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Original Article

Treatment of cystic lesion of mandible using combination of modified bone granules and calcium phosphate bone cement: A preliminary report

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ABSTRACT

Aims: This study was conducted to evaluate healing of bony cavity in mandible following enucleation of cystic lesion by obliterating the cavity using modified natural bone granules (G Graft) and calcium phosphate bone cement (G Bone).

Materials and method: In this technique, after enucleation of cystic lesion, peripheral osteotomy using No. 702 fissure bur and perforation of the inferior cortex using 1.5 mm drill bits were performed. Modified hydroxyapatite granules were used to fill the defect while calcium hydroxide bone cement was used to seal the cavity opening. Thirty-seven patients were treated using this technique. In 30 patients, quality and quantity of bone were within acceptable limits, and in 7 patients, there was extrusion of graft material and post-operative infection.

Conclusion: Treatment of cystic lesion of mandible using combination of modified bone granules and calcium phosphate cement is good alternative to other treatment methods. Long-term and comparative studies are required to evaluate its advantage over the other methods of treatment.

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1. Introduction

A number of techniques have been proposed for obliteration of bony cavity which is left behind after enucleation of cysts and cyst-like lesion from body of mandible. Obliteration of bony cavity is performed using special surgical techniques or by

limiting the volume of the blood clot in the cavity.¹ The former can be accomplished by approximating the bony walls of the cavity or by saucerization-like procedures, while the latter requires grafting with bone and bone substitutes or implantation with a variety of alloplastic materials. Surgical techniques like saucerization, application of osteoperiosteal flap and placement of autogenous bone graft are invasive and time

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Fig. 1 – Bovine derived and modified hydroxyapatite granules (G graft).

consuming surgical procedures and there is morbidity of donor site.² Allografts also have all the characteristics of autografts with the exception of osteogenesis due to the processing that they must undergo. Some are subjected to lyophilization and demineralization, which leaves them more brittle, while others undergo biomechanical alteration with the loss of compressive, bending and torsional strength. Xenografts are good alternative to autografts or allografts but are more costly compared to allografts. Both xeno- and allografts have advantage over other surgical techniques, as there is reduced morbidity of donor site. Continuous research work in field of biomaterials has greatly improved osteoconductive and osseointductive effects of bone substitutes.³ In the past, a number of studies have been done which used calcium phosphate bone cement or modified hydroxyapatite granules for obliteration of cystic cavity in bone.^{4,5} Our study is unique, as we used both natural hydroxyapatite and calcium phosphate bone cement to obliterate bony cavities (Figs. 1 and 2). This prospective study is conducted to evaluate healing of bony cavity in mandible following enucleation of cystic lesion by obliterating the cavity using modified natural bone granules (G graft) and calcium phosphate bone cement (Fig. 3).

Fig. 2 – Calcium phosphate bone cement (G Bone cement).

Fig. 3 – G bone cement after mixing with liquid becomes putty-like material.

2. Materials and method

Written consent was obtained from patients and study conformed to the ethical guidelines of the 1975 declaration of Helsinki. Thirty-seven patients in the age group of 12–58 years who were diagnosed to have cystic lesion in body of mandible were selected. Diagnostic criteria for presence of cyst in body of mandible were presence of well-defined radiolucent lesion seen on panoramic X-ray, presence of fluid on aspiration and histopathological confirmation regarding type of cyst and its origin.

Inclusion criteria:

- (a) Age between 12 and 58 years
- (b) Presence of cystic lesion in mandible

Exclusion criteria:

- (a) Presence of metastasis
- (b) Excessive destruction of bone (through and through defects, excessive thinning of lower border)
- (c) Infected cysts
- (d) Poor medical condition

Size of the cyst cavity was measured using CT scan. Depending upon size they were classified into three different groups: Group A – Cyst measuring less than 2 cm in greatest dimension, Group B – Cyst measuring less than 3 cm in greatest dimension and Group C – cyst measuring more than 3 cm in greatest dimension. Enucleation of cyst was done under local anaesthesia for cysts located in body of mandible (Fig. 4), and those located in molar-ramus area were operated under general anaesthesia. After reflection of mucoperiosteal flap, cyst lining was identified and carefully dissected from muco periosteal layer (Fig. 5), if nerve is present in surgical field, it was identified and preserved and cyst was carefully enucleated. After complete enucleation, peripheral ostectomy was performed using 702 fissure bur. A 1.5 mm drill bit was used to perforate the inferior cortex to increase vascularity at the graft placement site (Fig. 6). First bovine derived modified hydroxyapatite granules (G Graft, G. Surgiwear limited, India)

Fig. 4 – KCOT of anterior mandible in 14-year-old female patient before treatment.

