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ORIGINAL ARTICLE **OPEN ACCESS**

Evaluation and Comparison of Bone Mineral Density and Stability at Bone Implant Interface with and without 1% Metformin gel- A Pilot study

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ABSTRACT
Since the early 1970s, when dental implant retained prostheses were available, patient care has undergone a radical change. However, Osseo integration with good primary and secondary stability must be attained and maintained for the implant to be successful over the long term. Metformin (MF), an oral anti-hyperglycemic medication, is frequently administered. for managing type 2 diabetes which may have the ability to control osteoblast differentiation, hence increasing and promoting osseointegration. This study aims to evaluate the osseointegration around dental implants covered with 1% metformin gel clinically and radiographically, using resonance frequency analysis (OSSTELL® Device) and bone mineral density. A total of 10 (5 control group -5 experimental group) healthy patients with at least one tooth missing in premolar or molar region desirous of Dental implant placement will be selected.The sites will be divided into 2 groups-Group 1 - will consist of 5 patients receiving dental implants in premolar and molar region coated with 1% metformin gel. Group II - will consist of 5 patients receiving dental implants in premolar and molar region without coating of 1% metformin gel. 1% Metformin Gel demonstrated greater improvement in the osseointegration around bone-implant interface achieved at all-time intervals.
Key words: *Osseointegration, dental implants, RFI, ISQ*

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INTRODUCTION

Since the early 1970s, when dental implant retained prostheses were available, patient care has undergone a radical change. However, Osseo integration with good primary and secondary stability must be attained and maintained for the implant to be successful over the long term. Metformin (MF), an oral anti-hyperglycemic medication, is frequently administered. for managing type 2 diabetes. It has been demonstrated that this medication controls osteoblast activities by AMP-activated protein kinase (AMPK)[1] This shows that MF may have the ability to control osteoblast differentiation, hence increasing and promoting osseointegration. Pradeep *et al.* (2012) investigated the effectiveness of several concentrations (0.5 percent, 1 percent, and 1.5 percent) of MF gel as a local drug delivery system for treating intrabony defects (IBDs) in patients with chronic periodontitis [2]. Maximum improvement in clinical and radiologic parameters was observed to be achieved using the 1 percent MF gel in conjunction with SRP[3-4].

The osteogenic effect of MF has two potential modes of action: enhanced osteoblast proliferation and decreased osteoclast activity. According to studies, MF causes osteoblasts to proliferate more after absorbing it [5-6] Another study found that exposure to MF reduced osteoclast activity and bone resorption. MF increases the production of osteoprotegerin (OPG) from osteoblasts while down-regulating the production of receptor activator of nuclear factor kappa B ligand (RANKL). In order to achieve appropriate and quick osseointegration, a variety of procedures have been described in the literature to coat the dental implant with a bio-stimulant. This study aims to evaluate the osseointegration around dental implants covered with 1% metformin gel clinically and radiographically, using resonance frequency analysis (OSSTELL® Device) and bone mineral density[7].

MATERIAL AND METHODS

Study Design

A total of 10 (5 control group -5 experimental group) healthy patients with at least one tooth missing in premolar or molar region desirous of Dental implant placement will be selected from outpatient

Department of Periodontology, SGT Dental College, Hospital and Research Institute, Gurugram Delhi-NCR. Further procedures will only be carried out with patient's consent.

The sites will be divided into 2 groups-

Group 1 - will consist of 5 patients receiving dental implants in premolar and molar region coated with 1% metformin gel.

Group II - will consist of 5 patients receiving dental implants in premolar and molar region without coating of 1% metformin gel.

An informed written consent will be taken for all the patients selected for the study. All candidates shall be informed of the timeline and the bio stimulatory material used for the study.

Study Duration

All Participants in the study will be evaluated at Baseline and 3 months.

Inclusion Criteria

- Patient should be systemically healthy.
- Partially edentulous patients (at least one tooth missing).
- Patient with age group 18 to 60 years will be added.
- Patients with adequate maintainable oral hygiene.
- Adequate bone at the edentulous site for placement of implant.

Exclusion Criteria

- Presence of systemic disease preventing implantation.
- Having blood disease to prevent centrifugation.
- Presence of parafunctional habits.
- Acute infectious lesions in the areas intended for surgery.
- Pregnancy
- Smoking
- Allergy to one of the material to be used during operation.
- Individuals with severe periodontitis, in which periodontal therapy is indicated.
- Radiation therapy
- Corticosteroid and Bisphosphonate therapy
- Diabetic patients

Randomization

Participants will be randomly allotted by flip of the coin and will be randomly allotted to either of the two groups. Group I (Study group) - With 1% metformin gel or Group II (Control group) - without 1% metformin gel.

