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Clinical Outcome of Implants Placed in Grafted Maxillary Sinus Using Recombinant Human Bone Morphogenetic Protein-2: A 5-year Follow-Up Study

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Purpose: To investigate the 5-year outcome of dental implants placed in a grafted maxillary sinus using recombinant human bone morphogenetic protein-2 (rhBMP-2). **Materials and Methods:** We retrospectively analyzed 27 implants after maxillary sinus floor augmentation (MSFA) using rhBMP-2 in 16 patients between January 2016 and March 2017. The study evaluated two outcome variables: (1) 5-year cumulative survival and success rate of the implant after functional loading and (2) marginal bone loss (MBL) for implant failure. **Results:** The average residual bone height was 4.78±1.53 mm. The healing period before loading was 8.35±2.34 months. The crown-to-implant ratio was 1.31±0.26. The 5-year cumulative survival and success rate after functional loading were 100% and 96.3%, respectively. The 5-year average MLB was 0.89±0.82 mm. **Conclusion:** Placing dental implants with MSFA using rhBMP-2 is a reliable procedure with favorable long-term survival and success rates. [J Korean Dent Sci. 2024;17(1):45-52]

Key Words: Maxillary sinus floor augmentation; Bone morphogenetic protein; Marginal bone loss; Residual bone height

Introduction

The edentulous posterior maxilla frequently has been difficult for implant placement due to alveolar bone loss. Recently, maxillary sinus floor augmentation (MSFA) has become an optimal surgical option for implant placement in the atrophic maxillary posterior area[1]. The bone morphogenetic protein-2 (BMP-2) is known to have osteo-inductive characteristics[2]. Many studies have reported using recombinant human

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BMP-2 (rhBMP-2) in bone augmentation to promote bone formation and osseointegration for regenerating new bone[3-6]. However, further studies are needed to elucidate the long-term outcome of implants placed in the grafted sinus using rhBMP-2. Therefore, this study aimed to investigate the outcome of dental implants placed in a grafted maxillary sinus using rhBMP-2. We hypothesized that implants placed in the grafted sinus using rhBMP-2 would provide sufficient long-term implant stability. The specific aims of this study were to evaluate the more than 5-year implant survival rate and marginal bone loss (MBL) during functional loading.

Materials and Methods

1. Study design and sample size

We designed a retrospective study with a 5-year follow-up, including 27 implants of 16 patients who underwent implantation with MSFA using rhBMP-2 between January 2016 and March 2017. Data were collected from clinical and surgical records, panoramic radiographs, and cone-beam computed tomography (CBCT) images. Patients with maxillary sinusitis and incomplete medical records were excluded from this study.

2. Study variables

The study evaluated two outcome variables: (1) 5-year cumulative survival and success rate of the implant after functional loading and (2) MBL for implant failure. The following risk factors for implant failure in MSFA using rhBMP-2 were assessed: patients' age, sex, surgical site, residual bone height (RBH), implant length and diameter, graft material, staged or simultaneous implantation with MSFA using rhBMP-2, healing period, condition of the opposing dentition, prosthetic type (single or splinted), crown-to-implant ratio. The healing period was the length of time from implantation to functional loading. The crown-to-implant ratios were measured at the first follow-up using a panoramic radiograph taken at 3 months after functional loading. To measure preoperative RBH, the center of each inserted implant was measured on the preoperative panoramic radiographs. MBL was defined as the length from the implant-abutment junction to the alveolar bone and used the larger values in the mesial or distal sides of the implant.

3. Procedure

All procedures were performed via the sinus lateral approach under local or general anesthesia. The autogenous bone was harvested from either an intraoral (i.e., mandibular ramus) or extraoral (i.e., iliac crest) donor site. Freeze-dried cancellous bone (Allobone, CGbio, Seoul, Korea) was used as an allogeneic graft material. In some patients, orthoblasts (demineralized bone matrix paste with cancellous bone) were mixed and used. A 0.25 mg rhBMP-2 (Novosis, CGbio, Seoul, Korea) was used in the maxillary sinus of all patients, and collagen membranes (Ossguide, Bioland, Cheongju, Korea) were employed to cover the sinus windows.

