Original Article

Efficacy of calcium sulfate dihydrate as a bone graft substitute in odontogenic cystic defects of jaws following enucleation: A clinical study

ABSTRACT

Background: The treatment of osseous bone defects created following enucleation of a cyst is an arduous challenge. Autogenous bone grafts despite being the gold standard have various drawbacks such as donor site morbidity, limited availability of bone graft, and increased operative time. Hence, there are various bone grafts which are being investigated which could overcome the limitations of autografts. Thus, this study was conducted to evaluate the efficacy of calcium sulfate (CS), a bone graft substitute, for spontaneous bone regeneration of cystic defects.

Objectives: The purpose of this study is to evaluate bone formation in odontogenic cystic defects following enucleation and reconstruction with bone graft substitute by three-dimensional radiographic and clinical evaluation.

Methodology: A total of twenty patients diagnosed with odontogenic cysts were randomly divided into two groups, out of which the study group had undergone enucleation with bone grafting (tobramycin-impregnated CS dihydrate) and the control group had undergone enucleation without bone grafting. The patients were evaluated clinically and radiographically at the 1st, 3rd, 6th, and 12th months postoperatively.

Results: There was no bone formation observed at 1 month postoperative in both the groups. There was a statistically significant higher bone defect reduction observed radiologically on orthopantomogram and computed tomography scan in the study group than the control group at the 3rd, 6th, and 12th months postoperative. The rate of reduction in cystic volume of the study group at the 12th month was 94.4% and in the control group was 37.16%.

Conclusion: Immediate grafting of cystic cavity can avoid complications such as pathological fracture due to less bone support, delayed healing, etc., The utilization of a graft with a property of inducing rapid bone formation should be taken into consideration. The use of CS as a grafting material accelerated the rate of bone regeneration in the cystic defects, with minimal complications.

Keywords: Calcium sulfate dihydrate, enucleation, odontogenic cysts, volumetric analysis

INTRODUCTION

Odontogenic cysts are one of the most common pathologies encountered by an oral and maxillofacial surgeon. The most commonly occurring of all odontogenic cysts are radicular cysts comprising 48.67%, followed by follicular cysts (17.33%) and odontogenic keratocyst (OKC) (8%).[1] There are various factors influencing the management of cyst that includes age of the patient, size and site of cyst, and its histopathological nature.[2] Treatment modalities for cyst include marsupialization, enucleation followed by primary closure, enucleation with peripheral ostectomy and chemical cauterization, and segmental or marginal resection,

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all of which are intended to eradicate the vital cells within the defect.[3]

Enucleation has been the long-established, standard method of management of odontogenic jaw cysts. It creates a large bony defect which may act as an antecedent for complications such as infection, delayed healing, soft-tissue ingrowth, and pathological fractures. Bone defects heal through continuous remodelling and self repair, however, it fails to heal completely over a certain size, such defects are called critical size defects (CSDs).[4] Hence, the requisite properties of a bone graft must possess at least one of the four ideal characteristics that are osteogenesis, osteointegration, osteoinduction, and osteoconduction.

There are a variety of grafts although autologous bone grafts remain the "biologic gold standard" against which all other forms are assessed. Despite the benefits of autografts, allografts, and xenografts, there are limitations, which have given rise to an increasing interest in bone graft substitutes such as bioactive glasses, glass ionomers, aluminum oxide, calcium sulfate, calcium phosphates, a- and b-tricalcium phosphate, and synthetic hydroxyapatite.[5] Calcium sulfate (CS) has been in use for more than a period of 100 years as a bone graft substitute. This alloplastic material has key features such as high biocompatibility, osteoconductivity, and osteoinductive properties by reducing the local pH, hence leading to local bone mineralization,[6,7] fast rate of resorption, stimulates osteogenesis. It also has an advantage of delivering a high concentration of antibiotics and providing a scaffold for new bone formation, thus aiding in spontaneous bone regeneration which can be assessed radiographically and is proportional to its rate of resorption.[8]

There is sparse literature available on CS-bone graft substitute, in relation to the management of large odontogenic cystic lesions of jaw. Although it has been used immensely in the field of orthopedics in the treatment of infected bony defects, nonunions, osteomyelitis of long bones,[9] considering all of its advantages such as osteogenic, osteoconductive, and osteoinductive properties, we designed a study on odontogenic cystic defects using antibiotic (tobramycin) impregnated CS dihydrate, to evaluate spontaneous rate of bone regeneration potential by three dimensional (3D) radiographic and clinical analysis.

