Following article discusses the technique to use DentoGen® to treat anterior extraction socket.
HOW TO

GRAFT AN EXTRACTION SOCKET

DentoGen bone graft material is formulated to handle a variety of extraction socket grafting cases.

by DR. CHRISTOPHER PROTO
Information provided by Orthogen LLC.

Socket grafting is an increasingly common procedure. Current conventional wisdom is that the extraction socket should be grafted irrespective of whether a dental implant placement is planned. Socket grafting helps to maintain the ridge by regenerating new bone. The result is better both functionally and cosmetically.

DentoGen® is a medical-grade calcium sulfate hemihydrate-based bone graft material developed and sold by Orthogen LLC. DentoGen is indicated as:
- a bone graft by itself
- as a mixing agent with other bone grafts
- as a barrier to prevent ingrowth of soft tissues

Versatile material
Although DentoGen is approved for use as outlined above, it works best as a bone graft by itself in smaller defects such as incisor or premolar extraction sockets (any defect smaller than a premolar extraction socket). In larger defects, such as molar extraction sockets, the material works best in combination with other bone grafts such as allograft.

Packaging
A box of DentoGen contains two patient-specific kits with two grams of calcium sulfate material—one gram of material per patient-specific kit—regular setting solution (normal saline), and fast set solution (4% potassium sulfate). When the regular setting solution is added to the DentoGen powder, it forms a putty that can be implanted into the bone defect. DentoGen also can be mixed with the fast set solution to form a putty in an accelerated fashion.

WEB EXCLUSIVE
For more techniques and articles from our Cosmetic/Restorative team, go to dentalproductsreport.com.

AT A GLANCE
1. Patient at Initial presentation.
2. Extraction sockets for tooth Nos. 8 and 10.
3. An opened DentoGen Kit featuring powder and two setting solutions.
4. Add regular setting solution to the DentoGen powder.
5. Mix the powder with the regular setting solution.

DENTOGEN FEATURES
- Formulated with medical-grade calcium sulfate hemihydrate
- Stimulates bone growth into the defect
- Possesses soft tissue barrier properties

Orthogen LLC orthogencorp.com 877-336-8643
Clinical case
A 78-year-old female patient presented with hopeless tooth Nos. 8 and 10 (Fig. 1). After extensive examination and consultations, it was determined the teeth would be extracted.

Both teeth were extracted atraumatically. Fig. 2 illustrates the extraction sockets following the extraction procedure. Implants were not planned for the patient in this case.

Use the DentoGen Kit. Fig. 3 shows an opened kit with the powder, regular setting solution and fast setting solution. The extraction sites are grafted with DentoGen to maintain the alveolar ridge.

Regular setting solution is added to the DentoGen powder and mixed to form a putty (Figs. 4-5). Fig. 6 shows the resulting moldable putty of DentoGen.

The material is placed in the extraction sockets layer by layer. Rather than filling the entire extraction socket with one bolus of DentoGen, it is applied in at least 3-4 layers to achieve better bone regeneration (Fig. 7).

Slightly overfill the extraction socket.

The extraction sockets are slightly overfilled in layers with DentoGen bone graft material (Figs. 8-9).

After all sockets have been filled, mattress sutures are placed to contain the graft. DentoGen also acts as a barrier, which is a plus, and the fast set potassium sulfate solution can be applied after suturing to shorten the setting time (Fig. 10).

This socket grafting technique offers an alternative to bovine xenografts and human allografts in certain clinical situations. It aids in bone regeneration by the conversion of calcium sulfate hemihydrate into calcium phosphate, which is a principal component of human bone.

6. A moldable putty of DentoGen is formed and ready for placement.

7. The material is placed in the extraction sockets in layers. It is recommended to do so in at least 3-4 layers for optimal bone regeneration.

8. Slightly overfill the extraction socket.

9. The additional extraction socket is also filled in layers, and a mattress suture is placed.

10. Fast Set solution can be applied to accelerate the setting of grafted material.
Following case report discusses the use of DentoGen® in combination with allograft to treat infrabony defect. DentoGen® is also used as a barrier.
Bone Repair in Periodontal Defect Using a Composite of Allograft and Calcium Sulfate (DentoGen) and a Calcium Sulfate Barrier

Ziv Mazor¹
Sachin Mamidwar²
John L. Ricci³
Nick M. Tovar *2,3*

Deep bone defects are caused by the progression of periodontal disease, which breaks down bone and connective tissue that hold teeth in place. In this case, a 37-year-old male patient presented a deep bone defect with advanced periodontal disease around an upper canine. Medical-grade calcium sulfate was mixed with demineralized freeze-dried bone allograft and used to repair and regenerate the defect. Analysis of the radiographs at the 5-month time point showed the bone had completely regenerated.

Key Words: periodontal disease, calcium sulfate, allograft, composite

INTRODUCTION

Periodontal disease can result in the destruction of soft tissue and bone that support the teeth, leading to tooth loss. An estimated 75% of American adults are affected by this disease, of which 25% to 30% have severe forms.¹,² Periodontal disease is caused by highly organized bacterial biofilms that can trigger a destructive inflammatory response by the host.³,⁴ Factors such as smoking, diabetes, stress, genetic susceptibility, and so forth further aggravate periodontal disease.⁵,⁶ Some studies have also shown chronic periodontal disease to be correlated with systemic conditions such as coronary heart disease and stroke.⁷–⁹ To combat periodontal disease, an improvement in oral hygiene and removal of bacterial deposits are essential. In severe cases, surgical repair is necessary.

Surgical repairs using bone replacement grafts is a common method used to rapidly repair and regenerate bone. These grafts have been shown to statistically significantly increase bone and clinical attachment levels and reduce probing depths, as compared with open flap debridement procedures.¹⁰–¹³ In a study by Paolantonio et al,¹⁴ it was shown that when using pure calcium sulfate (CS) with a membrane barrier, there is a significantly greater improvement when compared with open flap debridement.¹⁴
Allogenic tissue, such as demineralized freeze-dried bone allograft (DFDBA), can also be used in combination with CS as a bone-filling binder.\textsuperscript{15,16} A CS or synthetic membrane barrier is then added to prevent ingrowth of cells. Nonresorbable synthetic membranes, such as expanded polytetrafluoroethylene, are far more invasive and time-consuming than is a resorbable CS membrane.\textsuperscript{17} Calcium sulfate, a material that has been used as a bone-filling material for more than 110 years,\textsuperscript{18} has been shown to be completely bioabsorbable,\textsuperscript{19} to be osteoconductive,\textsuperscript{14} to allow fibroblast migration,\textsuperscript{20} to not cause an inflammatory response,\textsuperscript{21} and to not elevate serum calcium levels.\textsuperscript{22} Recently, it has been shown that CS can be manufactured into a granular composite of CS and poly-L-lactic acid to decrease the degradation rate if the application calls for a slower dissolution.\textsuperscript{23} Strocchi et al observed significantly more blood vessel growth in defects filled with CS than those filled with autograft, proving its angiogenic properties.\textsuperscript{24} Blood vessels provide nutrition for growing bone and accelerate bone growth. Two parallel series of mechanisms are triggered by the degradation of CS into deep bone defect (Figure 1). The first mechanism involves the release of calcium and sulfur ions in the biological environment, which results in carbonate apatite formation and calcium ion stimulation of cellular activity.\textsuperscript{25} The second mechanism is the precipitation of calcium phosphate, which leads to a transient, local drop in pH. This causes surface demineralization of existing bone resulting in exposure of bioactive molecules and the release of growth factors such as transforming growth factors and bone morphogenetic proteins, which stimulates the growth of bone in defects filled with CS.\textsuperscript{25–28} Calcium sulfate has been used as a bone graft by itself, in combination with other bone grafts, and also as a barrier to treat extraction sockets.

**CASE REPORT**

A 37-year-old male patient presented with advanced periodontal disease around an upper canine. A deep bone defect of 8 mm was found in the distal aspect of the tooth, as seen grossly and by radiograph in Figure 2a and b.

