Bilateral Sinus Graft With Either Bovine Hydroxyapatite or β Tricalcium Phosphate, in Combination With Platelet-rich Plasma: A Case Report

Hadi Antoun, DDS,* Hassan Bouk, DDS,† and Ghizlane Ameur, DDS‡

Although the autograft is considered as the gold standard in sinus lifts, many biomaterials have been used with high success rates and less morbidity compared with intraoral or extraoral autogenous bone. Xenograft with bovine hydroxyapatite (BH), alloplast with tricalcium phosphate (TCP), or phycogene hydroxyapatite,2 and allograft,3-6 are described in the literature.

Optimal materials for bone augmentation should not only be bone substitutes but also bone regenerating material, which involve a complete resorption with the formation of new bone. Physically and chemically treated allografts have osteoconductive properties but immunologic reactions and infections remain of particular concern.7 Moreover, allografts seem to yield irregular and sometimes inadequate results.8,9

BH is a bone substitution material, which conserves natural bone mineral structure. It is produced by elimination of the organic components of the bovine bone. Because of its natural origin, it offers a substantial similarity with human bone.10 BH is a 60% to 70% per volume porous material, facilitating osteoblasts migration and vascularization.11,12 Crystals are about 10 nm and granules 0.25 to 1.00 mm³ of size. The frequent use of BH as grafting material in sinus lift procedures is supported by a close structure to human cancellous bone,10,13 a complete deproteinization of the inorganic component, the absence of antigenicity,11 and by its osteoconductive properties.1,12,14,15

The use of pure-phase TCP as a synthetic bone substitute material has recently gained growing attention. It is used in maxillofacial preprosthetic surgery, implant dentistry, traumatology, orthopedics, and hand surgery. The different treatment procedures in maxillofacial surgery included filling of large cysts, sinus grafting,16-20 augmentation, and filling of periodontal lesions.21,22 Granules of TCP are spherical with a porous structure. This material has been shown to be clinically suitable as bone substitute capable of biodegradation. It is gradually replaced by new mineralizing bone tissue.23,24

Platelet-rich plasma (PRP) has been recently used as an adjunct in oral and maxillofacial bone reconstructive surgery.25,26 Platelets are very important in the wound healing process as they quickly reach the wound site and begin coagulation. PRP is also a source of multiple healing growth factors and cytokines.27 The combina-
ation of TCP or BH with PRP is believed to accelerate and improve bone regeneration by increasing the concentration of autologous growth factors in the bone defect. In this case study, we report 2 different graft materials associated with PRP: TCP and BH in one patient referred for bilateral sinus augmentations.

MATERIALS AND METHODS

Case Presentation

A 74-year-old woman was referred for the replacement of missing teeth in the molar area of the right and left maxilla (Fig. 1). The residual bone under the maxillary sinus was between 2 and 4 mm on both left and right sides (Figs. 2 and 3). The treatment plan consisted in reducing the mucosal thickening at the level of the right maxillary sinus before bilateral sinus lifts and the placement of implants in the posterior areas 6 months later. Grafted biomaterial was BH (BioOss, Geistlich pharmaceutical, Wolhusen, Switzerland) mixed with PRP on one side and TCP (Cerasorb, Curasan pharma MGBH, Kleinert, Germany) with PRP on the other side.

Preoperative and Postoperative Medications

The patient was premedicated 1 hour preoperatively with prednisone, antibiotics (amoxicillin and clavulanic acid), and benzodiazepine. She also did mouth rinses with 0.2% chlorhexidine for 2 minutes. After surgery, antibiotics were prescribed for 7 days (500 mg three times per day) and prednisone was tapered over 2 days. The patient was also instructed to start chlorhexidine mouth rinses (3 times a day for 2 weeks) on the second day after surgery to reduce the risk of infection.