MATERIALS AND METHODOLOGY

The present prospective and randomized clinical study was conducted on systemically healthy patients diagnosed with cystic lesion of maxilla and mandible, between July 2018 and February 2020, reporting to the Department of Oral and Maxillofacial Surgery. Patients having cystic lesion of size more than 2 cm in greatest diameter were included in the study while those with a size more than 15 cm in greatest diameter were excluded from the study. A total of twenty systemically healthy patients with cystic lesions fulfilling the abovementioned criteria were recruited in the present study irrespective of age, gender, and site of lesion. They were randomly divided into two groups using a computer-generated table of random number. The study group underwent enucleation with bone graft substitute (tobramycin-impregnated CS dihydrate) and the control group underwent enucleation without bone grafting. Institutional Ethics Committee, D. M. I. M. S. (D.U.) Ref no. DMIMS(DU) /IEC/2018-19/7503 Date: 30.09.2018.

A detailed case history and written informed consent were obtained. A thorough examination was done clinically and radiographically. Routine analysis of blood was done to rule out any systemic disease. Preoperatively radiographic evaluation was done by: orthopantomogram (OPG) and computed tomography (CT) scan.

After obtaining a preanesthetic fitness, patients underwent surgical procedure under all aseptic precautions and standard surgical protocol. Suitable incision was given and full-thickness mucoperiosteal flap was reflected. Enucleation, curettage of cystic lesion, and peripheral ostectomy were performed. As per the random allocations of patients, in ten patients, primary closure was done without bone grafting and the other ten patients received bone graft substitute. All the surgical procedures were performed by a single experience senior surgeon. Postoperatively, antibiotics, analgesics, and antacids were prescribed.

Preparation of CS beads requires a RapidCure kit which contains 5 cc of CS hemihydrate powder, a premixing solution bulb, pellet mold, and spatula. 240 mg tobramycin liquid (6 ml) was blended with solution and 5 cc of CS in the mixing bowl and was mixed until "doughy" stage for 30 s. The paste formed was then applied to the molds and was set for 15 min. The beads impregnated with antibiotics were then implanted in the cystic cavity of the study group [Figure 1].

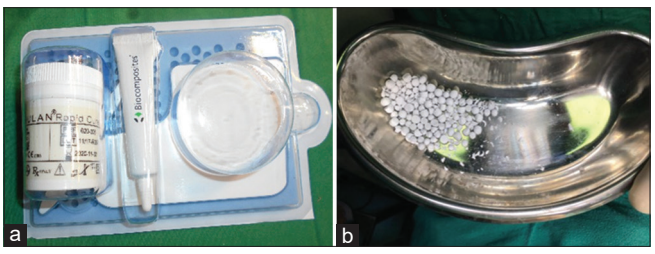

Figure 1: (a) RapidCure kit; (b) calcium sulfate beads

A patient was kept on regular follow-up when clinical and radiographical evaluation was done on OPG and CT scan at 1-, 3-, 6-, and 12-month intervals. An independent observer evaluated the patient on clinical and radiological parameters to minimize any intra-observer discrepancy. The clinical parameters assessed were soft-tissue healing and discharge from wound. Clinical appearance of the soft tissues was assessed postoperatively after 1 week using a Visual Analog Scale.[10] The presence of discharge from wound was assessed 1 week and 1 month postoperatively.

The radiological parameters assessed were rate of bone formation and shrinkage in the cystic volume. The rate of bone formation was assessed on the 1st-, 3rd-, 6th-, and 12th-month follow-up using the Radiopacity Scoring Scale by OPG.[11] The shrinkage in cystic volume was assessed preoperatively and postoperatively on the 1st, 3rd, 6th, and 12th months by CT scan. Using Medsynapse software, the maximum linear dimensions were measured in three planes, that is, coronal plane: maximum buccolingual width, axial plane: maximum anteroposterior length, and sagittal plane: maximum coronoapical height. The cross section of the lesion was demarcated on 2 mm slices of CT images, and volumetric measurement was assessed in three planes.

