A new biological approach to the maxillary sinus lift technique

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The maxillary sinus lift technique consists in grafting a bone substitute below the sinus membrane to achieve sufficient thickness for implant stability. The golden standard as a bone substitute is the patient's autologous bone, which is not only fully biocompatible but is also able to stimulate bone regeneration through the osteoinductive factors it contains. Nonetheless, it has to be withdrawn from a donor site, and this increases both the operative risk and creating increased patient discomfort.

In this case report, we present the results of a maxillary sinus lift achieved by grafting a heterologous bone substitute of equine origin, totally deantigenized through enzymatic treatment. The bone substitute was applied together with two osteopromoting heterologous compounds: an angiogenesis and a morphogenesis activator. At 6 months, the X-ray examinations show a greatly regenerated bone area at the grafting site. The histological examinations show that the grafted material was nearly completely remodeled and substituted by vital endogenous newly-formed bone tissue.

Key Words: Maxillary sinus lift, bone atrophy, bone substitutes, enzymatic deantigenation, osteopromoters.

INTRODUCTION

The maxillary sinus lift technique, introduced by Tatum\(^1\) and Boyne and James\(^2\) at the start of the 1980s, makes possible the rehabilitation implantology in the posterior sectors of the maxilla also in case of atrophy. It is an efficient procedure, based on scientific and biological grounds, the success of which depends — besides the surgical and implantological capabilities of the operator — by the intrinsic regenerative potential of the patient’s own bone tissue. This, also in the case of patients that based on their medical history and clinical examination do not present counter indications to the operation, result in being however limited due to anatomical\(^3,4\) or biological reasons.

From an anatomical point of view, in fact, the bone regeneration within the sinus results in being poor due to the presence of a single wall, the floor of the sinus, from which can initiate the osteogenic event. Further, the maxillary bone, having only the function of maintaining solidly anchored the teeth in place, results in being poor in growth factors in respect to the bone tissue of other parts of the body such as, for example, the limbs where, in the case of a traumatic event, the bone regeneration must be favored to be able to recuperate as soon as possible the ability to move. Such differences reflect the different modalities of apposition of the tissue to bone in the fetal development and of the postnatal phases of life. It is, in fact, known that the flat bone of the cranium and the facial bones are formed by direct, or mantellar, ossification, while the axial bones form by indirect membranous ossification, or, in other words, by substitution of pre-existing cartilaginous tissue.

These characteristics make it possible so that usually, in an operation of lifting of the maxillary sinus made with autologous bone as a substitute, the mean time necessary to obtain
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a sufficient quality of bone regeneration varies from 4 to 6 months, and represents the motivation for which implants of autologous bone are considered the golden standard for guarantying good bone regeneration. The autologous bone, in fact, contains those growth factors that are able to stimulate the bone regeneration at the implant site. The autologous bone implants, however, present a risk/benefit ratio that must be evaluated closely each time, asking for a surgical operation more complicated and hard to be accepted by the patient, whether it entails harvest from the chin bone or even from the iliac crest. These reasons have pushed for the use of allografts of diverse origins: synthetic and animal, and derived from corals as well as other sources. The action of such materials, of whatever type they may be, is in any case only osteoconductive, aimed therefore at guaranteeing adequate mechanical support for the vassal proliferation and the deposition of new endogenous bone tissue. A possibility to assure in site of the implant also in effect osteoinductive (or, in other words, the biological stimulation of the events that lead to bone regeneration) is represented theoretically by the use of the concentrated piastrinic PRP (Platelet Rich Plasma). Its use represents however practical problems that may limit the application in those countries in which extraction is permitted in dental offices where the intervention is made. In fact, it results difficult to optimize the extractive protocol to guarantee the repeatability both of the dose applied and of the optimal concentration of platelets present in the final compound. A number of authors have recently cast doubt on the efficiency of the methodology.

