学 位 論 文 の 要 旨

氏名　　小池　尚史

学位論文名　Histological Analyses of Bacterial Cellulose as a Carrier for BMP-2 in Bone Regeneration in Japanese White Rabbits

発表雑誌名　Journal of Bio-Integration
（巻，初頁～終頁，年）　(8: 95-100, 2018.)

著者名　Takashi Koike, Hiroto Tatsumi, Aya Yoshino, Katsumi Hideshima, Takaya Yamada, Takahiro Kanno

論 文 内 容 の 要 旨

INTRODUCTION

Dental implant treatment is often difficult in the posterior maxillary region because the height of the alveolar process is insufficient due to the presence of the maxillary sinus. When implants are placed in a region with extensive bone loss or atrophy, autogenetic bone transplantation is the best therapeutic option to avoid rejection. Nevertheless, there are limitations to this, including the invasive procedure required to harvest bone, the limited amount of bone collected, long treatment duration, postoperative complications, and grafted bone resorption. These limitations need to be overcome to improve alveolar bone augmentation.

We previously reported on the use of bacterial cellulose (BC) as a new intracanal treatment material for dental therapy. Due to its high water capacity and ability to maintain volume, BC may be suitable as a sustained-release bone morphogenetic protein-2 (BMP-2) carrier for bone regeneration.

In this study, we examined BC graft performance in a rabbit frontal sinus model considering pre-dental implant bone augmentation.

MATERIALS AND METHODS

All animal experiments in this study were approved by the Animal Care and Use Committee of Shimane University. Twelve male Japanese white rabbits (11 weeks old) were divided into four experimental groups: a sham control group, a BC-treated group with only a BC graft, a BMP-2 group treated only with BMP-2 solution (5 μg), and a BC + BMP-2 group treated with a BC graft soaked in BMP-2 solution (5 μg). The frontal sinus membrane was elevated using a mucosal elevator and graft material was placed. Rabbits were sacrificed at 4 and 8 weeks and sinus tissue and bone were extracted.

Tissues were sectioned and stained with hematoxylin-eosin (H&E), anti-proliferating cell nuclear antigen (PCNA) antibody, and anti-osteocalcin (OC) antibody. Newly formed bone amount was estimated as a ratio of the area of newly formed osteoid and bone relative to that of the entire bone defect. Sections stained with PCNA and OC antibodies were used to calculate the ratio of positively stained cells and stained area.

Statistical analysis was done using the analysis of variance (ANOVA) and Fisher's protected least significant difference test. Data were analyzed using SPSS ver. 24 for Macintosh (IBM, Armonk, NY, USA). A p-value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

We noted that BC retained its three-dimensional structure and observed pronounced new bone formation along the BC grafts. The amount of newly formed bone was significantly higher in the BC + BMP-2 group than in the other groups ($p < 0.05$). A significant difference in the amount of bone extracted was noted in the BC + BMP-2 group between weeks 4 - 8 ($p < 0.05$). Both PCNA and OC appeared around new bone, and there was a significant difference between the BC + BMP-2 group and the other groups ($p < 0.05$).

We speculated that PCNA can be effective for osteoblast proliferation in the space created during maxillary sinus floor augmentation. We predict that new bone formation can be initiated from a relatively early stage. In particular, because new bone formation was significantly increased in the BC + BMP2 group between weeks 4 and 8, a sustained release of BC is the most advantageous method for forming new bone.

Furthermore, staining confirmed the presence of osteoblasts and bone matrix in all groups with OC. Compared to the control group, the OC-positive region was more commonly located around new bone, and at weeks 4 and 8, the OC region was significantly increased in the BC + BMP-2 group. This suggests that a sustained release of BC could enhanced differentiation of osteogenic cells to osteoblasts through the sustained effect of BMP-2.

We expected to improve the activity of BMP-2 by suppressing its diffusion and absorption using BC as a carrier. Our results show that BP impregnated with BMP-2 promotes efficient bone formation by combining BC's sustainability and biocompatibility with BMP-2's ability to enhance osteoblast differentiation, creating a functional synergetic effect.

CONCLUSION

We aimed to improve the activity of BMP-2 by suppressing its systemic diffusion and absorption using a BC carrier. BP impregnated with BMP-2 showed the ability to induce osteoblast and chondroblast differentiation while maintaining graft space and providing sustained release to cells, thereby promoting efficient bone formation. We concluded that the sustained release of BMP-2 from BC has positive effects on bone regeneration and shows promise as a feasible carrier to promote clinical bone formation for pre-dental implant bone augmentation in the maxillary sinus.