The deep bone defect was accessed by elevating the full mucoperiosteal plate. The defect was debrided of all granulation tissue, and the root surface was carefully planed. DFDBA was mixed with medical grade CS (trade name DentoGen, Orthogen, LLC, Springfield, NJ) at a ratio of 75:25 (DFDBA: DentoGen; Figure 3a). Fast-setting solution was added to this mixture to form the bone graft composite. The composite was grafted into the deep bone defect using a spatula, as shown in Figure 3b. It was tightly compressed to thoroughly fill the defect. The defect was closed with a pure CS (DentoGen) barrier to prevent the ingrowth of soft tissue. Fast-setting solution was added to CS to form the putty, which was implanted as a barrier (Figure 3c). Nonresorbable suture was placed to reposition the flap (Figure 3d). Preoperative digital radiographs of the deep bone defect were taken to facilitate comparison with future time points. Digital radiographs of the grafted site were taken at 1- and 5-month postoperative time points. All of the radio-
graphs were taken using a long cone beam. A standard bite holder was placed while taking a radiograph. The patient was followed every month for up to 6 months.

When observed grossly, the site was healing well at the 1-month time point, and radiographs showed the grafted material was slowly resorbing (Figure 4a). At the 5-month postoperative time point, the site was grossly observed to have healed well, and the deep bone defect observed in the preoperative radiograph was now replaced with bone, as evidenced by radiographs (Figure 4b).

Figure 2. (a) Preoperative periodontal deep bone defect around upper canine. (b) Preoperative radiograph of periodontal deep bone defect around upper canine.

Figure 3. (a) Mixture of allograft and DentoGen. (b) Allograft and DentoGen composite implanted in periodontal deep bone defect. (c) Defect closed with DentoGen membrane barrier. (d) Sutures placed over the top.
DISCUSSION

A severe form of periodontal disease has been surgically treated using a 75% DFDBA/25% CS composite graft and a pure CS membrane barrier. Because CS has significant bone regeneration properties of its own as a bone graft, it not only acts as a binder that prevents DFDBA from migrating out of the deep bone defect but also further aids in bone growth by depositing a calcium phosphate trellis, preventing ingrowth of soft tissues, stimulating blood vessel formation, and affecting the release of growth factors.

When comparing the gross initial bone defect to the 5-month time point, a complete healing of the bone with no gingival recession was noted. At both the 1- and 5-month time points, the patient showed no signs of discomfort, and no infection was observed. Analysis of the radiographs verified the gross observations as the bone showed signs of remodeling at the 1-month time point and complete bone growth at the 5-month time point. As DFDBA underwent remodeling, CS degraded and slowly resorbed, leading to the formation of a calcium phosphate trellis, which further stimulated bone growth. This resulted in the deep bone defect’s being filled with regenerated bone at the 5-month postoperative time point.

These results were similar to previous clinical studies on 19 patients with chronic periodontitis, which indicate that CS, used as a binder and barrier in combination with DFDBA, supports significant clinical improvement in intrabony defects. The authors observed that after 6 months, there was a reduction in probe depth, gains in clinical attachment level, and defect fill and resolution. A similar study by Harris evaluated a CS porous hydroxyapatite and tetracycline binder combined with DFDBA and a CS barrier in 100 patients. Their technique also found a decrease in probe depth and an increase in clinical attachment level after 6 months. A

Figure 4. (a) Radiograph obtained 1 month postoperatively. (b) Radiograph obtained after 5 months shows degradation of grafted material and bone growth in the original defect.
long-term, 6-year study of 12 patients by Orsini et al also yielded similar results. 31 They used a combination of autogenous bone grafting plus CS as a binder and barrier and compared it to a defect treated with a bioabsorbable membrane. 31 After 6 years, there was no significant difference found between the two techniques. There was also a decrease in probe depth and an increase in clinical attachment level. It was also observed that there was no statistically significant difference when comparing the long-term, 6-year results to their short-term, 6-month data.

CONCLUSION

In this surgical case report, medical-grade CS mixed with DFDBA was found to be a biocompatible composite graft with the ability to provide radiographic evidence of hard-tissue repair of a periodontal intrabony defect. The incorporation of CS improves the handling characteristics of DFDBA as well as the cost-effectiveness of the procedure.

ABBREVIATIONS

CS: calcium sulfate
DFDBA: demineralized freeze-dried bone allograft

REFERENCES


Following case report discusses the use of DentoGen® in combination with ß-TCP to treat molar extraction sockets.
Patients present for extraction of teeth for numerous reasons. Whether teeth are being removed in preparation for orthodontic therapy, malposition or to eliminate dental disease, the sites require reconstruction. Many patients will have restorations placed over or adjacent to these areas of reconstructed bone. In current times, most will have implants inserted in the regenerated bone. For successful maintenance of aesthetic implant-supported restorations, maximal volume in the restored site containing vital bone with keratinized tissue will enable the surgical/restorative team to design functional and aesthetic restorations. In this manner, the patients are returned to an ideal state, maintainable for many years.

**KEY WORDS:** Site preservation, alloplast, dental implants

2. Private Practice Periodontics and implant Dentistry Ra’anannah, Israel.
3. Senior Researcher, Department of hard Tissue Research, U. of Minnesota, Minneapolis, Minnesota.
4. Professor and Director, Division of Oral and Maxillofacial Pathology, Director Hard Tissue Research Lab, University of Minnesota, School of Dentistry, Minneapolis, Minnesota.
INTRODUCTION

Before a tooth or multiple teeth are extracted, a determination should be made regarding hard and soft tissue volume in the area. Periodontally involved teeth are typically missing supporting bone which must be replaced at the time of extraction. The roots of the teeth also take up space which must be filled in with vital bone to enable osseointegration. Determination of the combined volume of these two defects and if/where there may be missing walls will assist the surgeon at the time of extraction. In the aesthetic zone, forced eruption may be incorporated into the treatment plan. This technique utilizes orthodontic forces to augment, non-surgically, both the alveolar bone and keratinized tissue. In this manner, extraction sites can be diminished in volume prior to removal of the tooth.

More often, patients present for extraction without the luxury of time on the side of the dental team. In many instances, patients require the removal of a tooth or teeth and do not have the ability to wait 3 to 6 months for forced eruption to regenerate gingiva and bone. In these cases, bone and the surrounding soft tissue have to be reconstructed in one or more procedures at the time of extraction. This is accomplished by a combination of bone replacement graft materials, barriers, and in some cases, growth enhancing factors as well.

Previous studies have documented the preservation of alveolar volume utilizing various graft materials. These papers demonstrate that placing a biocompatible material will minimize the decrease in socket dimensions after the procedure. Although the height and width of the remaining bone are not significantly altered by using this type of material, the histologic appearance in the socket is different than native alveolar bone.

The materials documented in this case series have been shown in human and animal studies to be completely resorbable in the time normally used between tooth extraction and delayed implant placement, 4 – 6 months. The synthetic betricalcium phosphate (β-TCP) has no incidence of disease transmission and, as a salt, is dissolved rather than depending on the action of osteoclasts to resorb it. The material has been shown to be equivalent in resorption and vital bone formation to autogenous bone in maxillary sinus augmentation. Calcium sulfate has been used as a bone replacement graft and/or graft enhancer for 100 years. This material as well is both synthetic and fully resorbable. The purpose of this article is to demonstrate the use of β-TCP alone or in combination with calcium sulfate as predictable materials for maintenance and/or enhancement of bone volume after tooth extraction.

MATERIALS AND METHODS

Three cases are presented in which extraction sites and their associated defects were treated with β-TCP (figure 1). After adequate healing time, bone cores were harvested from the surgical sites at the time of dental implant placement. The trephines containing the bone were fixed in 10% neutral buffered formalin. Upon receipt in the Hard Tissue Research Laboratory at the University of Minnesota Dental School, the specimens were immediately dehydrated with a graded series of alcohols for nine days. After dehydration, the specimens were infiltrated with a light-curing embedding resin (Technovit 7200 VLC, Kulzer, Wehrheim, Germany). Following twenty days of infiltration with constant shaking at normal atmospheric pressure, the specimens were embedded and polymerized by 450 nm light with the tem-
perature of the specimens never exceeding 40°C. The specimens were then prepared to by the cutting/grinding method of Donath.8,9 The specimens were cut to a thickness of 150 µm on an EXAKT cutting/grinding system (EXAKT Technologies, Oklahoma City, USA). The slides were then polished to a thickness of 45 µm using the EXAKT microgrinding system followed by alumina polishing paste and stained with Stevenel's blue and Van Giessen's picro fuchsin. Following histologic preparation, the cores were evaluated morphometrically. All the cores were digitized at the same magnification using a Zeiss Axiolab microscope and a Nikon Coolpix 4500 digital camera. Histomorphometric measurements were completed using a combination of Adobe PhotoShop (Adobe Systems, Inc.) and the public domain NIH Image program (developed at the U.S. National Institutes of Health and available on the Internet at http://rsb.info.nih.gov/nih-image/). At least two slides of each core were evaluated. Parameters evaluated were total area of the core, percentage of new bone formation, and percentage of residual graft material.

