A Clinical and Histological Case Series Study on Calcium Sulfate for Maxillary Sinus Floor Augmentation and Delayed Placement of Dental Implants

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ABSTRACT

Background: Maxillary sinus floor augmentation is a procedure that is indicated in cases when the volume of the posterior maxillary bone is inadequate. The goal of this treatment is to obtain sufficient amount of bone tissue in order to gain osseointegration of endosseous implants.

Purpose: The purpose of this study was to conduct a clinical and histological analysis of calcium sulfate (CaS) as bone graft substitute in sinus floor augmentation.

Material and Methods: Ten patients with edentulous maxillas were included in this study. They had moderate to severe atrophy of the posterior maxilla. Surgiplaster (Classimplant®, Rome, Italy) was used as graft material in the maxillary sinus and was covered by BioGide® (Geistlish Pharmaceutical, Wolhusen, Switzerland). After 4 months of graft healing, 40 dental implants were placed and a biopsy for histomorphometry was taken at these occasions. The specimens were viewed by light microscope, and the extent of bone regeneration and remaining graft material was evaluated. Radiographs were taken at the time of sinus augmentation and after 4 months of graft healing.

Results: At the time of abutment surgery, one implant was considered as a failure and was consequently removed, giving a survival rate of 97.5% after 1 year of loading. Radiographs showed a mean of 26.5% shrinkage of the augmented area. A significant resorption of CaS was noted with a mean value of 8.8% of remaining graft material after 4 months of healing. The biopsies also revealed new bone formation with a mean value of 21.2% of the total biopsy area. Histology showed signs of an acellular substitution of CaS with bone-like tissue.

Conclusion: The results of this study show that new bone regeneration occurs in the maxillary sinus after augmentation with CaS. This enabled successful placement, integration, and loading of dental implants in the posterior maxilla, as only 1 of 40 implants was lost during 1 year of follow-up.

KEY WORDS: bone substitute, histology, maxillary sinus augmentation

INTRODUCTION

Osseointegration of endosseous dental implants is an important factor in order to gain implant stability and obtain good prognosis for a future prosthetic restoration. The clinical manifestation of osseointegration is the absence of implant mobility; thus, achieving and maintaining implant stability are prerequisites for successful long-term function of bone-anchored

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prostheses.[1] Because of sinus pneumatization and alveolar bone loss following tooth extraction and severe periodontitis, the inability of sufficient bone formation in buccolingual and apico-occlusal direction may result in insufficient bone volume for placement of an implant. According to Scarano and colleagues,[2] it becomes difficult in this situation to obtain primary stability because of the absence of useful quantity of cortical bone and because of the presence of loose structure of type IV spongious bone.

In order to gain useful amount of cortical bone in the posterior maxilla, the idea of maxillary sinus floor elevation (sinus lift) was first formulated by Tatum,[3] and the surgical procedure was later described and published by Boyne and James.[4]

There are several grafting materials that have been used for this treatment. According to several studies, autogenous bone from the iliac crest and oral cavity has been considered to be the preferred bone graft material.[5,6] The reasons may be lack of immunological reactions and the presence of healing stimulating factors and stem cells that induce osteoinductive and osteoconductive properties.[7,8] In his thesis, Hallman[9] has indicated that autogenous bone grafts are both osteoinductive, with the potential for initiating new bone formation and successively replaced by vital bone, and osteoconductive, in that they act as a scaffold for ingrowth of bone-forming cells. Furthermore, it is suggested that the graft consists partly of surviving cells (preosteoblasts and preosteoclasts) and also proteins capable of converting undifferentiated mesenchymal cells into bone-producing cells.[9]

However, because of the negative factors that involve harvesting autogenous bone, that is, additional surgery at a donor site which, according to several clinical reports in the literature,[7,10] may result to donor site morbidity, requirement of anesthesia in cases of extraoral bone harvesting, and a limited amount of available bone graft[10]; it is beneficiary to use other types of grafting materials. In a review article, Esposito and colleagues[11] have evaluated the efficiency of various bone augmentation procedures for dental implants. According to this article, autogenous bone grafts could be replaced by bone substitutes in maxillary sinus lift procedures having less than 5 mm residual alveolar bone.

