IN VITRO, CLINICAL AND IMMUNOCHEMICAL EVALUATION OF A LOCAL DRUG DELIVERY SYSTEM DOXYCYCLINE HYCLATE IN THE MANAGEMENT OF SEVERE CHRONIC PERIODONTITIS

Ghada A.Mansour and Shahira A. El –Domiaty *

ABSTRACT

The purpose of this study was to evaluate in vitro, clinically and immunochemically the effectiveness of two doxycycline gel formulations based on chitosan (Ch) and pluronic (Pl) polymers in management of moderate to severe chronic periodontitis cases. 25% Doxy Pluronic gel and 2% Doxy chitosan gel were prepared in faculty of Pharmacy, Alexandria University. They were submitted to an in vitro study ,including evaluation of their viscosity , injectability, Doxy drug release and gel dissolution. Pl changed into stiff gel at temperature around ~21°C. Change of pH from 4.4 to physiological pH, and changes in Ch solubility did not influence its viscosity . The injectability results showed that Pl was expelled from the syringe under the influence of a weight < 2kg; whereas the Ch gel needed about 3.7 kg. Release from Pl 25% gel formula indicated drug release of ~18% after 1 hour, and ~26% after 7 hours. Cumulative Doxy release profile from Ch was about 30% after 1 hour and 48% after 7 hours. Ch dissolution profile showed initial lag period followed by slow dissolution in the first 4 hours. Ch 2% revealed significantly higher %dissolution efficiency than Pl 25%, (36.77% and 20.93% respectively).The clinical and immunochemical studies were conducted on 15 patients with moderate to severe chronic periodontitis. 45 matched pockets in these patients (3 in each patient) located anteriorly on single rooted teeth constituted the study sample. All patients received scaling and root planning. Qualifying defects were randomly assigned as either receiving subgingival chitosan based Doxy gel, pluronic based Doxy gel or placebo gel. At baseline, 6 weeks and 3 months post-therapy, clinical evaluation included plaque scores (PI), papillary bleeding scores (PBI), probing depth (PD), and clinical attachment level (CAL).Post treatment results showed a significant improvement in all studied variables at 6 weeks and 3 months when compared to baseline in terms of plaque index reduction (PIR), papillary bleeding reduction (PBIR), pocket depth reduction (PDR),and gain in attachment levels (ALG), except for placebo group that did not show significant ALG post therapy. Intergroup data analysis showed significantly better results in Doxy groups when compared to placebo group, with chitosan treated sites manifesting the best clinical improvement.For the immunochemical study, GCF samples were withdrawn from treated sites and were evaluated using ELISA for crevicular elastase level. For all patients, GCF elastase decreased significantly following therapy, with Doxy groups revealing

* *Assistant Professor of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Alexandria University.*

statistically significant reduction in comparison to placebo group, and chitosan treated sites having significantly decreased elastase level than pluronic treated sites. In conclusion, both chitosan and pluronic showed promising results as polymers used for controlled release intra-pocket doxycycline therapy, both in vitro, clinically and immunochemically.

INTRODUCTION

It is well established that periodontal disease is the result of a local bacterial infection by a pathogenic microflora within the periodontal pocket. Moreover, it has been shown that only pockets of less than 3 mm in depth can be maintained plaque-free by home care, and that regular professional non-surgical care can maintain the stability of deeper pockets over the years. [1]

The treatment strategy of chronic periodontitis is focused on reducing to an acceptable level, and preferably eradicating the periodontal pathogens. Currently, the most common therapy for periodontal inflammatory diseases consists of repeated

professional supra- and subgingival plaque and calculus removal (scaling and root planning: SRP) . However, after non-surgical therapy, several deep periodontal pockets may persist, and in such a case, the treatment consists of surgery. [2]

Adjunctive antimicrobial and chemo-therapeutic agents may be necessary to control the disease process . They can be administered by a variety of routes broadly defined as local or systemic.[3]

Systemically applied antimicrobials have been advocated for the treatment of severe forms of periodontitis. Indeed, side effects including hypersensitivity, gastrointestinal intolerance, decreased patient's compliance, and the development of bacterial resistance have been described. [4] Some studies also reported poor results due to the fact that the active product could not achieve an adequate concentration at the site of action and/or due to the inability of the active product to be retained locally for a sufficient period of time. These drawbacks would be markedly reduced if antimicrobial agents applied locally could be used.[5]

Drugs administered locally have the advantage of providing higher concentration of medication to the target site, with limitation to adverse effects of systemic administration. A constant high concentration of the antibiotic in the crevicular fluid increases the possibility of eliminating or at least disrupting the periodontal plaque for a longer period of time.[6]Gels and semi-solid formulations are currently receiving much interest as drug delivery vehicles for their ability to reach deeper area in the periodontal pocket .[7]The local delivery devices used in periodontology can be divided into two classes according to the duration of drug release: sustained-release devices (drug delivery for less than 24 hours) and controlled delivery devices (drug release exceeding 1 day). [8]

Tetracycline, doxycycline and minocycline are used extensively in the management of periodontal diseases. They are bacteriostatic antibiotics that interfere with bacterial protein synthesis and also inhibit tissue collagenase activity. They have a broad spectrum of activity inhibiting both Gram negative and Gram positive organisms, including the beta-lactamase producing strains which occur in approximately 50% of 6-7 mm deep periodontal pockets, and against which penicillins are ineffective. At high concentrations, such as