CASE REPORTS

Case 1
After a second course of antibiotics prescribed by another dentist, this patient presented to for definitive therapy around tooth #30. She had a history of pain and swelling on the tooth that had endodontic therapy but was never restored with a crown. When a radiograph was taken of the lower right first molar, it was apparent that there was significant bone loss in the furcation (figure 2). Clinical inspection of the tooth revealed a vertical fracture through the remaining coronal portion of the tooth (figure 3).

After administration of local anesthesia, the tooth was sectioned and the individual roots extracted. Minor flap elevation enabled complete debridement of the area and visualization of the sites where the residual buccal plate was very thin (figure 4). To prevent site collapse and to enable the possibility of future implant placement, the site was grafted with Cerasorb® M (Riemser Inc., Research Triangle Park, North Carolina, USA) mixed with the patient’s
own blood (figures 5,6). Combining the graft particles with blood from the site enabled the mixture to handle like a gel or putty and kept the material where it was placed in the socket without washing out during the procedure. To enhance guided bone formation in the defect, the graft was covered by a resorbable barrier (EpiGuide®, Riemser Inc., Research Triangle Park, North Carolina, USA). This three layer synthetic membrane has the ability to maintain its’ own shape and allow fluid transfer to the graft beneath it. A recent study comparing resorbable barriers has demonstrated that Epiguide® has one of the best abilities to facilitate early osteoblast cell attachment, ideal for promoting maximal bone formation in an extraction socket.10 The area was closed with sutures, but primary closure was not obtained (figure 7). By the three month postoperative visit, the tissues had fully keratinized and radiographic evidence of bone fill was apparent (figures 8,9).
Figure 5: β-TCP alloplast mixed with patient’s blood.

Figure 6: Extraction site grafted with β-TCP. Note resorbable membrane.

Figure 7: Case 1 surgical closure. Note that full primary closure was not obtained and portions of the resorbable membrane are visible.

Figure 8: Note full soft tissue closure and keratinization of the surgical site in Case 1.
Case 2
This patient presented with pain in a maxillary molar tooth. Though the tooth was vital, inspection revealed a complete vertical fracture through the central portion of the tooth incorporating the distobuccal root (figure 10). To minimize trauma to the alveolar bone, the tooth was sectioned and the other roots extracted utilizing Piezosurgery (Mectron, Verona, IT). Previous papers have shown the effectiveness of this type of instrument as an aid to numerous types of oral surgical procedures.\textsuperscript{11} The tooth was extracted with minimal trauma to the bone and surrounding soft tissue (figure 11). Elevation of a full thickness flap was only needed for access to and debridement of the defect on the mesiobuccal region. After careful debridement, the graft material (Cerasorb M) was mixed with a calcium sulfate containing a methylcellulose binder (CalMatrix, Keystone Dental, Boston, MA). This mixture was utilized to give more of a putty-like consistency (figure 12), enabling maximal volume preservation in the mesiobuccal region. The addition of calcium sulfate to the graft material has also been shown in other studies to enhance vital bone formation and turnover of the graft material to vital bone.\textsuperscript{12} A recent paper has shown more complete healing when calcium sulfate has been added to $\beta$-TCP.\textsuperscript{14} In this animal study, better bone was formed and the bone fill was to a higher level coronally compared to sites grafted without the extra graft additive. For complete graft containment and to further enhance healing,
a calcium sulfate barrier (Bone Gen, Ortho- gen, NJ) was placed over the coronal portion of the graft (figure 13). The flaps were closed, but primary closure was not obtained and sutures were placed (figure 14). An immediate postsurgical radiograph demonstrated alloplastic fill of the extraction site (figure 15).

Over the next two months, the soft tissues fully granulated over the calcium sulfate barrier and closed the coronal portion of the socket (figure 16). Six months after extraction and grafting, the site was opened. Clinical evaluation revealed an absence of graft particles, but full volume and width reconstruction from the surgical procedure (figures 17,18). A one-stage dental implant was placed with an osteotome technique to facilitate the placement of a longer implant and to enable better stabilization at the sinus floor. A 5 year postsurgical radiograph is presented in figure 19.
Figure 13: Extraction site grafted with β-TCP and covered with calcium sulfate barrier.

Figure 14: Case 2 surgical closure. Note that full primary closure was not obtained and portions of the resorbable barrier are visible.

Figure 15: (right)  
Immediate postsurgical radiograph demonstrating alloplastic fill of the extraction site.

Figure 18: (bottom right center)  
Case 2 radiographic presentation at 6 months after surgery. Note bone fill.

Figure 19: (bottom far right)  
5 year follow up radiograph of Case 2.
Figure 16: Note full soft tissue closure and keratinization of the surgical site in Case 2.

Figure 17: Case 2 clinical presentation at 6 months after surgery. Note bone fill.
Case 3

This patient presented with a failing restoration on a mandibular right first molar tooth (figures 20, 21). Upon evaluation, the tooth was deemed to be non-restorable and atraumatically extracted (figure 22). After debridement of the socket, the site was grafted with a mixture of blood from the site and a pure phase, beta-tricalcium phosphate (Cerasorb M) to ideal contour (figure 23). The graft material was covered with a resorbable collagen membrane and the flaps closed.

The site was followed radiographically, observing resorption of the graft particles and concomitant vital bone formation in the site (figure 24). Six months after the extraction, the site was opened for placement of a dental implant. No graft particles were evident on visual inspection of the site. After retrieving a core of the regenerated material for histologic analysis, the implant was placed. The alveolar ridge volume was sufficient to enable placement of a wide body, wide neck one stage dental implant that was fully stable at insertion (figure 25).
All Cases
Dental implant fixtures were delivered in all cases. At the appropriate time after implant placement, restorative procedures were performed. The implants were restored with cemented ceramo-metal restorations to return the patients to ideal form and function. Alveolar crestal height was followed radiographically from the time of extraction through placement of final restoration to assist in determination of stability of the crestal attachment apparatus. In all cases, there has been no loss of alveolar bone from the crestal region over the time frame studied (1-5 years). There has also been no change in the level of the facial gingival margin over the same time period.

CONCLUSIONS
The techniques of extraction and simultaneous graft and barrier placement presented in this article are very predictable for restoring volume.
of the alveolar ridge. When resorbable barriers are utilized to cover the graft, certain materials can be safely left partially exposed to the oral environment. The cases shown in this report demonstrated this principle with various materials. If primary closure cannot be maintained leaving a large area exposed, or is not desired, the surgeon may benefit by the placement of a dense PTFE barrier over the grafted site.\textsuperscript{15,16}

Synthetic graft materials are advantageous in their ability to be used in any country around the world. The same is not true for all products of human and/or animal origin. Patients must make informed decisions on the materials that surgeons place with respect to the origin of these products and their expected biologic results. In the cases shown in this paper, vital bone was formed in all re-entered, regenerated sites. In the maxillary molar site, 32\% vital bone was formed and only 8\% residual graft was left (figure 26). In the mandibular molar site, 51\% vital bone resulted with less than 1\% remaining bone replacement graft material (figure 27). This is in contrast to studies with bovine graft materials where anywhere from 25-35\% residual graft has been shown.\textsuperscript{17}

The predictable formation of vital bone in the treated extraction sockets of this and other studies has led to 100\% success rates in implant placement and loading.\textsuperscript{18} Additionally, this bone has maintained radiographic integrity and enabled support of keratinized tissue with no dimensional alterations over time. Additional studies are needed comparing vital bone formation in sockets and in maxillary sinus augmentation with \textsuperscript{\beta}-TCP compared to other graft materials.

\noalign{\vspace{1cm}}

**Correspondence:**

Dr. Robert Horowitz
2 Overhill Rd, Suite 270
Scarsdale, NY, 10583
RAHDDS@gmail.com
**Disclosure**

Drs. Horowitz and Mazor report receiving an honorarium from Reimser, Inc.