Platelet-rich Plasma Preparation

PRP was prepared as previously described. Briefly, several minutes before surgery, 40 mL of blood was drawn into 8 citrated tubes. Tubes were centrifuged for 10 minutes at 2400 rpm (Curasan pharma GmbH, Kleinostheim, Germany) leading to 3 basic layers: erythrocytes at the bottom of the tube, plasma rich in growth factors in the middle, and plasma poor in growth factors at the top of the tube. The upper part of the tubes and the upper 1 to 2 mm of the red blood phase were collected and centrifuged for 15 minutes at 3600 rpm to concentrate the platelets. The supernatant was then separated into a lower PRP and an upper platelet-poor plasma growth factor layer. The volume of the cell-free plasma was reduced to approximately 0.3 mL. The PRP obtained was activated by CaCl solutions and finally mixed with either BH or TCP.

Surgical Procedure

After local anaesthesia (articaine 4%; adrenaline 1/100,000) of the maxillary edentulous region, a crestal incision displaced toward the palatal
Figs. 4 and 5. Cerasorb mixed with freshly prepared PRP is used on the left maxillary sinus. Fig. 6. BioOss mixed with freshly prepared PRP is used on the right maxillary sinus.

side was performed. Divergent releasing incisions were made buccally in the canine and tuberosity regions and a full thickness flap was elevated at the buccal side of the jaw to expose the lateral wall of the maxillary sinus. An ovoid antrostomy was outlined with a round bur under abundant sterile saline irrigation and along the inner limits of the maxillary sinus. The bone in the center of the window remained attached to the Schneiderian membrane which was carefully elevated within the sinus cavity, leaving it completely free from the original floor of the sinus cavity, anteriorly, posteriorly, and medially. Concurrently, the lateral wall was elevated inward to create the new relocated sinus floor. The antral space was then grafted with a mixture of BH/PRP on the right side and TCP/PRP on the left side (Figs. 4–6). Finally, the mucoperiosteal flap was approximated and sutured with horizontal mattress and single interrupted sutures.

The re-entry procedure was done at 6 months after a panoramic radiograph and a CT scan control (Figs. 7–9). A modification of the implant site preparation protocol included the use of a 2 mm internal diameter trephine (3 mm external diameter) and 10 mm long for histologic evaluation. Four nonsubmerged Branemark MK
IV Wide Platform TiUnit implants (Nobel Biocare, Paris, France) were placed at maxillary molar sites reaching a final insertion torque of 50 Ncm.

Biopsy Procedure
Both grafted sites were biopsied at the time of implant placement. After fixation, the biopsies were dehydrated and embedded in polymethylmethacrylate without previous decalcification. A 150 μm thick piece was cut from each resin block with a specific cutting system (EKAKT Microcutting System). Using the Donath technique, the pieces were then ground to 20 μm thickness and their surface colored (using paragon) to identify the different underlying tissues. The pieces were examined qualitatively under a Nikon eclipse microscope E600 and photographed with a Nikon DN 100 numeric camera. The histomorphometric analysis was done with a Zeiss microscope (Axioskop) and analyzed with the Samba images analyze system (Samba technologies, France).

The following parameters were then quantified: (1) the density of the implanted material, the preformed bone tissue and fibro-connective tissue (2) the percentage of contact between the biomaterial and bone tissue, fibrous tissues and bone layers.

RESULTS
Radiographic Observations
Postoperative panoramic radiographs and CT scan showed the positions of both types of graft materials and the height of the new sinus floor (Figs. 7–9). Bone height augmentations were considered successful to place oral implants in good conditions. Panoramic and retro-alveolar follow-up radiographs showed a normal and stabilized bone level at 4 years.

Clinical Observations
There were no postoperative complications. Normal wound healing was observed after both surgeries. The 4 implants were clinically successful as suggested by the absence of mobility and the complete bone coverage of all implants up to the first thread.