RESULTS

Among the total twenty patients who were included in the study, the mean age of the patients in the study group was 35.70 ± 15.63 years (15–66 years) and the control group was 30.70 ± 14.84 years (17–66 years). A distinct male gender predilection was seen with a male: female ratio of 3.59:1. The mean initial cystic volume found in patients of the study group was 16.43 ± 16.44 mm^3, and in patients of the control group, it was 11.49 ± 10.66 mm^3. The rate of bone formation was assessed at 1, 3, and 6 months postoperative by using OPG. No bone formation was observed at 1 month postoperative. There was a statistically significant higher bone defect reduction observed in OPG in the study group than the control group at the 3rd, 6th, and 12th months postoperative, $P = 0.043$, $P = 0.0001$, and $P = 0.006$, respectively, by using Chi-square test. On 3D computed tomographic volumetric analysis, it was noted that there was a 3.67%, 35.43%, 81.78%, and 94.4% reduction in the cystic volume in the study group in the 3rd, 6th, and 12th months postoperative ($P = 0.077$, $P = 0.019$, $P = 0.014$, and $P = 0.005$) [Figure 2]. While the reduction in the cystic volume in the control group at the 3rd, 6th, and 12th months postoperative was 0.35%, 9.76%, 18.55%, and 37.16%, respectively ($P = 0.34$, $P = 0.077$, $P = 0.12$, and $P = 0.005$). The soft-tissue healing was assessed at 1 week postoperative where all patients of the control group had normal mucosa. The Fisher's exact test was used to compare discharge from wound, where it was noted in 70% of the study group and 20% of the control group at 1 week postoperative. At 1 month postoperative, both the groups showed the absence of discharge from wound.

DISCUSSION

The purpose of the study was to evaluate the rate of bone formation in odontogenic cystic defects in terms of radiologic volumetric analysis by utilizing CS as bone graft substitute in surgical defects. The defect created within the bone after enucleation of cystic cavities renders the bone fragile and prone to pathological fracture. Such CSDs require more than 1 year for its complete regeneration.[4] To prevent such

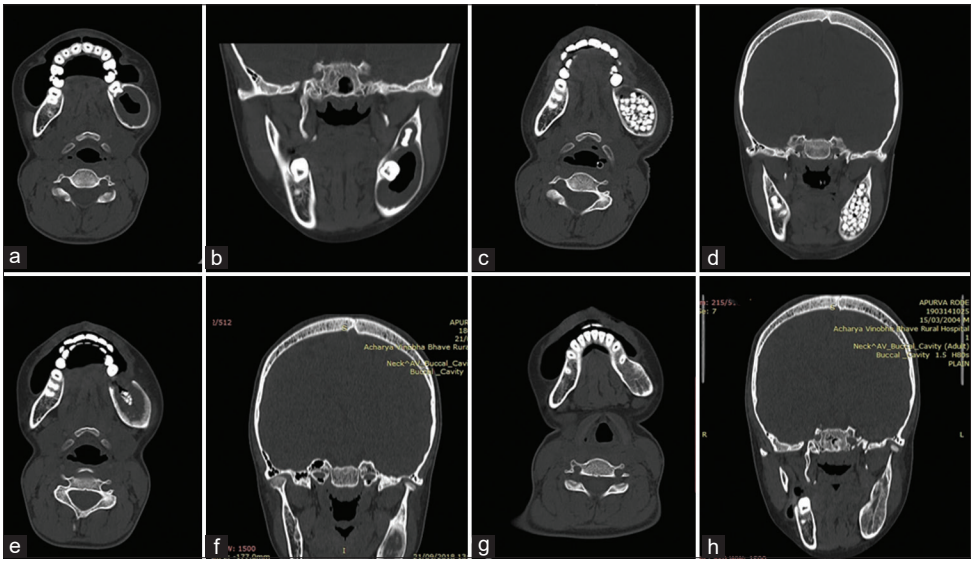

Figure 2: (a and b) Preoperative axial and coronal cut; (c and d) axial and coronal cuts at 1 month postoperative; (e and f) Axial and coronal cuts at 3 months postoperative; (g and h) Axial and coronal cuts at 3 months postoperative

consequences, various bone graft substitutes have been searched, particularly CS is one such bone graft substitute which has been studied in literature recently by Pecora *et al*. due to its resorbable property in a short duration leading to a localized increase in the concentration of the calcium ions which may induce the osteoblastic activity and acts as a scaffold for regeneration of bone.[12]