4. Statistical analysis

The variables and treatment data were evaluated using a descriptive analysis (mean±standard deviation, frequency, and range).

Results

Sixteen patients underwent 27 implantations with MSFA using rhBMP-2 during the study period. The average age of 16 patients (5 men and 11 women) was 52.69±10.75 years. The parameters such as patients' demographic information, surgical site, RBH, implant length and diameter, bone graft material, the healing period before loading, condition of the opposite dentition, prosthesis type, crown-to-implant ratio, and MBL are summarized in Table 1. The average RBH was 4.78±1.53 mm, and the average implant diameter was 4.44±0.47 mm. The average implant length was

Table 1. Patient demographic and clinical data

Sex (M/F)	Age (year)	Surgical site	RBH (mm)	Implant diameter & length (mm)	Graft material	Staged or simultaneous	Healing period (months)	Opposite dentition	Prosthetic type	Crown implant ratio	MBL (mm)
M	64	M1	3.3	4.0×8.5	Autobone & allobone	Staged	16	Natural dentition	Splinted	1.97:1	0.61
		M2	5.6	4.0×10	Autobone & allobone	Staged	16	Natural dentition	Splinted	1.52:1	0.46
F	63	M2	5.7	4.5×10	Allobone	Simultaneous	8	Natural dentition	Single	1.12:1	1
F	59	P2	5.6	4.0×10.5	Autobone & allobone	Simultaneous	11	Implant	Splinted	1.07:1	1.62
		M1	4.6	5.0×10.5	Autobone & allobone	Simultaneous	11	Implant	Splinted	1.2:1	1.38
F	65	P1	6.2	4.1×10	Allobone	Simultaneous	9	Natural dentition	Single	1.03:1	1.01
F	50	M1	5.5	3.5×10	Autobone & orthoblast	Simultaneous	7	Natural dentition	Splinted	1.26:1	1
		M2	6.3	5×8.5	Autobone & orthoblast	Simultaneous	7	Natural dentition	Splinted	1.77:1	0
F	40	P2	5.7	4.1×10	Autobone & allobone	Simultaneous	8	Natural dentition	Splinted	1.09:1	1.61
		M1	2.1	4.8×10	Autobone & allobone	Simultaneous	8	Natural dentition	Splinted	1.06:1	0.41
M	27	M1	5.5	4.8×10	Allobone	Simultaneous	9	Natural dentition	Splinted	1.26:1	0.69
		M2	4.9	4.8×10	Allobone	Simultaneous	9	Natural dentition	Splinted	0.97:1	0
M	51	P2	5.1	4.1×10	Autobone & allobone	Simultaneous	9	Natural dentition	Splinted	1.24:1	0.54
		M1	3.3	4.8×10	Autobone & allobone	Simultaneous	9	Natural dentition	Splinted	1.28:1	0.54
		M2	3.6	4.8×10	Autobone & allobone	Simultaneous	9	Natural dentition	Splinted	1.36:1	0.63
F	60	M1	4.1	4.5×10	Allobone	Simultaneous	7	Implant	Single	1.44:1	0.54
F	48	M1	4.6	5.0×10.5	Autobone	Simultaneous	10	Implant	Splinted	1.77:1	2.03
F	55	P2	3.3	3.5×10.5	Autobone & allobone	Simultaneous	10	Implant	Splinted	1.43:1	0.85
		M1	3.9	5.0×10.5	Autobone & allobone	Simultaneous	10	Implant	Splinted	1.46:1	1.79
F	56	M1	1.7	4×9	Orthoblast	Simultaneous	9	Implant	Splinted	1.7:1	2.53
F	37	M1	6	5×10	Allobone	Simultaneous	7	Natural dentition	Single	0.96:1	0.54
F	46	P1	6.3	4×10.5	Autobone	Simultaneous	10	Implant	Splinted	1.34:1	1.15
		P1	6	4×9	Autobone	Simultaneous	10	Implant	Splinted	1.56:1	1.2
M	55	M1	6.3	5×10	Allobone	Simultaneous	10	Natural dentition	Single	1.32:1	2.01
		M1	1.1	4.5×10	Autobone & allobone	Staged	8	Natural dentition	Single	1.22:1	1.77
M	67	M1	6	4.5×10	Autobone & allobone	Staged	12	Natural dentition	Splinted	1.16:1	1.79
		M2	6.7	4.5×8.5	Autobone & allobone	Staged	12	Natural dentition	Splinted	1.05:1	1.79

