Comparison of rhGDF-5/β-TCP and rhPDGF/β-TCP effects on Periodontal Wound Healing/Regeneration in One-Wall Intrabony Defects

Hyuk-Rak Kwon

The Graduate School

Yonsei University

Department of Dental Science

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of Hyuk-Rak Kwon is approved.

Thesis Supervisor： Chong-Kwan Kim

Kyoo-Sung Cho

Seong-Ho Choi

Kyoung-Nam Kim

Yun-Jung Yoo

The Graduate School

Yonsei University

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감사의 글

본 논문이 완성되기까지 졸업 후부터 늘 끊임없는 지도와 관심을 보내주신 김종관 교수님께 진심으로 감사 드립니다. 그리고 박사 과정 동안 많은 관심으로 이끌어 주신 채중규 교수님, 조규성 교수님, 최성호 교수님께도 감사의 말씀 올립니다. 또한 논문 완성 과정에서 많은 조언을 해 주신 김경남 교수님, 유윤정 교수님께도 감사 드립니다.

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그리고, 언제나 아낌없는 사랑과 헌신적인 도움으로 나의 버팀목이 되어준 사랑하는 아내와 항상 끊임없이 뛰어 노는 예쁜 딸 지인이와 개구쟁이 아들 순헌이에게도 사랑하는 마음을 전합니다.

마지막으로, 항상 곁에서 든든하게 기도해주시는 양가 부모님께 감사의 마음을 담아 이 논문을 드립니다.

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Abstract

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Platelet Derived Growth Factor (PDGF) is known to induce chemotactic and mitogenic activity in osteoblasts and stimulate type I collagen synthesis. In human study, rhPDGF was considered effective in the treatment of periodontal osseous defects. Recombinant human growth/differentiation factor-5(rhGDF-5) is reported to have abilities of chondrogenesis, osteogenesis and angiogenesis. It has shown strong osteoinductive ability with limited risk of excessive bone formation. β-Tricalcium Phosphate is biocompatible and biodegradable material.

The objective of this study was to compare periodontal wound healing/regeneration following application of the rhGDF-5/β-TCP and PDGF/β-TCP in one-wall intrabony periodontal defects in dogs

Bilateral, critical-size (5-mm), one-wall, intrabony periodontal defects were surgically created in the mandibular premolar regions in five Beagle dogs. Defects on one side received rhGDF-5/β-TCP while the other defects in other side received PDGF/β-TCP. The histologic and histometric analysis was performed following an 8-week healing interval.

Clinical healing was generally uneventful. Sites implanted with rhGDF-5/β-TCP exhibited significantly enhanced cementum and bone formation compared to rhPDGF/β-TCP. Cementum regeneration averaged 4.49±0.48mm (Mean±SD) vs 2.72±0.91mm($p<0.05$) for the rhGDF-5/β-TCP, rhPDGF/β-TCP respectively. Corresponding values for bone regeneration height averaged 3.08±0.74mm vs 1.29±0.78mm ($p<0.05$). Cementum regeneration included cellular/acellular cementum with or without a functionally oriented periodontal ligament in rhGDF-5/β-TCP sites, whereas rhPDGF/β-TCP sites showed acellular cementum predominantly Also in PDL fiber, mixed (extrinsic, intrinsic) fibers was observed in both groups. Regenerated cementum generally extended above the alveolar crest in both treatment groups. In newly formed bone, lamellar bone with primary osteon was seen in rhGDF-5/β-TCP, whereas PDGF/ β-TCP showed newly formed bone including woven and lamellar bone. Both sites receiving rhGDF-5/β-TCP or rhPDGF/β-TCP showed some residual biomaterial apparently undergoing resorption. Sites receiving rhPDGF/β-TCP commonly showed more residual biomaterial sequestered in connective tissue than rhGDF-5/β-TCP.

In conclusion, rhGDF-5/β-TCP shows significance in supporting regeneration of the periodontal healing/regeneration compared to rhPDGF/β-TCP.

Key words: Recombinant human growth/differentiation factor-5, Platelet Derived Growth Factor, β-Tricalcium Phosphate

Comparison of rhGDF-5/β-TCP and rhPDGF/β-TCP effects on Periodontal Wound Healing/Regeneration in One-Wall Intrabony Defects

Hyuk-rak Kwon, D.D.S., M.S.D.

Department of Dental Science

Graduate School, Yonsei University

(Directed by Prof. Chong-kwan Kim, D.D.S., M.S.D., Ph.D.)

I. INTRODUCTION

The object of periodontal regeneration is not only the recovery of connective tissue and epithelium, but also the recovery of bone and periodontium. For regeneration of periodontal apparatus, many clinical trials like flap surgery, bone graft and guided tissue regeneration were performed. Recently tissue engineering came into the spotlight. Recombinant human bone morphogenetic protein-2(rhBMP-2) and recombinant human platelet-derived growth factor (rhPDGF) have received FDA approval for use in orofacial indications and is now available for clinical uses. This is very encouraging in that periodontal regeneration can be controlled in an active way.

For tissue engineering, three components: cells, scaffolds, and signaling molecules (Babensee et al., 2000; Bartold et al., 2006) are needed. Blood supply could be the fourth factor. Many scaffolds like collagen sponge which is concerned as the ‘gold standard’ for BMP carriers have been studied. (McPherson, 1992; Wikesjo et al., 1999; Uludag et al., 2001) β-Tircalcium Phosphate, which is regarded as the best carrier for signaling molecules, and poly(lactic-"co"-glycolic acid)(PLGA).

However, there is weak point with this carrier such as collapse of the provided space. For these reasons, other carriers were developed for the new delivery systems. β-TCP can be a good substitute for collagen (Urist et al. 1984; Jung et al. 2006). β-TCP can support the frame and release the signaling molecules slowly.

Recombinant human platelet-derived growth factor (rhPDGF) is known to induce chemotactic and mitogenic activity in osteoblasts and stimulate type I collagen synthesis (Rutherford et al., 1992; Park et al., 1995; Giannobile et al., 1996). In human study, rhPDGF was considered safe and effective in the treatment of periodontal osseous defects (Oates et al., 1993; Camelo et al., 2003; Nevins et al., 2003; Nevins et al., 2005).

