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ORIGINAL ARTICLE

Comparison of recombinant human bone morphogenetic protein-2-infused absorbable collagen sponge, recombinant human bone morphogenetic protein-2-coated tricalcium phosphate, and platelet-rich fibrin-mixed tricalcium phosphate for sinus augmentation in rabbits

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absorbable collagen sponge;
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TCP

Abstract *Background/purpose:* Numerous grafting materials have been used in the bone regeneration of maxillary sinus to obtain a sufficient amount of new bone in implant dentistry. The objective of this study was to compare the potentials of Type I absorbable collagen sponge (ACS) impregnated with recombinant human bone morphogenetic protein (rhBMP)-2, rhBMP-2-coated tricalcium phosphate (TCP), platelet-rich fibrin-mixed TCP for enhancing bone regeneration in sinus augmentation in rabbits.
Materials and methods: The sinus defects were grafted with rhBMP-2+ACS (Group A), rhBMP-2-coated TCP (Group B), and platelet-rich fibrin-mixed TCP (Group C). The specimens underwent decalcification, and were stained for histomorphometric analysis.
Results: There were no significant differences in inflammatory features among the groups 1-week postoperation. In a histomorphometric analysis, the new bone formation ratio showed significant differences between groups at 2 weeks. rhBMP-2+ACS showed a larger and more rapid bone formation area at 2 weeks than those of Groups B and C.

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Conclusion: Our histological evaluation demonstrates that Type I ACS can be used as a carrier of rhBMP-2, and rhBMP-2+ACS showed rapid bone formation, remodeling, and calcification at Week 2 in rabbit.

Introduction

After tooth loss, edentulous posterior maxillae often present with insufficient alveolar bone quantity and quality, with maxillary sinus pneumatization.[1] To overcome these structural deficiencies and ensure successful implant surgery, most surgeons used to perform maxillary sinus augmentation.

Autogenous bone, known as the *gold standard*, is a well-established material used to fill insufficient maxillary sinus, because it has osteogenic, osteoinductive, and osteoconductive characteristics.[2] However, some disadvantages and systemic limitations, such as the need for a second surgical site and postoperative morbidity, are well documented.[3] Owing to these limiting characteristics, recent studies have investigated an ideal bone substitute and growth factors to reduce surgical morbidity, and the addition of growth factors and numerous grafting materials to promote bone formation has set high expectations for their clinical potential. Similarly, some studies have focused on early bone formation for early implant loading[4,5]; reduced sinus augmentation operating time and cost are greatly desired by surgeons for successful implantation and meeting patient expectations.

We previously reported the usefulness of tricalcium phosphate (TCP) as a carrier for recombinant human bone morphogenetic protein (rhBMP)-2 and platelet-rich fibrin (PRF) in sinus augmentation in rabbits, and demonstrated the early bone formation capacity of rhBMP-2-coated TCP and PRF-mixed TCP.[6] However, the use of TCP as a carrier for rhBMP-2 still has limitations because particulate artificial bone can remain in the maxillary sinus surrounded by the Schneiderian membrane, and act as a focus for unwanted infection during the healing period, especially in the event of Schneiderian membrane tearing; if sinus infection is detected after augmentation, the surgeon must remove all of the infected grafted materials.[7] Likewise, PRF has early and good bone formation potential, but its use is limited by the recommendation of additional venous blood sampling.

Type I collagen is one of the best rhBMP-2 carriers because of its versatility, high biocompatibility, low immunogenicity, ease of use, and relatively low cost. The first rhBMP-containing products approved by the Food and Drug Administration for the treatment of several spinal disc diseases and open tibial fractures were absorbable collagen sponge (ACS)-based devices impregnated with rhBMP-2.[8,9] Tripplet et al[10] conducted a multicenter, randomized, prospective clinical trial and demonstrated the effectiveness and safety of rhBMP-2/ACS compared with bone graft for sinus floor augmentation.

Thus, the aim of this histological study was to compare the potential of Type I ACS impregnated with rhBMP-2, rhBMP-2-coated TCP, or PRF-mixed TCP to enhance bone regeneration, and to evaluate the usefulness of Type I ACS as a carrier for sinus elevation in rabbits.

Materials and methods

Animals and group design

Thirty-six New Zealand white adult female rabbits, aged > 6 months and weighing 2.5—3.5 kg, were used in this study. The animals were housed individually in standard rabbit cages at an ambient 20°C. All of the sinus procedures were performed under general anesthesia, using intramuscular ketamine HCl (50 mg/kg; Ketara; Yuhan, Seoul, Korea) and xylazine (10 mg/kg; Rumpun; Bayer, Seoul, Korea) in a mixture ratio of 5:1 under sterile conditions.

The dorsal area of each rabbit's cranium was shaved before surgery, and the surgical field was prepared with an iodine solution. A midline skin incision was made on the skull, and the periosteum was reflected laterally, exposing the maxilla. Two symmetric ovoid bone defects were then created in the anterior maxilla wall using a round bur under constant irrigation. Special care was taken to avoid injury to the sinus membrane. The defects were grafted with Type I ACS (Ateloplug; Bioland, Chungbuk, South Korea) impregnated with rhBMP-2 (Group A), rhBMP-2-coated TCP (Group B), or PRF-mixed TCP (Group C; Table 1). Each group included 12 rabbits. After obtaining adequate hemostasis, the periosteum was closed with a 4-0 Vicryl suture, and the skin was closed with a 4-0 nylon suture. The animals were given 5 mg/kg gentamycin (Kookje, Seoul, Korea) postoperatively to prevention infection. The postoperative course in all of the cases was uneventful (Figure 1).

The rabbits were killed at 1 week, 2 weeks, 4 weeks, and 6 weeks after surgery, and the six sites of the sinus area were harvested and subjected to histologic examination. All of the experiments were conducted in accordance with the Dong-A University Medical Research Institute's ethics

Table 1 Group design.

	Group A	Group B	Group C
Graft material	rhBMP-2+ACS	rhBMP-2+TCP	PRF+TCP
No. of rabbits	12	12	12
Sinus lift site	24	24	24

ACS = Type I absorbable collagen sponge; rhBMP-2: = recombinant human bone morphogenetic protein-2; PRF = platelet-rich fibrin; TCP = tricalcium phosphate.