

## CLINICAL EFFICACY OF BIODEGRADABLE DENTAL IMPLANTS OF TINIDAZOLE IN PERIODONTITIS

R. NAGARAJU<sup>1</sup>, N. UDUPA\*, JACOB MATHEW<sup>2</sup> AND B. R. R. VARMA<sup>3</sup>

<sup>1</sup>*Visveswarapura Institute of Pharmaceutical Sciences, BSK II Stage, Bangalore - 560 070,*

*\*College of Pharmaceutical Sciences, Manipal - 576 119,*

<sup>2</sup>*College of Dental Surgery, Manipal - 576 119 and*

<sup>3</sup>*Yenapoyya College of Dental Sciences, Mangalore*

( Received on October 6, 1998 )

**Abstract :** Dental implants of tinidazole were formulated using poly ( $\epsilon$ -caprolactone), a biodegradable polymer and evaluated. Clinical evaluation was carried out in ten patients with acute periodontitis. Various clinical parameters viz., gingival index, plaque score, attachment gain, reduction in pocket depth were evaluated after 10, 20, 30 and 40 days of treatment and compared with placebo as control. There was significant improvement in the healing of periodontal pockets treated with tinidazole implants as compared to the control sites. Estimation of tinidazole in gingival crevicular fluid (GCF) revealed that the drug levels above the minimum inhibitory concentration (5.9  $\mu\text{g}/\text{mg}$ ) for many of the periodontal pathogens was maintained throughout the period of study (40 days). This confirms the clinical efficacy of the dose and the duration of the study. It was found that biodegradable carrier was better accepted than the non-biodegradable carriers reported earlier.

**Key words :** biodegradable                      tinidazole                      dental implants

### INTRODUCTION

Periodontal disease is a localised infection with a primary bacterial etiology. The conventional treatment is root planning and scaling along with high doses of antibacterial agents for longer periods of time to achieve sufficient concentration in gingival crevicular fluids (GCF). This might result in undesirable side effects such as gastrointestinal disorders, over growth of fungal microorganisms, development of

resistant bacterial strains, superinfection etc. (1, 2). Keeping in view, the disadvantages of the conventional oral antibiotic therapy, a sustained release, cost effective, potent and biodegradable local drug delivery device is developed and evaluated.

Dental implants of antiinfective agents in hydroxypropyl methylcellulose, ethylcellulose and other non-biodegradable polymers have been reported (3-7). The main disadvantages of these implants

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\*Corresponding Author

include need for surgical removal of the polymer strip at the end of the therapy and patient non-compliance. To overcome these problems a biodegradable polymer, poly ( $\epsilon$ -caprolactone) was used in the present study.

## METHODS

*Preparation of Dental Implants:* Poly ( $\epsilon$ -caprolactone) (900 mg) was weighed and dissolved in minimum quantity of dichloromethane (DCM). Tinidazole (60 mg) and carbopol (974P NF) (180 mg) were dispersed uniformly by using sonicator. The resultant viscous mass poured into a glass mould of 5 × 3 cm size lined with aluminium foil. DCM wall allowed to evaporate at room temperature. The dried film was then cut into 0.5 × 0.5 cms size. Each film contains 1 mg of the drug. The drug, carbopol and polymer ratio was 1:3:15 respectively. Various physicochemical properties viz., size (length and breadth), thickness, content uniformity and weight variation test were performed on the prepared implants. The drug content uniformity and weight variation were found to be within the limits of  $\pm 5\%$ .

*Clinical studies:* Ten patients with deep periodontal pockets who visited College of Dental Surgery, KMC, Manipal were selected. Patients with any systemic disease were excluded. The informed consent was obtained and the protocol was approved by Ethical Committee of Kasturba Hospital, Manipal.

After collecting subgingival plaque, one implant with the drug was placed in the experiment pocket (test site) while another

implant without drug was kept in the control pocket. The implants were retained in the pockets without any sutures or periodontal dressings. The patients were asked to continue the oral hygiene procedures.

Gingival index, probing depth, attachment gain and microbiological examinations were evaluated on 10th, 20th, 30th and 40th day as described by Loe et al (8, 9).

Gingival crevicular fluid (GCF) was collected by placing a filter paper disc of 6 mm diameter. The drug present in the GCF was extracted with 5 ml of isotonic phosphate saline (pH 7.2). The drug content was estimated by measuring absorbance at 316 nm by Shimadzu UV/Visible Spectrophotometer (10).

The statistical significance of the data between the groups as well as within the group were analysed using ANNOVA (PAD STAT, Copy right © 1990 software package).