An alternative approach, aimed at obtaining a more rapid osseous regeneration and qualitatively better, could be that based on the osteoinductive materials containing growth factors able to act, similarly to BMPs (Bone Morphogenetic Proteins, the bone’s own morphogenetic proteins) inducing the differentiation in osteoblasts of mesenchymal cells brought into the implant site from the vassal circulation, and thus inducing the acceleration of the deposition of the matrices collagen that will be subject to successive mineralization. An additional approach, complementary or alternative to the preceding one, could consist in the utilization of substances able to stimulate the angiogenesis in the implant site (the vascularization of which is, as is well known, a necessary condition so that bone regeneration may occur).

The scope of the present work is that of presenting the results obtained in a case of a maxillary sinus lift where there have been used in combination an activator of angiogenesis and an activator of the differentiation of mesenchymal cells together with osteoconductive enzymatically deantigenized equine bone tissue.

**Clinical case and treatment plan**

A male patient, 59 years of age, presenting grave bilateral bone atrophy in the upper right maxillary region in correspondence
with the teeth number 17 and 16, with a bone height of less than 2 mm, and in the left maxillary region with a bone height of approximately 4 mm (Fig. 1). The decision to effectuate a major lifting of the right sinus maxillary contextually with a contemporaneous augmenting of the vertical crest was made, and, after 6 months, to perform the positioning of an implant. On the left side, it was decided to perform a mini-lifting of the left maxillary sinus utilizing the Sommers technique. The results and the surgical procedure described in the present article regard only the major lifting of the sinus maxillary performed in the upper right quadrant.

MATERIALS AND METHODS

Grafting material with osteoconductive action: flexible bone tissue sheets (Spongy Osteoplant Flex, Bioteck Srl, Arcugnano – VI) have been used and a mixture of granules of spongy and cortical bone of between 0.5 and 1 mm in dimension (Biogen MIX, Bioteck). It is material of equine origin, completely without the antigenic organic component through enzymatic treatment, and is completely reabsorbable osteoclastically in the physiological time period necessary for the remodeling of the implant. Such materials have been used for years in orthopedics7-10, for major bone reconstructions (for example, hip prosthetic revisions) and are utilized with success also in orthodontic dentistry11-13.

Material additives with osteopromoting action: an activator of angiogenesis in gel form (Osteoplant Angiostad, Bioteck) and an activator of morphogenesis in granule form (Osteoplant Activagen, Bioteck) have been utilized. Osteoplant Angiostad is a hydrogel containing dissolved factors of protein origin able to activate the production of VEGF (Vascular Endothelial Growth Factor), a cytokine which stimulates the proliferation of vassal endothelia. The action of Osteoplant Angiostad is immediate and is exhausted in over a period of 96 hours.

Osteoplant Activagen is a material composed of lyophilized granules of type 1 collagen (degradable only osteoclastically) containing factors of protein origin belonging to the super family of the TGFb-1 (Tissue Growth Factor Beta 1). The half life of morphogenic proteins has not ever been estimated with any accuracy, but it is logical to suppose that it does not reach the order of several hours14. This fact renders scarcely efficient their exogenous application in cases in which the ossification must be stimulated directly, in that the time in which these are degraded is less than the time necessary for the vessel elements to colonize the implant site. Due to this fact, when in the implant site, through the vessels, the pre-osteoblastic cells, the morphogenic exogenous protein, are not able to activate the differentiation in osteoblasts in that they are already degraded.

In the Activagen product, instead, the protein factors in lyophilized form (and therefore not subject to degradation) are protected by a shell of type I collagen, and its degradation can only occur when in the implant site are present osteoclasts. In this phase, there are certainly present the pre-differentiated mesenchymal cellule. The lyophilized protein factors freed undergo hydration and, reacquiring their original conformation, are able to exercise the morphogenetic effect on such elements cellular, inducing the differentiation in osteoblasts and stimulating the activity, accelerating of consequence the formation of new bone tissue.

Modality of intervention
The patient’s pre-surgical preparation has been made starting with a prophylactic treatment of antibiotics, administered 1 day before the operation and after the therapy continues two times a day for 6 days, with Amoxicilin/clavulanic acid (Augmentin, Glaxo Smith Kline). An hour before the operation, a pre-medication with Diazepam (Valium 2, Roche) had been administered.

