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Effect of Local Apllication of Simvastatin on Bone Rgeneration after Peri-Radicular Sugery: A Case Report

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ABSTRACT

This case report examines the impact of locally administered simvastatin on bone regeneration subsequent to peri-radicular surgery. Peri-apical lesions persisting despite non-surgical endodontic interventions prompted the investigation. Two cases, involving young female patients with refractory peri-apical lesions, are presented. After unsuccessful non-surgical treatments, peri-radicular surgery was performed, with one case incorporating simvastatin application within the peri-apical defect. Over a three-month follow-up period, both cases exhibited enhanced bone density and reduced lesion size, with greater improvement observed in the simvastatin-treated case. The discussion delineates the inflammatory processes within peri-radicular tissue and elucidates simvastatin's mechanisms in bone regeneration. Findings suggest that simvastatin adjunctive therapy in peri-radicular surgery facilitates bone healing and tissue regeneration.

Keywords: Periradicular surgery , Simvastatin, Gel foam, Collagen matrix, Bone defect, Bone healing, Dental pulp, Non-surgical endodontics, Peri-apical lesions, Bone regeneration, Inflammatory processes, Pleiotropic effects, Mitochondrial dysfunction, Osteoclast expression, Pro-inflammatory mediators, Bone morphogenic protein-2, Odontogenic differentiation, Local application, Case report, Bone density, Lesion size, Peri-radicular tissue, Peri-apical score, OPG (Orthopantomogram), Flap elevation, Root end resection, Fibrous connective tissue, Cholesterol lowering agent, Inflammatory role, BMP-2 production, Osteoblast differentiation, Healing, Thrombotic potential, Periodontal pocket, Osteogenic activity, Histological study, Alveolar bone, Anti-inflammatory properties, Bone morphogenic protein-2 (BMP-2), Osteoinductive properties, Accelerated healing, Alveolar Ridge preservation, Pleiotropic effects

INTRODUCTION

Dental pulp is sterile connective tissue. Injury to pulp chamber leads to inflammation and result in pulp necrosis if left untreated and infection can also spread to peri-radicular area. Non-surgical endodontics can heal most of the lesions, but further modalities like peri-radicular should be undertaken if infection persists.

Tissue injury following surgery or trauma is complex process involving multiple steps. Repair can be with replacement of tissue which structurally and functionally resemble normal tissue or can be with fibrous connective tissue [(1)].

Statins (co-enzyme- A) major lipid lowering agents, have other pleiotropic effect like sepsis, wound healing etc[(2)]. Simvastatin aids in healing of peri-apical lesion by Alleviating mitochondrial dysfunction due to hypoxia.Simvastatin enhances bone formation by -alleviates mitophagy and apoptosis, Decreases Cyr61 expression of osteoclast, Reduce expression of pro-inflammatory & inflammatory mediators like IL-6 and 1beta., Increasing expression of bone morphogenic protein-2 and reduces bone resorption marker and beneficial for bone catabolic diseases. It induces odontogenic differentiation of human dental pulp cells and promote bone regeneration in pulpitis.
Various method for local application of statins includes collagen gel, gelfoam etc. GELFOAM was initially used as hemostatic agent because it can hold within its network large amount of blood and other fluid[(3)].

The purpose of study compares the bone regenerative power after application of simvastatin and without simvastatin after peri-radicular surgery.

The inclusion criteria used in this studywell-motivated patients requiring surgery in anterior teeth. Failed RCT with recurrent sinus and pus discharge. Lesion of peri-apical score 4 & 5 were included. Smokers , alcoholics, pregnant, lactating were excluded. Lesion measured in 3 directions Bucco palatal, mesiodistal and diagonal on IOPA taken with parallel technique.

CASE REPORT

Case report 1:
A 17-year-old female reported to Department of Conservative dentistry and Endodontics with chief complain of swelling in upper front region of mouth. On examination, there is Ellis class III fracture with respect to 11 with formation of abscess on palatal aspect. On radiographic examination there is open apex present with respect to 11 and periapical radiolucency of about 13*15mm present with respect to 11,12. BMP done upto 80k file and metapex was pushed inside the canal and patient prescribed antibiotics for 5 days. Cap. Novamox 500mg t.d.s * 5 days, Tab Metrogyl 400mg t.d.s * 5 days and Tab Combiflame t.d.s.*5 days. Follow up was done for a period of 3 months. After 3 months there is not much improvement in peri-apical lesion so peri radicular surgery was done in relation to 11, 12 region.

