Review Article

Application of calcium sulfate as graft material in implantology and maxillofacial procedures: A review of literature

ABSTRACT

Calcium sulphate (plaster of Paris) has been used since 1892 to fill bone defects and as a good bone graft substitute. Calcium sulphate is an osteoconductive, inorganic substance. Following 75 years, many other authors reported variable and a better result in grafting of bone defects and in several cases of immediate and delayed dental implants for good osseointegrations, with no complications attributed to the calcium sulphate. Early results were variable, because of its conflicting crystalline structure, purity, and quality of the calcium sulphate. Apart from this, calcium sulphate also shows predictable resorption rate *in vivo*, presence of minimal trace elements and extremely uniform crystalline structure. Calcium sulphate is a bio-inert material and get resorbed over a period of weeks and fibrovascular tissue takes its place which eventually allows neovascularization and bone formation within the area. Use During the conventional surgical treatment addition of calcium sulphate as a bone graft of in case of placement of dental implants and pathological bony defects it improves the clinical outcome. Calcium sulphate also act as a barrier and filling material for the treatment of "through and through" bony lesions. Use of calcium sulphate as a bone graft substitute avoids the complications and morbidity associated with autograft like infection, second surgery.

Keywords: Bone substitute, calcium sulphate, dental implant, oseoconductive

INTRODUCTION

In context with the dental treatments, there are several circumstances where an osseous grafting might be required. These grafting could be of immense help in restoring the osseous anatomy of the defects created during the treatment procedure or any pathological defects. Grafting may also be useful in the augmentation of resorbed bony contours for dental implants placements. However, treatment of large bony defects is challenging.[1] Osseous grafts primarily act as a scaffold, allowing the native bone formation gradually while maintaining the volume.[2]

A wide array of osseous grafting material has been reported in the literature and also in the clinical application. This encompasses allograft, autograft, xenograft, and non-biological derived products (both mineral and synthetic based). Autologous bone grafting is nevertheless the "biologic gold standard" against all other forms. Autograft provides osteoconductive, osteoinductive, and osteoprogenitor properties enhancing union of the fracture, non-union,

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and osseous defects.[1] The morbidity of such surgeries is approaching 30%. Furthermore, non-availability of autograft is a major concern in young children.[2,3] Calcium sulfate (CS) holds a unique position in the domain of regenerative material.

It has also been used as bone defect filler, binder, grafting material, and as a delivery vehicle for pharmacologic agents and growth factors for more than a century. Calcium sulfate (CaSO4 ½H20) is an inorganic compound which is popularly known as Plaster of Paris or gypsum plaster.[4] It is available in powder and liquid form and assumes its solid form when mixed together. CS has a high compressive strength than that of a cancellous bone and a slightly lower tensile strength when compared to a cancellous bone.[5,6] The key highlight of CS is its biocompatibility, ability to promote osteogenesis and rapid resorption rate.

The maxillofacial application of CS includes the treatment of osteomyelitis, radicular cyst defect repair, socket preservation, ridge augmentation, sinus augmentation, and as an adjunct to dental implant placement. When calcium sulfate is embedded in the body, it dissolves completely and leaves behind deposits of calcium phosphate which invigorate bone growth.[5] Calcium sulfate disintegrates into its component elements naturally occurring in the body; making this bone graft material a well-tolerated and non-immunogenic material.[1]

The release of calcium ions from CS causes activation of platelet to release platelet derived growth factors and bone morphogenic proteins that stimulate osteogenic differentiation and proliferation of mesenchymal stem cells. After placement, it can be monitored radiologically with ease due to its radio-opaque property.[7,8] However, it gradually transforms into newly formed uncalcified bone within the first three weeks rendering it a radiolucent characteristic.[9,10] Over the time, it resorbs by 5th–7th weeks through dissolution and gradually calcifies again at around 12th week and becomes radio-opaque again.[5,11]

CS, in comparison with the other grafting materials such as autogenous graft and freeze-dried bone, shows a faster rate of resorption. Furthermore, it was also observed that the cases where infection was present, CS was able to drain out the pus with no evidence of sequestrate presence, when placed in the infected site.[11] No adverse reaction or failure to heal of CS has been reported in the literature, this makes this osseous graft material well tolerated and non-immunogenic.[12] This paper aims to emphasize on calcium sulfate, its properties along with its clinical implications in context with oral surgery and to provide future perspective in this regard.

