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Clinical Evaluation of Demineralized Bone Allograft for Sinus Lifts in Humans: A Clinical and Histologic Study

조 선 대 학 교 대 학 원

치 의 학 과

원 영 훈

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탈회 동종골을 이용한 상악동 거상술의 임상 평가:
임상 및 조직학적 연구

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조선대학교 대학원

치 의 학 과

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지도교수 김 수 관

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조 선 대 학 교 대 학 원

치 의 학 과

원 영 훈

원영훈의 석사학위논문을 인준함

위원장 조선대학교 교수 김 학균 인

위원 조선대학교 교수 문 성용 인

위원 조선대학교 교수 김 수관 인

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조선대학교 대학원

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원 영훈
지도교수 : 김 수관
조선대학교 치의학과
구강악안면외과학 전공

본 연구의 목적은 탈회 동종골을 이용하여 상악동 거상술을 시행하고 조직검사를 시행하여 조직학적 평가를 시행하여 임상 검사와 함께 이의 임상적인 유효성에 관해 평가하는 데 있다.

본 연구에서는 상악동 거상술 및 임프란트 식립 등의 외과적 술식으로 인한 합병증이나 병발증은 관찰되지 않았다. 상악동 거상술 9개월 후 임프란트의 식립시 충분한 일차 고정을 얻을 수 있었으며 안정성 평가 시행시 높은 안정성을 보였다. 상악동의 거상된 양은 충분하였으며 정상적인 골밀도와 이식된 높이가 유지되었다. 조직학적인 소견으로 이식재의 흡수와 함께 신생골 형성을 관찰할 수 있었으며 이식재 입자 표면에 골이 직접 침착되어 있는 긴밀한 접촉을 보였다. 또한 임상 관찰 기간 동안 안정화된 양상을 보였다. 이러한 결과 탈회 골기질의 단독 사용은 임프란트 식립을 위한 상악동 거상술시 유용한 방법이라 생각된다.

Introduction

After the loss of teeth in the posterior maxillary region, due to the pneumatization of the maxillary floor, the maxillary sinus floor approaches the alveolar area, and the height of the remaining alveolar bone may decrease markedly, making implant placement difficult. Consequently, bone grafting within the maxillary sinus is often required for the placement of implants in this area. For sinus bone grafting, Tatum first reported inlay bone grafting in 1977. Subsequently, the technique has been improved greatly, and it is now widely applied for implant placement with sufficiently predictable results[1)]. Autograft, allograft, xenograft, and alloplast materials can be used for bone grafts in the maxillary sinus floor. Autografts include block bone fragments, cortical bone, and mixtures of cortical and cancellous bone; allografts include freeze-dried bone and demineralized freeze-dried bone. Synthetic bone may be various types of hydroxyapatite powder. The development of bone graft materials has been ongoing, and many case reports have been published. Autologous bone is used most widely and with high success rates. Consequently, it is recognized as the gold standard. Autologous bone has excellent new bone formation capacity, will not spread infectious diseases, and has excellent biocompatibility; however, it requires additional surgery and may lead to complications in the donor sites. Therefore, the development of bone graft materials that can replace autologous bone is in continuous development.

Since its introduction in 1889 as a bone graft material, demineralized bone matrix (DBM) has been used clinically. DBM contains bone morphogenic proteins and stimulates osteoinduction. On the other hand, demineralized bone is readily resorbed, which makes maintaining a space difficult. Hence, it is often mixed with other allograft bones or synthetic graft materials. Many products contain DBM, and the ratio of DBM in

carrier varies. The bone graft material used in this study was DBX® (Synthes), which contains 32% DBM with sodium hyaluronate as the carrier.

In this study, maxillary sinus lifts were performed using only DBX®, and the results were analyzed histologically and clinically after 9 months to evaluate its usefulness.

Study subjects and methods

The study included eight patients whose ages were ranged from 48 to 64 years old (average, 57.2). The patients were non-smokers, had no history of systemic disease or drug abuse, and presented with an edentulous maxillary molar area. A total of 10 maxillary sinus lift procedures were performed in the eight patients. On the presurgical panoramic x-ray, the height of the residual alveolar bone, from the maxillary sinus floor to the alveolar crest, ranged from 4.5 to 7.8 mm and averaged 5.9 mm. Any paradental cysts adjacent to the implant placement area or lesions in the root apex observed radiologically were treated preoperatively. Before surgery, panoramic x-rays and Water's view were used to determine the shape of the maxillary sinus and the presence or absence of maxillary sinus disease.

