

## Original Research

### Evaluating the oseoinductive properties of simvastatin in patient undergoing mandibular third molar surgery- A pilot study

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#### ABSTRACT:

**Aim:** This study focused to evaluate the potency of osteotrophic agent - simvastatin by assessing the rate of bone regeneration and the density in patients with third molar impaction by using Cone Beam Computed Tomography. **Materials and methods:** Totally 10 patients diagnosed as having impacted third molars within the age of 18- 25 years was enlisted in this study, post removal of third molar gel foam was blended with crushed smaller particles of Simvastatin tablets and dampened with normal saline (2 ml) was surfaced in the freshly extracted socket. **Results:** Normality tests, Shapiro-Wilks tests, Kolmogorov-Smirnov test stated that the study followed normal distribution. The result of the study concluded that there is significant increase in bone regeneration. **Conclusion:** The present study concluded that the simvastatin when applied locally is effective in inducing early bone regeneration and it is very cost effective. Simvastatin use decreased the need for autogenous graft and thereby reducing donor site morbidity. It as an effective tool for bone healing in minor oral surgical procedural defects.

**Key words:** Bone substitute, Simvastatin, Osteotrophic agent

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#### INTRODUCTION

Surgical removal of mandibular third molar is a common procedure practiced routinely in the field of dentistry. Some of the commonly encountered complications following this procedure are alveolar bone loss around the distal part of second molar tooth causing the formation of distal pocket, sensitivity. To prevent this complication, preserving the socket, bone, and the alveolar ridge after tooth removal or extraction is important. Bone loss following any oral surgical procedures will lead to functional and aesthetic problems. Regeneration of bone requires the three major key components osteo-induction, osteogenesis, and osteoconductive actions. Bone grafts such as autograft, allograft, and xenograft have been used for the regeneration of bone. There is always a formidable challenge in the selection of ideal graft material. Autogenous bone graft have all the major key elements for bone regeneration, and

thereby, it remains as an excellent material for bone grafting:

Simvastatin is a non-hygroscopic white crystalline powder and have been proven to have pluripotent effect. This study focused to evaluate the potency of osteo-trophic agent simvastatin by assessing the rate of bone regeneration and the density in patients at different intervals of wound healing with bilateral symmetrical third molar impaction by using CBCT.

#### STUDY DESIGN & MATERIALS AND METHODS

The research study was conducted in the Department of Oral and Maxillofacial Surgery, SRM dental college, Ramapuram, Chennai with acceptance from Review panel of the institution. The patients were explained about the treatment, review protocol and informed consent was obtained. Totally 10 patients diagnosed as having impacted third molars within the age of 18- 25 years were enlisted in this study. All the patients were assessed pre operatively using OPG for

the angulation of the impacted tooth to the adjacent second molar teeth. (FIGURE 1). Inclusion criteria were Patients diagnosed with mandibular third molar impaction, Patients without any active infection and

any history of systemic disorders and abusive habits. Exclusion criteria were Patients with systemic diseases, impacted third molar with large periapical pathologies.



**FIGURE 1- OPG showing identical impacted mandibular third molar**



**FIGURE 2.1- Simvastati      FIGURE 2.2- Gel foam**

**SURGICAL TECHNIQUE**

All the third molar surgery was performed by a single surgeon. The surgical site was prepared and mandibular nerve block was given. The impacted tooth was removed and the extracted socket was examined for any sharp bony margins which were filled, smoothed and irrigated to remove the debris using normal saline. (0.9%) (Figure 3.1 and 3.2)