Nevins et al.(2005) reported that treatment with rhPDGF stimulate a significant increase in the rate of CAL gain, reduce gingival recession at 3 months post-surgery, and improve bone fill when compared to β-TCP bone substitute at 6 months(Nevins et al., 2005).

Recently, FDA (Food and Drug Administration, USA) approved the clinical use

of rhPDGF for chronic skin wounds in diabetic patients (Regranex, Ethicon, USA) and for periodontally related osseous defects (GEM21s, BioMimetic Therapeutics, USA).

Recombinant human growth/differentiation factor-5(GDF-5) is also called Cartilage-derived morphogenetic protein-1(CDMP-1) or bone morphogenetic protein-14(BMP-14). This growth factor is known to have a chondrogenic effect. It is reported that rhGDF-5 is a suitable factor for enhancing healing in bone defects and ectopic bone formation (Spiro et al., 2000; Poehling et al., 2006; Yoshimoto et al., 2006).

The objective of this study was to compare periodontal wound healing/ regeneration following rhGDF-5/β-TCP and PDGF/β-TCP application in one-wall intrabony periodontal defects in beagle dogs.

II. MATERIALS AND METHODS

A. MATERIALS

1. Animals

Five male Beagle dogs, approximately 15 months old, weight 10-15 kg, bred exclusively for biomedical research purposes, were used. The animals exhibited an intact dentition with a healthy periodontium. Animal selection and management, surgical protocol, and preparation followed routines approved by the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea. The animals had *ad libitum* access to water and a pelleted laboratory diet with the exception of one week immediately postsurgery when they were fed a canned soft dog food diet (Prescription Diet Canine i/d, Hill's Pet Nutrition, Inc., Topeka, Kansas, USA).

2. Materials

The rhGDF-5/β-TCP technology (MD05, Scil Tchnology GmbH, Martinsried, Germany) comprises rhGDF-5 coated onto a synthetic carrier, β-TCP (Calciresorb, Ceraver Osteal, Roissy, France), at a concentration of 500μg/g β-TCP using a proprietary protocol. The β-TCP carrier comprises micro- and macro-porous, irregular

500-1000㎛ diameter granules of a phase purity > 95%. Analysis of the interconnecting porosity display a 43.7% microporosity, average pore diameter 2.12㎛, and pore area 0.647m^2/g. The macropore diameter ranges between 100 and 400㎛, and the pore area is estimate to 1.2m^2/g (Poehling et al., 2006). The applied dose was estimated to 20㎍ rhGDF-5/defect. All materials were supplied by Scil Technology and stored at -80℃ until use.

rhPDGF/β-TCP (GEM21s, BioMimetic Therapeutics, Franklin, Tennessee, USA) comprises 0.5 ㎖ of the rhPDGF 0.3mg/ml in 0.5cc carrier, β-TCP using a proprietary protocol. It was applied as described as package inserted.

B. EXPERIMENTAL PROCEDURES

1. Surgical procedure

All surgical procedures including extraction and experiment were performed under general anesthesia. General anesthesia was induced intravenously with atropine‖ and intramuscularly with a combination of xylazine¶ and ketamin# and maintained with inhalation anesthesia**.

After the extraction of first premolar and third premolar, 8 weeks were given for complete socket healing. The extraction sites were allowed to heal for 2 months. The remaining dentition received oral prophylaxis in conjunction with the extraction procedures. Under infiltration anesthesia, full thickness mucoperiosteal flap was

elevated to make 1-wall defect at the pre-extraction site. The surgically created one-wall “box-type” (4 mm width, 5 mm depth) intrabony bilateral defects were made distal to the first premolar and mesial to the third premolar (Kim et al., 2004; Kim et al., 2005). Defects on one side was filled with rhGDF-5/β-TCP and on the other side filled with rhPDGF/β-TCP.

Next, the mucoperiosteal flaps were advanced, adapted, and sutured with resorbable suture materials[††].

Post-surgical management included intramuscular administration of antibiotics[‡‡] for 3 days and daily topical dressing of 0.2% chlorhexidine solution[§§] for infection control for 7 days.

The animals were euthanized 8 weeks following the first surgical procedure and block sections including the surgical sites were removed for the histological analysis.

2. Clinical and Radiographic Records

Clinical photos and radiographs were taken before and after each extraction, surgery and necropsy.

3. Histologic and Histometric Analysis

The animals were sacrificed using an overdose of pentobarbital (90 -120 mg/kg;

IV). Block sections including defect sites and tooth, surrounding alveolar bone and soft tissues were collected. The block specimens were fixed in 10% buffered formalin for 10 days, decalcified in 5% nitric acid for 7 days, trimmed, dehydrated and embedded in paraffin. Serial sections, 4μm thick, were cut in a mesial-distal direction at 80μm intervals. The sections were stained using hematoxylin and eosin.

The four most central sections of each defect site were observed using light microscopy‖‖. Histometric analysis was performed using image analysis software¶¶. The following parameters were recorded.

◦ Defect height: distance from the apical extension of the root surface notch to the cemento-enamel junction (CEJ)

◦ Epithelial attachment: distance from the CEJ to the apical extension of an epithelial attachment on the root surface. This parameter included any gingival recession.

◦ Cementum regeneration: distance from the apical extension of the root surface notch to the coronal extension of newly formed cementum or a cementum-like substance on the root surface.

◦ Bone regeneration (height): distance from the apical extension of the root surface notch to the coronal extension of newly formed bone along the root surface;

◦ Bone regeneration (area): new alveolar bone within the standardized template that served as a proxy for the defect site (Figure 2). The template was aligned parallel to the root surface interfacing the apical extension of defect at the root surface notch.

◦ Unresorbed biomaterial: volume of the remained biomaterial in newly formed bone and connective tissue.

◦ Root resorption

◦ Ankylosis

4. Statistical Analysis

The experimental groups of rhGDF-5/β-TCP and rhPDGF/β-TCP were compared using student *t*-test ($p < 0.05$) with Statistics software[##].