In an article, Orsini and colleagues[12] have discussed that the material of choice should be completely resorbable, safe, and inexpensive. It should be able to maintain space in order to act as a reservoir for calcium ions and to act as a barrier to create a protected space for the organizing of blood clot and for the migration of osteoprogenitor cells into the defect.

Calcium sulfate (CaS) is a highly biocompatible material and has a track record of more than 100 years.[5,10,12] It has been used successfully to treat periodontal disease, endodontic lesions, alveolar bone loss, and maxillary sinus augmentation.[12] CaS has been proved to be tissue compatible and does not interfere with the healing process.[12] Furthermore, calcium powder functions as a source of calcium supply and may allow a more rapid ingrowth of osteoprogenitor cells.[12]

The aim of this work was to histologically study bone regeneration after maxillary sinus floor augmentation, using CaS as the grafting material. The aim is, moreover, to conduct a clinical examination.

MATERIALS AND METHODS

Patients

Ten consecutive patients (six females, four males) with a mean age of 70 years (range 53–79) participated in this study. The patients were referred to the Department of Oral and Maxillofacial Surgery, Gävle Hospital in Gävle, Sweden, for maxillary sinus augmentation because of the lack of sufficient bone tissue for the placement of endosseous implants.

The inclusion criterion for maxillary sinus augmentation was less than 5 mm alveolar bone that remained in the floor of the sinus as determined by conventional tomography.

No age limit was set. Patients receiving steroid treatment, those with known leukocyte dysfunction, those currently undergoing chemotherapy, and those with uncontrolled endocrine disorders, psychotic disorders, or known current alcohol abuse were excluded. Only 1 of 10 patients in this study was a smoker. That patient was not excluded in this study, but was asked to reduce or stop smoking before undergoing treatment.

Preoperative clinical examination and radiographs, including panoramic radiograph and computer tomography (Scanora®, Soredex Orion Corporation Ltd., Helsinki, Finland), revealed severe atrophy classified as level V–VI[13] in the posterior maxilla in six of the patients.

The remaining four patients, who were totally edentulous, were classified as class III–IV, all according to Cawood and Howell.[13] After being informed about the study, the patients signed a consent form. The study was approved by the Research Ethics Committee at the University of Gothenburg, Sweden.

Anesthesia and Surgery

The patients were given perioral sedation (midazolam, Dormicum®, Roche AB, Stockholm, Sweden). Local anesthesia was given to the patients using lidocaine 2% with epinephrine (1:80.000) (Xylocaine/Adrenalin®, Astra AB, Södertälje, Sweden). The patients were also given a prophylactic dose of penicillin V 2 g × 2 during 10 days (Kåvepenin, Astra AB) starting with the first dose 1 hour before surgery. The surgery was performed by elevating a partial thickness flap from the palatal side of the edentulous ridge, followed by a full thickness flap, exposing the underlying buccal and palatal bone. An osteotomy with infraction was performed on the lateral side of the sinus wall, combined with a careful elevation of the sinus (schneiderian) membrane in order to create a subsinus cavity where the graft material could be placed.

Surgiplaster (Classimplant) was used as the graft material to augment the floor of the sinus. In order to cover the graft material, a resorbable membrane BioGide (Geistlish Pharmaceutical) was placed after the augmentation.

Implant Placement and Biopsy Retrieval

After a healing period of 4 months, implant placement was carried out, using TiUnite™ (Nobel Biocare AB, Göteborg, Sweden) (Figure 1, A and B).

A total number of 40 implants were inserted, 39 implants had a diameter of 3.75 mm and one implant was 5 mm in diameter (TiUnite) (Table 1).