Before obturation apexification was done with biodentine followed by customized gutta-percha placement peri-radicular surgery was performed. After period of 1 week surgical procedure was carried out. The surgical procedure included the flap elevation, curettage, root end resection and filling the defect with collagen gel foam and simvastatin. Initial lesion measure about 13*15mm. Follow up X-ray shows improvement in bone density and size of lesion is 10*12mm in 3 months follow up.

CASE 2:A 18 years old female reported to Department of Conservative dentistry and Endodontics with chief complain of pain in upper front region with previous history of root canal treatment in the upper front tooth region.On radiograph there was a evidence of previous attempt of access opening with persistent periapical radiolucency of about 13*15mm.Access opening with BMP done till 55K file and metapex is placed inside the canal and follow up is done for 3 months.

There is not much improvement of radiolucency so peri-radicular surgery was planned for apicectomy of root and simvastatin was placed inside peri-apical lesion.Initially the size of the lesion was13*15mm but after follow up of 3 months lesion size was 9*10mm and there is increase in bone density (radioopacity).Initial lesion 13*15mm, follow up after 3 months lesion size 9*10mm, increase in bone density (radio-opacity).

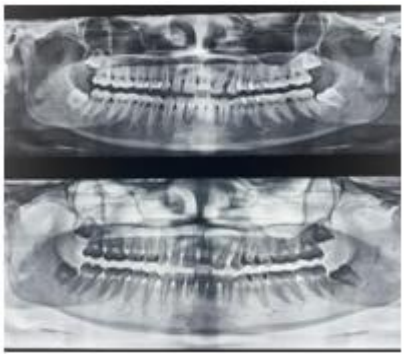

Figure 1.1: OPG

Figure 1.2: Incision placed

Figure 1.3: flap elevation

Fig. 1.4: marking for the trephination site.

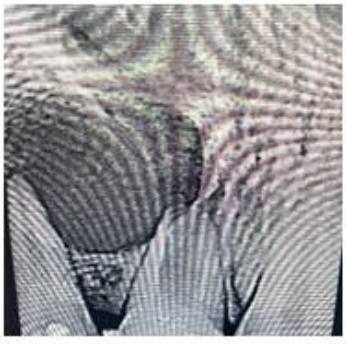

Fig 1.5: preoperative radiograph.

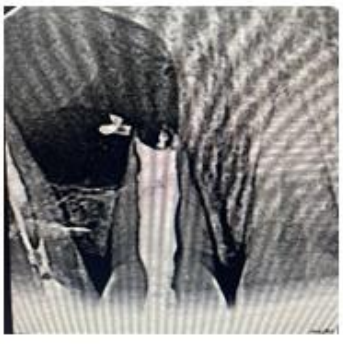

Fig 1.6: calcium hydroxide placed

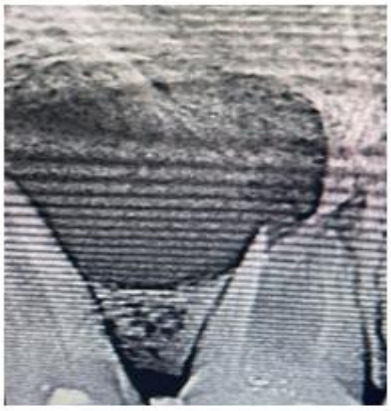

Figure 1.7: Inter appointment radiograph

Figure 1.8: after 3 months follow up

Figure 2.1: flap reflection and curettage

Figure 2.2: orthograde cavity preparation using retrograde tips.

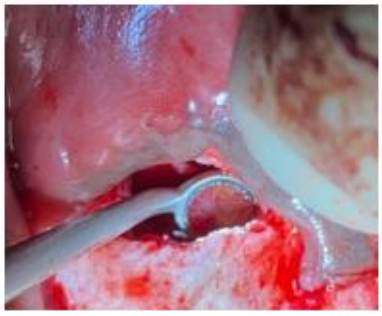

Figure 2.3: inspection of retrograde cavity

Figure 2.4: simvastatin placed in the defect. Figure 2.5: suturing done

Figure 2.6 preoperative radiograph

Figure 2.7: calcium hydroxide placed

Figure 2.8: inter appointment radiograph Figure 2.9: 3 months after follow up.

