The effect of rhBMP-2 bonegraft on infrabony defects

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Abstract

rhBMP-2 bone graft has been used in orofacial defect and alveolar ridge augmentation. This clinical trial aims to evaluate the effect of rhBMP-2 compared with bioactive glass on the periodontal tissue regeneration in 2- and 3-wall infrabony periodontal defect

Method: 23 patients(male 13 and female 10) who had probing depth above 5 mm in one wall and the more of tooth walls received Biogran® bone grafts in 14 control sites and CowellBMP® in 13 experimental sites. The probing depth and gingival recession were measured at the base line, 3 month and 6 months after surgery.

Results: The experimental group showed the significant decrease in probing depth 3.78 mm and 3.96 mm on 3 and 6 months after surgery compared to 2.64 and 2.71 mm of the control group ($p<0.05$). Gingival recession of both group were significantly decreased to 0.63 mm on 3 months and 0.65 mm on 6 months in experimental group after surgery and 0.50 mm on 3 months and 6 months in control group($p<0.05$) but there were no difference between two groups. Probing attachment level were significantly increased to 2.93 mm in experiment group on 6 months compared to 4.04 mm in control group ($p<0.05$).

Conclusion: Biogran® and CowellBMP® were effective in treatment of infra-bony periodontal defects. CowellBMP® was more significantly effective in decrease of probing depth and the increase of probing attachment level than Biogran®.

The periodontal treatment aims to the decrease of periodontal pocket for easy plaque control and the regeneration of periodontal tissue in the defects. Gottlow and Nyman et al. used the barrier membrane with the various bone materials of autogenous, allogenous, xerogenous and synthetic bone graft [1,2].

The autogenous bone graft is the gold standard, but the additional surgery and adverse effects limits the graft uptake practice [3-6]. The allogenous bone graft has osteoinductive property, but the safety could not be proven [7]. The xerogenous bone graft and synthetic bone graft have the osteoconductive property but do not have the osteoinductivity. Piorellini et al. reported that these grafts could not be successful in graft surgery.

The mesenchymal stem cells and growth factors have been recently tried in the periodontal tissue regeneration. The effect of recombinant human bone morphogenetic protein (rhBMPs) of growth factors on bone regeneration was reported by Urist in 1965 [8].

The DNA sequence and recombinant technique of

rhBMPs was identified and established [9-11]. It was reported that the bone matrix saturated with rhBMP-2 induced the new isotopic bone in the muscle of mice according to the transformed osteoblast from myoblasts [12,21].

rhBMPs, the superfamily of TGF-beta (transforming growth factor-beta), have the major key of mammalian skeleton development due to the effect on osteoblast, chondroblast and osteoclast [13,14]. The bone regeneration effect of rhBMP-2 had been proven in the clinical trials[16-20]. It was reported the effect of rhBMP-2 on the periodontal tissue regeneration was positive in the animal experience [22-26].

The effect of rhBMP-2 on the periodontal tissue regeneration in human was not studied. This clinical trial aims to evaluate the effect of rhBMP-2 compared with allograft on the periodontal tissue regeneration in 2- and 3-wall infrabony periodontal defect

Ⅰ. Material and methods

1. Study Subject

The study was designed as a prospective, randomized controlled study documenting the response of the rhBMP-2 bone graft material and bioactive glass bone graft material in the periodontal department of Dankook dental school, Cheonan, Korea.

23 patients(male 13 and female 10) who had probing depth above 5 mm in one wall and the more of tooth which have over 2 mm kerantinized gingiva and under 1 degree mobility received Biogran® bone grafts in 14 control sites and CowellBMP® in 13 experimental sites.

2. Material

The control group was treated with the bioactive glass bone graft material, Biogran®(Biomet 3i Co., Ltd. Warsaw, United States) and the experiment group was done with the rhBMP-2 and HA/beta-TCP particles, CowellBMP®(Cowellmedi Co., Ltd, Busan, Korea).

3. Treatment

1) Pre-operative treatment

The scaling, root planning and tooth brushing instruction were done at first visit. In case of traumatic from occlusion, the occlusal adjustment was done. At second visit, the periodontal control was evaluated and the additional oral hygiene instruction was done.

2) Surgical procedure

Infiltrate anesthesia was done in treatment site with 2% Lidocanine (1:80000 Epinephrine) injection. The sulcular incision and additional vertical incision (if need) was used. The full thickness flap was elevated with the periodontal elevator. The calculus removal and root planning were done in infrabony defect after the removal of granulation tissue. The planed root surface was treated with Tetracycline HCl for 2 minute. The defect was filled with Biogran® in control group and CowellBMP® in the experiment group. The flap was sutured with 4-0 Ethilon silk. The stitch were removed on 7~15 days after surgery(Fig 1).