A biopsy for histology was taken at the time of implant placement. In 1 of 10 patients, the graft resorption was severe and did not permit a biopsy to be taken. In nine patients, core samples were taken in a lateral direction from the alveolar crest with a trephine bur (2–4 mm in diameter). The implant placement and biopsy retrieval was carried out during local anesthesia using lidocaine 2% with epinephrine (1:80.000) (Xylocaine/Adrenalin). All patients were also prescribed a prophylactic dose of penicillin V 2 g × 2 during 10 days (Kåvepenin).

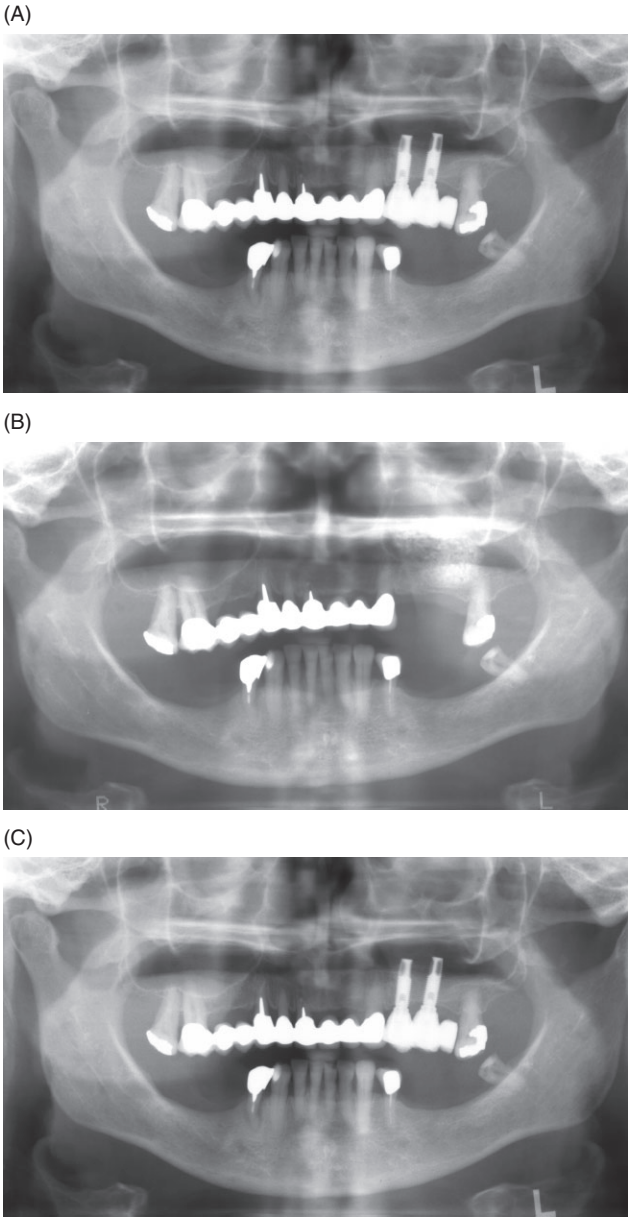

Figure 1 Series of radiographs showing (A) the preoperative situation with missing teeth and minor bone area for implant placement in the left maxilla, (B) after augmentation with calcium sulfate, and (C) permanent bridge at the first annual checkup.

Specimen Preparation and Analysis

The biopsies were fixed by formalin and were dehydrated in a graded series of ethanol. They were embedded in light-curing methacrylate (Technovit® 720 VCL, Kulzer, Friedrichsdorf, Germany). In order to make ground sections approximately 10 µm thick, the specimens were prepared by using a sawing and grinding technique (Exakt® Apparatbau, Norderstedt, Germany). The sections were then stained with toluidine blue.