M: male; F: female; P1: first premolar; P2: second premolar; M1: first molar; M2: second molar; RBH: residual bone height; MBL: marginal bone loss.

9.87±0.60 mm. The healing period before loading was 8.35±2.34 months. The crown-to-implant ratio was 1.31±0.26. The 5-year cumulative survival and success rate after functional loading were 100% and 96.3%, respectively. The 5-year average MBL was 1.07±0.65 mm. One implant did not meet the success criteria, exhibiting an MBL of 2.53 mm. Among the implants, nine were opposing other implants, whereas 18 were opposing natural dentition. Regarding the prosthesis type, six were single, and 21 were splinted.

Discussion

Autologous bone, which contains osteoblasts capable of bone production, is considered the superior bone graft material. However, it has drawbacks, such as potential complications, tissue damage, and bone resorption at the donor site[7]. Despite having osteo-inductive effects, allografts are associated with significant bone resorption and limited bone regeneration[8]. Xenografts and synthetic bone graft substitutes are osteo-conductive materials; however, their ability to form bones is slow and poor[9,10]. To overcome this problem, various growth factors were developed to promote bone formation. In 1988, Wozney successfully generated BMP-2 and BMP-4 through genetic recombination[11]. This process involved the expression of these factors in mammalian cells, Chinese hamster ovary cells, and Escherichia coli via the recombination of complementary deoxyribonucleic acid, ultimately resulting in the production of rhBMP-2[12,13]. BMP is a growth factor belonging to the transforming growth factor beta family, consisting of more than 20 types. Among them, BMP-2, BMP-4, BMP-5, BMP-6, and BMP-7 promote bone formation[14]. Among them, rhBMP-2 obtained by recombinant DNA has been reported to exhibit the best osteoinductivity[15]. In an animal experiment using a vertebral model, osteogenesis, observed three months after the application of rhBMP-2 obtained through genetic recombination in Escherichia coli, exceeded 70%, and the osteoconductivity in the treated group was 1.5 times higher than in the control group[16].

As the rhBMP-2 is easily diffused and lost in the body, a carrier that can release BMPs slowly and continuously has more advantages in bone formation, allowing them to act properly on target cells[17]. The carrier should exhibit strong binding with rhBMP-2 and possess excellent biocompatibility[18,19]. Ideally, the carrier should also be capable of absorption, dispersion, or incorporation into the bone[18,19]. In this study, bone graft materials were used as carriers for rhBMP-2.

In this study, MBL was evaluated to assess the long-term outcomes of implants during the follow-up period after implantation with rhBMP-2. An objective indicator crucial for determining long-term implant success is the marginal bone level, significantly impacting surrounding soft tissue height and affecting esthetic implant treatment[20]. Furthermore, the stress dispersion around the implant is different depending on the bone quantity and quality, and more stress concentration has been reported in the low-density cancellous bone. Notably, failures often occur in the maxillary posterior region due to the limited cortical bone presence and abundant cancellous bone, leading to inadequate bone-implant contact. Moreover, as the pneumatization of the maxillary sinus increases, the inferior border of the maxillary sinus descends, reducing the vertical diameter of the residual bone[21,22]. Peñarrocha et al. reported that 108 implants had greater MBL in the maxilla[23]. In 1986, Albrecktsson et al. proposed a criterion for implant success, suggesting that the amount of marginal bone absorption around implants during the first year should be less than 1 - 1.5 mm and subsequently less than 0.2 mm per year[24]. Adell et al. reported that 1.2 mm of marginal bone is absorbed during the first year, followed by 0.1 mm of MBL per year, and that this initial change in marginal bone occurs during the adaptation process of the bone around the implant when occlusion load is applied[25].

