

## Study Protocol

# Comparative Analysis Of Bone Regenerative Potential Of Simvastatin Vs Platelet Rich Plasma In Mandibular Third Molar Extraction Socket- A Study Protocol

### ABSTRACT

**BACKGROUND:** Third Molar Extraction is a treatment used by oral and maxillofacial surgeons in which distal bone loss to the second molar is a major concern due to consequences such as pain, mastication difficulty, and pocket development. Platelet -Rich Plasma (PRP), a novel adjunct to promote bone regeneration. The method of its preparation is cumbersome and need a costly centrifuge machine. Hence many studies have been conducted to find an effective alternative to Autologous PRP. Statins have also proved effective in inducing bone regeneration of which Simvastatin has been more effective. It can also be used in immediate implant cases where faster and better bone healing is necessary for osseointegration.

**AIM:** To assess the effectiveness of simvastatin and PRP in regenerating bone in third molar extraction sockets.

**MATERIAL AND METHODS:** All together 15 patients will be selected with identical bilateral third molar impaction. All the patients will be divided into two groups of simvastatin and PRP.

**EXPECTED RESULTS:** If the results prove significant, Simvastatin can be used as an osteoinductive agent for bone healing.

**CONCLUSION:** If the outcomes favor the bone regeneration potential of Simvastatin to be equivalent or superior than PRP, then Simvastatin can be used for osteoinduction in Third Molar Extraction socket or other small bony defects.

**KEYWORDS:** Third Molar Extraction, Platelet-Rich Plasma (PRP), Simvastatin.

### INTRODUCTION:

Third Molar Extraction is a treatment used by oral and maxillofacial surgeons in which distal bone loss to the second molar is a major concern due to consequences such as pain, mastication difficulty, and pocket development, thus preservation of alveolar ridge or bone after extraction is essential.<sup>[1]</sup> Bone grafting with different types of bone graft is considered as one of the most accepted method for bone regeneration. Theoretically, grafting of autologous bone into the extraction socket can favorably influence defect healing. This treatment creates a secondary injury as well as is difficult to fit in the irregular shape of an extracted socket.<sup>[2]</sup>

Platelet -Rich Plasma (PRP), a novel adjunct to promote bone regeneration. It is a descendant of platelets which consist of numerous growth factors(GFs) which are GF- $\beta$ , vascular endothelial growth factor (VEGF) and epithelial GF all of which help to accelerate bone healing.<sup>[3,4]</sup> In spite of its advantages, the method of its preparation is cumbersome and need a costly centrifuge machine. Hence many studies were conducted to find an effective alternative to Autologous PRP.

It was first reported that statins induce bone morphogenetic protein 2 (BMP-2) gene expression within osteoblasts and cells of bone marrow, indicating that statins play a vital function in modulating bone regeneration.<sup>[5,6,7]</sup> Simvastatin is one of the most effective and widely prescribed statins.<sup>[8]</sup> Almost all trials on the use of simvastatin as a topical treatment for bone abnormalities have had positive results.<sup>[9]</sup>

Although there are many studies which prove Simvastatin as potent bone regenerative agent, its efficacy is still a matter of investigation. In light of this, we will undertake a study to compare the efficacy of Simvastatin against PRP in terms of bone regeneration potential in the mandibular third molar extraction socket.

## **OBJECTIVES-**

1. To assess the efficacy of Simvastatin in bone regeneration in third molar extracted socket.
2. To assess the efficacy of PRP in bone regeneration in third molar extracted socket.
3. To compare the efficacy of Simvastatin and PRP in bone regeneration in third molar extraction socket.

## **METHODOLOGY-**

The research will take place at Sharad Pawar Dental College and Hospital in Sawangi (M), Wardha, in the Department of Oral and Maxillofacial Surgery. A total of 15 patients with identical bilateral third molar impaction will be chosen. Before participating in the study, all patients will be informed about it and will be asked to sign a written informed consent form. All the patients will be split in two categories:

Group A: Simvastatin group (n = 15)

Group B: PRP group (n = 15)

### **Inclusion criteria**

1. Age of subject between 16-45 years.
2. Patients who require bilateral transalveolar third molar extractions.

### **Exclusion Criteria**

1. Patients having a localized infection in the third molars of the mandible.

2. Patients with any systemic illness or any bleeding disorder.
3. Associated pathology like cyst and tumor.

### **Pre-operative preparation**

Orthopantomogram (OPG) and Intraoral Periapical (IOPA) radiograph will be done to evaluate the nature of impacted tooth and any pathology associated.