TABLE 1 Various Lengths of Inserted Implants

Length (mm)	Number	Failure
7	2	
8.5	1	
10	12	
11.5	1	
13	20	1
15	4	
Total	40	1

The sections were viewed and analyzed in a light microscope (Nikon Eclipse 80i, Tekno Optik AB, Göteborg, Sweden) connected to a personal computer with a software for morphometry (Easy Image Measurements 2000, Tekno Optik AB).

The extent of bone regeneration and remaining CaS were measured in each biopsy site, and the values were calculated in percentage. Finally, the mean value of bone regeneration and remaining CaS were measured.

Follow-Up of Implants and Superstructures

The patients were treated with screw-retained metal–ceramic fixed prostheses, and all of them were followed up during 1 year of loading (see Figure 1C). All prostheses were removed after 1 year of loading in order to check the stability of the individual implants and to tighten the abutments and bridge screws.

Intraoral radiographs were taken at the baseline (at the time of implant insertion) and after 1 year of functional loading. The mesial and distal marginal bone levels were measured for each implant. All radiographs were evaluated by one surgeon. The measurements were made using a peak scale loop with a magnifying factor of 7× and a scale in tenths of millimeters.

An implant was considered to be successful if the following criteria were met:

1) A clinically stable implant, examined after removing the fixed prosthesis and tightening the abutments.
2) No sign of pathological reaction, pain, or infection in the hard or soft peri-implant tissue.
3) No peri-implant radiolucency.
4) Marginal bone loss did not exceed 2 mm after 1 year of functional loading.

An implant was considered a failure if removed for any reason. Implants that were not removed but did not meet the success criteria were regarded as survivals.

Graft Resorption

The resorption of the graft was evaluated using panoramic radiographs. The height of the graft was measured immediately after the surgery and also after 4 months of healing at the time of implant insertion.

After 1 year of implant loading, the resorption around the apical part of the implant was also measured.

RESULTS

Clinical and Radiological Evaluation

Healing following the grafting procedure was uneventful. All mucosal membranes were intact. At abutment surgery, 1 implant (operated in a nonsmoking patient) of 40 failed to integrate and was removed, giving an early failure rate of 2.5%. When removing the bridges after 1 year of functional loading, all the other implants were found to be stable. The stability of the implants was measured by forceps and percussion before the prosthetic treatment and after 1 year of loading. No resonance frequency analysis was conducted. Radiographs revealed shrinkage of the grafted area varying from 0 to 70% with a mean value of 26.5%. The apical parts of the placed implants were, in two cases, surrounded by bone, while the other implants showed exposed apical parts varying from 1 to 6 mm (mean: 2.7 mm) after 1 year of functional loading.

The mean marginal bone loss was 0.6 ± 0.5 mm for all implants after 1 year of functional loading (Table 2). Only one implant had a marginal bone resorption exceeding 2 mm.

Histological Evaluation

Histological examination of the specimens revealed new bone formation and various amounts of CaS remnants after 4 months of healing. There were no traces of CaS in the biopsies of 3 of 10 patients, which showed a significant amount of new bone formation (Table 3 and Figure 2). In the specimens that showed remnants of grafting material, the area of remaining CaS ranged from 3.2 to 22.7%. The bone area in all specimens ranged from 3.3 to 34.0% (see Table 3). A loose connective tissue rich of cells and vessels were seen between bone trabeculae and remaining graft material.

TABLE 2 Results from Marginal Bone Measurements

	n	Minimum	Maximum	Mean	SD
Marginal bone loss	39	0.00	2.50	0.6474	±0.54325

In biopsies with remaining CaS, the material seemed to be substituted with bone without the presence of cells (Figure 3, B–D). In high magnification, small granulae could be distinguished, which seemed to fuse together to larger areas (see Figure 3C). In other more mature areas, CaS could be seen incorporated in the newly formed bone.