Presurgical Preparation

After having entered into the study, all patients at baseline visit will receive the following procedure by the same operator which includes supportive periodontal treatment consisting of professional prophylaxis (scaling and root planing), oral hygiene instructions, impression recording, blood tests, radiographic investigations) and clinical photographs.

Treatment Phase

Following initial examination and treatment planning, the selected patients will undergo patch test for checking any hypersensitivity reaction to MF and then subjected to Phase I therapy.

The surgical technique used in the treatment group will consists of following steps:

After achieving adequate local anesthesia, full thickness flaps will be elevated and implant site will be prepared. For the Study Group the implant will be placed into osteotomy site with an insertion torque at the crestal level. For Study Group before the placement, implants will be coated with 1 %MG from the sterile vials, 1ml of 1%MG will be drawn out from sterile syringe. The stability of the implant will be evaluated at baseline in both groups, using ostell device and the flap will be sutured after placement of cover screw. Post-operative instructions will be given and the patient will be prescribed with antibiotics, analgesics and mouthwash. Patient will be recalled 10 days after surgery for suture removal and postoperative evaluation. Also, patients will be reinforced with oral hygiene instructions at every visit.

At Baseline (V_0) -On the day of placement

IOPA will be taken to assess the correct placement of dental implant using paralleling technique.

Implant Stability Quotient will be recorded at baseline.

The stability of the implants will be evaluated with resonance frequency analysis (RFA). The measurements will be carried out with the Osstell® device by connecting the transducer (SmartPeg) to the implant. RFA measurements will be recorded immediately after surgery and repeated at the 3 months after implant placement.

Visit 1(V_1) – 3 months

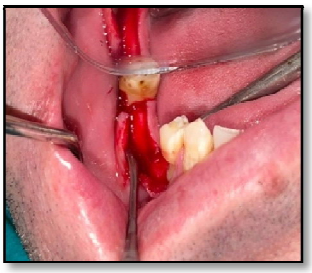
ISQ values will be recorded to check implant stability

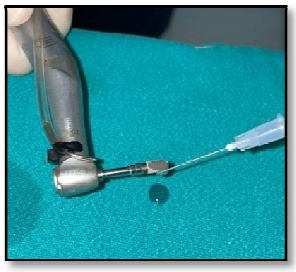
IOPA using paralleling technique will be done to evaluate bone mineral density at bone implant interface. The implant was divided in length into three equal parts in coronal section and images will be sliced at 1mm. BMD will be recorded at the mid-point of each divided section using ImageJ software. Then the average BMD was calculated by adding the values at the middle and the apical section. Coronal BMD values are excluded, keeping in mind the crestal bone loss.

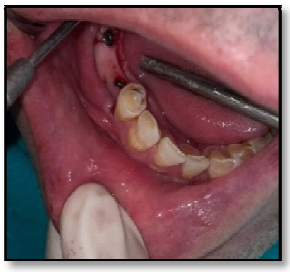
Statistical Analysis

All the clinical parameters will be recorded and subjected to suitable statistical analysis. Student t-test was done as two groups are to be compared. Probably value of <0.05 will be considered as statistically significant for all the comparisons.

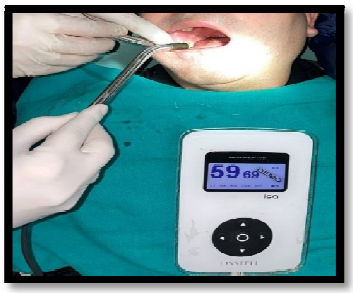
Clinical Presentation

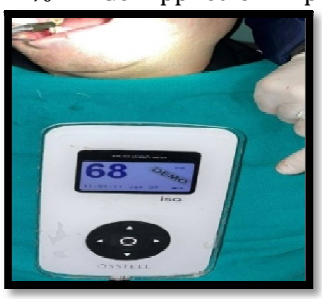


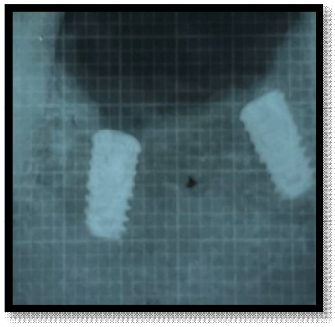




Pre-Operative Edentulous site 1% MF Gel Applied on Implant Implant Placement done