## RESULTS

The mean reduction in gingival index scores at the tinidazole treated sites were 0.93, 1.45, 1.52 and 1.50 at 10, 20, 30 and 40 days respectively, whereas at the control sites it was 0.88, 1.15, 1.15 and 1.13 (Table 1).

The mean plaque scores at tinidazole treated sites and control sites were 0.32, 0.42, 0.53 and 0.53 whereas at control sites these were 0.35, 0.47, 0.58 and 0.63 at 10, 20, 30 and 40 days (Table I).

TABLE I : Clinical parameters.

Clinical parameters	Days of treatment							
	10th day		20th day		30th day		40th day	
	Control	Test	Control	Test	Control	Test	Control	Test
Gingival index	0.88±0.24	0.93±0.12	1.15±0.38	1.45±0.16	1.15±0.34	1.52±0.18*	1.13±0.32	1.50±0.17*
Plaque score	0.35±0.21	0.32±0.24	0.47±0.07	0.42±0.12	0.58±0.12	0.53±0.18	0.63±0.13	0.53±0.18
Gain in attachment	0.33±0.33	1.50±0.41***	0.68±0.29	2.00±0.35***	0.87±0.17	2.13±0.21***	0.90±0.20	2.15±0.20***
Reduction in pocket depth	1.63±0.55	2.24±0.41**	2.02±0.50	2.76±0.48***	2.04±0.53	2.49±0.92**	2.05±0.53	2.82±0.49**

Statistical significance: Test vs. Control \*P<0.05, \*\*P<0.01, \*\*\*P<0.001

The mean gain in attachment levels at the experimental site were 1.50 mm, 2.00 mm, 2.13 mm and 2.15 mm whereas at control sites these were 0.33 mm, 0.68 mm, 0.87 mm and 0.90mm at 10, 20, 30 and 40 days respectively (Table I). The mean reduction in pocket depth of drug treated sites were 2.24 mm, 2.76 mm, 2.49 mm and 2.82 whereas at control sites these were 1.63 mm, 2.02 mm, 2.04 mm and 2.05 mm (Table 1). The mean GCF concentration of drug in the experimental group was  $9.36 \pm 0.43$  µg/mg,  $7.89 \pm 0.688$  µg/mg,  $6.81 \pm 0.53$  µg/mg and  $5.89 \pm 0.84$  µg/mg at 10, 20, 30 and 40 days respectively. The mean salivary drug concentration was  $2.80 \pm 0.52$  µg/mg,  $2.32 \pm 0.45$  µg/mg,  $1.65 \pm 0.23$  µg/mg and  $0.75 \pm 0.18$  µg/mg at 10, 20, 30 and 40 days.

## DISCUSSION

The knowledge that specific bacteria are associated with chronic adult periodontitis provides a rationale for the use of antibiotics as adjunctive therapy to scaling and root planning. Theoretically, the addition of a

chemotherapeutic agent should effectively eliminate the bacteria harboured at the bottom of deeper pockets *on in* dentinal tubules which can not be removed with mechanical treatment. Slow releasing devices which have the capacity to release the drug for a prolonged period of time and maintain the effective concentration of drug within the periodontal pocket will naturally be more effective in periodontal therapy.

Poly ( $\epsilon$ -caprolactone) controlled release devices developed in the present study were found to be capable of releasing tinidazole in quantities above that of the minimum inhibitory concentration (4 µg/ml) for a period of 40 days (11, 12, 13). Carbopol used in the preparation of film improves the adhesiveness of the implant due to swelling in aqueous environment thereby negating the use of the mechanical retention aids or periodontal packs to support the implant in the periodontal pocket. The low drug concentration in saliva as observed is desirable to prevent development of bacterial resistance.

The present clinical study in ten patients with periodontitis demonstrated that administration of tinidazole controlled release drug implants into periodontal pockets deeper than 5 mm following removal of supragingival surface deposits was more effective in improving various clinical parameters when compared to control sites where placebo inserts were placed. Similarly studies were carried out by Dollet et al (1995) for dental implants containing ciprofloxacin and norfloxacin in non-biodegradable polymer, ethylcellulose. These dental implants had shown significant

improvement of various clinical parameters (4).

The development of tinidazole release implants using biodegradable polymer may offer significant therapeutic advantage in the treatment of isolated deep pockets which do not respond to conventional antimicrobial therapy. As the polymer used was biodegradable, there is no need of surgical removal of the polymer strip at the end of the treatment. However, more detailed study is required to fully establish this therapeutic modality.

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