PROPERTIES OF CALCIUM SULFATE

Calcium sulfate is a ubiquitous material and is often used as an industrial and laboratory chemical. It has been perceived that the quality of the calcium sulfate and its physical characteristics are the crucial factors for its reproducible performance inside the human body. It was seen that by controlling the shape and size of the calcium sulfate hemihydrate crystals of medical-grade, a product that can get absorbed in the body at a rate consistent with the growth of new bone was possible to obtain. In the form of γ-anhydrite (the anhydrous form), it is used as a desiccant hygroscopic substance that promotes or incites a state of dryness in its surrounding area.[13]

PHYSICAL PROPERTIES

Having a similar chemical structure, the three forms of calcium sulfate vary in the physical structure in context with its crystal size, lattice imperfection, surface area, and hardness.

Anhydrite

It is in the orthorhombic crystal system, having three directions parallel to the perfect three planes of symmetry. The structure of anhydrite consists majorly of cleavage masses and rarely composed of well-developed crystals. The hardness is 3.5 and the specific gravity 2.9. The color varies from white, sometimes greyish, bluish, and to purple with a white streak. It also possesses a vitreous to pearly luster.[14,15]

Calcium sulfate dihydrate

Frequently occurring in nature, as flattened and transparent crystals. It has a monoclinic crystal lattice structure where crystals are found to contain hydrogen bonding and anion water. It has a moderate water-soluble property (~2.0–2.5 g/l at 25°C). Moreover, when compared to the other salts available, CS demonstrates a retrograde solubility, i.e., it becomes less soluble at higher temperatures.

Calcium sulfate hemihydrate

It has two forms—a (alpha) and ß (beta) forms, which, although, possess similar chemical properties, and differ in several aspects [physical properties] including the crystal size, lattice structure, and surface area.[16]

Alpha—Calcium sulfate hemihydrate

Alpha calcium sulfate hemihydrate is manufactured when gypsum is calcined in an autoclave at 120–130-degree Celsius at 17 lbs/sq. inch under steam pressure for 5-7 hours. This process of obtaining CS hemihydrate is also known as wet calcination. The structure constitutes cleavage fragments

and rod and prism-shaped crystals. Generally, the crystals comprise of small particle size.

Beta—Calcium sulfate hemihydrate

It is obtained by milling and heating gypsum at a temperature of 110-130 degrees Celsius through a procedure known as dry calcination. They constitute fibrous aggregates of fine crystals with capillary pores. They are then, pulverized to break up the needle-like crystals. Doing so ameliorates the packing properties. The particle size of CS is larger, irregular, and porous; however, this reduces the hardness and strength.

It is also hygroscopic, and therefore, should be stored in air-tight containers. Moreover, it may tend to assimilate moisture accelerating the setting reaction of CS, when exposed to a relative humidity greater than 70%. It also consists of an aggregate of irregular crystals with interstitial capillary pores.[17]

APPLICATIONS OF CALCIUM SULPHATE

Bone defects

The first to report the utilization of CS as a regenerative material in the late nineteenth century was Dressman.[18] Over 60 years later, Lillo and Peltier used CS rods to repair bone defects in a canine model and reported that CS did not promote bone growth unless covered by periosteum.[19]

When periosteum was present, however, there was total dissipation of the CS in 45–72 days. Furthermore, in approximately three months, a complete regeneration of the defects was observed. They also noted an absence of inflammation and the presence of normal morphology of the bone-related cells.[20,21]

Extraction-socket grafting and ridge preservation

There are multiple options available for socket grafting. The use of autologous bone was originally considered to be the ideal grafting material,[22] as it is completely replaced with vital bone but studies shows that it might lead to significant loss in ridge dimension.[23] Allografts have been found to resorb slower than autologous grafts and provide more dimensional stability to the ridge, and sites grafted with allograft showed less residual graft particles (approximately 15%)[24] when compared to xenograft materials (approximately 30%).[25] Majzoub *et al*.[26] conducted a study on socket grafting with different materials found minimal differences in resorption rate when comparing alloplastic grafts to both allogeneic and xenogeneic grafting materials.

In the sites grafted with CS, the mean trabecular bone was found higher (58% vs. 46%) than nongrafted sites Guarnieri *et al*.[27] used a technique in which a BG/CS composite graft was placed in extraction sockets and subsequently covered with a layer of CS. Vance *et al*.[8] used an allograft combined with putty composed of CS (a-hemihydrate) and sodium carboxy methylcellulose (CMC) to preserve ridge dimensions following tooth extraction. The sites were covered with a CS barrier after the experimental putty was placed in the sockets. The putty was compared with a bovine-derived xenograft covered with a collagen membrane. Dimensional changes post-extractions were similar in both groups, but there was significantly more vital bone in the experimental putty group (61%) versus the xenograft group (26%).