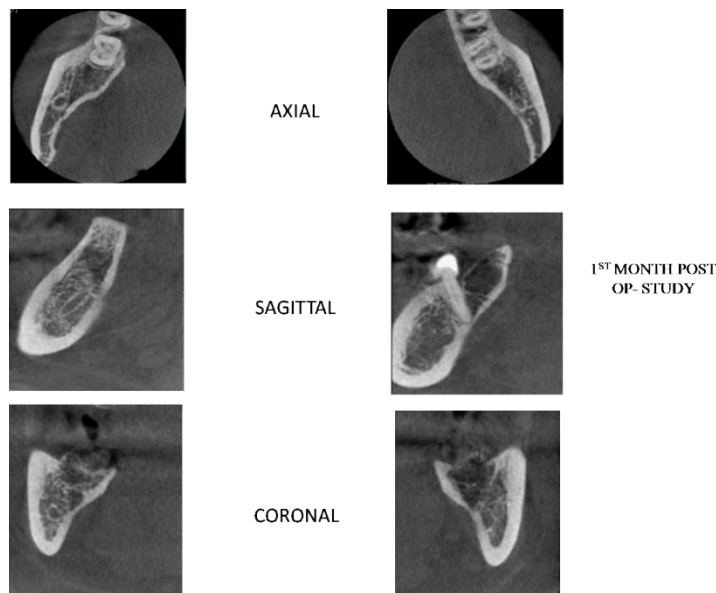
**FIGURE 3.1      FIGURE 3.2**  
**FIGURE 3.1 and 3.2- Extraction of mandibular third molar done under local anesthesia**

The gel foam was blended with crushed smaller particles of Simvastatin tablets (figure 2.1) and dampened with normal saline (2 ml) was surfaced in the freshly extracted socket

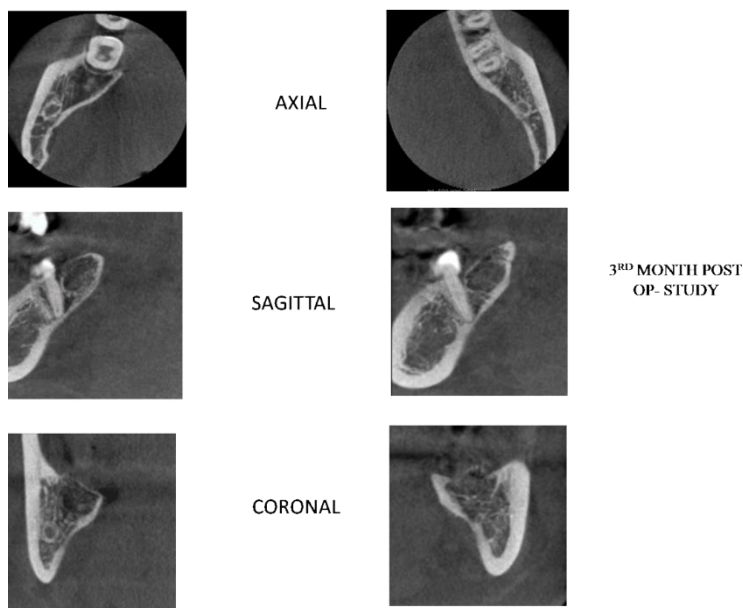


**FIGURE 4.1- Gel foam with simvastatin placed into the extracted socket      Figure 6 - Gel foam along with simvastatin**  
**FIGURE 7- Gel foam with simvastatin placed into the extracted socket**

The surgical site flap was approximated and closed using 3-0 silk suture. The postoperative pain and swelling were evaluated by first and seventh day. Bone height, width and density measurement was assessed using CBCT (ON DEMAND 3D) by first and third month. ( Figure 8 and 9)



**FIGURE 10- Bone width, height, density assessment on 1<sup>st</sup> post operative month**



**FIGURE 11- Bone width, height, density assessment in study on 3<sup>rd</sup> post operative month.**

The parameters which were taken into considerations were Pain based on VAS score, Swelling - Fixed reference points in the face were used to assess the swelling A- The posterior most point on the tragus, B- The lateral canthus of the eye, C- The lateral most point on the angle of the mouth, D- The soft tissue

pogonion. E-The inferior most point on the mandibular angle.AC, AD and BE linear measurements were measured and the swelling score was obtained using the formula AC+AD+BE and Bone density

**RESULTS**

**Table 1: Age distribution among the study participants**

Age distribution (in years)	Study participants
18-21	45%
22-24	55%

Mean	21.12
Standard deviation	2.01

**Table 2: Gender distribution among the study participants**

Gender distribution	Study participants
Male	60%
Female	40%

**Table 3: Descriptive statistics of VAS score during the time intervals**

Intervals	Mean	S.D
Post operative at 1 <sup>st</sup> day	4.77	0.73
Post operative at 7 <sup>TH</sup> day	1.65	0.62

