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Evaluation of hyaluronic matrix efficacy in sinus augmentation: a randomized-controlled histomorphometric and micro–computed tomography analysis

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Abstract. The objective of the present study was to test the hypothesis that the addition of hyaluronic acid–based matrix to collagenated heterologous bone graft for sinus augmentation would enhance bone formation compared to collagenated heterologous bone graft alone in the early healing period, by micro−computed tomography and histomorphometry. Thirteen systemically healthy patients requiring bilateral two-stage maxillary sinus augmentation (residual crest height $\leq$ 4 mm) were enrolled in this split-mouth prospective randomized controlled study. One sinus side as a control group was grafted with only collagenated heterologous bone graft; the other region as a test group was grafted with hyaluronic matrix and collagenated heterologous bone graft. Bone biopsy samples were taken after 4 months during the dental implant surgery and analyzed using micro−computed tomography and histomorphometric parameters. According to the micro−computed tomography and histomorphometric results, a significantly higher percentage of new bone was observed in the test group when compared to the control group after 4 months of healing.

This study confirmed the hypothesis that the addition of hyaluronic matrix to collagenated heterologous bone graft for sinus augmentation enhances bone formation compared to collagenated heterologous bone graft alone in the early healing period.

Key words: maxillary sinus augmentation; dental implant; hyaluronic matrix; histomorphometry; micro computed tomography.

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The rehabilitation of partially or completely edentulous patients with implant-supported prostheses has been a routine treatment in recent decades, with reliable outcomes[1]. The long-term stability of dental implants in the function and prognosis of implant-supported prostheses are directly associated with the quality and quantity of the available bone for implant placement[2].

Clinicians usually have to deal with insufficient bone height in the posterior maxilla due to alveolar bone atrophy and pneumatization of the maxillary sinus after teeth loss. Maxillary sinus augmentation procedures have been used to obtain sufficient bone quantity and quality to allow implant placement. Since Tatum[3] first described a maxillary sinus augmentation procedure using the lateral window technique, various grafting materials have been used for this purpose[4,5]. These include autografts, allografts, xenografts, alloplasts, and combinations of these in various forms[6].

Autograft is believed to be the gold standard in augmentation procedures due to its osteogenic, osteoinductive, and osteoconductive properties; however; it has main disadvantages in sinus grafting such as the availability of only limited quantities, the need to include additional surgical sites, donor site morbidity, and a tendency towards resorption which may compromise long-term implant stability[7,8]. Recent studies have shown higher implant survival/success rates with xenografts than with autografts in sinus augmented areas[9]. In addition to bovine bone being used frequently for sinus augmentation, a collagenated heterologous bone graft (CHBG) has been used recently in augmentation procedures[10]. CHBG is similar to human bone in that it is osteoconductive and integrates well at host sites. Although many studies have evaluated the suitability of materials of different origins, it still remains unknown which is the most convenient graft material for maxillary sinus augmentation[11].

To obtain successful sinus augmentation outcomes, regeneration of well-vascularized, healthy bone is critical[12]. Other than the type of graft material used, the duration between sinus augmentation and implant placement influences regenerative outcomes in maxillary sinus augmentation[13–15].

Longer healing periods increase the amount of newly formed bone. However, for patient comfort and quality of life, shortening the length of surgical treatment time is an important issue[1].

The application of exogenous hyaluronic acid and hyaluronic acid–based materials have provided good results in manipulating and accelerating wound the healing process in a large number of medical disciplines, as evident in ophthalmology, dermatology, dentistry, and rheumatology[16]. Hyaluronic acid is a naturally occurring, nonsulphated glycosaminoglycan that is normally present in great quantities in extracellular matrixes such as basal laminae, connective matrixes, and synovial fluid[17]. Through its complex interactions with matrix components and cells, hyaluronic acid has multifaceted roles in biology using both its physicochemical and biological properties[18]. It plays a predominant role in tissue morphogenesis, cell migration, differentiation, and adhesion[19]. Hyaluronic acid also has osteoconductive properties and accelerates bone regeneration by means of chemotaxis, proliferation, and successive differentiation of mesenchymal cells[20].

According to the literature, there is a limited number of studies using hyaluronic acid for sinus augmentation. Schwartz et al.[21] reported the use of hyaluronic acid as a carrier material with demineralized bone allograft (DFDBA) for sinus augmentation in human patients. Their results showed that hyaluronic acid can be used as a carrier for DFDBA without reducing the clinical effectiveness of the graft.

Butz et al.[22] evaluated the time-dependent efficacy of bovine hydroxyapatite/synthetic peptide in a sodium hyaluronate carrier (PepGen P-15 Putty) for maxillary sinus augmentation. Emam et al.[23] also aimed to test the efficacy of PepGen P-15 Putty as a sole graft material for sinus augmentation.

Imaging techniques such as micro–computed tomography (micro-CT) have made it possible to obtain high-resolution three-dimensional images to directly examine the bone architecture. With this technique, no specimen preparation is required, and testing is nondestructive compared to conventional histomorphometry[24]. This method allows evaluation of the three-dimensional architecture of grafted bone after a period of bone healing. However, despite improvements in micro-CT, the histomorphometric techniques still remain a gold standard for analysing bone formation and allow more accurate evaluation of the association between graft particles, newly formed bone, and the cellular characterization[25].

This clinical study aimed to testing the hypothesis that the addition of hyaluronic matrix to CHBG for sinus augmentation would enhance bone formation in the early healing period compared to CHBG alone, using micro-CT and histomorphometric evaluation.

Materials and Methods

Thirteen systemically healthy patients requiring bilateral maxillary sinus augmentation (residual crest height $\leq$ 4 mm) were included in this prospective randomized controlled study.

Eight female and five male patients (mean age, 0 years; range, 33–69 years) were enrolled between September 2013 and June 2015. The exclusion criteria were advanced systemic diseases, chronic medication use, maxillary sinus disease, current pregnancy or lactation, and smoking habit. At baseline, a comprehensive oral examination, panoramic radiographs, and cone beam computed tomography (CBCT) scans were performed. CBCT scans were analyzed for residual crest height, residual crest width, intrasinusal pathologies, and morphology of the bony walls. Patients with good oral hygiene and no active periodontitis underwent two-stage maxillary sinus augmentation.

The study was performed according to the Declaration of Helsinki as revised in 2001[26,27]. The study protocol was approved by the clinical research ethics board of the university (2014/08 - 16 (KA-14030)). The patients were fully informed about the procedures and could terminate their participation in the study at any time. All patients provided written informed consent.

The present study has been registered to the clinicaltrials.gov system as a randomized controlled trial with identifier number NCT02692261.

All patients received bilateral sinus augmentation via a lateral window approach as described by Tatum[3]. After local anesthesia, this approach began with a crestal incision on the top of the alveolar ridge, which was supplemented by two releasing incisions at the anterior and posterior extent of the crestal incision. A full-thickness mucoperiosteal flap was raised, and a small buccal window was then created using a round bur under sterile saline irrigation on the lateral wall of the sinus until the bluish hue of the sinus membrane was visible. The Schneiderian membrane was elevated from the bony floor with sinus elevation curettes freely anteriorly, posteriorly, and medially to ensure tension-free elevation. The space created below the membrane was available for graft placement. If the sinus membrane was inadvertently perforated, collagen membrane was applied to seal the opening and to ensure the confinement of the graft material. As larger perforations occurred, the augmentation procedure was postponed and patient was excluded from the study.