Histologic and Histomorphometrical Observations

Biopsy 1. TCP with PRP (Figs. 10 and 11). The grafted bone substitutes appeared as granules up to 600 μm in diameter occupying 60.3% of the studied surface. The centripetal trabecular penetration was important with bone density of 19.9% and bone tissue-biomaterial contact of 36.8% (Tables 1 and 2). The density of bony lacunae was 75.4% with very few fibrous tissues 0.4%. The bone tissue showed a peripheral lamellar structure and a central and peripheral primary structure. Direct bone apposition did not reach all BioOss debris. Few debris and very few signs of implants degradation were noticed. There was no local inflammation or immunologic reaction.

DISCUSSION
In this case study, 2 bone substitutes, BH and TCP, used in a sinus augmentation procedure, increased vertical bone height and allowed for the placement of implants in good clinical conditions. Restored implants remained clinically stable over a follow-up period of 4 years (Figs. 14–16). The osteoconductive properties of both these bone substitutes and the lack of complications could make BH a...
TCP gave a nonsignificant higher percentage of bone formation than BH (19.9% vs. 13.9%). The newly formed bone was immature with BH whereas a combination of primary bone and lamellar bone was found with TCP, raising the hypothesis that TCP may induce faster bone regeneration and maturation. This needs to be confirmed in a large controlled comparative study. The impact of biomaterials on bone healing time and regeneration in this case study remains unknown. The results obtained with BH are similar to published data on bone regeneration without PRP. In 15 patients, Valentini et al., showed that the regenerated bone at 12 months was lamellar in structure and supported the biomechanical charges.33 The slight decrease in material density after 12 months could indicate a very slow but active resorption. In the present case study, BH did not show any sign of resorption after 6 months, as previously described in the literature.14 On the other hand, higher resorption rates, have been reported by others.35,36 In chimpanzees, McAllister et al. reported a decrease of material 1.5 years after the sinus graft; BH still being found in small quantities.36 Histologic examinations showed zones of resorption of the particles, replaced by newly formed bone. Fugazzotto et al. showed that after 12 to 13 months, only 0.13% of the particles of the xenograft were still present in comparison to an average 68.8% of bone regeneration at the same site.35

In our case study, the percentage of remaining particles was higher with TCP (60.3%) than BH (45.5%). However, TCP showed some signs of resorption that are consistent with an experimental study investigating TCP in extraction sockets of beagle dogs.37 Sockets were filled with Cerasorb (Curasan, pharma MGBH, Kleinert, Germany) associated, or not, with PRP. The histologic findings suggested early signs of resorption of the graft particles at 12 weeks postsurgery. New bone was formed both in the widened pore system of the granules and along their scalloped surfaces. After 24 weeks, high bone density in the grafted area was achieved through integration of the granules into the newly formed bone network. These results must be taken with caution because conditions in animal experiments differ greatly from those encountered in human.

Zerbo et al. used TCP in 2 patients to augment alveolar bone before the placement of dental implants.24 TCP was used in one patient to fill a large alveolar defect in the posterior mandible after removal of a residual cyst, and in another patient to augment the sinus floor. Biopsies were taken at the time of implant placement, 9.5 and 8 months after grafting, respectively, and processed for hard tissue histology. The 9.5-month biopsy of the mandible showed 34% of mineralized bone tissue and 29% of remaining TCP, whereas the 8-month biopsy after sinus floor augmentation showed 20% mineralized bone and 44% remaining TCP, comparable with our case study. Bone and osteoid were lying in close contact with the remaining TCP and were also seen within the micropores of the grafted particles. Tartrate resistant-acid phosphatase multinuclear cells, presumably osteoclasts, were found surrounding, within and in close contact with the TCP particles, suggesting active resorption of the bone substitute. Remodeling of immature woven bone into mature lamellar bone was also found, as in our study. The limited data presented from these 2 cases suggest that TCP, possibly by virtue of its porosity and chemical nature, is a suitable bone substitute that can biodegrade and be replaced by new mineralizing bone tissue.