**Table 4: Descriptive statistics of assessment of swelling during the time intervals**

Intervals	Mean	S.D
Pre operative	37.78	3.24
Post operative 36-48 hours	40.16	2.74
POST OP 6 <sup>TH</sup> -7 <sup>TH</sup> DAY	38.58	2.62

**Table 5: Descriptive statistics of assessment of bone according to height, width and density during the post operative after 1 month**

Intervals	Mean	S.D
Height	3.09	0.38
Width	2.82	0.40
Density	785.04	48.37

**Table 6: Descriptive statistics of assessment of bone height, width, density during the post operative after 3 month**

Intervals	Mean	S.D
Height	7.12	1.16
Width	5.98	1.24
Density	1857.80	126.62

## DISCUSSION

Surgical removal of the mandibular 3<sup>rd</sup> molar is a most common surgical procedure in the field of oral and maxillofacial surgery. There are chances of formation of bony defect on the distal aspect of 2<sup>nd</sup> molar intra operatively during bone guttering and luxation of tooth. In order to correct these defects bone grafting has played a significant role. The ideal material of choice for bone grafting is autogenous graft due to their inherent capacity like osteoinduction, osteoconduction but it has its own drawbacks like donor site morbidity, patient discomfort, limited availability [1]. Various studies have been performed and shown satisfactory results in bone regeneration. The major need for grafting after extraction of impacted third molar surgery is due to bone removal distal to the second molar that may lead to distal pocket formation and periodontally compromising the second molar tooth post operatively. Simvastatin a commonly used cholesterol lowering drug which basically works by inhibition of HMG-CoA reductase, in turn prevents the conversion of substrate form to the product form of the enzyme. Their use in the craniofacial region has been reported in the recent years, in bone grafting which states that

these drugs have the osteoinductive property. The reported positive findings for use of simvastatin in the literature are: fastens osteogenesis in bone graft [1][2][3], increases the thickness of trabecular pattern [1][4][5], ensures the availability of growth factors and BMP in early stages [1][21-24], enhances early amalgamation [7][8], expedite graft mineralization [9][10], increases bone regeneration [11][12], accelerates wound healing [13][14].

Mundy et al initial research started with osteoinductive properties of statin which states that they reduce vascular and systemic inflammation, thereby reducing the expression of C reactive protein. Through local application, significant bone regeneration with no local and systemic complications which has been reported in the literature [6][15]. According to US food and drug administration the accepted dose of simvastatin upto 80mg/day reduces the risk of developing myopathy and rbdomyolysis. Simvastatin are generally applied locally with carrier so they are usually mixed with ethanol, chloroform and methanol or with bone graft materials.

George et al study states that comparing with simvastatin 0.1mg and 0.5mg and they assessed the

outcome post operatively on the 28<sup>th</sup> day, concluded that 0.5mg showed reduction in the inflammatory changes and increased rate of bone formation than 0.1mg simvastatin which fraternize on previous studies which were based on the various dosage for simvastatin<sup>[8]</sup>.

In our study we used simvastatin 10mg which is accepted as a safe dosage by US food and drug administration, was placed with gelfoam as a carrier, in the extracted Mandibular third molar socket. The patient was reviewed on 1<sup>st</sup> and 7<sup>th</sup> day for pain, swelling and restricted mouth opening clinically. Radiographically, bone density measurement was done using CBCT (3D demand software) post operatively on 1<sup>st</sup> and 3<sup>rd</sup> month. In the postoperative 1<sup>st</sup> and 3<sup>rd</sup> month, showed significant increase in the bone formation. The study results affirmatively showed evident acceleration of bone formation followed by maturation.

Facial swelling was measured pre and post operatively, there were no any significant difference which concludes that local application of simvastatin doesn't provide any adverse soft tissue reaction. Pain was assessed using VAS scale, there was no any significant severity of pain. The height, width and the density had significant increase as compared over a period of 3 months, indicating that Simvastatin has a bone regeneration property and can be considered an alternative for autografts which is minimally invasive and with minimal side effects.

## CONCLUSION

The present study concluded that the simvastatin when applied locally is effective in inducing early bone regeneration and it is very cost effective. Simvastatin use decreased the need for autogenous graft and thereby reducing donor site morbidity. So simvastatin can be considered as an effective tool for bone healing in minor oral surgical procedural defects. As a future perspective, it needs more clinical trial for usage in major cranio- maxillofacial procedures.

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