Using conventional methods, the inside and outside of the oral cavity were sterilized, and local anesthesia was administered with 2% lidocaine containing 1:100,000 epinephrine. A transverse incision was made on the alveolar crest, together with a sufficient vertical buccal incision, and a full-thickness flap was lifted. Using a diamond round bur or Piezosurgery, a lateral window osteotomy, approximately 10 × 15 mm in size, was made in the lateral maxillary wall, and the maxillary sinus membrane was lifted. The bone window was fractured internally to avoid its inclusion in the future bone tissue

harvest (Fig. 1). As bone graft material, DBX® was used without a barrier membrane (Fig. 2). The average amount of DBX® used was 1.7 cc. The flap was replaced using conventional methods and was sutured. No postsurgical nasal hemorrhage, maxillary sinusitis, or other complications were detected in any of the patients.

The patients were assessed clinically and radiologically after a day, a month, and 6 months postoperatively. Bone tissue segments were harvested 9 months later, at the time of implant placement. To minimize the inclusion of original bone tissues in the sample, a core was harvested from the healed side of the bone window using a trephine bur with an internal diameter of 2.0 mm, and the new bone formation in the maxillary sinus was analyzed. In all, 24 implants were placed, with a mean diameter of 4 mm and mean length of 11.8 mm.

Fig. 1. The internal fracture after lateral window osteotomy.

Fig. 2. Lifting the Schneiderian membrane, followed by DBX® filling.

The collected bone samples were immediately fixed in 10% formalin for 24 h and then decalcified with Calci-Clear Rapid™ (National Diagnostics, Atlanta, GA, USA) for 12 h. The decalcified tissues were washed under running water, processed automatically (Hypercentre XP, Shandon, Cheshire, UK), embedded in paraffin, sectioned at 4- to 5-μm thickness, stained with hematoxylin-eosin (H&E), and analyzed using light microscopy.

Results

None of the patients developed complications such as infection or maxillary sinusitis.

When the tissue samples were harvested, the lateral window area did not differ greatly from the adjacent normal bone tissues, and the border was not obvious. In all patients, sufficient initial fixation was obtained during implantation. A second procedure was performed approximately 6 months after surgery. During abutment connection, the stability was evaluated with Periotest® and ranged from –1 to –4 (average, –2.7). Using conventional methods, a permanent prosthesis was placed approximately 3 months postoperatively.

In the radiographic evaluation, the amount of lifted maxillary sinus was sufficient, the bone density was normal, and the initial grafted height was maintained. The radiographic results showed normal condition implant placement. The bone near the implant was examined using root apex radiographs, and the resorption of the marginal bone ranged from 0.6 to 2.9 mm (average, 1.13). After placing the final prosthesis, occlusal loading was added, and no macroscopic movement or displacement was detected during a year of follow-up period.

Histologically, resorption of the graft materials and new bone formation were observed, and there was direct deposition of bone on the surface of the graft particles. New bone filled the spaces between graft particles, most of which were buried within new bone. Osteoid was detected in some cases, indicating active bone formation within the graft material. Bone marrow cavity formation by osteocytes and new connective tissues were observed. The bone marrow cavities contained new connective tissues and abundant blood vessels, and osteoclasts were seen near the graft material in some cases. No infiltration of inflammatory cells was detected, although irregular invasion of graft particles by new bone was present in some cases (Figs. 3 and 4).

Fig. 3. Histopathological findings after DBX® grafting. Woven bone (arrows) has formed around the implant chips (black asterisk). Partly resorbed implant chips (white asterisks) are scattered in the background. H&E staining, ×100.

Fig. 4. Higher magnification of Fig. 3, showing woven bone (arrows) around an implant chip (black asterisk) and intervening fibrosis (white asterisks). H&E staining, ×200.

