with a molecular weight of 72,000 (72 kd) and a microenvironment of pH of 7.4.

The study subjects were randomly assigned to either CLM or control group. Clinical parameters, i.e., Plaque Index (PI)[15] (Turesky-Gilmore-Glickman modification of Quigley Hein PI, 1970) and Gingival Index (GI)[16] (Loe and Silness, 1963) were recorded for all patients. Pocket PD and clinical attachment level (CAL) were assessed in the selected sites using a custom made stent and University of North Carolina-15 periodontal probe (UNC-15, Hu-Friedy, Chicago, IL) probe to standardize all measurements.