In our case study, the histomorphometric comparison between BH

<table>
<thead>
<tr>
<th>Implant Surface (%)</th>
<th>Bone Tissue Surface (%)</th>
<th>Lacunas Surface (%)</th>
<th>Fibrous Tissue Surface (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCP</td>
<td>60.3</td>
<td>19.9</td>
<td>15.4</td>
</tr>
<tr>
<td>BH</td>
<td>45.5</td>
<td>13.9</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Table 2. Contact Tissue-material Parameters in Sinus Grafting at 6 Months Showing More Bone Contact, no Lacunas Contact and Significant More Fibrous Tissue Contact With BH Particles When Compared to TCP Particles

<table>
<thead>
<tr>
<th>Bone Tissue Contact (%)</th>
<th>Lacunas Contact (%)</th>
<th>Fibrous Tissue Contact (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCP</td>
<td>36.8</td>
<td>54.3</td>
</tr>
<tr>
<td>BH</td>
<td>44.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Table 1. Surface Parameters (Density) in Sinus Grafting at 6 Months Showing More Residual Particles. Bone Formation and Lacunas With TCP When Compared With BH. Fibrous Tissue Surface Was Much More Pronounced in BH Biopsy

and TCP the materials of choice in sinus augmentation as an alternative to autogenous bone.
and TCP showed an important difference in the lacunae present and the proportion of fibrous tissue surface. The lacunae were shown in 15.47% proportion of fibrous tissue surface.

The percentage of bone contact between the remaining particles and the bony tissue was higher with BH. However, some particles of BH were not in contact with bone but with connective tissue, as opposed to particles of TCP which were all in contact with the bony tissue.

CONCLUSIONS

In conclusion, BH and TCP have resulted in bone formation after the sinus lift procedures. Histomorphometric analysis showed lamellar structure with TCP versus primary bone structure with BH. TCP showed signs of resorption though most of the biomaterial was still present. However, BH did not show any signs of resorption. TCP led to lacunae formation between the remaining particles and fibrous tissue with BH. BH particles showed more bone contact compared with TCP but both biomaterials allowed for stable clinical results. They deserve further evaluation and comparison in large controlled studies and long-term histomorphometric examination.

Disclosure

The authors claim to have no financial interest, directly or indirectly, in any entity that is commercially related to the products mentioned in this article.

REFERENCES


Abstract Translations

**GERMAN / DEUTSCH**

**AU T OR (E N):** Hadi Antoun, DDS, Hassan Bouk, DDS und Ghizlane Ameur, DDS. **Korrespondenz an:** Dr Hadi Antoun, DDS, 11 bis avenue Mac Mahon, 75017 Paris, Frankreich. **Telefon:** +33 1 47 23 83 25, **Fax:** +33 1 47 20 31 58, **eMail:** hadi@antoun.fr

**Bilaterales Sinustransplantat mit entweder Rinderhydroxyapatit oder β-Trikalkiumphosphat, in Verbindung mit Trombozytenreichem Blutplasma: Eine Fallstudie**


**SPANISH / ESPAÑOL**

**AU T OR (E S):** Hadi Antoun, DDS, Hassan Bouk, DDS, y Ghizlane Ameur, DDS. **Correspondencia a:** Dr Hadi Antoun, DDS, 11 bis avenue Mac Mahon, 75017 Paris, France. **Teléfono:** +33 1 47 23 83 25, **FAX:** +33 1 47 20 31 58, **Correo electrónico:** hadi@antoun.fr

**Injerto bilateral del seno con hidroxiapatita bovina o β-fosfato tricalcico, en combinación con plasma rico en plaquetas: Informe de un caso**