‖ 0.04 mg/kg; Kwangmyung Pharmaceutical Ind. Co. Ltd., Seoul, Korea

¶ Rompun, Bayer Korea Co., Seoul, Korea

Ketara, Yuhan Co., Seoul, Korea

** Gerolan, Choongwae Pharmaceutical Co., Seoul, Korea

†† Vicryl 5.0 Polyglactin 910, Ethicon, Johnson & Johnson, New Jersey, USA

‡‡ Cefazoline Sodium 20mg/kg; Yuhan Corporation, Seoul, Korea

§§ Hexamedin®, Bukwang Pharmaceutical Co., Seoul, Korea

‖ ‖ Olympus Multi-view microscope BH2, Tokyo, Japan

¶¶ Image-Pro Plus, Media Cybernetic, Silver Springs, MD, USA

Microsoft Office Excel 2007, Microsoft Co., Redmond, Washington, USA

III. RESULTS

1. Clinical and Radiographic Observations

All sites including rhGDF-5/β-TCP and rhPDGF/β-TCP groups healed uneventfully. Figure 1 and Figure 3 showed the clinical and radiographic observation at surgery and after 8 weeks healing. Both groups showed bone formation at defect sites.

2. Histomorphometric Analysis

Histomorphometric analysis is shown on Table 1.

Defect height of rhGDF-5/β-TCP group was 5.16±0.43 mm and the defect height of rhPDGF/β-TCP group was 5.15±0.17 mm. These values had no significant difference ($p>0.05$). But, bone regeneration height and area showed significant differences between the 2 groups. Bone regeneration height was 3.08±0.74 mm and 1.29±0.78 mm in rhGDF-5/β-TCP and rhPDGF/β-TCP group ($p<0.05$). Cementum regeneration height was 4.49±0.48 mm and 2.72±0.91 mm in rhGDF-5/β-TCP and rhPDGF/β-TCP group. Values of epithelial attachments averaged 0.52±0.40 mm and 1.17±0.52 mm in rhGDF-5/β-TCP and rhPDGF/β-TCP group Values of connective tissue attachments averaged 0.14±0.25 mm and 1.25±0.84 mm in rhGDF-5/β-TCP

and rhPDGF/β-TCP group. rhPDGF/β-TCP group showed significantly higher epithelial attachment ($p<0.05$)(Figure 9).

Mean values of bone regeneration area were 6.51±0.93 mm^2 and 1.44±1.04 mm^2 for rhGDF-5/β-TCP and rhPDGF/β-TCP respectively with significant differences between the 2 groups ($p<0.05$)(Figure 10).

The total volume of residual materials was 0.79±0.58 mm^2 , 0.91± 0.42 mm^2 for rhGDF-5/β-TCP and rhPDGF/β-TCP respectively. The volume of residual materials were 0.65±0.55 mm^2 and 0.22±0.17 mm^2 for rhGDF-5/β-TCP and rhPDGF/β-TCP respectively in the newly formed bone. On the other hand, in the connective tissue. the values were 0.14±0.03 mm^2 and 0.69±0.42 mm^2 rhGDF-5/β-TCP and rhPDGF/β-TCP respectively. There was a significant difference in the volume of the residual material inside the connective tissue. But, there was no significant difference between 2 groups in total residual material volumes (Table 2, Figure 11).

3. Histologic Analysis

Histologic observations are shown on Figure 4, 5, 6, 7, 8.

Both groups showed significant bone and cementum formation. In newly formed bone, predominant lamellar bone with primary osteon was observed in rhGDF-5/β-TCP. In contrast, lamellar and woven bone was observed in rhPDGF/β-TCP. Both groups showed enhanced cementum regeneration. However, not only the length of

cementum, but also the density and thickness were enhanced in rhGDF-5/β-TCP group(Figure 5). The rhPDGF/β-TCP groups were mostly acellular, but the rhGDF-5/β-TCP groups were mixed (cellular/acellular,) cementum. Periodontal ligament fibers were seen perpendicularly and parallelly in both groups (Figure 5, 6).

Most of the β-TCP particles in rhGDF-5/β-TCP were seen in the bone area, which was lined with osteoid representing biodegradation. Besides, Most of β-TCP particles in rhPDGF/β-TCP were sequestered in the connective tissue area (Figure 8).

IV. DISCUSSION

Dennison et al(1994). reported that PDGF might be valuable in promoting new connective tissue attachment in the periodontal wound. Mumford et al(2001). reported the effect of PDGF-BB on the proliferation of PDL and concluded that there may be cell-specific differences critical to periodontal wound healing. These studies supported that PDGF-BB promoted periodontal wound healing. And when PDGF-BB is delivered to promote periodontal tissue engineering of tooth-supporting osseous defects, there is a direct effect on bone turn-over (Sarment et al. 2006).

Recombinant human platelet-derived growth factor-BB (rhPDGF-BB) is potent mitogenic and chemotactic protein for PDL fibroblasts and alveolar bone cells and improves angiogenesis, while bone allograft offers a biological matrix conductive to cell growth and may contribute osteoinductive bone matrix proteins (Nevins et al. 2003). And Nevins et al. demonstrated that the use of rhPDGF-BB was safe and effective in the treatment of periodontal osseous defects in human clinical study (Nevins et al. 2005).

Recently, rhPDGF-BB (GEM21s, Biomimetic Therapeutics) and rhBMP-2 (Infuse, Medtronic sofamor Danek) received FDA approval for a clinical use. These are the first proven safe materials for clinical use in tissue engineering.

Recombinant human growth/differentiation factor-5 (rhGDF-5) is a member of the transforming growth factor-β superfamily and plays a pivotal role in the process of

joint formation (Chang et al. 1994; Storm et al. 1994). In addition to joint development, rhGDF-5 has shown activity in promoting angiogenesis and tendon/ligament morphogenesis (Wolfman et al. 1997; Yamashita et al. 1997). As well as these basic properties, rhGDF-5 was reported suitable factor for enhancing healing in bone defect and ectopic bone formation with chondrogenesis, osteogenesis properties (Francis-West et al. 1999; Spiro et al. 2000; Yoshimoto et al. 2006).

rhPDGF-BB, which was first reported as having wound healing properties, and rhGDF-5, which was first reported as having chondrogenesis properties, were both applied to periodontal defects and studied for periodontal regeneration. In this study, the 1-wall intrabony defects may provide the proper preclinical model for the evaluation of the periodontal regeneration(Kim et al. 2004).