**References**


Following article reviews the extensive use of calcium sulfate for bone grafting purposes in clinical implant dentistry.
Medical-Grade Calcium Sulfate Hemihydrate in Clinical Implant Dentistry: A Review

Ahmad Kutkut1 & Sebastiano Andreana2*

Departments of 1Prosthodontics and 2Restorative Dentistry, State University of New York at Buffalo, School of Dental Medicine, Buffalo, New York

*Address all correspondence to: Sebastiano Andreana, DDS, MS, Associate Professor, Director of Implant Dentistry, Department of Restorative Dentistry, State University of New York at Buffalo, School of Dental Medicine, 235E Squire Hall, 3435 Main Street, Buffalo, NY 14214, USA; Tel.: 716-829-6645 or 716-829-2923; Fax: 716-829-2440; andrean@buffalo.edu.

ABSTRACT: Medical-grade calcium sulfate has been successfully used for several decades as a bone filler and as a carrier with medications or bone growth factors for the treatment of bone defects. The present review illustrates the biological behavior and clinical outcomes of this material when used in clinical implant dentistry. Furthermore, the review illustrates the different indications specifically related to implant dentistry when medical-grade calcium sulfate has been used alone or in combination with bone grafting materials. The histological published evidence is reviewed together with successful clinical results. This material, well known since the 1800s, continues to be used by clinicians and researchers worldwide, and the latest scientific evidence clearly indicates that medical-grade calcium sulfate can be used alone or in combination with biologically active proteins in applications such as socket preservation, ridge augmentation, and sinus lift procedures.

KEY WORDS: calcium sulfate, implant dentistry, bone regeneration

I. INTRODUCTION AND HISTORY OF USE

Gypsum plaster, also referred to plaster of Paris, is first documented as being used for fracture treatment by the Arabs in the 10th century.1 The first internal use to fill bony defects was reported in 1892 by Dreessmann.2 The application of plaster of Paris as a bone void filler and antibiotic-laden plaster in the treatment of infected bony defects has been supported by various studies.3–6 Calcium sulfate (CaSO4), generally known as plaster of Paris, has long been used in its partially hydrated form. Bone grafting is a common procedure in dental implant surgery. The clinical use of medical-grade calcium sulfate hemihydrate (MGCSH) has a much longer history than most of the currently available biomaterials. This material undergoes rapid and complete resorption without significant inflammatory response, and its biocompatibility when used to fill bone defects is well documented. The primary advantage of using MGCSH is that it can be used in the presence of infection. The raw material from which it is made is relatively inexpensive and readily available. In addition, MGCSH can be used as a carrier to deliver growth factors.

MGCSH has found wide use in orthopedics and dentistry. In the latter field, it has been used in a variety of clinical applications, including periodontal defect repair, sinus augmentation, extraction socket preservation, and endodontic treatments. In addition, it has been used as a membrane barrier to prevent the loss of grafted material and as an adjunct to dental implant placement.

It has been shown that MGCSH could serve as a matrix that holds other graft material particles and does not interfere with the healing processes.7–15 Despite these advantages, this material has not gained the same popularity as many other currently available regenerative materials.16
II. CALCIUM SULFATE PROPERTIES

Medical-grade calcium sulfate is crystallized in highly controlled environments producing regularly shaped crystals of similar size and shape.\(^\text{17}\)

\(\text{CaSO}_4\) goes through a process called calcination when it is heated at 110 °C, and during this process it loses water. The product obtained from this reaction is calcium sulfate hemihydrate. The reaction is described below in detail:

\[
\text{CaSO}_4 \cdot 2\text{H}_2\text{O} \rightarrow \text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O} + \frac{1}{2}\text{H}_2\text{O}
\]

Calcium sulfate hemihydrate can be obtained in 2 forms: denominated \(\alpha\) and \(\beta\). The main differences between these 2 forms are crystal sizes, crystal surface area, and lattice imperfections. Although these forms are chemically identical, they differ considerably in physical properties.\(^\text{16}\) Particularly, “the \(\beta\) form is a fibrous aggregate of fine crystals with capillary pores, whereas the \(\alpha\) form consists of cleavage fragments and crystals in the form of rods or prisms.”\(^\text{18}\) Furthermore, the crystals of the \(\beta\) form have a “sponginess and irregular shape,” whereas crystals in the \(\alpha\) form are denser and have a prismatic shape.\(^\text{18}\)

Three essential principles for bone regeneration are: osteogenesis, osteoinduction, and osteoconduction. Osseointegration is defined as the final bonding between host bones and grafting material. Osteoprogenitor cells living within the donor graft may survive during transplantation, and could potentially proliferate and differentiate to osteoblasts and eventually to osteocytes. These cells represent the osteogenic potential of the graft.\(^\text{19}\)

Osteoinduction, on the other hand, is the stimulation and activation of host mesenchymal stem cells from the surrounding tissue, which differentiate into bone-forming osteoblasts. This process is mediated by a cascade of signals and the activations of several extracellular and intracellular receptors, the most important of which belong to the transforming growth factor-beta (TGF-\(\beta\)) family.\(^\text{19}\)

Osteoconduction describes the facilitation and orientation of blood vessels and the creation of the new Haversian systems into the bone scaffold.\(^\text{20}\) Calcium sulfate is considered an osteoconductive bone substitute.\(^\text{20}\)

III. CLINICAL ADVANTAGES

MGCSH has ideal regenerative properties. In fact, this material undergoes complete resorption in a relatively short period of time, is extremely biocompatible, provides a resorbable scaffold for bone growth, provides a plentiful supply of calcium ions that can stimulate osteoblastic activity, is easily used as a delivery vehicle for growth factors, and is relatively inexpensive. Nevertheless, it does have some disadvantages, including handling technique sensitivity associated with the clinical application of the paste form. The rapid resorption can, under some circumstances, be disadvantageous in the healing process. This is because the grafted area does not maintain the preferred shape. Lastly, the material is not particularly strong, even when preset forms are used, which makes it difficult to fulfill the space preservation or scaffold function often required in bone regenerative applications.\(^\text{16}\)

IV. CLINICAL USES OF CALCIUM SULFATE IN IMPLANT DENTISTRY

IV.A. Extraction Socket Preservation Prior to Implant Placement

An in vivo study on a canine model by Cardaropoli et al. described the histological events into an extraction socket.\(^\text{21}\) Following tooth extraction, the first 24 hours are characterized by blood clot formation. Within 2 to 3 days, the blood clot contracts and is replaced by the formation of granulation tissue with blood vessels and collagen fibers. After 4 days, an increased density of fibroblasts is visible in the clot and the proliferation of fibroblasts from wound margins is apparent. Remodeling of the sockets begins with the presence of osteoclasts inducing bone resorption. One week after extraction, the socket is characterized by granulation tissue consisting of a vascular network, young connective tissue, and osteoid formation in the apical por-
tion, and epithelial coverage over the wound. Three weeks after the extraction, there is dense connective tissue overlying the residual sockets, which are filled with granulation tissue. A trabecular pattern of bone starts to merge. At 2 months’ observation, bone formation in the socket is not yet complete, with a not fully mineralized osteoid being present, the bony height of the original socket not yet reached, and the trabecular pattern still undergoing remodeling.21

Several articles in the literature report the use of MGCSH in extraction sockets. An overall level of agreement from these studies indicates that at 3 months, a good bone consistency and an almost completely preserved volume are achieved, which are fundamental to an ideal implant placement. The use of calcium sulfate has been shown both clinically and histologically to improve new bone formation in intact extraction sockets before implant placement. Histologically, MGCSH was not observed in most of the grafted sites. This observation requires further explanation. The demineralization processes for the histological preparation of the specimen remove the mineral content of the calcium sulfate, thus not making it visible at the light microscope observation. However, if the bulk of the calcium sulfate were still present, a homogeneous mass would be visible. This is not the case with calcium sulfate use, in which a network of truly newly regenerated tissue is visible. Newly formed bone with lamellar arrangements is in fact identified in histological sections of studies. This makes MGCSH an ideal graft material in extraction socket bone regeneration, in which the resorbable material allows a new trabecular bone arrangement at 3 months.22–26

Furthermore, when histologically comparing bone cores from calcium sulfate-filled sites versus unfilled sites, a mean regenerated bone trabecular area of 58% was seen in the grafted sites and an area of 48% was seen in the unfilled control sections 3 months after the extractions.22,23,26

The ability to uneventfully enhance tissue coverage would further support reports of the compatibility of calcium sulfate to gingival fibroblasts. Calcium sulfate facilitates cell attachment and spreading of cells with the greater potential for guided tissue regeneration in surgical sites in which primary wound closure cannot be obtained.27

Aimetti et al.26 clinically and histologically evaluated the healing of human extraction sockets filled with calcium sulfate. Their results showed that healing was uneventful, with neither infectious episodes nor untoward clinical symptoms. Complete epithelial closure of the grafted areas was achieved after 21 to 28 days. A similar time frame for epithelial closure was observed in the unfilled sockets. At the time of implant insertion, the MGCSH-treated sockets were completely filled by a hard material, which exhibited the consistency of bone on probing. Vertical bone resorption of the buccal socket walls and reduction of the buccopalatal width were more pronounced at unfilled sites than at MGCSH sites.