Fig. 5 – Bony cavity seen after enucleation of cyst.

Fig. 7 – Final stage after placement of G graft granules and sealing the opening of cavity using calcium phosphate bone cement.

Fig. 6 – Perforation of inferior cortex using 1.5 mm drill bit.

of size 1 mm were used to fill the cavity, after that calcium phosphate bone cement (G-Bone, G. Surgiwear limited, India) was applied to seal the opening of cavity (Fig. 7). Collagen sheet was used to cover the defect followed by layered closure using resorbable sutures. All patients received i.v. ceftriaxone 1 g twice daily, inj. metrogyl 500 mg thrice daily and oral anti-inflammatory (Aceclofenac 100 mg + paracetamol 375 mg) thrice daily for 7 days. Initially, patients were followed after every 2 days and then after every 7 days for next 4 months.

3. Results

Of 37 patients, 15 patients were female and 22 patients were male. Seven patients were children (mean age 11.5 years) and 30 patients were adults (mean age 38 years). Depending upon size of cyst, 16 patients were included in group A, 15 patients were in group B and 6 patients were in group C. Odontogenic keratocystic tumour was present in 52% of cases followed by dentigerous cyst which was present in 28% of cases while unicystic ameloblastoma (Fig. 9), periapical cyst and residual cyst were present in 8%, 7% and 5% of cases, respectively (Graph 1). In 30 patients, healing was accelerated and completed in 3- to 5-months time (Figs. 8 and 10). Healing time was directly proportional to size of cyst (Graph 2). Complaints of excessive pain, swelling and flap dehiscence were seen in 7 patients. In all 7 patients, there was extrusion of graft material. Quality of bone, which was formed after complete healing, was assessed on CT scan (Figs. 11 and 12); it was found that the bone was predominantly cortical which conformed to D1 type of bone.

4. Discussion

In developing countries like India, treatment of cystic lesion with enucleation and placement of autologous bone graft is

Graph 1 – Type of cyst in study group (in percentage).

Fig. 8 – Follow-up panoramic radiograph after 3 months.

Fig. 9 – Unicystic ameloblastoma in 28-year-old male patient.

Fig. 10 – Follow-up panoramic radiograph after 4 months.

expensive procedure. Patients do not readily agree for such extensive procedures. Removing the cyst contents, then packing it with Iodoform gauze and changing the pack at regular intervals is very effective and economical method of

Graph 2 – Healing time (in weeks) in relation to size of cyst.

Fig. 11 – 3D reconstruction of healed cavity to evaluate quality and quantity of formed bone.

Fig. 12 – Dentascanner examination of healed cavity to check quality of formed bone.

treatment. There is a growing concern among patients for an economical one stage management of such lesions, as many patients feel uncomfortable with Iodoform gauze in oral cavity and some patients who are from remote locations cannot come for regular follow-up and for changing Iodoform dressing. Authors were greatly influenced by advancement in biomaterials, which lead them to focus on new and cost-

effective technique of cyst management. Studies done in past for obliteration of cystic cavity in bone using bone substitute have few limitations. These were slow absorption of graft material,⁶ poor osseointegration properties of material^{6,7} and expulsion of graft material from placement sites.⁸ To overcome these difficulties, authors choose very small bovine-derived and collagen-modified hydroxyapatite granules (G graft), which gets resorbed in a considerable time and collagen molecules present in granules attract multinucleated giant cell initiating degradation of granules. Small size and large quantity of G graft granules greatly increased the amount of blood retained within granules. Perforation of inferior bony cortex to increase vascularity was another step to overcome the limitation of poor osteoinduction. This process establishes direct communication between G graft granules and bone marrow (Fig. 13).