The prevalence of odontogenic cyst in relation to age, gender, and site of involvement has been reported by various studies. In this study, the average age of the population was 15–66 years with male predilection with a ratio of 3.59:1.[13,1] As per anatomic location, the mandible was observed to be the most commonly affected.[14,11] The distribution of odontogenic cysts according to diagnosis was as follows: OKCs (55%), radicular cysts (35%), and infected dentigerous cysts (10%).

In this study, the rate of bone formation was evaluated radiographically by OPG at the 1st-, 3rd-, 6th-, and 12th-month intervals. At the 3rd, 6th, and 12th months postoperative, there was a statistically significant difference in bone formation in the study group on OPG evaluation. At the 6th and 12th months postoperative, there was a significant bone formation noted in the control group on OPG evaluation. The rate of regeneration of bone into a bone defect is related to the rate of resorption of pellet. Radiological evaluation of bone healing is reliable and predictable to assess the healing of bone graft.

In order to assess the rate of shrinkage and the reduction in volume, measurement of the initial cystic volume is essential. The mean cystic volume was detected on the basis of CT scan by measuring the maximum linear dimensions in three planes: in the study group, it was 16.43 mm^3, and in the control group, it was 11.70 mm^3. There was a statistically significant reduction in the volume of cystic defects noted in the study group by 3D CT scan in the 3rd, 6th, and 12th months, i.e. 5.79 ± 6.41 ($P = 0.019$), 14.35 ± 14.92 ($P = 0.014$), and 16.43 ± 16.44 ($P = 0.005$), respectively. In addition, we found that there was a 3.67%, 35.43%, 81.78%, and 94.4% rate of reduction in the size of the cystic defects of the study group, while in the control group, there was 0.35%, 9.76%, 18.55%, and 37.16% at the 1st, 3rd, 6th, and 12th months postoperative. It was noted that during the follow-up, the CS dihydrate had resorbed gradually and was replaced by new bone from the adjacent tissue, which was assessed radiographically.

Similar studies have been reported to evaluate the efficacy of CS with respect to spontaneous bone healing. Early studies in orthopedic literature reported that the incorporation of CS in cystic defects showed spontaneous bone healing along with 99% resorption within 6 months postoperatively on radiographic examination.[9,15,16]

In any surgical procedure, soft-tissue healing is the main goal to achieve better functional and esthetic outcomes. The most potential complication such as wound dehiscence, infection, and discharge from wound will adversely affect the course of a very well-executed treatment plan. Hence, monitoring at a regular basis is required to check the proper healing of the wound. The study group showed statistically significant soft-tissue healing at 1 week postoperative ($P = 0.004$). The common finding associated in both the groups was discharge from wound. The probable explanation reported for this is related to the serous discharge until the resorption of CS from the wound by the osmotic effect.[9,17,18] Discharge from wound was statistically significant at 1 week postoperative, in the study group ($P = 0.06$) while it was insignificant at 1 month postoperative. Similar studies noticed the presence of serous discharge until complete resorption of CS pellets.[9,17] There was no such complication found after the complete resorption of CS pellets.

In this comparative study, radiographic evaluation of bone formation in the cystic defects was done. The purpose of using a graft material is to treat the enucleated cystic cavity to avoid the dead space. The results of the study validate that the application of CS as a bone graft substitute for regeneration of bone defects in cysts of the oral and maxillofacial region may prove as a useful alternative for bone grafts. It also has an additional property of releasing antibiotics locally.