These findings demonstrated that calcium sulfate does not interfere with the clinical healing process when applied in fresh extraction sockets with favorable morphologic features. In addition, it seems to reduce alveolar ridge resorption following tooth extraction and to positively influence the bone volume over a 3-month period. Histomorphometric measurement data are suggestive of a consistently greater bone maturation rate from the superficial to the deeper part of the healed sockets, as compared to the normal course of healing without grafting material.26

IV.B. Peri-Implant Bone Defects

In a case report, Scarano et al.28 suggested that MGCSH, being completely resorbable and having osteogenic activity, may represent a valid alternative to autogenous bone graft for filling peri-implant bone defects. A bone biopsy was harvested 4 months after implant insertion and graft placement with MGCSH, and was then processed and analyzed. Under light microscopy at low-power magnification, regenerated trabecular bone was clearly visible. At higher magnification, osteoblasts and osteoclasts were observed. Histomorphometry showed that newly formed bone constituted 40% ± 3.1%; marrow spaces constituted the rest.
Transmission electron microscopy examination of the collected bone biopsy showed an abundant quantity of newly formed bone. Bone tissue at the interface with the implant was detached from the titanium surface, and it showed an amorphous layer in some regions, in close contact with the implant, followed by osteoid seam, followed by mature bone. In different areas, a very thin electron-dense line separated the bone tissue from the implant surface. Scarano et al. concluded that the calcium sulfate–augmented site presented many newly formed blood vessels, with accompanying histological evidence of mature bone tissue.

IV.C. Sinus Augmentation Procedure

After tooth extraction in the maxillary posterior region, crestal bone resorption and pneumatization of the maxillary sinuses can often occur, resulting in an inadequate volume of bone for implant placement. For optimal sinus augmentation, a bone graft substitute that can regenerate high-quality bone and enable the osseointegration of implants is needed in clinical practice. Pecora et al. reported the results of sinuses grafted with calcium sulfate in 2 patients. These authors reported that a bone biopsy was collected at the time of implant placement, which was 9 months after the augmentation procedure. In the first patient, titanium threaded cylinder implants were inserted in the maxillary sinus after 9 months, whereas in a second case, an implant was placed at the time of the sinus lift procedure. Histological evaluation of the bone cores indicated bone formation with remodeling and lamellar maturation in the specimens. As in previous reports, the graft material was not detectable in the biopsies. At the second-stage surgery to uncover the implants, the implants were clinically osseointegrated in both cases. These early case reports allowed the researchers to conclude that MGCSH can be considered for sinus augmentation procedures. Of particular interest, to indicate healthy bone, the medullary spaces seen under the microscope were filled by adipose marrow with normal blood vessels.

Andreana et al. reported that calcium sulfate could be successfully used alone or in combination with demineralized freeze-dried bone allograft (DFDBA) for sinus lift procedures. In this particular report, the histologic evidence showed that when calcium sulfate was used in combination with DFDBA, remaining particles of the grafted DFDBA could be found within the newly generated bone several months after the surgery. As in the previous report by Pecora et al., calcium sulfate alone led to bone regeneration in the sinus with no adverse events. All implants had primary stability when placed into the regenerated sites. Stability was also reported at the uncovering surgery when prosthetic treatment started. Periapical radiographs of the area showed peri-implant bone health with no loss. All implants were successfully restored.

Iezzi et al. histologically evaluated the bone around an immediately loaded implant retrieved 7 months after placement in a sinus that was simultaneously grafted with calcium sulfate. At low-power magnification, native and newly formed bone were visible, and small osteocyte lacunae were also detectable around and in contact with the implant surface. The regenerated bone was in close and tight contact with the implant surface. The analyzed histological sections did not indicate the presence of any gaps, epithelial cells, or connective tissues at the bone–implant interface. Furthermore, inflammatory cells were not visible. In some areas of the interface, unorganized woven bone was seen. However, in other areas, wide marrow spaces were present near the implant surface. At higher magnification, osteoblasts with adjacent osteoid matrix were seen. Cortical mature bone was present near the implant surface, and bone undergoing remodeling was in direct contact with the implant surface. A large quantity of vessels was present in the marrow spaces around the implant. The percentage of bone–implant contact (BIC) was 55–68%. Histomorphometry showed that the grafting material (calcium sulfate) was replaced by the formation of new bone in a maxillary sinus.

Additional studies by De Leonardis and Pecora and Guarnieri and Bovi further demonstrated that calcium sulfate as a grafting material for sinus
augmentation predictably leads to new bone formation that is viable for implant placement. The proposed technique to place calcium sulfate in the sinus seems to reduce the possible shrinkage of the grafted material during healing and to improve the quality of bone formation.30,31

V. CALCIUM SULFATE AS A DELIVERY VEHICLE FOR GROWTH FACTORS

Intini et al. reported on a composite graft engineered by the absorption of platelet-rich plasma (PRP) onto calcium sulfate based on in vitro osteoblast proliferation and scanning electron microscopy (SEM) analyses.32,33 The combination of calcium sulfate and PRP presented a preserved crystalline structure well integrated by organic matrix. This combination showed the highest cell proliferation levels and demonstrated that the PRP was activated and the subsequent release of growth factors is detectable when combined with calcium sulfate. In fact, when calcium sulfate was used as a carrier for platelet-derived growth factors (PDGFs), it showed increased cell proliferation and was an efficient carrier for PRP or PDGFs. These findings support the in vivo use of these combinations as bioactive matrices.32,33

Shi et al. evaluated the combination of surgical-grade calcium sulfate (SGCS) and PRP for alveolar ridge preservation prior to implant placement in a canine model.34 Less ridge resorption was observed in the calcium sulfate/PRP-filled sites compared with the unfilled sites. Bone scintigraphy showed that sites filled with SGCS/PRP showed a significantly higher count/pixel at 2, 4, and 6 weeks and a significantly higher percentage of bone-implant contact than unfilled sites. The results of Shi et al. suggest that grafting extraction sockets with SGCS/PRP reduces alveolar ridge resorption and promotes bone formation.34

VI. GUIDED TISSUE/BONE REGENERATION

The clinical observation of epithelial wound healing as well as bone fill would seem to support the clinical use of a combination of guided bone regeneration with MGCSH and PRP in fresh extraction sockets without flap mobilization. This technique may provide faster soft tissue healing. The ability to enhance tissue coverage would further support reports of the compatibility of calcium sulfate with gingival fibroblasts.27 In vitro studies by Payne et al. have shown that calcium sulfate facilitates gingival fibroblast cell attachment and physiological spreading of cells over calcium sulfate substratum, with potential for guided tissue regeneration in surgical sites in which primary wound closure cannot be obtained.27

Calcium sulfate enhances bone formation by the mechanism of its particles binding to adjacent bone and then resorbs, providing a mechanism to guide bone growth.35 Strocchi et al. created bone defects in the tibiae of rabbits, which were then filled with calcium sulfate granules or autogenous bone.36 Microvascular density was increased in the calcium sulfate–treated defects, suggesting a positive effect on angiogenesis.36 The release of calcium ions during physiological dissolution of calcium sulfate in high concentrations may affect osteoblast genesis and function, and the ions may act as a stimulus to osteoblast differentiation.37 One additional factor is the alteration of tissue pH. Locally altered pH by calcium sulfate may play a role in osteogenesis. More specifically, as suggested by Walsh et al., increased acidity related to the dissolution of calcium sulfate could cause localized bone demineralization. Subsequently, the bone matrix would release specific bone growth factors previously entrapped into the bone matrix during the mineralization of the extracellular bone matrix. Moreover, MGCSH shows great potential for guided bone regeneration in surgical sites.38 Pecora et al. followed the principles of guided tissue regeneration in a rat model. These authors used 40 male Sprague-Dawley rats and induced 5-mm through-and-through bony defects in the mandible bilaterally. One side received a sterile medical-grade prehardened calcium sulfate disk both lingually and buccally to “cover” the defect. In the control side, the bone circular defect was left uncovered.