After surgery, mouth rinsing with chlorhexidine 0.1% or 0.12%, twice daily for 10 days, was prescribed, together with the recommended medication prescribed by the surgeon (such as analgesics, anti-inflammatory compounds or antibiotics).

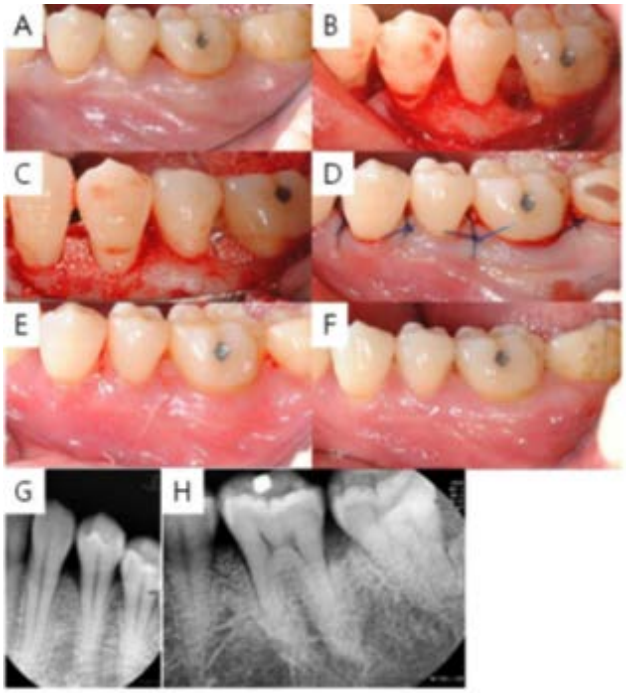

Figure 1. Surgical procedures and periapical view in experimental group
A : Preoperative status
B : Incision and flap reflection
C : Application of rhBMP-2
D : Suturing
E : Stitch out
F : Healing status after 3 months later
G : Periapical view of #34 teeth, 3 months after treatment
H : Periapical view of #36 teeth, 3 months after treatment

3) Measurement

All measurements were carried out by well-trained calibrated examiners independent from the surgeons placing the implants. The probing depth and gingival recession were measured on the pre- and post-operation, 3 months and 6 months after surgery at buccal, mesiobuccal, distobuccal, lingual, mesiolingual and distolingual sites with periodontal probe of 1 mm unit scale. Probing attachment level was measured on pre-operation, post-operation and 6 months after surgery.

4) Statistical method

The probing depth and gingival recession at the site of maximal probing attachment level was analyzed on the pre-operative, post-operative, 3 months and 6 months after surgery with SPSS ver. 13.0. The change of measurement in two group according to periods was identified with Wicoxon signed ranks test. The difference between the measurement of two group according to periods was identified with Mann-Whitney test.

Ⅱ. Result

1. The change of clinical index according to periods

1) The change between baseline and 3 months

The change of probing depth between baseline and 3 months was higher 3.78±0.26 mm in experiment group than 2.64±0.13 mm in control group with significant difference.($p<0.01$)(Table 1)

2) The change between 3 months and 6 months

The change of probing depth between 3 months and 6 months was 0.18±0.09 mm in experiment group and 0.07±0.07 mm in control group without significant difference.($p>0.05$)

Table 1. Changes of clinical indexes between baseline and 3 months (mm)

Parameter	Group	Baseline	3 Months	Difference	Significance
PD	control	6.58±0.25	3.93±0.22	2.64±0.13	<0.001*
	experimental	7.62±0.72	3.84±0.32	3.78±0.26	<0.001*
	p value			<0.01*	
GR	control	0.21±0.11	0.71±0.16	0.50±0.14	<0.008*
	experimental	0.33±0.25	0.96±0.15	0.63±0.21	<0.001*
	p value			NS	

PD : Probing pocket depth; GR : Gingival recession

NS : difference not statistically significant.

* = statistically significant difference (P <0.05)

Table 2. Changes of clinical indexes between 3 months and 6 months (mm)

Parameter	Group	3 Months	6 Months	Difference	Significance
PD	control	3.93±0.22	3.86±0.21	0.07±0.07	0.32
	experimental	3.84±0.32	3.66±0.26	0.18±0.09	0.17
	p value			NS	
GR	control	0.71±0.16	0.71±0.16	0.00	1.00
	experimental	0.96±0.15	0.98±0.12	0.02±0.05	0.46
	p value			NS	

PD : Probing pocket depth; GR : Gingival recession

NS : difference not statistically significant.