TABLE 3 Results from Histometric Measurements of Biopsies Taken after 4 Months of Healing

Patient	Mean value of bone regeneration	Mean value of calcium sulfate
1	13.3	14.1
2	33.0	3.2
3	34.0	5.9
4	32.3	0
5	9.7	22.7
6	33.4	0
7	17.1	20.1
8	19.5	6.5
9	16.6	15.4
10	3.3	0
Mean	21.1 ± 11.2	8.8 ± 8.6

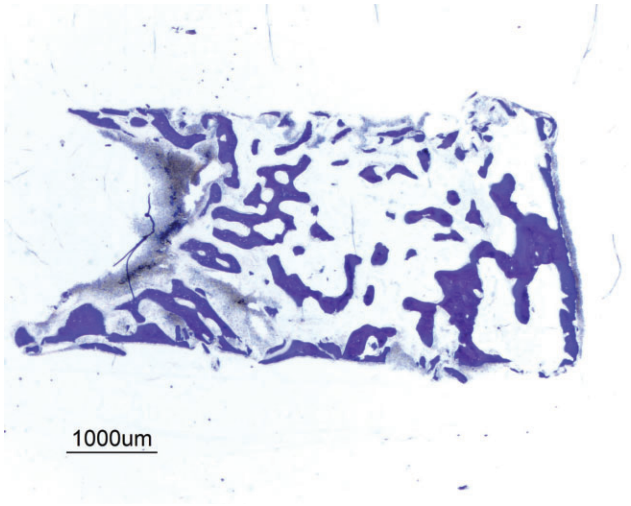

Figure 2 Light micrograph of a biopsy with no remnants of calcium sulfate. Note the slender bone trabeculae surrounded by a loose connective tissue.

DISCUSSION

The histomorphometric results in the present study indicate that CaS can function as grafting material prior to implant placement. It appeared to resorb quickly and to have osteoconductive properties. In the biopsies taken after 4 months of healing, a mean remaining graft material area value of 9% was calculated and a bone area value of 23.7% was found in all nine patients. This observation is in accordance with other studies supporting the use of CaS as a bone substitute.[5,7]

When CaS is used as a grafting material, the resorption mechanism is chemical and the material is converted into ions (calcium and sulfate). It is believed that the osteoconductive ability of CaS is due to its nature of dissolving rapidly and converting to calcium phosphate (CaP) deposits. This mineral, which is a biological apatite, appears to form as calcium ions are released from CaS that reacted with body fluids. In an article, Ricci and colleagues[14] concluded that these deposits became incorporated into new bone. While no direct contact between CaS and bone, as was observed by the authors, the deposits left by the CaS appeared to be osteoconductive. This suggests that CaS acted as a resorbable calcium releasing substrate that produces a CaP lattice in adjacent tissue. This lattice functioned probably as an osteoconductive matrix for bone ingrowth. This is in accordance with the findings of the present study except for the fact that some CaS particles seemed to be incorporated with new bone. In a previous study, we have examined the biopsies of the present study by field emission scanning electron microscopy and energy dispersive x-ray spectroscopy.[15] That study demonstrated the presence of CaP as well as CaS in the biopsies, and the results suggested that as CaS dissolves, it is replaced by precipitated CaP.

Guarnieri and colleagues[7] have explained this mechanism as a result of formation of an amorphous