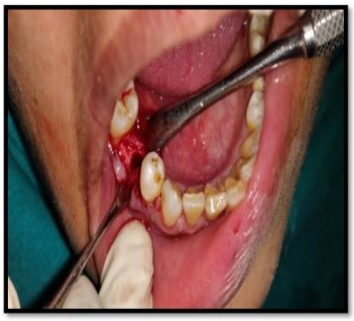




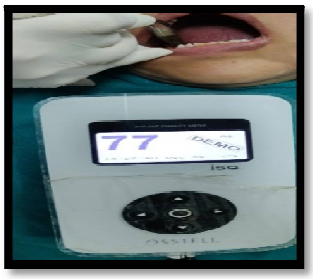


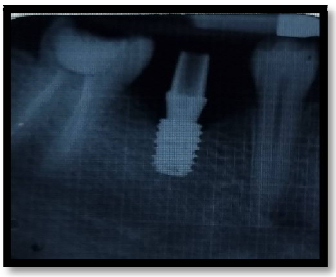
IOPA taken at baseline IOPA taken after 3 Months

GROUP 1 - IMPLANT WITH 1% METFORMIN GEL



Implant Placement done ISQ taken at baseline IOPA taken at baseline





ISQ taken after 3 months IOPA taken after 3 months.

GROUP 2- WITHOUT 1% METFORMIN GEL

RESULTS AND DISCUSSION

There was an overall increase in the BMDs in both the groups at 3 months interval. But when compared at 3 months, Test group showed a greater improvement in the BMD at 3 months than the control group. There was a marked increase in the ISQ values in both the groups during the 3 months interval.In this pilot study, a three months course of 1% metformin gel at bone implant interface was associated to be with improvements in osseointegration around dental implants and with better RFA in terms of Implant stability within a period of 3 months. A dose-dependent increase in osteoblast-like cell proliferation employing a variety of clinical trials has been demonstrated in various studies [8-9]. In osteoblastic cells, this medication functions as a mild mitogen, and long-term exposure to metformin in osteoblastic cultures results in osteogenic effects. Additionally, it has been demonstrated that MF increases the expression of the Runx2/Cbfa1 transcription factor, which is thought to be the mechanism by which MF increases the expression of osteocalcin, BMP-2, mRNA expression, endothelial nitrous oxide metabolism, osteoblastic alkaline phosphatase, type I collagen, and mineral deposition. However, with the use of local application of 1% metformin gel reported to be more advantageous including advantages of reduced dosage, fewer administrations, and high patient acceptability, as well as an advantage of enhanced drug concentration at the target site[10-11]. In this current study, the mean bone mineral density at implant site was around 121 Grey scale value using Image J software which was in accordance with various other studies. The bone density value, however, should be taken into consideration that it cannot be standardised because the usual value ranges from one person to another. This shows a statistically significant increase in bone density on the lingual aspect in both groups throughout the course of the 3-month period. However, the test group had shown a greater increase in 3-month time interval. The mean ISQ value increased in both the test and control groups at all time intervals, which may have been caused by the implant achieving secondary stability at that time due to corticalization of the surrounding bone [12-13].

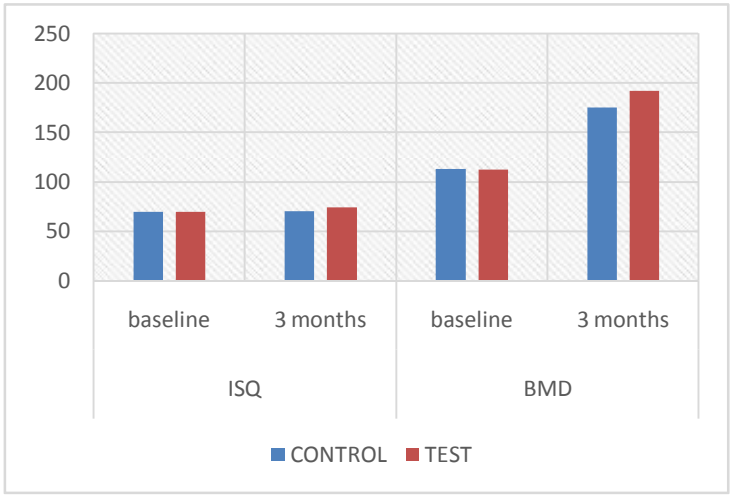


Figure 1 correlation of ISQ and BMD

CONCLUSION

Within the limits of this study, 1% Metformin Gel demonstrated greater improvement in the osseointegration around bone-implant interface achieved at all-time intervals. Further studies with larger

samples sizes, longer follow up periods need to be conducted with histological evaluation of the new bone formed to derive conclusive evidence.

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