Vitals like Temperature, Pulse and Blood Pressure will be recorded. Blood investigations like Bleeding Time, Clotting Time, Hemogram, , Random Blood Sugar test will be performed. These tests will be done to rule out any systemic diseases and bleeding disorders.

### **Extraction of Third Molar and Packing of Extraction Socket-**

A conventional inferior alveolar, Lingual and Long buccal nerve blocks will be given, and the third molar will be extracted under all aseptic precautions. Then curettage of extraction socket will be done and irrigation will be done thoroughly with saline and betadine. In first session the extraction socket of one side will be packed with prepared simvastatin with gel foam as a carrier. In another session other side extraction socket will be packed by PRP.

### **Preparation of PRP-**

10 ml of intravenous blood will be withdrawn from the cubital fossa area of the patient with the help of flashback blood collection needle, which was collected in a bulb containing EDTA. This bulb will be centrifuged for 10 minutes at 1200 rpm to separate the collected blood into a lower part containing Red Blood Cells and an upper part containing straw colored plasma. The plasma part contains low platelet concentration and boundary layer called Buffy Coat contains relatively high concentration of platelet.

In a glass tube, the upper portion, buffy coat, and upper 1 ml RBC layer will be collected and centrifuged for 10 minutes at 2000 rpm. The upper half of supernatant fluid will now be discarded, while lower half will be combined to make PRP. PRP will be mixed with 0.5-1ml of 10% calcium chloride and immediately inserted into the extraction socket.

### **Preparation of Simvastatin with Foam Base-**

Simvastatin (10 mg) tablet will be crushed and mixed with 2ml of 0.9% normal saline and will be applied using gel foam as a carrier.

### **Bone Density Measurement-**

Subject will be recalled for evaluation at 1,2,4 and 12 weeks respectively and will be evaluated using IOPA of the particular side at 4<sup>th</sup> week and at 12<sup>th</sup> week. Follow-up CBCT (at day 1 and

12<sup>th</sup> week) will be used for comparison in new bone density. Analysis will be done using the mean gray -scale value and in Hounsfield units.

## **DISCUSSION:**

Bone regeneration in extraction socket after removal of third molar is one of the most important factors in successful surgery of third molar extraction. This led to the scope of finding materials which can be used in extraction socket to promote bone regeneration post-surgery.

According to Saikrishna Degala and Nikita A. Bathija et. al., Simvastatin has shown positive results bone morphogenetic protein-induced osteoclastic activity is inhibited, while osteoblastic activity is accelerated. The effects of local application of simvastatin (10 mg) on bone repair after surgical removal of bilaterally impacted mandibular third molars were investigated in this split-mouth randomized clinical experiment. Dr. Saikrishna Degala and Dr. Nikita Bathija et al analyzed whether local application of simvastatin (10 mg) on bone regeneration following extraction of bilaterally impacted mandibular third molars is effective or not. A total of 30 patients between the ages of 18 and 40 were chosen to have their bilateral impacted mandibular third molars surgically removed. Patients were free of any other systemic diseases. Standard IOPA radiographs were taken using parallel technique of X-ray taking at the end of 1,4,8,12 weeks for each patient at exposure of 70 kVp and 8mA to calculate bone regeneration. It was digitalized and using gray-scale histographic values. Results were that at the end of each evaluation according to weeks there was increase in value of study group as compared to study group. CBCT was used as another guide which showed increased bone regeneration in the study sockets.

According to Ravi Bhujbal and Neelima Maliket al healing can be aided by the GF's included within platelet-rich plasma (PRP), which has ability to shorten the postoperative recovery period. The primary goal of this study was determination of the function of PRP in socket healing, oedema, discomfort, and bone regeneration after extraction of impacted mandibular third molars. The findings suggested that wound healing and debridement could be improved. Effectiveness of Platelet Rich plasma in healing of different types of wounds is reflected in a number of studies<sup>[10-22]</sup>.

## **IMPLICATIONS-**

Bone regeneration is the desired outcome whenever there is formation of bony defect due to any surgical procedure such as Cystic enucleation and extraction of tooth. Simvastatin can be used as an osteoinductive agent for bone healing. It can also be used in immediate implant cases where faster and better bone healing is necessary for osseointegration.

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