Discussion

The bone density in the maxillary molar area is relatively low. Thus, when severe bone loss follows the resorption of the residual alveolar bone or when the pneumatization of the maxillary sinus is marked, implantation becomes difficult, usually requiring surgical intervention such as a maxillary sinus lift and bone grafting[2)]. Improved maxillary sinus lift techniques and diverse bone graft materials have been used for this purpose. Autologous bone was originally used for most maxillary sinus lifts and is still considered to be the best bone graft material[3)], owing to its exceptional osteogenesis ability, near-zero possibility of rejection or transmitted infection, and excellent biocompatibility. Nevertheless, bone harvesting requires additional surgery, with its accompanied complications, and it can be difficult to obtain sufficient autologous bone from the oral cavity[4,5)]. Bone substitutes have been developed to replace autologous bone, and these are used alone or together with autologous bone. However, their osteogenesis and bone maintenance abilities are controversial. In addition, it is not clear which bone graft material is the best for maxillary sinus lifts.

Demineralized bone matrix consists of bone matrix that preserves the organic substances and proteins and is produced by removing inorganic substances from cortical

bone obtained from cadavers. The osteogenic proteins within the bone matrix stimulate osteoinduction, giving DBM excellent osteoinductive ability.

DBM was first used as a bone graft material in 1889. Initially, the inorganic substances were removed for the purpose of sterilization; however, because this process increased osteoinduction, numerous studies have been performed on DBM[6]. Animal studies of DBM placed in bone defects have shown that the mechanical strength and level of osteogenesis are comparable to those of autologous bone. Consequently, numerous clinical studies have been conducted[7-10]. In 1975, Libin *et al* first used DBM in the maxillofacial area[11], and it has been reported to give satisfactory clinical results[12-16].

Numerous recent studies on maxillary sinus lift using DBM have demonstrated remineralization and new bone formation leading to increased levels of inorganic substances, which allows implant placement. Schwartz *et al* used DBM alone and in combination with Bio-Oss and found that the rate of new bone formation and trabecular bone volume did not show significant difference between the two groups[17]. In a study comparing patients who had received demineralized freeze-dried bone (DFDB) grafts with those who had received autologous bone grafts, Nishibori *et al* found sufficient bone volume and quality for implant placement in the patients with the autologous bone graft, whereas the volume and quality of bone were insufficient in those with the DFDB graft; at least 12 months were required for maturation of the DFDB graft material[18]. The success rate of some graft materials can exceed 90%, but the success rate with demineralized bone can be as low as 75%[19-21].

Numerous graft materials containing DBM have been introduced, with the DBM content ranging from 17 to 100%. The osteoinductive ability of these materials varies with the DBM content[22]. The carriers, which include calcium sulfate, lecithin, sodium

hyaluronate, porcine collagen, and glycerol, cause slight differences in the clinical results[23]. The carrier in DBX® is hyaluronic acid, a non-toxic, biocompatible, natural polymer that is absorbed in the body and is used in dermal lesions[24] and joints. Hyaluronic acid does not reduce the clinical efficacy of DBM transplants. The pH of DBX® (7.5 versus 4.5 for DBM with glycerin as a carrier) is comparable to that of blood, and thus it does not cause cellular hemolysis. In rats, DBX® resulted in significantly greater osteogenesis in the femoral bone in comparison with DBM in glycerin[25]. Hyaluronic acid consists of different polymers, making DBX® malleable like putty. Therefore, unlike other bone substitutes, DBX® does not scatter in maxillary sinus lifts and is readily manipulated, allowing sufficient amounts to be grafted[17]. It can be used in combination with other bone substitutes, possibly shortening treatment times.

Conclusion

In our series of maxillary sinus lifts performed using DBX®, no complications or adverse sequelae of maxillary sinus lifting and implant placement were observed. With implant placement performed 9 months after maxillary sinus lifting, sufficient initial fixation was obtained, with high resulting stability. The lifted amount of the maxillary sinus was sufficient, and normal bone density and alveolar ridge height were maintained. Histologically, resorption of the graft materials and new bone formation were observed, with bone directly deposited on the surface of the graft particles. The results remained stable during the clinical observation period of 1 year. Based on these results, demineralized bone matrix graft material can be used alone in maxillary sinus lift surgery for implantation.

(1) The mean alveolar crest bone resorption was 0.09 mm around a single upper

prosthesis, 0.39 mm near a fixed partial prosthesis, and 0.5 mm with a full arch prosthesis and overdenture.

(2) Overall, the prognosis of a one-stage implant in Koreans who have strong masticatory force was good.