For evaluation of periodontal regeneration, cementum and bone regeneration height, and bone regeneration area were measured. In both groups, bone was enhanced, although bone regeneration area and height were significantly higher in the rhGDF-5/β-TCP group than in rhPDGF/β-TCP group (Table 1, Figure5, 6). rhPDGF/β-TCP group has bone regeneration in 1-wall intrabony defects approximately 30 percent of the defect height, rhGDF-5/β-TCP group(3.08±0.74 mm) has better effect on bone regeneration in 1-wall intrabony defects compared to rhPDGF/β-TCP group.(1.29± 0.78mm)(Table 1)

Both groups showed enhanced cementum regeneration, 4.49±0.48mm and 2.72±0.91mm, rhGDF-5/β-TCP and rhPDGF/β-TCP respectively. However, there

was stastically significant enhancement in rhGDF-5/β-TCP than rhPDGF/β-TCP (Table 1, Figure 5). Moreover, not only the length of cementum, but also the density and thickness were more enhanced in rhGDF-5/β-TCP group in histologic analysis (Figure 5). rhPDGF/β-TCP groups were mostly acellular but the rhGDF-5/β-TCP groups were mixed (cellular/acellular,) cementum. Periodontal regeneration includes *de novo* cementogenesis, osteogenesis and the formation of periodontal ligament fibers. Cementum seems to have the potential for the regeneration of periodontal apparatus.

The properties of cementogenesis should be regarded as an important factor for the periodontal regeneration. In this aspect, rhGDF-5 seems to be optimal for periodontal regeneration.

Both groups showed little resorption of tooth. Unlike BMPs, both growth factors could be applied to periodontal defects without ankylosis or resorption of tooth (Wikesjo et al. 1999; Wikesjo et al. 1999).

Periodontal ligament, which is the major reference point of periodontal regeneration, were found regulary arranged in both groups. Periodontal ligament fibers were seen perpendicularly and parallelly in both groups (Figure 5, 6). Most of the β-TCP particles in rhGDF-5/β-TCP were seen in the bone area, which was lined with osteoid representing biodegradation. Besides, Most of β-TCP particles in rhPDGF/β-TCP were sequestered in the connective tissue area (Figure 8). That means that rhGDF-5/β-TCP has more potential for the new bone formations.

A remarkable finding about these growth factors is that both groups showed hypercellularity in the newly formed bone (Figure 7). Regardless of the quantity of bone formation, both groups showed active cellularity. It could be concluded that, both growth factors accelerate biodegradation of a biomaterial used as a carrier in the periodontal defects, being displaced with bone in an active way (Koo et al. 2007). Biodegradation and formation of bone are the results of activities of growth factors. The rhGDF-5 seems to have more potent capacity of osteoconduction and osteoinduction than rhPDGF.

Though rhGDF-5/β-TCP showed enhanced effect on bone and cementum formation compared to rhPDGF/β-TCP group, both groups showed characteristics of hypercellularity and cementum formation. In the point of cementogenesis, long-term studies about these biomaterials are needed.

V. CONCLUSION

The results show that rhGDF-5/β-TCP has a higher efficacy in bone and cementum regeneration compared to rhPDGF/β-TCP in one-wall intrabony defects of dogs. The β-TCP carrier exhibited timely resorption and no appreciable adverse reactions affecting bone formation making it a candidate matrix for rhGDF-5 and rhPDGF.

In conclusion, rhGDF-5/β-TCP supports bone and cementum formation in advanced periodontal defects. Application of rhGDF-5/β-TCP appears safe as it is associated with limited adverse effects, if any.

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LEGENDS

Figure 1. Representative surgical procedure. Surgically created, critical-size, one-wall, intrabony periodontal defect at the distal aspect of the mandibular 2nd and mesial aspect of the mandibular 4th premolar teeth (left). Application of rhPDGF/β-TCP and rhGDF-5/ß-TCP (left center). Mucoperiosteal flaps adapted and sutured for primary intention healing (right center). Healing at week 8 (right). upper: rhPDGF/β-TCP, lower: rhGDF-5/ß-TCP

Figure 2. Schematic drawing of landmarks/parameters used in the histometric analysis.

Figure 3. Representative radiographs showing a defect site presurgery(upper), and defect sites at 8 weeks following beagle dog surgery, implantation of rhPDGF/β-TCP (left), and implantation of rhGDF-5/β-TCP (right).

Figure 4a. Representative photomicrographs from defect sites receiving rhPDGF/β-TCP. (X10, X40)

Figure 4b. Representative photomicrographs from defect sites receiving rhGDF-5/β-TCP. (X10, X40)

Figure 5. Representative photomicrographs defect sites receiving rhPDGF/β-TCP(left), and rhGDF-5/β-TCP(right). Newly formed cementum appears denser at sites receiving rhGDF-5/β-TCP compare to rhPDGF/β-TCP(X200)

Figure 6. Representative photomicrographs defect sites receiving rhPDGF/β-TCP(left), and rhGDF-5/β-TCP(right). Newly formed PDL denser at sites receiving rhGDF-5/β-TCP compare to rhPDGF/β-TCP. (x200)

Figure 7. Representative photomicrographs of hypercellularity in receiving rhPDGF/β-TCP(left, X100), and rhGDF-5/β-TCP (right, X100)

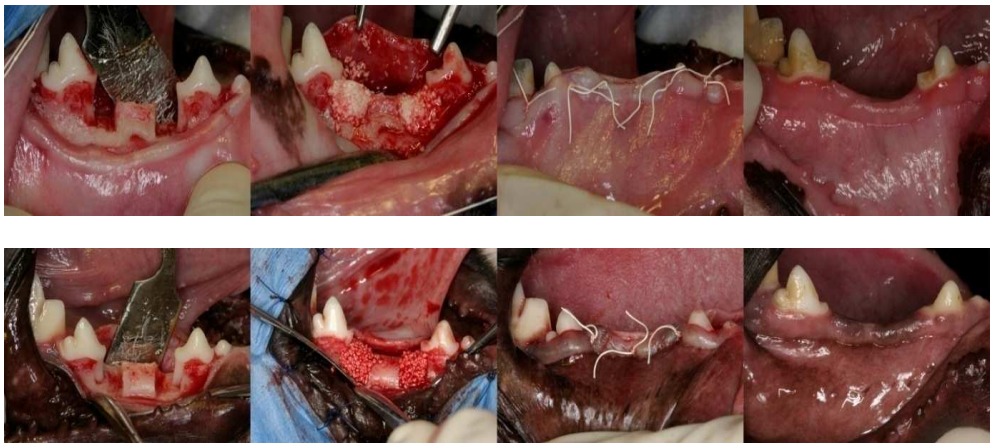
Figure 8. Representative photomicrographs of residual biomaterials in receiving rhPDGF/β-TCP (left), and rhGDF-5/β-TCP (right). Osteoclasts may be observed around the residual biomaterial, and osteoblasts around woven bone and residual biomaterial. (X100)