Specimens were then harvested at 3, 9, 18, and 22 weeks. The histologic analysis demonstrated
that at 3 weeks all sites protected with calcium sulfate disks showed partial or complete bone healing. However, to validate the model and to demonstrate the efficacy of calcium sulfate, the unprotected jaw defects showed no bone growth at 3 and 9 weeks and only partial bone healing at 18 and 22 weeks. This study demonstrated that calcium sulfate could be used in guided tissue regeneration.

VII. CONCLUSIONS

The published experience of several clinicians, supported by in vitro and in vivo studies, as presented in the text of the present article, undoubtedly indicates that medical-grade calcium sulfate is an excellent material for use in bone regeneration in implant dentistry. Its safety and very long history further support its use.

REFERENCES


Following poster discusses the use of DentoGen® to stabilize failing dental implant. This poster was presented at American Academy of Implant Dentistry (AAID) meeting in Boston in October 2010.
Bone Regeneration Using Calcium Sulfate (DentoGen) After Bone Loss Around Dental Implant

M. Chen1, S. Mamidwar2, J. Ricci3, H. Alexander3, N. Tovar2,3
1California Center for Implant Dentistry, San Jose, CA 95123, USA; 2Orthogen, LLC, Springfield, NJ 07081, USA; 3New York University College of Dentistry, New York, NY 10010, USA

ABSTRACT

Regeneration and preservation of alveolar bone surrounding a dental implant is essential for implant success. This process can be affected by a number of local and general factors. In this study, medical grade calcium sulfate hemihydrate (MGCSH) served as an effective barrier to prevent soft-tissue interdigitation. Clinical examination revealed that bone was completely healed. The patient showed no signs of pain or discomfort. MGCSH was found to be cost-effective, with simple handling characteristics and the ability to enhance bone regeneration around a dental implant.

INTRODUCTION

Rapid alveolar bone regeneration is essential for the incorporation of a dental implant. Regeneration is orchestrated by the careful conservation of the wound healing process. This process can be affected by infection of the extracted tooth, difficulty during tooth extraction, patient's age, heavy tobacco use, and/or dental implant allergy. The goal is to regenerate lost bone during extraction with minimal postoperative pain in preparation for the dental implant. Once placed, the implant-bone interface must be preserved to prevent implant failure.

Since soft tissue grows 15 times faster than woven bone, it can interfere with the regeneration of bone and prevent the bond between implant and bone. A membrane barrier can be used to isolate the bone-implant interface from soft tissue, epithelium and gingival crevice. Medical Grade Calcium Sulfate Hemihydrate (MGCSH) serves as a bone graft that allows for the rapid regeneration of bone. MGCSH has been used as a bone graft for over 110 years, is completely bioabsorbable, osteoconductive, and does not cause an inflammatory response. Two concurrent mechanisms are triggered by the degradation of MGCSH. The first mechanism involves the release of calcium and sulfate ions in the defective area. This results in the formation of carbonated apatite and stimulation of calcium ion cellular activity. The second mechanism is the temporary, local drop in pH as a result of precipitation of carbonated apatite. This drop causes deminerilization of the existing bone's surface resulting in exposure of bioactive molecules and the release of growth factors and bone morphogenic proteins (BMPs). These proteins stimulate the growth of bone in defects filled with CS.

CASE REPORT

A patient presented in good health with a complaint of a dental implant that was sensitive to pressure and uncomfortable. The patient had the implant placed by a periodontist 2 years ago in tooth #8. Clinical examination showed the threads of the dental implant were exposed through the gingival tissue on the labial side (figure 1A). The implant was fully exposed after surgical procedures. The area was cleaned and MGCSH was placed over the exposed surface (figure 1B), as both a bone graft and membrane barrier. Non-resorbable suture was used to reposition soft tissue over the MGCSH (figure 1C). At the one year time point radiographs show bone had fully grown around the implant (figure 1D). The patient no longer complained of discomfort and the area was no longer sensitive when masticating.

DISCUSSIONS

The careful and rapid regeneration of bone in a defective area is essential in normalizing tissue function. Various bone graft materials can be used for the rapid regeneration of bone. MGCSH is a bone graft that can be used alone, as a binder with other bone graft materials, or as a membrane barrier to separate a defective area from soft tissue.

In this case report, MGCSH was successfully used as a graft and membrane to enhance the bone growth process by separating soft tissue from the dental implant-bone interface, hence allowing the stimulation and formation of bone vessels and preventing tissue ingrowth. After the one year time point, no gingival recession or inflammatory response was observed. Based on radiographic analysis, bone has completely healed and the patient showed no signs of pain or discomfort.

CONCLUSIONS

In this surgical case report, medical grade calcium sulfate, MGCSH was found to be an effective bone graft and membrane barrier with the ability to provide radiographic evidence of bone regeneration in a dental implant-bone interface defective area. MGCSH is a cost-effective option with simple handling characteristics that prevent soft tissue ingrowth and assist in the regeneration of bone.
Following poster discusses the use of DentoGen® to treat anterior type I extraction sockets. This poster was presented at International Congress of Oral Implantologists (ICOI) meeting in Las Vegas, in February 2011.
Computerized Tomographic Evaluation of Guided Bone Regeneration in Type I Extraction Sockets Grafted with Calcium Sulfate; 1,3Robert Bagoff, DMD, FAGD; 1,2Nick Tovar, PhD; 2Sachin Mamidwar, MBBS, MS

1New York University College of Dentistry, New York, NY 10010, USA, 2Orthogen, LLC, Springfield, NJ 07081, USA and 3Private Practice, Livingston, NJ 07039, USA

INTRODUCTION

Extraction socket grafting is commonly performed to rebuild the bone for future placement of dental implants. Xenografts (mainly bovine bone), allografts and various alloplastic materials are used for this purpose. Allografts, after placement in the extraction socket, undergo remodeling and heal the extraction socket. Alloplastic materials like calcium phosphate and bioglass also undergo remodeling and are replaced by bone. Calcium sulfate (CS) based materials degrade after placement in the bone defect. As they degrade they leave behind a calcium phosphate network which serves as a stimulus for further bone growth. CS is biocompatible and osteoconductive. Degradation of CS leads to a local drop in pH, which causes demineralization of the surface layer of bone leading to release of growth factors (e.g. PDGF, BMP2). These growth factors further stimulate bone formation.

METHODS

A male patient in his 50s was referred with complaints of bad breath and broken teeth. On examination, teeth (nos 4 and 13) were found not to be restorable and hence needed extraction. Both of these extraction sockets were found to be type I sockets, meaning all 4 walls were intact. No. 4 extraction socket was grafted with a mix of irradiated cancellous bone (ICB, Rocky Mountain Tissue Bank, Aurora, CO) and calcium sulfate (DentoGen®, Orthogen, LLC, Springfield, NJ) in a 1:1 ratio. No. 13 extraction socket was grafted with calcium sulfate (DentoGen®, Orthogen, LLC, Springfield, NJ) alone. CT scans were taken just before the implant placement.

RESULTS

Flaps were elevated after 4 months in each of these sites for the placement of dental implants. Solid ridge formation was observed in each of these sites. Computerized tomographic evaluation of each of the sites revealed new bone formation to the center of the site (Fig 2 and 3), making it possible for implant placement. The patient was followed regularly; abutment and temporary restorations were placed 6 months after placement of dental implants. Implants in both sites are doing well; patient is chewing and implant is strongly supported by bone.

DISCUSSION

CS degrades at a fast rate. In posterior extraction sockets (which are usually larger than anterior sockets), materials that degrade more slowly are usually used for bone grafting procedures. However, this case report demonstrates that CS is effective at strong bone formation in type I sockets. It is a very cost-effective bone graft.

CONCLUSIONS

Calcium sulfate was effectively used for bone regeneration in type I extraction sockets. It is an excellent cost-effective alternative for bone grafting purposes in such extraction sockets.