Regarding implant length, Pierrisnard et al. studied the stress applied to the implant according to the length of the implant using a three-dimensional finite element analysis and reported that the maximum stress transmitted to the bone around the implant is similar regardless of the length of the implant[26], suggesting that the difference in length of the implant will not have a significant effect on the MBL because stress is concentrated in the cervical area of implant regardless of the length of the implant[27]. Moreover, larger implant diameters reduce stress in the alveolar crest region. Hertel et al. emphasized the importance of increasing implant size to minimize the stress transmitted to the bone, especially in the case of small-diameter implants[28].

From a healing period perspective, maxillary sinus floor augmentation involves two approaches: delayed implantation methods that entail placing the implant several months after bone grafting and immediate implantation methods where the implant is placed simultaneously with bone grafting. In the past, the residual bone height of 5 mm was generally accepted as the minimum criterion for obtaining the initial stability and osteointegration of the implant during maxillary sinus floor augmentation. Consequently, immediate implantation was recommended for cases with 5 mm or more of bone height, whereas staged implantation was suggested for cases with less than 5 mm[29]. Recently, due to the development of implant surface treatment and design, immediate implantation has been implemented even in cases of less than 5 mm, and similar to staged implantation, this approach has yielded positive clinical outcomes[30].

For the long-term success of the implant, effective dispersion of the occlusal load is crucial, and the implant prosthesis type and the condition of opposite dentitions can be considered. The patterns in which implants and natural teeth respond to occlusal forces are different. Due to the absence of a periodontal ligament, implants and natural teeth respond differently to biomechanical forces. Overloading can lead to the breakdown of osteointegration at the bone-implant interface and potential implant fractures[31]. Unlike natural teeth, implants placed to bone can cause loss of implants due to microfractures at the implant-bone interface, mechanical breakage of the implant fixture, and fatigue breakage of the prosthetic component when excessive occlusal force is applied. In implants, splinting increases the area of support tissue and efficiently distributes occlusal load between implants, minimizing harmful stress on the implant-bone interface[32].

Furthermore, when considering the marginal bone, which experiences the greatest stress among adjacent bones, any deterioration in the crown-to-implant ratio caused by MBL can lead to increased stress concentration. This heightened stress may elevate the risk of peri-implantitis, potentially leading to the formation of a periodontal pocket around the implant[33,34].

In general, an increase in the crown-implant ratio can cause overload and non-axial load due to the leverage effect, causing implant MBL[35]. In a finite element analysis of 889 single-tooth implant prosthetic cases spanning 13 years, a survival rate of 98.2% was reported for a crown-implant ratio of 1.3:1[36]. Malchiodi et al. reported that MBL increased with a crown-implant ratio of 2 or higher when studying 259 short-length implants for 36 months[36]. Hingsammer et al. observed 74 implants with a length of 6.5 mm and reported a strong correlation between bone absorption and the crown-implant ratio. They found that early bone absorption did not increase unless the crown-implant ratio exceeded 1.7[37].

In this study, one implant exhibited a significant amount of MBL. In the patient's history, all teeth, except for the mandibular anterior teeth, were extracted during her forties due to chronic periodontitis. Hardt et al. suggested that a significant amount of MBL may be related to the patient's previous history of chronic periodontitis. Patients with destructive periodontal disease experienced more than twice the rate of implant failure compared to patients with a healthy periodontal status[38]. Moreover, oral hygiene is a critical factor influencing dental implant survival. Numerous studies highlight the importance of effective plaque control and regular periodontal maintenance in promoting dental implant survival[38-40]. Therefore, for the long-term success and survival of implants, maintaining oral health care and preserving the level of marginal bone through regular follow-ups is crucial.

Conclusion

In conclusion, dental implant placement with MSFA using rhBMP-2 ensures long-term implant survival and prevents MBL effectively. Furthermore, rhBMP-2 is beneficial for implants in the grafted maxillary sinus when RBH is unfavorable.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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