Periodontal defects

CS pellets have been used as implantable filler in treating periodontal bone defects. Alderman placed this material in intra-bony lesions in 35 patients and showed radiographic evidence of bone fill in 79% of the defects. The material was well-tolerated, and there was no evidence of inflammation or infection noted in any of the test sites.

Shaffer and colleague also used CS in treating periodontal intra-bony defects in a small number of patients clinical measurements and radiographs were obtained at initial surgery and surgical re-entry after 6 months.[28] Another study showing Class II/III furcation defects which uses a composite graft comprising of CS as a transporter for carrying tricalcium phosphate mixed with doxycycline hyclate,[29] reported a defect four times more likely to have approximately 50% defect fill and 3.7 times more than nongrafted sites. Histological analysis revealed that the sites grafted with autogenous bone plus CS had the highest proportion of newly formed bone (58%). This percentage was significantly greater than that seen with the other materials.

Barrier membrane

Procedures requiring the use of barrier membranes for both GTR and guided bone regeneration favor the use of resorbable over non-resorbable materials to avoid the chance for a second surgery for the removal of the membrane. Therefore, many absorbable materials, including CS, have been utilized to be used in such procedures.[5]

An *in vitro* study found CS to enhance tissue coverage and compatibility with gingival fibroblast, as well as facilitate cellular attachment when compared to polytetrafluoroethylene (PTFE) and polylactic acid membranes.[30]

Distraction osteogenesis

CS has also been as an adjuvant with distraction osteogenesis of mandible. In a small study consisting of 13 patients, Kim *et al*.[31] demonstrated that addition of CS pellets to the 4 mm

surgical osteotomy wound resulted in a significant increase in bone mineral density at the sites as compared with control sites, which received no CS. It has been suggested that the application of CS may shorten the treatment time.[32] Song *et al*.[33] reported that addition of the CS/CMC composite increased the rate of osteogenesis and calcification. Some workers have also used hyaluronic acid in combination with CS in DO sites and reported positive results.[34]

Osteomyelitis management

The adjunctive delivery of antibiotic therapy for treating osteomyelitis using CS as a carrier has shown promising results. One *in vitro* study showed that in carrying and delivering 11 different antibiotics, the use of dried CS implants proved effective against osteomyelitis.[35] Several human[36] and animal[37] studies reported fascinating results with the use of antibiotic-impregnated locally delivered CS in surgically debrided areas with osteomyelitis. A clinical study utilizing vancomycin-impregnated CS in the surgically-debrided osteomyelitis areas of the jaw showed positive results.[38]

Sinus augmentation

Pecora *et al*.[39] reported the application of CS in sinus augmentation. In an initial report of two cases, they described the successful osseointegration of four implants 9 months after CS was used as a graft material. De Leonar dis and Pecora subsequently performed a prospective, longitudinal study consisting of a "pilot group" of 15 sinuses in 12 patients and a "test group" of 50 sinuses in 45 patients and followed for at least 1 year. Type II or III bone was found in all specimens, and the overall success rate was 98.5%.[40] Several human and animal clinical studies have shown promising outcomes when using CS in sinus augmentation for implant placement. A study reported new bone formation 8–9 months after grafting with no residual bone grafting. Successful osseointegration of implants with both simultaneous and staged approaches kept in CS-grafted sinuses was noted.

Peri-implant defects

Studies shows that trabecular bone formation with no CS remnants while treating peri-implant defects during implant placement through light microscopy, while histomorphometry showed 40% of new bone formation.[41] Compared to other grafting materials, histological and immune histochemical analyses of animal models report no differences compared to CS when used for bone augmentation around titanium implants.[42] For peri-implantitis, one case reported a 2-year successful result after using a combination of inorganic bovine bone and CS following surface decontamination of implant.[43]

CONCLUSION

An ideal bone graft alternative which is suitable for all circumstances does not exist as per the literatures present till date. However, depending on the large array of clinical complications, a wide variety of graft materials are available. Although numerous alterable, such as size and type of the defect along with the time of healing response, and the difference in host response make comparison and interpretations difficult, alloplastic graft materials have an important role as an autograft extender, which when mixed with the available autogenous bone, provides a good total volume of graft material.

CS exhibits many desirable qualities of an ideal regenerative material: (1) In a relatively small period of time, it undergoes complete resorption, (2) It is biocompatible in nature, (3) It lays out a resorbable scaffold for bone growth, (4) It supplies calcium ions, which may stimulate osteoblastic activity, (5) It acts as a transporter for growth factors, small molecule drugs, and antibiotics, and (6) It is relatively inexpensive CS offers further advantage for its use. Future assessments, recognizing both the advantages and shortcomings of CS, must include randomized prospective clinical trials within the wide range of applications indicated for this material.

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Conflicts of interest

There are no conflicts of interest.

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