One-half hour before the operation, the patient had been administered an anti-inflammatory substance (Naproxen sodium) and had continued to be prescribed for 2 times a day for a total of 4 days (Synflex forte, 550, Recordati). Successively, before the start of the operation, the patient had rinsed with Chlorhexidine Gluconate at 0.2% (Corsodyl, Glaxo Smith Kline). Then, the patient was covered with sterile gauze. The operation had been performed in local anesthesia with

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Articain at 4% and Epinephrine 1:100.000 (Citrocartin 100, Molteni).

The surgical procedure was initiated with an incision along the crest slightly vestibular in the keratinized mucosa, approximately 3 cm in length. Then, a distal and mesial incision was performed and the tissue was released completely. Then, a continuous periosteal release was made to connect the vertical, mesial and distal release incisions, to obtain a total release of the margin and to be able to suture it at the end of the operation without tension being present.

After having removed with extreme accuracy all of the residual connective tissue above the bone crest, it was possible to proceed with the opening of the lateral wall of the maxillary bone, following the technique of the "lateral window" as described by Tatum and Misch\(^1\). With a rosette shaped diamond bur mounted on a contra angle high velocity head, a window is made with an elliptical form with a dimension of 12 mm x 8 mm. Then, the operation proceeded with the release of the sinus membrane utilizing retractors designed for the sinus (Hufriedy). Successively, the vestibular window is mobilized delicately towards the medial wall of the sinus, in such a way so as to make a roof for the cavity in which the graft is inserted. The graft material was prepared by hydrating for several minutes in sterile physiological solution the sheet of spongy Osteoplant FLEX, that was then successively cut in pieces appropriate for insertion within the sinus access window (the sheet, once hydrated, assumes a flexible consistency; it can be bent and compressed to introduce it in the sinus, where it will reassume its original shape). At the same time, 1 gram of granulate (Biogen MIX) is mixed with 1 gram of Activagen additive: the mixture obtained in this way was hydrated for several minutes in sterile physiological solution and to this is added the Angiostad gel in a 1:10 volumetric proportion (1 part Angiostad: 10 parts granular mixture), following the producer's indications.

The filling operation had been performed placing a first sheet of spongy within the sinus, in contact with and as a protection for the Schneider membrane, and successively alternating a layer of granular mixture, injected utilizing the supplied syringe, and a sheet of spongy, until a complete filling of the cavity is obtained. A membrane in collagen for guided regeneration (Biocollagen, Bioteck) was hydrated in sterile physiological solution for several minutes and was then placed over the bone window to obtain a complete closure of the graft site.

At the same time of the grafting operation on the right side, the insertion of the two implants, in positions number 12 and 14, was also performed. Then, the intervention proceeded with the repositioning of the mucoperiosteum and suturing with vertical "mattress sutures" (Gore-tex, WL Gore) alternated with simple interrupted sutures. The sutures were removed after 12 days; the patient had control visits once a month for a period of six months, and at the end of this period had a control OPT (shown in Fig. 2a).

**Grafting procedure**

After 6 months, the graft was reopened with a marginal cut with a vestibular incision, exposing the osseous crest. In the point where it was decided to insert the graft, in position number 16, a part of the cortical bone (approximately 1,5 mm.) was removed, using a rosette-shaped multiple blade bur mounted on a contra angle surgical drill head, until arriving at the tissue of the graft.

Then, with a 3 mm diameter bone harvesting drill bit, a core of bone was harvested approximately 10 mm long. The core was immediately placed in a suitable container containing formalin at 10% and successively sent to a histological laboratory.

The alveolus obtained in this manner was then enlarged to 4 mm, to permit the insertion of a 5 x 13 mm implant (Sustain, Lifecore Biomedical). The consistency of the bone found was of D2-D3 quality.
Once the graft was positioned, the margins were sutured utilizing horizontal "mattress sutures". The sutures were removed after 10 days. After an additional 6 months, the graft was connected with a temporary prosthesis and, after an additional 6 months of functioning with the temporary prosthesis, a permanent prosthesis in gold-ceramics was positioned (Fig. 2c).
**Fig. 2a** OPT before the positioning of the last graft. Note in correspondence with the graft at the position of the right maxillary sinus the regeneration of a noticeable radio-opaque mass. The transcortical screws fix a sheet of cortical Osteoplant Flex placed to perform at the same time an augmentation of the vertical crest (not described in the present article). On the left side, it is possible to observe the insertion of a graft in position 27 following the mini-lifting of the maxillary sinus following Sommers, made with Bio-Oss (Geistlich, Switzerland).