Collagen, when used in conjugation with other osteoconductive carriers like hydroxyapatite or tricalcium phosphate and further when these composites are combined with fresh blood, acts as an osteoinductive material.⁹ Small and irregular shape granules greatly increase the surface area of G graft granules which absorb considerable amount of blood, and in time, the intergranular spaces are filled with granulation tissue, which include fibroblasts, lymphocytes, monocytes and macrophages as well as newly invaded blood vessels.

Multi-nucleated giant cells appear on the surface of granules, which differentiate into osteoclasts and start resorbing it. At the same time, osteogenesis starts from osteoblasts, which are derived from mesenchymal stem cells.

Study by Pandey et al.⁹ and Kattimani et al.¹⁰ proved that G graft or collagen-modified natural hydroxyapatite is capable of regenerating good quality bone in extraction socket and cyst cavities which is much superior to hydroxyapatite only. Similar observation was seen in our study. Defects were filled in 3- to 5-months time, and upon CT scan investigation, adequate and good quality bone was found to be present. Calcium phosphate cement was used to seal the opening of cavity to limit the clot at the grafting site. Furthermore, it

prevents wound dehiscence by providing a strong base against which mucosa can rest. The G graft granules are small in size and lack structural durability, so they cannot prevent flap dehiscence in larger defects. In previous studies in which small-sized hydroxyapatite granules were used, incidence of flap dehiscence was high in larger size defects.^{4,10,11} The explanation for this phenomenon is that, when the granules come in contact with blood they become soft and shrink to 10–12% smaller compared to original size. This shrinkage creates dead space between flap and bony defect causing accumulation of inflammatory fluid or saliva which later leads to flap dehiscence.¹² The calcium phosphate bone cement sets up into a hard mass in 24 h (Fig. 3), which is resistant to shrinkage and prevents entry of inflammatory fluid and saliva into cavity.

Calcium phosphate bone cement is osteoconductive material which rapidly integrates into the bone structure and transforms into new bone by the action of multinucleated giant cells and mesenchymal stem cells responsible for the local bone remodelling.^{4,6} However, in spite of these good properties, it has limitations due to its slow biodegradation. More the amount of calcium phosphate used, more time it will take to heal the bony cavity. The authors modified its application by reducing its quantity, and only little amount was used to seal the cavity and to support overlying mucosa. Some surgeons have attempted to augment the activity and physical properties with composite grafts combining molecular, cellular and genetic tissue engineering technologies.^{13,14}

The molecular approach using Bone morphogenetic protein (BMP) has received the most attention over the past decade. BMPs are differentiation factors that are part of the transforming growth factor superfamily, but many other factors also contribute, such as transforming growth factor (TGF- β s), insulin-like growth factor (IGFs), fibroblast growth factor (FGFs) and platelet-derived growth factor (PDGFs). Recombinant BMP is available for use in reconstructive surgery but high cost limits its use in poor countries. Perforating the inferior cortex makes it possible for blood to make direct contact with G graft bone. Fresh blood itself is a source of various growth factors and mesenchymal stem cells and when combined with G graft, it exhibits osteoinductive properties.^{8,15}

Calcium phosphate bone cement has been shown in previous studies to attract multinucleated giant cells after implantation, although at different rates.^{16,17} These cells multinucleated cells are thought to be responsible for the degradation of the bone substitute materials and at the same time induce vascularization by releasing vascular endothelial growth factor (VEGF) and other biologically active compounds, such as chemokines. Pain, swelling and paraesthesia complaints were nominal in treated patients. Though 30 patients successfully completed the procedure with satisfying results, 7 patients had post-operative infection and extrusion of graft material. Saliva played a crucial role in development of these complications. Saliva contamination not only prolongs setting of calcium phosphate cement but also causes infection if G graft granules are contaminated with saliva.

This method is technically feasible and it is up to the expertise of surgeon to carefully place the G graft and calcium phosphate cement preventing them from getting contaminated with saliva. This study proves that G graft granules along

Fig. 13 – Schematic diagram showing calcium phosphate cement on the top layer which was used to seal the bony cavity, modified hydroxyapatite granules used to fill the defect and perforation of inferior cortex at the lowermost layer. The red arrow showing direction of blood flow.

with calcium phosphate bone cement is a good option for economical one step treatment of cystic lesion of mandible. Further long-term and comparative studies are needed to evaluate its usefulness and advantage in comparison to other techniques.

Conflicts of interest

The authors have none to declare.

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