DISCUSSION

Peri-radicular tissue consists of apical root, cementum, PDL & alveolar bone. Apical periodontium consists of sensory, motor nerve fibre, ground substance like fibroblast, cement oblast, osteoclast, undifferentiated mesenchymal cells, epithelial rest of malassez. Irritation of peri-radicular tissue causes inflammatory changes include Vasodilatation ,Vascular stasis , Increased vascular permeability , Leakage of fluid and components into surrounding tissue.

These changes lead to redness, heat, swelling, pain, which are cardinal sign of inflammation.

Hydroxymethylglutaryl-coenzyme A reductase inhibitors (statins) are most commonly used cholesterol lowering agent. It has anti-inflammatory role by attenuating the effect of tumor necrosis factor which has major role in synthesis of CCL-2 and cysteine rich-61. It also decreases CD-68 positive macrophage chemotaxis into lesion. Simvastatin is known to improve BMP-2 production which is responsible for differentiation of multipotent stem cell into osteoblast like cell. Statins also stimulate production of bone in experimental animal studies.

In present case report healing of peri-apical lesion was compared with and without simvastatin. 10mg of simvastatin was crushed and dispersed into 0.9% of 2ml normal saline. 10mg is considered to be safe dose to insert in socket and inserted with gelfoam as direct powder can cause severe inflammation.Initial peri-apical lesions measure about 13*15 mm. After 3 month follow up, lesion measure 10*12mm withoutsimvastatin and 9*10mm with simvastatin.

So from present case report, this can be concluded that simvastatin aids in overall healing of peri-radicular lesion.
Mundey *et al*. have studied the osteo conductive properties of simvastatin. Simvastatin consist of osteoinductive and conductive properties which are similar to BMP 2 gene[(4)]. They produce heat shock protein 27 They help in vascular endothelial growth and reduce as the kinease activity assosiated with rho in osteoblast. clinical studies on paitent have shown that statins could reduce the risk of osteoporosis and fracture of bone [(5)].

Simvastatin was used to treat periodontal pocket by applying 2.5% of topically. This show improve results by elimination of periodontal pocket. In the in vitro studies statins have showed promotion in osteogenic activity and impose vascular Endothelial cells[(6)].

Statins have thrombotic potential hence they were used to treathypercholesterolemia[(7)].
Chauhan AS*et al* reported there was improved healing with significant decrease in the size of swelling in 2-3 days post-operatively.[(8)]

Nyan *et al* In their study concluded, the effects of Simvastatin could be do depended or carrier dependent. The ultra-structural and cytological studies Shows bone formation and lamellar appearance of matrix in the rats [(9)].
Ayukawa In the histological study, concluded when application of simvastatin locally in the bony defect Showed evidence of osteogensis at the site[(10)].

Mouhamed *et al*used mixture of simvastatin and tricalcium phosphate in the bony defect and examined radiographically and histologically and reported the evidence of bone formation and improved healing.[11]

Hassan *et al* studied the effects of simvastatin In alveolar Ridge preservation procedures, and concluded there was accelerated healing tendency with preservation of bone volume[(12)].

CONCLUSION

This case report explores the effect of local application of simvastatin on bone regeneration following peri-radicular surgery. Simvastatin, known for its pleiotropic effects including anti-inflammatory properties and promotion of bone formation, was applied locally in conjunction with peri-radicular surgery. The study involved two cases, both of which showed improvement in bone density and reduction in lesion size following the application of simvastatin.

Simvastatin's mechanisms of action, including its ability to increase bone morphogenic protein-2 (BMP-2) production and stimulate osteoblast differentiation, are discussed. Additionally, previous studies supporting the use of simvastatin in bone regeneration and periodontal treatment are referenced, providing further context for its effectiveness in this case report.

Overall, the case report suggests that simvastatin aids in the healing of peri-radicular lesions and promotes bone regeneration when applied locally during peri-radicular surgery. The findings align with existing literature on the osteoinductive and anti-inflammatory properties of simvastatin, further supporting its potential therapeutic use in dental procedures aimed at promoting bone regeneration and tissue healing.

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