**Fig.2b** Close-up of the graft in position 14.  
**Fig.2c** OPT with rehabilitation completed.  
**Fig.2d** Close-up of the graft at the grafting site in position 16.

**Histological analyses**

The sample was fixed in a formalin tampon at 10%, dehydrated in ethylic alcohol, decalcified with Decalcifying K with EDTA (Kaltek) and enclosed in paraffin (Paraplast Plus, Kaltek). There were obtained sections the thickness of 6-7 micron, which were stained with hematoxylin and eosin, and, successively, evaluated by optical microscopy (Olympus BX 45).

**RESULTS**

The radiographic analyses utilizing OPT showed, at 6 months, the presence within the cavity of the maxillary sinus of a radio-opaque mass of noteworthy dimension (Fig. 2a-2d). The histological analysis of the biopic sample harvested in the graft implant site, approximately 10 mm in length, showed the presence of spongy bone constituted of thick and irregular trabecola of newly formed bone with an osteonic structure in which can be recognized numerous well conserved osteocytes and Havers canals (Fig. 3-5). In the medullar spaces there were found connective fibril of varying denseness and richly vascularized including spicules of transplanted bone, necrobiotics and which were in large part reabsorbed, delimitated by osteoclastic elements and fibrocytes (Fig. 6). The graft’s vitality was confirmed, besides by the presence of the osteocytes, by the evidence of the newly deposited collagen fibrils, visible in polarized light (Fig. 7). The newly formed bone tissue demonstrated overall a good level of maturation in the grafting site.
**Fig. 3** Tissue stained with hematoxylin and eosin. There is an evident presence of spongy bone organized in thick irregular trabecula.

**Fig. 4** Tissue stained with hematoxylin and eosin. Detail at a greater magnification.

**Fig. 5** Tissue stained with hematoxylin and eosin. The lamellar organization of the newly formed bone tissue is testimony to the elevated level of graft maturation.

**Fig. 6** Tissue stained with hematoxylin and eosin. Marrow rich in connective fibrils in which are enclosed spicules of transplanted bone, necrobiotic and largely reabsorbed.

**Fig. 7** Tissue stained with hematoxylin and eosin, and illuminated with polarized light. The presence of newly formed collagen fiber is observable and confirms the graft’s vitality.

**DISCUSSION AND CONCLUSIONS**

The results that have been presented in this case report show how the use of a heterologous bone substitute that has been opportunely deantigenized, in combination with compounds able to stimulate both angiogenesis and morphogenesis in the grafting, was able, in the considered case, to provide in a brief period of time optimal results in relation to the quality of the regenerated bone tissue.

It is known that the specific bone substitutes employed undergo complete remodeling thanks [SESTA PAGINA/SIXTH PAGE]
to the enzymatic deantigenation process by which they are obtained by, that does not alter the chemical and physical characteristics of the mineral component of the equine bone, conserving its possibility for complete remodeling.

Nevertheless, in our opinion, particularly significant are the elevated levels of remodeling and of graft maturation found that we believe are due instead to the stimulating action produced by the osteopromotor compounds utilized in combination with the cited bone substitutes.

The importance of such results, if confirmed by additional cases, is evident if one thinks of the possible case of abbreviating the time necessary for the completing of a patient’s implant and prosthetic rehabilitation.

At the time of this case report’s writing, one of the authors (Ludovichetti) has obtained analogous results, employing the same association of materials, in at least ten other cases. The clinical effectiveness of such associations will now be the subject of study through a research protocol aimed at the obtaining of a statistically significant number of cases.

**BIBLIOGRAPHY**


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