References

1. Tatum H Jr: Maxillary and sinus implant reconstructions. Dent Clin North Am, 30: 207, 1986.

2. Boyne PJ, James RA: Grafting of the maxillary sinus floor with autogenous marrow and bone. J Oral Surg, 38: 613, 1980.

3. Wallace SS, Froum SJ: Effect of maxillary sinus augmentation on the survival of endosseous dental implants; A systematic review. Ann Periodontol, 8: 328, 2003.

4. Lauri SWS, et al: Donor site morbidity after harvesting rib and iliac bone. Plastic and Reconstructive Surg, 73: 933, 1984.

5. Sommers BN, Eisenstein SM: Donor site pain from the ileum; a complication of lumbar spine fusion. J Bone Joint Surg Br 71: 677, 1984.

6. Block JE, Poser J: Does xenogeneic demineralized bone matrix have clinical utility as a bone graft substitute? Med Hypotheses, 45: 27, 1995.

7. Tiedeman JJ, et al: Treatment of nonunion by percutaneous injection of bone marrow and demineralized bone matrix. An experimental study in dogs. Clin Orthop, 268: 294, 1991.

8. Gepstein R, et al: Bridging large defects in bone by demineralized bone matrix in the form of a powder. A radiographic, histological, and radioisotope- uptake study in rats. J Bone Joint Surg Am, 69: 984, 1987.

9. Gebhart M, Lane J: A radiographical and biomechanical study of demineralized bone matrix implanted into a bone defect of rat femurs with and without bone marrow. Acta Orthop Belg, 57: 130, 1990.

10. Einhorn TA, et al: The healing of segmental bone defects induced by demineralized bone matrix. A radiographic and biomechanical study. J Bone Joint Surg, 66: 274, 1984.

11. Libin BM, et al: Decalcified, lyophilized bone allografts for use in human periodontal defects. J Periodontol, 46: 51, 1975.

12. Glowacki J, et al: Application of the biological principle of induced osteogenesis for craniofacial defects. Lancet, 1: 959, 1981.

13. Mulliken JB, et al: Use of demineralized allogeneic bone implants for the correction of maxillocraniofacial deformities. Ann Surg, 194: 366, 1981.

14. Kaban LB, et al: Treatment of jaw defects with demineralized bone implants. J Oral Maxillofac Surg, 40: 623, 1982.
15. Sonis ST, et al: Clinical trial of demineralized bone powder in the treatment of periodontal defects. J Oral Med, 38: 117, 1983.
16. Glowacki J, Mulliken JB: Demineralized bone implants: Clin Plast Surg, 12: 233, 1985.
17. Schwartz Z, et al: Clinical evaluation of demineralized bone allograft in a hyaluronic acid carrier for sinus lift augmentation in humans: a computed tomography and histomorphometric study. Clin Oral Implants Res, 18: 204, 2007.
18. Nishibori M, et al: Short-term healing of autogenous and allogenic bone grafts after skinus augmentation: a report of 2 cases. J Periodontol, 65: 958, 1994.
19. Jensen OT, et al: Nasal fossa and maxillary sinus grafting of implants from a palatal approach: report of a case. J Oral Maxillofac Surg, 50: 415, 1992.
20. Block MS, Kent JN: Maxillary sinus grafting for totally and partially edentulous patients. JADA, 124: 139, 1993.
21. Lozada JL, et al: Root-form implant placed in subantral grafted sites. J Calif Dent Assoc, 21: 31, 1993.
22. Edwards JL: In vivo osteoinductivity of two human DBM materials: comparative histologic evaluation at 14 and 28 days. IsoTis OrthoBiologics, 0166.0, 2003.
23. Han B, et al: Quantitative and sensitive in vitro assay for osteoinductive activity of demineralized bone matrix. J Orthop Res, 21: 648, 2003.
24. Weindl G, et al: Hyaluronic acid in the treatment and prevention of skin diseases: molecular biological, pharmaceutical and clinical aspects. Skin Pharmacol Physiol, 17: 207, 2004.
25. Oakes D, et al: An Evaluation of the Osteoinductive Potential of Human Demineralized Bone Matrices in an Athymic Rat Femoral Defect Model. 47th Annual Meeting: Orthopaedic Research Society: February, 2001.
26. Groeneveld EH, et al: Mineralization processes in demineralized bone matrix grafts in human maxillary sinus floor elevations. J Biomed Mater Res, 48: 393, 1999.