CONCLUSION

The use of CS in the osseous defects has been popularly used by orthopedic surgeons. It is the most biocompatible bone substitute with rapid rate of resorption and its ability to induce osteogenesis. It also undergoes creeping substitution. Therefore, with a comparable rate of bone formation in the cystic defects, CS can be used as a bone graft substitute. The most accurate and reliable method for evaluating bone formation in large cystic defects by 3D volumetric analysis confirms the complete bone formation within 6 months.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kambalimath DH, Kambalimath HV, Agrawal SM, Singh M, Jain N, Anurag B, *et al.* Prevalence and distribution of odontogenic cyst in

Indian population: A 10 year retrospective study. J Maxillofac Oral Surg 2014;13:10-5.
2. Vasudev S, Vakade CD, Paramesh RC, Prerna R, Deepak S, Mathew AE. Hydroxyapatite and B-tricalcium phosphate for bone regeneration in large cystic cavities. Int J Oral Health Med Res 2017;4:7-11.
3. Stoelinga PJ. The management of aggressive cysts of the jaws. J Maxillofac Oral Surg 2012;11:2-12.
4. Schlegel KA, Lang FJ, Donath K, Kulow JT, Wiltfang J. The monocortical critical size bone defect as an alternative experimental model in testing bone substitute materials. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:7-13.
5. Kumar CY, Nalini KB, Menon J. Calcium sulfate as bone graft substitute in the treatment of osseous bone defects, a prospective study. J Clin Diagn Res 2013;7:2926-8.
6. Moore WR, Graves SE, Bain GI. Synthetic bone graft substitutes. ANZ J Surg 2001;71:354-61.
7. Dimitriou R, Jones E, McGonagle D, Giannoudis PV. Bone regeneration: Current concepts and future directions. BMC Med 2011;9:66.
8. Sheikh Z, Sima C, Glogauer M. Bone replacement materials and techniques used for achieving vertical alveolar bone augmentation. Materials 2015;8:2953-93.
9. McKee MD, Wild LM, Schemitsch EH, Waddell JP. The use of an antibiotic-impregnated, osteoconductive, bioabsorbable bone substitute in the treatment of infected long bone defects: Early results of a prospective trial. J Orthop Trauma 2002;16:622-7.
10. Sivolella S, Berengo M, Bressan E, Di Fiore A, Stellini E. Osteotomy for lower third molar germectomy: Randomized prospective crossover clinical study comparing piezosurgery and conventional rotatory osteotomy. J Oral Maxillofac Surg 2011;69:e15-23.
11. Nakkeeran KP, Saravanan K, Babu P, John RR. Evaluation of bone regeneration in periapical osseous defects with and without platelet rich plasma, combined calcium sulfate and autologous bone graft – A comparative study. J Stomatol Oral Maxillofac Surg 2019;120:196-202.
12. Pecora G, de Leonardis D, Ibrahim N, Bovi M, Cornelini R. The use of calcium sulphate in the surgical treatment of a 'through and through' periradicular lesion. Int Endod J 2001;34:189-97.
13. Ramachandra P, Maligi P, Raghuveer H. A cumulative analysis of odontogenic cysts from major dental institutions of Bangalore city: A study of 252 cases. J Oral Maxillofac Pathol 2011;15:1-5.
14. Jones AV, Craig GT, Franklin CD. Range and demographics of odontogenic cysts diagnosed in a UK population over a 30□year period. J Oral Pathol Med 2006;35:500-7.
15. Kelly CM, Wilkins RM, Gitelis S, Hartjen C, Watson JT, Kim PT. The use of a surgical grade calcium sulfate as a bone graft substitute: Results of a multicenter trial. Clin Orthop Relat Res 2001;382:42-50.
16. Bibbo C, Patel DV. The effect of demineralized bone matrix-calcium sulfate with vancomycin on calcaneal fracture healing and infection rates: A prospective study. Foot Ankle Int 2006;27:487-93.
17. Ferguson JY, Dudareva M, Riley ND, Stubbs D, Atkins BL, McNally MA. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis: A series of 195 cases. Bone Joint J 2014;96-B: 829-36.
18. Podaropoulos L, Veis AA, Papadimitriou S, Alexandridis C, Kalyvas D. Bone regeneration using B-tricalcium phosphate in a calcium sulfate matrix. J Oral Implantol 2009;35:28-36.