**ABSTRACTO:** Antecedentes: Se usan varias técnicas y muchos biomateriales en los aumentos del piso mandibular. **Propósito:** Para comparar dos diferentes materiales de injertos, se utilizó hidroxiapatita bovina (BH) y β-fosfato tricalcico de fase pura (TCP) asociada con plasma rico en plaquetas (PRP) en un paciente derivado para el aumento bilateral del seno. **Materiales y Métodos:** Se realizaron dos aumentos bilaterales del seno con BH mezclada con PRP de un lado y con TCP con PRP en el otro lado. Se realizaron biopsias seis meses después y se colocaron 4 implantes. **Resultados:** La curación de la herida ocurrió sin inconvenientes después de...
ambas operações e os quatro implantes foram clínicamente exitosos. La BY e TCP em combinação com PRP lograron un aumento satisfactorio en la dimensión vertical del hueso. El análisis histomorfométrico demostró diferencias en el número de lagunas y la proporción de tejido fibroso entre ambos materiales. El tejido óseo demostró una estructura laminar y una estructura primaria en la región inyectada con TCP/PRP mientras que fue una estructura principal exclusiva en el lado con BH/PRP. **Conclusión:** BH y TCP resultaron en la formación de hueso después de los procedimientos de elevación del seno. El análisis histomorfométrico demostró algunas diferencias pero ambos biomateriales permitieron resultados clínicos estables. Merecen más evaluaciones y comparación en estudios controlados más numerosos y examen histomorfométrico a largo plazo.

**PORTUGUÊS / PORTUGUESE**

**AUTORES:** Hadi Antoun, Cirurgião-Dentista, Hassan Bouk, Cirurgião-Dentista e Ghizlane Ameur, Cirurgião-Dentista. **Correspondência para:** Dr Hadi Antoun, DDS, 11 bis avenue Mac Mahon, 75017 Paris, France. **Telefone:** +33 1 47 23 82 25, **Fax:** +33 1 47 20 31 58, **E-Mail:** hadi@antoun.fr

**Enxerto da cavidade bilateral com hidroxiapatita bovina ou fosfato de tricálcio B, em combinação com plasma rico em plaquetas: Relato de caso**

**RESUMO:** Antecedentes. Diversas técnicas e muitos biomateriais são usados em aumento da superfície da cavidade maxilar. **Objetivo:** Comparar dois materiais de enxerto diferentes, hidroxiapatita bovina (BH) e fosfato de tricálcio B de fase pura (TCP) associados com plasma rico em plaquetas (PRP) em um paciente encaminhado para aumentos da cavidade bilateral. **Material e Métodos:** Aumentos da cavidade bilateral foram realizados com BH misturada com PRP num lado e TCP com PRP no outro lado. Foram realizadas biópsias seis meses mais tarde e 4 implantes foram colocados. **Resultados:** A cura da ferida foi desigual depois que ambas as cirurgias e os quatro implantes foram clinicamente bem-sucedidos. BH e TCP em combinação com PRP levaram a um aumento satisfatório na dimensión vertical do osso. A análise histomorfométrica mostrou diferenças no número de lacunas e na proporção de tecido fibroso entre ambos os materiais. O tecido do osso mostrou uma estrutura lamelar e uma estrutura primária na região enxertada com TCP/PRP enquanto era estrutura exclusivamente primária no lado de BH/PRP. **Conclusão:** BH e TCP resultaram em formação de osso após os procedimentos de elevação da cavidade. A análise histomorfométrica mostrou algumas diferenças, mas ambos os biomateriais proporcionaram resultados clínicos estáveis. Eles merecem avaliação adicional e comparação em grandes estudos controlados e exame histomorfométrico de longo prazo.