Figure 9. Representative of results of histometric analysis. (mm)

Figure 10. Representative of bone area of histometric analysis (mm^2)

Figure 11. Representative of residual materials volume in CT and bone. (mm^2)

FIGURES



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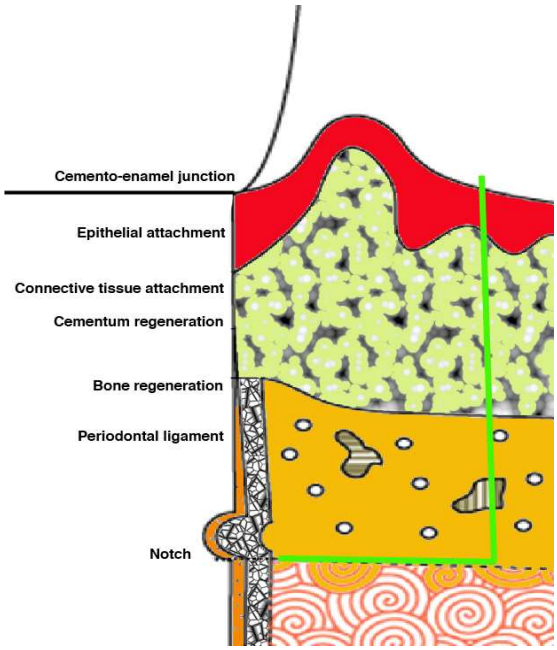

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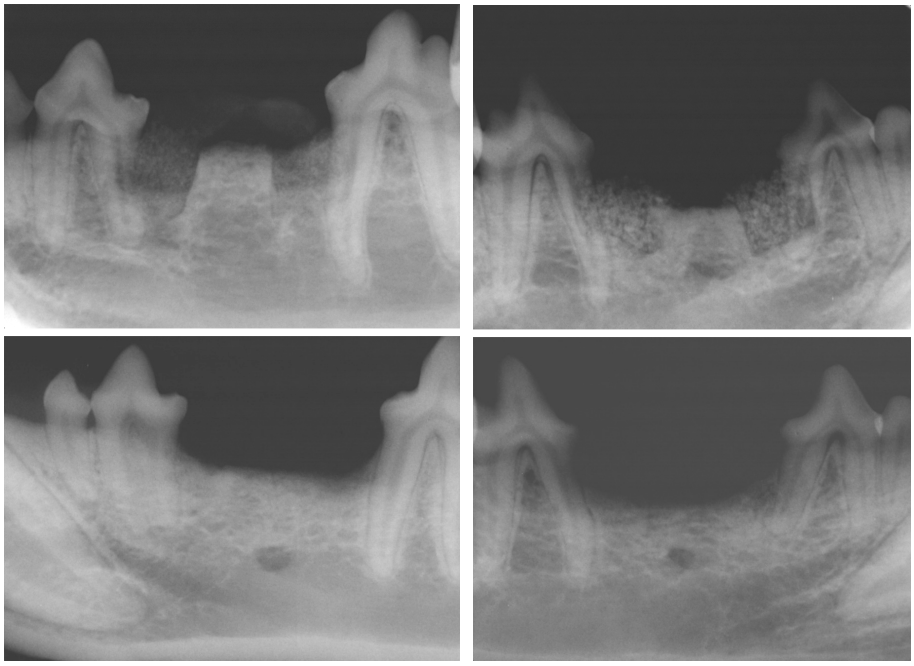

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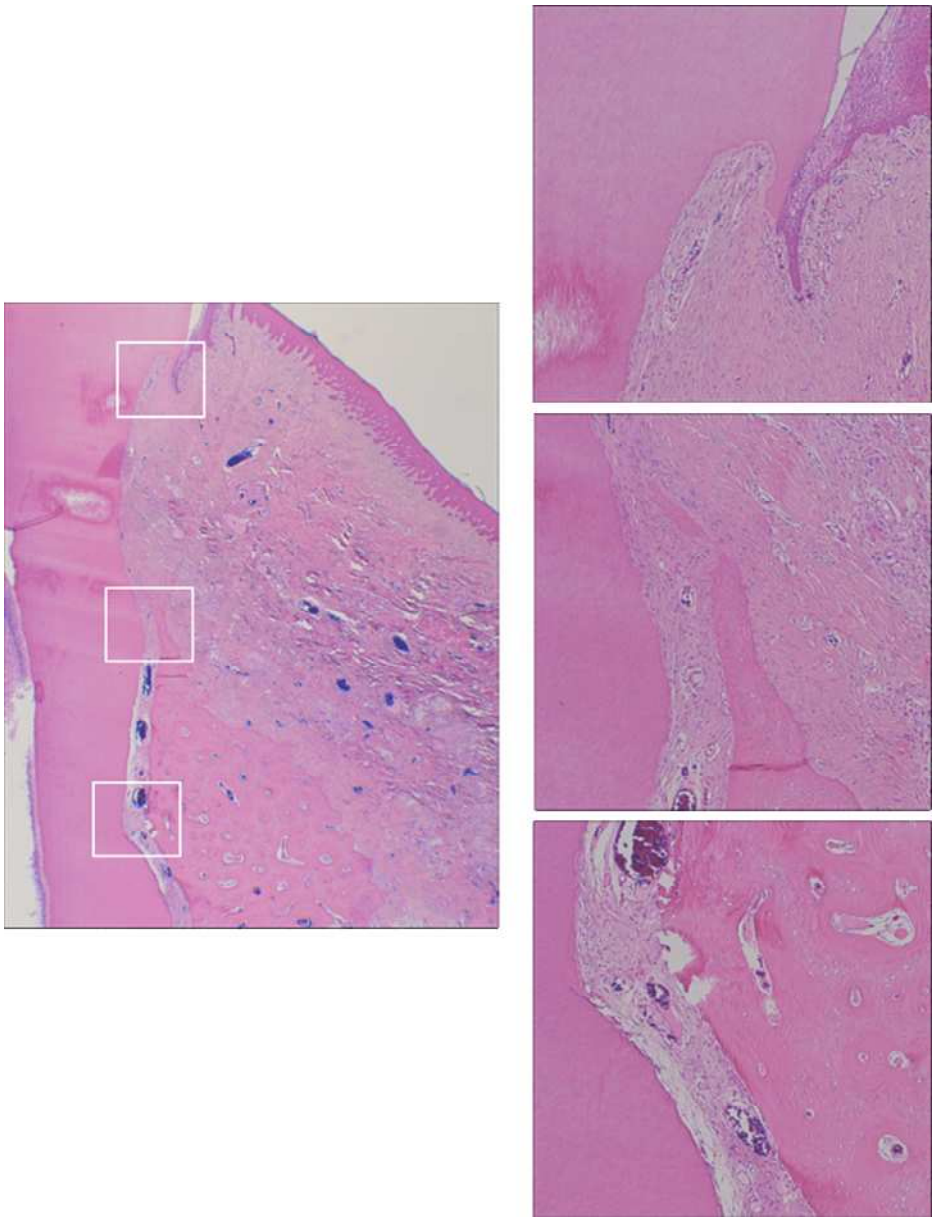