REFERENCES

Following poster discusses the use of DentoGen® as a guided tissue regeneration barrier membrane. This poster was presented at International Congress of Oral Implantologists (ICOI) meeting in Las Vegas, in February 2011.
The Use of Calcium Sulfate as a Barrier in GTR
Mamidwar S†, Chesnoiu-Matei I†, Horowitz R‡
†Orthogen LLC, NJ, USA
‡New York University College of Dentistry, NY, USA

Abstract

Introduction: The concept of guided tissue regeneration (GTR) was introduced in the 1980s to prevent soft tissue infiltration and to assist bone formation in various defects, allowing for placement of dental implants. Calcium sulfate (CS) barrier is resorbable and therefore does not require a removal surgery; furthermore, it has demonstrated superior fibroblast migration compared to Poly(lactic acid) (PLLA) or Polytetrafluoroethylene (PTFE) barriers. Methods: This report is based on several cases where CS (DentoGen®, Orthogen, LLC, NJ) was used as a barrier. Following tooth extraction, bone graft was packed in the defect and closed with a CS barrier. Patients were followed regularly. Implants were placed between 4 to 6 months. Results: Four-months following guided tissue and bone regeneration (GTR and GBR), soft tissue showed adequate healing with bone regeneration to support implant placement. Conclusions: CS barrier supports wound healing and facilitates bone regeneration. It prevents the infiltration of epithelial and connective tissue. Its complete resorption eliminates the need for a second, removal surgery.

Methods

This report is based on 5 cases where CS (DentoGen®, Orthogen, LLC, NJ) was used as a barrier membrane in combination with an alloplastic bone graft to preserve the alveolar height and width. Following socket debridement, a bone graft was packed in the defect, filling to an ideal biologic contour (Figure 1A and B). CS was mixed in the form of a putty and molded over the superior portion of the socket (Figure 1C). The ideal consistency is dry enough to stick together as it is picked up with a spatula, but wet enough to be spread over bone and the graft material. The barrier was approximately 1.5-2 mm thick and extended 2-3 mm on to the surrounding bone. Suturing was used to reposition the soft tissue before the CS barrier fully set (Figure 1D). Patients returned for implant placement approximately 4 months following grafting. At this time point bone cores were collected for histological analysis. Prosthetic restoration was later achieved. Patients were followed for a two-year period. In the case presented below, parallel to the grafting procedure, an implant was inserted to replace tooth #28 without any GTR or GBR and was not included in this study.

Results

Patients were followed 2 weeks, 1 and 4 months after placement of bone graft and barrier. Soft tissue was seen to be healing well. By 2 weeks, in most cases, soft tissue grew over the grafted material (Figure 2A). At an average of 4 months following grafting, the sites were re-entered and evaluated. Soft tissue was healing properly, with no signs of inflammation. Upon probing, the underlying bone presented as regenerated, fully healed tissue. Histological analysis of cores obtained from the grafted site showed the presence of vital woven and lamellar bone and increased osteoblastic activity (Figure 3). There were no signs of epithelial or connective tissue infiltration and no remnants of the initial graft were noticed. Implants became osteointegrated and maintained their stability after prosthetic rehabilitation.

Objectives

The purpose of this case study is to examine the effect of a calcium sulfate barrier used in combination with alloplastic bone grafts, on the regeneration and preservation of bone following extraction procedures.

Summary

- The biocompatibility of CS in the human body has been attested for over 110 years. Properties such as the ability to promote new blood vessel formation, resist infection, and facilitate fibroblast and PDL cell migration, have promoted the use of CS as a barrier in the field of GTR.
- CS used as a barrier showed good soft tissue healing with full closure of the wound. Epithelial and connective tissue cells were prevented from infiltrating the healing socket. By four months, the grafting material has been completely resorbed and replaced by living, vital bone.
Following case report discusses the use of DentoGen in combination with allograft to treat extraction socket in a smoker with a 10 year history of bisphosphonate use.
Socket Preservation and Implant Insertion in a Smoker With a 10-Year History of Bisphosphonate Use: A Case Report

Sasikumar Sunkara,1 Carla Beneduce,2 & Sebastiano Andreana2*

Departments of 1Periodontics and Endodontics and 2Restorative Dentistry, State University of New York at Buffalo, School of Dental Medicine, Buffalo, New York

*Address all correspondence to: Sebastiano Andreana, DDS, MSc, Associate Professor, Director of Implant Dentistry, State University of New York at Buffalo, School of Dental Medicine, Department of Restorative Dentistry, 235E Squire Hall, 3435 Main Street, Buffalo, NY 14214, USA; Tel.: 716-829-6645 or 716-829-2923; Fax: 716-829-2440; andrean@buffalo.edu.

ABSTRACT: A 63-year-old woman was seen as self-referred at the School of Dental Medicine, State University of New York at Buffalo, for the evaluation and management of a root perforation on a maxillary premolar (or bicuspid). The tooth was diagnosed as untreatable and extraction was indicated. Simultaneously, the patient was advised that tooth number 14 was missing and offered options for replacing the missing tooth. The patient was informed about the risks associated with both smoking habits and bisphosphonate intake. Amoxicillin was started the day prior to extraction and continued for 10 days. The tooth was extracted without raising the flaps, and the socket was degranulated and filled with calcium sulfate (DentoGen) and 50% cortical/50% cancellous bone allograft (AlloOss). The orifice was protected with a collagen barrier (Conform). The patient applied chlorhexidine over the wound site (bid) for 14 days; follow-up visits were at 2, 7, 14 and 21 days. Although the patient continued smoking, healing was uneventful. After 4 months, 2 implants (Nobel Biocare) were inserted to replace missing teeth. The full thickness flap was raised and completely repositioned after insertion. Healing was uneventful. Three months later, implants were exposed using a diode laser and were prepared for restoration. Implants were clinically stable and no soft/hard tissues deficiencies were noted. This clinical case may indicate that a minimally invasive surgical extraction combined with regenerative techniques and antibiotic/antimicrobial therapy, followed by implant placement with complete wound closure, may be considered when treating patients with known health risk factors.

KEY WORDS: calcium sulfate hemihydrate, bisphosphonate, smoking, dental implant

I. INTRODUCTION

Bisphosphonates are a class of drugs used to treat cancer, osteoporosis, and other bone-related conditions. As part of cancer therapy, bisphosphonates are generally administered via intravenous (IV) infusion to reduce bone pain and hypercalcemia of malignancy. However, bisphosphonates are also used orally to inhibit bone resorption in patients diagnosed with osteoporosis, Paget’s disease, or conditions such as osteogenesis imperfecta. In patients with osteoporosis, the oral administration of bisphosphonates aims to slow or stop the osteoclastic activity, the natural process that dissolves bone tissue, thus resulting in maintained or increased bone density and strength. Bisphosphonates tend to reside in bone for long periods of time. Some literature reports propose that the half-life of these drugs ranges from months...
to several years, suggesting that bisphosphonates could be found in bone tissue over a decade after the initial administration.4–6 Even though both routes of administration have been shown to be clinically effective, they also carry associated risks.5 Oral administration of bisphosphonates has been primarily associated with adverse gastrointestinal events and, rarely, with osteonecrosis of the jaw.5,7 On the other hand, in some cases, higher IV infusion and increased dosages of bisphosphonates have been associated with adverse renal function, higher frequency of exposed bone of the mandible or maxilla (osteonecrosis), and problems with bone healing, particularly after dental surgery.5,7–9 According to the American Academy of Oral and Maxillofacial Surgeons, the estimated cumulative incidence of osteonecrosis of the jaw in patients taking IV bisphosphonates varies from 0.8–12%.10 In addition, Li and Wang suggest that patients undergoing IV infusion of bisphosphonates are 4 times more prone to develop osteonecrosis of the jaw.9 Although the frequency of osteonecrosis is much lower in patients taking oral bisphosphonates,7,40 this clinical condition remains difficult to manage because it does not respond to standard clinical treatment.7 Furthermore, other factors including prolonged corticosteroid therapy, diabetes, and health-threatening habits such as smoking, alcohol use, and poor oral hygiene are thought to be risk factors for the onset of osteonecrosis of the jaw in patients taking bisphosphonates.6,10 In a study conducted in 2007, Yarom et al. reported that 4 of the 11 patients evaluated for osteonecrosis of the jaw were heavy smokers (at least 1 pack/day for the last 10 years or more) and suggested that cigarette smoking may further aggravate the necrotic process as well as affect the expected treatment outcome.11 At the present time, oral bisphosphonates are the most commonly prescribed drugs for the prevention and treatment of osteoporosis. Although it is preventable and treatable, osteoporosis is a chronic disease that is caused by the loss of bone mineral tissue. A 2010 report from the National Osteoporosis Foundation indicates that as many as 44 million Americans may be affected by this disease.12 At the same time, the placement of dental implants for the rehabilitation of partially and/or fully edentulous healthy and medically compromised patients has also become a valid alternative to the conventional fixed and/or removable prosthodontic approaches.7 Li and Wang suggested that the presence of systemic disorders and unhealthy habits cannot be underestimated as they may play a counterproductive role in the implant treatment; thus, it is preferable to select patients who do not have local or systemic contraindications to implant therapy.4 Failure of implant placement may result from 3 major etiologies: compromised host healing, challenged bone-to-implant interface, and bacterial load.4 A key factor for patients who are taking bisphosphonates for osteoporosis and are seeking implant treatment is the likelihood that this systemic disease alters the quality of bone or its healing ability to the extent that osseointegration of the implant may be jeopardized.5 However, literature reports on the long-term use of oral bisphosphonates and their effects on bone healing, mainly after implant therapy, are yet very limited.5 Failure of implant treatment has also been associated with behavioral factors and habits such as smoking. In a systematic review and meta-analysis, Strietzel et al. reported that smoking was in fact identified as a significant risk factor for implant therapy.13 Li and Wang reported that because smoking seems to affect the revascularization of the bone tissue in regenerative procedures, the outcome of the implant treatment could be further compromised.9 Furthermore, Levin et al. also reported that cigarette smoking may possibly impair wound healing and that patients with a history of smoking had a higher failure rate of implants and implant-related surgeries (bone regeneration, sinus lift, etc.), regardless of the amount of cigarettes smoked.14 The current report presents the treatment modalities implemented to successfully achieve rehabilitation in a partially edentulous and medically complex patient seeking implant therapy.