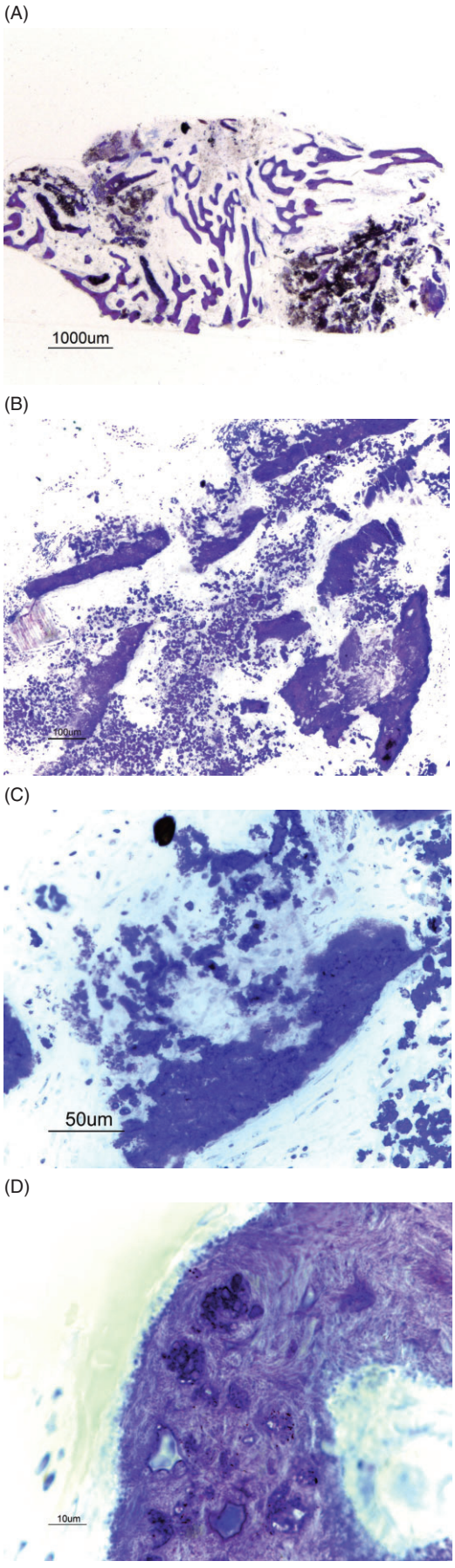

Figure 3 (A) Overview light micrograph of a biopsy with remnants of calcium sulfate (CaS) seen to the right. (B) Magnification of *A* showing a mixture of granular CaS and new bone areas. (C) Ongoing bone formation and/or bone replacement of CaS particles. (D) Light micrograph of a more mature area of the biopsy showing incorporated CaS in the newly formed bone.

substance which develops due to complete resorption of CaS. This amorphous substance has been found to be close to bone trabeculae and has been referred to as CaP trellis too, left by the resorption process that may act as an osteoconductive scaffold.

The radiological evaluation of the post-sinus floor augmentation in this study was only limited to two-dimensional anatomic planes taken by either intraoral radiographs or orthopantomography. This observation does not give a complete assessment of the extent of resorption since the amount of bone resorption in buccopalatal plane cannot be observed. According to Peleg and colleagues,[16] computed tomography scans used to analyze three-dimensional anatomic planes have become the "gold standard" by which a comprehensive implant treatment plan is determined and a postoperative assessment for cancellous and cortical bone is achieved.

The current study of sinus floor augmentation using CaS as a grafting material was successful. However, one implant was lost at the time of abutment connection (a nonsmoker), leading to a failure rate of 2.5%. Furthermore, all patients received implant-supported bridges that were functionally loaded during 1 year without any further complication.

According to De Leonardis and Pecora,[5] the increase in bone volume is likely the result of many factors, such as vascularization. Angiogenesis or the process of vascular induction plays an important role in all biological regenerative processes. In a study on rabbits, Strocchi and colleagues[17] have examined the microvessel density in sites treated with CaS and autogenous bone with or without expanded polytetrafluoroethylene nonresorbable membranes. Microvessels were present in all three groups, with the highest mean number in sites treated with CaS. The presence of blood vessels among CaS sites indicates the start of a tissue repair process. The formation of blood capillaries precedes the new bone formation and is therefore an important issue for development and remodeling of new bone tissue.

CONCLUSION

The results of this study show that new bone regeneration occurs in the maxillary sinus after augmentation with CaS. This enabled successful placement, integration, and loading of dental implants in the posterior maxilla as only 1 of 40 implants was lost during 1 year of follow-up. Smoking had no significance in this study, since only 1 out of 10 patients was a smoker, and the failed implant was not associated with a smoking patient.

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