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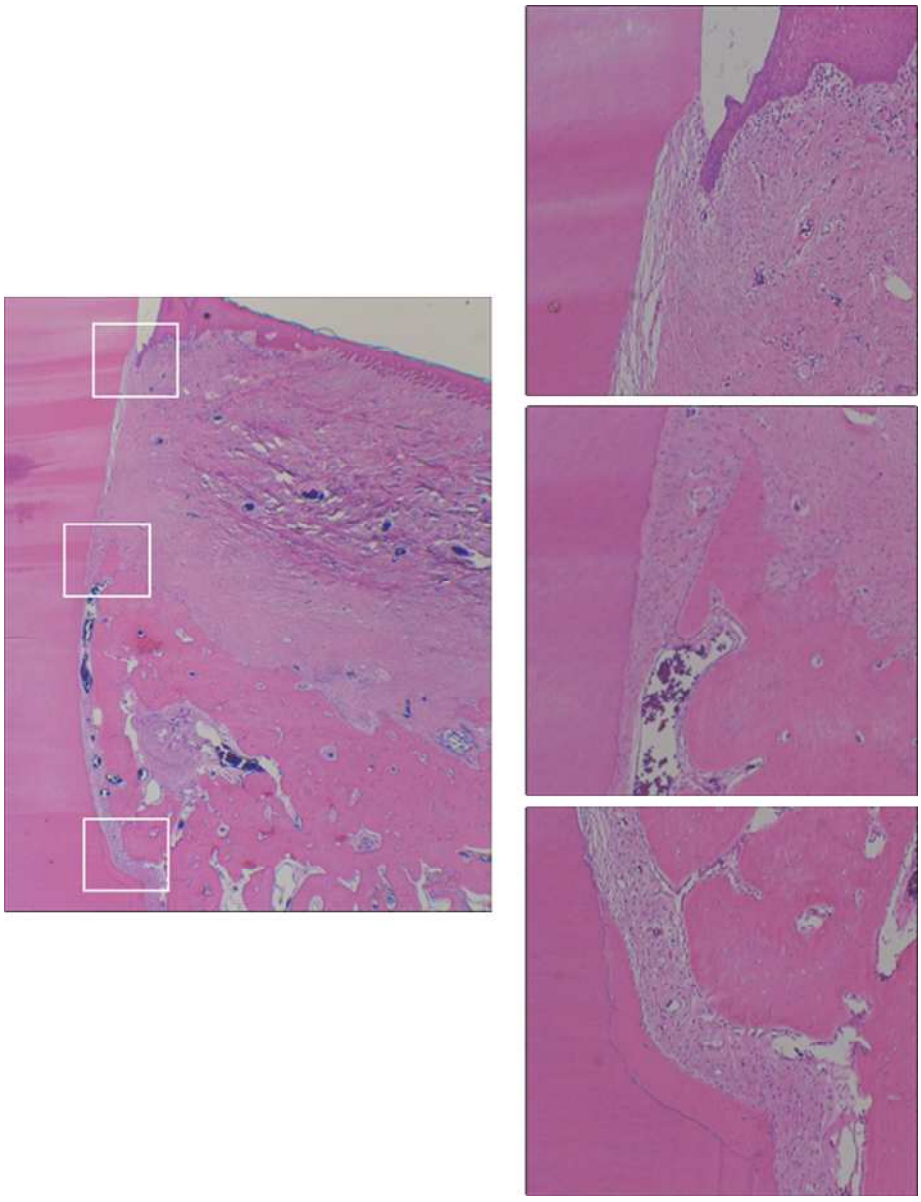
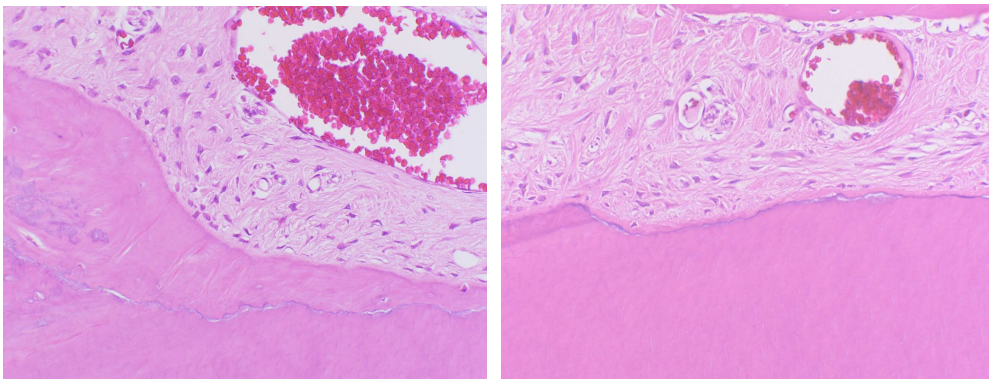