* = statistically significant difference (P <0.05)

3) The change between baseline and 6 months

The change of probing depth between baseline and 6 months was higher 3.96±0.23 mm in experiment group than 2.71±0.13 mm in control group with significant difference.($p<0.05$)

Probing attachment level were significantly increased to 2.93±0.02 mm in experiment group on 6 months compared to 4.04±0.13 mm in control group ($p<0.05$).(Table 2)

Table 3. Changes of clinical indexes between baseline and 6 months (mm)

Parameter	Group	Baseline	6 Months	Difference	Significance
PD	control	6.58±0.25	3.86±0.21	2.71±0.13	<0.001*
	experimental	7.62±0.72	3.66±0.26	3.96±0.23	<0.001*
	p value			<0.05*	
GR	control	0.21±0.11	0.71±0.16	0.50±0.14	<0.008*
	experimental	0.33±0.25	0.98±0.12	0.65±0.13	<0.005*
	p value			NS	
PAL	control	9.07±0.32	6.14±0.29	2.93±0.22	<0.001*
	experimental	9.92±0.22	5.88±0.21	4.04±0.13	<0.001*
	p value			<0.01*	

PD : Probing pocket depth; GR : Gingival recession;

PAL : Probing Attachment Level; NS : difference not statistically significant.

* = statistically significant difference (P <0.05)

2. The change of clinical index at each periods(Fig.2)

The change of probing depth between baseline and 3 months was higher 3.78±0.23 mm in experiment group than 2.64±0.13 mm in control group with significant difference.($p<0.05$)

The change of probing depth between baseline and 6 months was higher 3.96±0.23 mm in experiment group than 2.71±0.13 mm in control group with significant difference.($p<0.05$)

The change of gingival recession between baseline and 3 months was higher 0.63±0.21 mm in experiment group than 0.5±0.14 mm in control group without significant difference.

The change of gingival recession between baseline and 6 months was higher 0.65±0.13 mm in experiment group than 0.5±0.14 mm in control group without significant difference.

Probing attachment level were significantly increased to 2.93±0.02 mm in experiment group on 6 months compared to 4.04±0.13 mm in control group ($p<0.05$).