**RUSSIAN / РУССКИЙ**

**АВТОРЫ:** Hadi Antoun, доктор стоматологии, Hassan Bouk, доктор стоматологии, и Ghizlane Ameur, доктор стоматологии. **Адрес для корреспонденции:** Dr Hadi Antoun, DDS, 11 bis avenue Mac Mahon, 75017 Paris, France. **Телефон:** +33 1.47.23.82.25, **Факс:** +33 1.47.20.31.58, **Адрес электронной почты:** hadi@antoun.fr

**Проведение двусторонней синусовой трансплантации с применением либо бифосфонатов, либо B-трикальцийфосфата, в сочетании с насыщенной тромбоцитами плазмой: описание проведенного лечения**

**РЕЗЮМЕ:** Исходные данные. При наращивании основания верхнечелюстной пазухи используются различные методики и биоматериалы. **Цель.** Сравнить два различных материала для трансплантации: бифосфонат (BH) и бифосфонат B-трикальцийфосфата (TCP) в сочетании с насыщенной тромбоцитами плазмой (PRP) применительно к двустороннему наращиванию верхнечелюстной пазухи. Материалы и методы. Двустороннее наращивание верхнечелюстной пазухи проводилось с применением BH, смешанного с PRP, с одной стороны и с применением TCP, смешанного с PRP, с другой стороны. Через шесть месяцев была проведена биопсия и установлено 4 имплантата.

**Результаты.** Заживление раны прошло без особых осложнений после обеих операций, и переход четырех имплантатов прошла успешно. BH и TCP в сочетании с PRP положительно сказались на вертикальном размере кости. Гистоморфометрический анализ показал различия в количестве пустот и количестве волокнистой соединительной ткани между обоими материалами. Костная ткань продемонстрировала пластинчатую структуру и первичную структуру в области, где трансплантация была проведена с применением TCP/PRP, в области, где трансплантация была проведена с применением BH/PRP, была выявлена только первичная структура. **Вывод.** BH и TCP обеспечили остеогенез после проведения процедуры наращивания пазухи. Гистоморфометрический анализ показал некоторые различия, но применение обоих биоматериалов способствует получению стабильных клинических результатов. Следует провести дальнейшее исследование и сравнение этих материалов в рамках масштабных контролируемых клинических испытаний, а также долговременный гистоморфометрический анализ.

**TURKISH / TÜRKÇE**

**YAZARLAR:** Hadi Antoun, DDS, Hassan Bouk, DDS, Ghizlane Ameur, DDS. **Yayışım için:** Dr Hadi Antoun, DDS, 11

**İMPANT DENTISTRY / VOLUME 17, NUMBER 3 2008** 357

JAPANESE / 日本語

ウシ由来ハイドロキシアパタイトまたはβ-リーン酸三カルシウムを多血小板血漿と組合わせて補填したバイオテラルサイナスグラフト：ケースレポート

共同研究者氏名: ハディ・アントウン (Hadi Antoun) DDS, ハッサン・ボウク (Hassan Bouk) DDS, ギズレーン・アムア (Ghizlane Ameur) DDS.

研究概要: 背景: 多様な技術と多数のバイオマテリアルが上顎洞底増大術に使用されている。 目的: バイオテラルサイナスグラフト委託治療患者1名に各々多血小板血漿 (PRP) と組合わせたウシ由来ハイドロキシアパタイト (BH) と純相β-リーン酸三カルシウム (TCP) を補填し、2種類の異なる補填材の比較を目的とした。 素材と方法: 一侧面にはBHとPRP そして反対側側面にはTCP とPRP を補填してサイナス増大術を行った。6ヶ月後に生検を行い4本のインプラントを埋入した。 結果: 術創は両側面とも術後順調に治癒し、4本のインプラントも臨床的に成功した。BHならびにTCPのPRP混合補填材はそれぞれ垂直面骨形成に成功している。一方で組織形態測定学分析では2種類の補填材に骨細胞数と織維組織比率の差異が見られた。TCP/PRPでグラフトを行った部位では骨組織にラメラ構造と初期構造が見られたが、BH/PRP側では骨組織は初期構造のみに限られていた。 結論: BHとTCPはサイナスリフト術後に骨形成を生じる。組織形態測定学的観点では多少の差異が見られたものの、両バイオマテリアル共に安定した臨床結果が得られる可能性がある。これらの補填材は今後も大幅な対照研究や長期的組織形態測定学上検査で評価と比較を続ける価値を示している。