Figure 4b. Representative photomicrographs from defect sites receiving rhGDF-5/β-TCP. (X10, X40)



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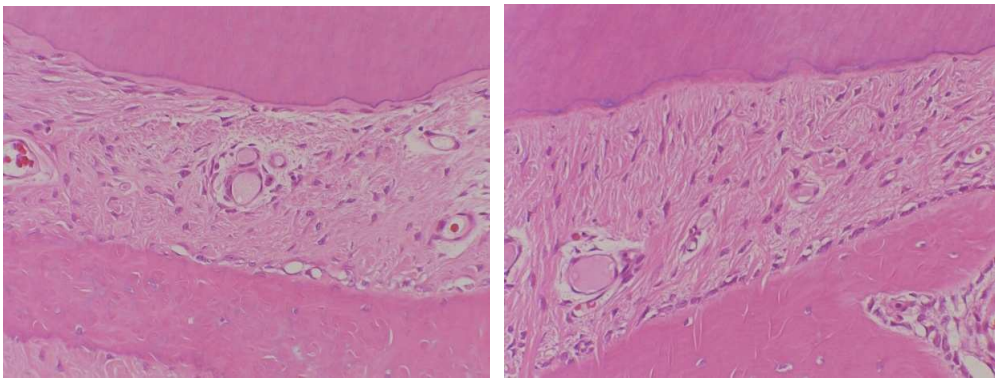

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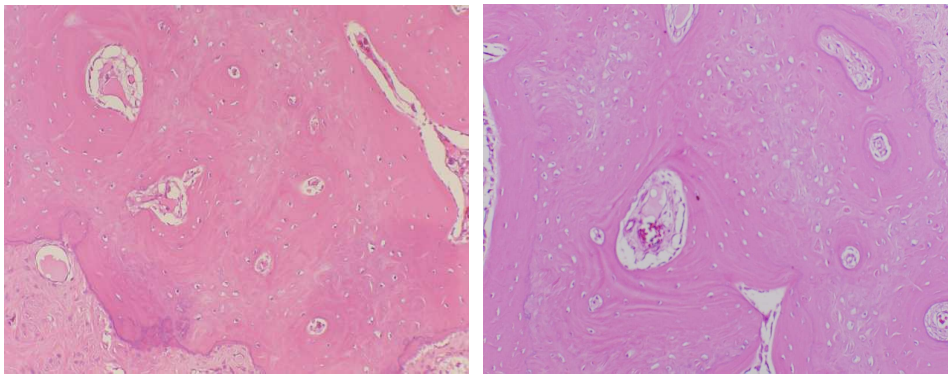

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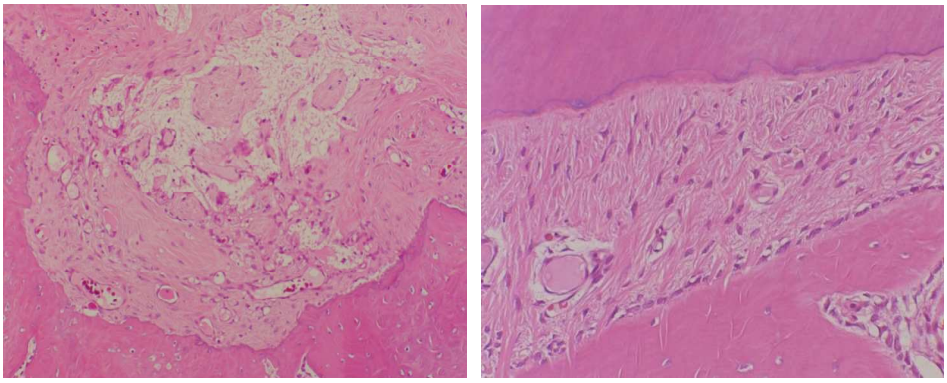

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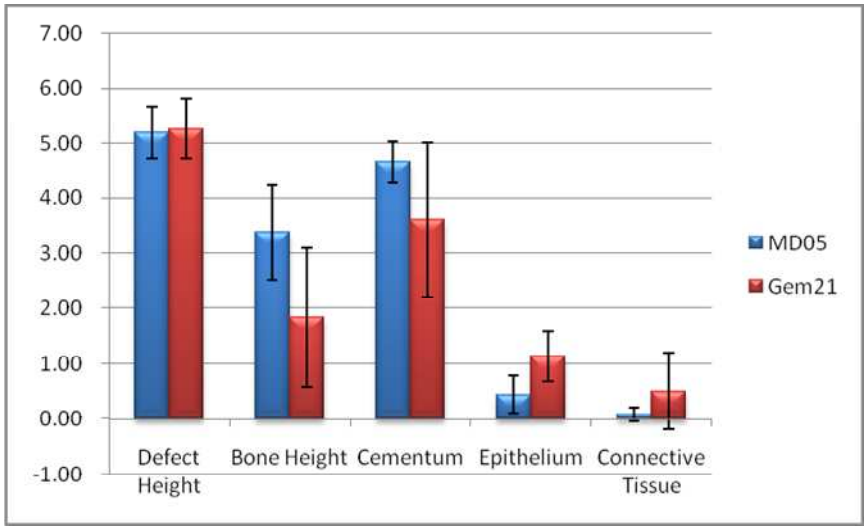

Figure 9. Representative of results of histometric analysis. (mm)

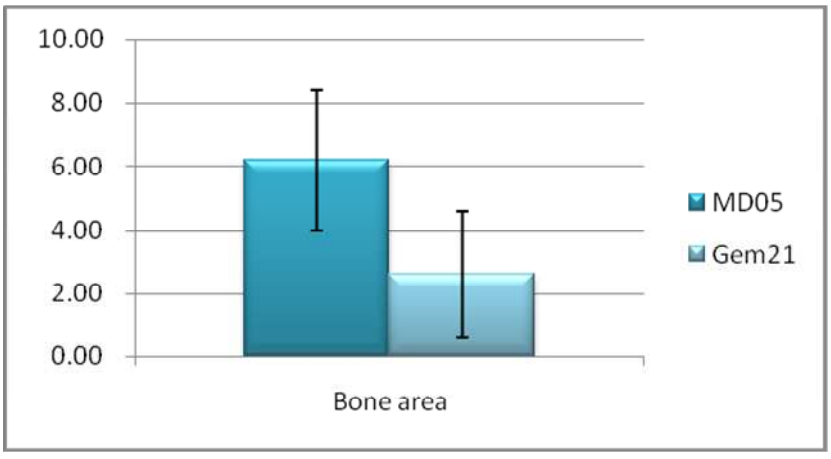

Figure 10. Representative of bone area of histometric analysis (mm^2)