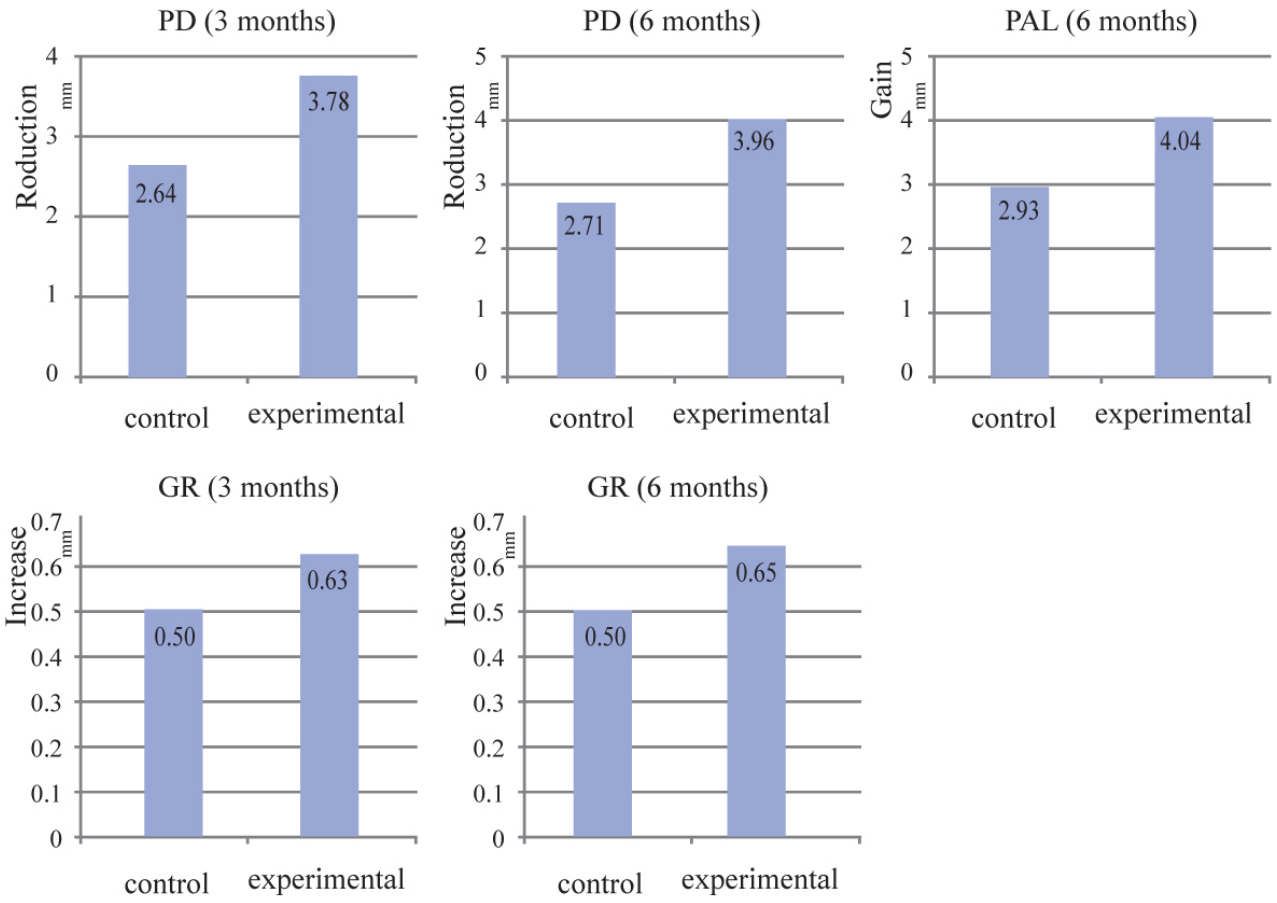

Fig 2. Changes of clinical indexes at each time from baseline
PD : pocket depth, PAL : probing attached level, GR : Gingival recession
* Compared with control group ($p<0.05$)

Ⅲ. Discussion

rhBMP-2 bone graft was reported to be effective in oral maxillofacial bone defects, sinus bone augmentation and socket preservation [27-29]. It was reported that the longitudinal marginal bone change of implant placement and simultaneous rhBMP-2 bone graft was stable [20,80,81]. Jung et al. (2008) reported that the rhBMP-2 experiment group had been more effective than the control group in the 43 of total 45 studies of periodontal tissue regeneration, socket preservation and peri-implant defect regeneration and the growth factor like as BMP-7, GDF-5 and PDGF [82].

It was reported that rhBMP-2 had the potential property of the regeneration of cement and periodontal ligament [22-26]. It was reported that the cementoid tissue regenerated by rhBMP-2 prevented the epithelial migration [88]. But Sigurdsson et al. reported that rhBMP-2 induced the ankylosis in periodontal regeneration site [84,86] . It was reported that the high dose of rhBMP-2 could induce the dentinal resorption [88]. The bone regeneration effect of rhBMP-2 was supported by various studies. In contrast, there are the controversy in periodontal tissue regeneration.

Bioactive glass, Biogran® used in the control group of this study is reported to bind bone and contact with soft sissue [87, 88]. Wilson and Low et al. reported that Bioactive glass has the osteoconductive property and effectiveness in infrabony periodontal defect [89]. Zamet et al. reported that the probing depth was reduced to 3.82 mm and the gingival recess was 1.09 mm in Biogran® treatment group [40,41]. Lovelance et al. reported that Biogran® and DFDBA reduced the probing depth without significant difference [42]. Therefore, Biogran® was used in this study.

The carrier of rhBMP-2 is composed of the absorbable collagen sponge, decalcified bone matrix and synthetic bone graft material. CowellBMP® carrier is 70% beta-TCP/30%HA which the bone regeneration effect was proven [46].

The change of probing depth and gingival recession between pre-operative and post-operative periods was effective in both group. The control group received Biogran® was same result as Lovelance et al. study [42]. The change of probing depth between baseline and 6 months was higher 3.96±0.23 mm in experiment group than 2.71±0.13 mm in control group with significant difference.($p<0.05$) Probing attachment level were significantly increased to 2.93±0.02 mm in experiment group on 6 months compared to 4.04±0.13 mm in control group ($p<0.05$).(Table 2)

In recent clinical studies, the adverse effect of rhBMP-2 was reported to the facial swelling which was increased to proportional of the dose of rhBMP-2 [46,48]. In this study, there were no this adverse effect due to the low dose of rhBMP-2.

Ⅳ. Conclusion

Biogran® and CowellBMP® were effective in treatment of infra-bony periodontal defects. CowellBMP® was more significantly effective in decrease of probing depth and the increase of probing attachment level than Biogran®. rhBMP-2 might to be effective in periodontal tissue regeneration even in this limited enroll clinical study.

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