II. MATERIALS AND METHODS

The patient, a 63-year-old female, presented to the School of Dental Medicine, State University of New York.
York at Buffalo, seeking treatment for root perforation of the maxillary left premolar (tooth no. 13). The tooth was diagnosed as untreatable and extraction was therefore indicated. The patient’s medical and dental history was reviewed and a further interview was performed by the clinician to gather additional information to complete the overall medical assessment. The medical history revealed diagnoses of osteoporosis and high cholesterol, in addition to regular smoking habits (1–2 packs of cigarettes/day) for several years. At the time of the initial assessment, the patient was taking a cholesterol-lowering medication (atorvastatin, 10 mg/day), daily aspirin therapy (aspirin, 81 mg/day), medication to prevent and treat osteoporosis (risedronate, 150 mg/mo), and vitamins (vitamin D and calcium combination, 2000 IU daily; vitamin C, 1000 IU daily). The patient also confirmed that she had been taking osteoporosis medication for 10 years and that she had discontinued the 150 mg/mo dose and started taking the vitamin combination only 4 months prior to dental treatment. A scrupulous intraoral clinical and radiological exam was performed and the following diagnosis was made: perforation of the middle third of the root on tooth number 13 (Figs. 1 and 2). Other intraoral structures were found within the normal limits. The individualized treatment plan included extraction and socket preservation, followed by the implant insertion and a related restorative plan. The patient was informed of the risks associated with both smoking habits and bisphosphonate use (10 years/once a week oral treatment) and was later asked to sign a treatment informed consent form. The patient was then scheduled for the extraction of tooth number 13. Amoxicillin (500 mg every 8 h) was prescribed starting the day prior to extraction and continued for 10 consecutive days. The premolar was extracted without raising the flaps and the alveolar socket was degranulated (Figs. 3–5). Bleeding within normal limits was noted. Following degranulation of the socket, the extraction site was then filled with DentoGen calcium sulfate (Orthogen, Springfield, NJ, USA) and cc of AlloOss 50% cortical/50% cancellous bone allograft (Ace, Brockton, MA, USA) (Figs. 6–8). The orifice was protected with a 15-mm × 20-mm hydrated Conform collagen barrier (Ace) (Fig. 9). The entire extraction site was secured with a Vicryl 4.0 suture (Ethicon Inc, Somerville, NJ, USA). Postoperative oral hygiene instructions were given to the patient. The instructions included the application of 0.12% chlorhexidine over the wound site with a toothette (Sage Products Inc, Crystal Lake, IL, USA), twice a day for 14 consecutive days. The patient was instructed to take ibuprofen (600 mg) as needed. Follow-ups visits were scheduled at 7, 14, and 21 days (Fig. 10). Even though during this initial surgical phase, the patient did not limit her smoking habits and had recently stopped taking osteoporosis medication, the healing of the extraction site was uneventful. Approximately 4 months later, the patient was scheduled to receive dental implants (Fig. 11). One week prior to implant placement, impressions

![FIGURE 1. Presence of fistula on tooth number 13: initial assessment.](image1)

![FIGURE 2. Occlusal view of the preoperative site: initial assessment.](image2)
of both arches were taken to fabricate a radiographic surgical guide to aid the implant placement. On the day of implant placement, no changes in medical and medication history were reported and the patient also reported no changes in her smoking behavior. The full thickness flap was then raised and 2

Nobel Biocare implants (Yorba Linda, CA, USA) were inserted with a torque of 35 Ncm at tooth number 13 (NobelReplace Tapered 4.3 × 10) and tooth number 14 (previously missing; NobelReplace Tapered 5 × 10) following standard implant placement surgical protocol, which included the
use of the surgical guide (Figs. 12 and 13). Cover screws (Nobel Biocare) were inserted over both implants. The flap was repositioned and sutured (Fig. 14) after insertion to fully cover the surgical area. A radiograph was taken to evaluate the placement of implants and postoperative instructions were given to the patient, similar to the previous surgery. Postoperative evaluation was performed after 1 week and 3 weeks (Fig. 15) of the implant placement, and healing of the wound site was again uneventful.

Four months after placing the implants, the patient returned to expose the implants and prepare them for the restorative phase (Figs. 16 and 17). Exposure of the implant was performed using a diode laser (Odyssey 2.4G; Ivoclar Vivadent Inc, Amherst, NY, USA) (Fig. 18). All postsurgical periods were uneventful (Fig. 19). At that time, no signs of hard and soft tissue pathology were noted. Bone height and quality of soft tissue were sufficient to proceed with the restorative phase (Fig. 20).

III. DISCUSSION

The association between implant failure and bisphosphonate use (either orally or intravenously) cannot be overlooked, and clinicians must be aware of the possible risks of treating patients undergoing
Some literature reports have shown that the incidence of implant failure was minimal in patients using oral and IV bisphosphonates. The American Dental Association Council on Scientific Affairs reported in 2008 that the possibility of developing a bisphosphonate-related osteonecrosis of the jaw in patients taking oral bisphosphonates is low. A retrospective study by
Zahid et al.\textsuperscript{16} on implants placed in patients taking bisphosphonates showed that implant thread exposure might be a long-term possible outcome. In our case, the minimally invasive technique used for the extraction, in combination with the placement of calcium sulfate and cortico/cancellous human bone followed by coverage with a collagen barrier, led to the growth of bone that later allowed placement of the implants with primary stability of 35 Ncm. Calcium sulfate has been used successfully alone or in combination following tooth extraction\textsuperscript{17,18} to preserve the alveolar ridge. In our case, we speculate that the following factors played a fundamental role in the final outcome: 1) the alveolar bone was never left exposed, 2) the extraction site was properly bled immediately after the extraction and, 3) clot stabilization was achieved with the graft composite. The complex medical history of the patient, together with the long-term heavy smoking habit, might have played against bone regeneration; however, this was not noted in this clinical case. Furthermore, at the time of implant site preparation and implant insertion, the surgical time was kept to a minimum, and correct soft tissue coverage was achieved, again, without leaving any osseous surface exposed. The second-stage surgery was performed flapless with the use of a diode laser\textsuperscript{19}; therefore, exposure of the underlying bone surface did not occur. Based on this case, a minimally invasive surgical technique, use of tissue-friendly materials, antibiotic coverage and antimicrobial treatment, and reduced surgical time might have played a role in the successful outcome, considering the co-morbidities of the patient’s several-year smoking habit and 10-year use of bisphosphonates. Therefore, we conclude that dental implants in patients taking oral bisphosphonates can osseointegrate and remain functionally stable\textsuperscript{11} and can be considered as one of the treatment modalities available to the clinician.

**IV. CONCLUSION**

This clinical case may indicate that a minimally invasive surgical extraction combined with regenerative techniques and antibiotic/antimicrobial therapy, followed by implant insertion with complete wound closure, may be considered when treating patients with known health risk factors for implant surgery.

**REFERENCES**