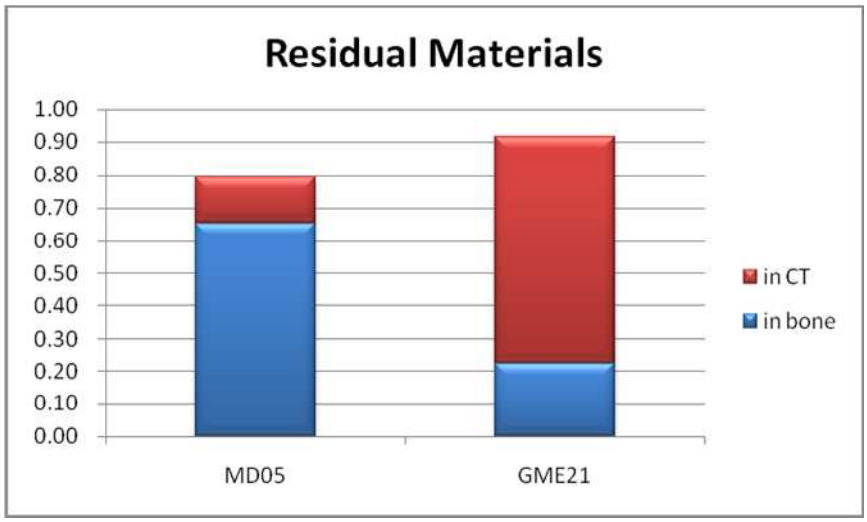

Figure 11. Representative of residual materials volume in CT and bone. (mm^2)

TABLES

Table 1. Histomorphometric analysis (group means ± SD in mm/mm^2)

	Defect Height	Epithelial Attachment	Connective tissue Attachment	Cementum Regeneration	Bone Regeneration Height	Bone Regeneration Area
rhGDF-5/ β-TCP	5.16±0.43	0.52±0.40	0.14±0.25	4.49±0.48*	3.08±0.74*	6.51±0.93*
rhPDGF/ β-TCP	5.15±0.17	1.17±0.52*	1.25±0.84	2.72±0.91	1.29±0.78	1.44±1.04

* : statistically significant differences ($p<0.05$)

Table 2. Residual materials (mean ± SD in mm^2)

Residual Materials Area	in bone	in C-T	Total
rhGDF-5/β-TCP	0.65±0.55	0.14±0.03	0.79±0.58
rhPDGF/β-TCP	0.22±0.17	0.69±0.42*	0.91±0.42

* : statistically significant differences ($p<0.05$)

국문요약

일벽성 골내결손에서 rhGDF-5/ β-TCP와 rhPDGF/ β-TCP의 치주조직 치유 및 재생에 대한 비교

< 지도교수 **김 종 관** >
연세대학교 대학원 치의학과

권 혁 락

치주조직 재생의 목표는 결합조직, 상피뿐만 아니라 골과 인대 백악질의 재생에 있다. 치주조직의 재생에 많은 노력과 시도가 있어 왔으며 최근에는 조직공학이 주목을 받고 있다. Platelet Derived Growth Factor (PDGF)는 콜라겐 1형의 합성을 촉진하며 골 합성세포의 화학주성 및 유사분열의 활동성을 촉진한다고 알려졌으며 Recombinant human growth/differentiation factor-5(rhGDF-5)는 과잉의 골을 형성할 정도의 제한된 위험성을 갖고 연골형성,

골형성, 혈관형성 능력을 보인다고 보고되어졌다. 하지만 PDGF와 rhGDF-5는 이식되어진 부위에서 일정기간 역할을 할 수 있도록 도와 주는 매개체가 필요한데 현재 β-Tricalcium Phosphate가 적합하다고 보고되어지고 있다. 이 연구의 목적은 성견의 치주결손 부위에 새롭게 개발되어진 rhGDF-5/β-TCP를 적용시켜 이미 많은 논문에서 치주조직 재생에 유용하다고 보고되어진 PDGF/β-TCP와 비교하여 rhGDF-5/β-TCP의 가능성을 평가하는데 있다.

5마리의 성견 하악 소구치 부위에 수술적으로 양측에, 5mm 간격의 일벽성의 골내 결손을 양측성으로 형성하였다. 결손 부위의 한 편에는 rhGDF-5/β-TCP을 수여하였고 다른 부위에는 PDGF/β-TCP를 이식하여 비교부위를 형성하였다. 이후 8주의 치유기간을 가지고 희생 되어졌으며 조직학적분석과 조직계측학적 분석을 시행하였다.

임상적으로 염증소견 등 부작용이 양쪽 모두에서 발견되어지지 않았다. 조직학적 관찰결과 세포성/무세포성을 포함한 백악질의 양쪽 모두에서 재생되었으며 재생 되어진 백악질은 양쪽 실험 그룹 모두에서 치조골 위

부위까지 재형성이 이루어진 것이 관찰된다.

rhGDF-5/β-TCP와 rhPDGF/β-TCP이 이식 되어진 양쪽 부위에서 흡수가 진행되어지고 있는 잔존 이식재가 관찰되어졌다. 그러나 rhPDGF/β-TCP가 이식되어진 부위에서 공통적으로 보다 많은 잔존 이식재 들이 존재 하였다.

rhGDF-5/β-TCP가 이식되어진 부위에서 rhPDGF/β-TCP가 이식되어진 부위보다 백악질과 골의 형성에서 통계학적으로 유의하게 우수한 능력을 나타냈다.

결론적으로 rhGDF-5/β-TCP 가 rhPDGF/β-TCP 보다 백악질, 골 형성 등에서 우수한 치주조직의 재생능력을 보여주고 있다. 이는 rhGDF-5/β-TCP 의 임상적인 가능성을 나타낸다고 할 수 있을 것이다.

핵심되는말: 조직공학, 이식재, 재생된 치주조직