Transforming Growth Factor-ß$_1$ Accelerates Resorption of a Calcium Carbonate Biomaterial in Periodontal Defects

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감사의 글

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2006년 12월

저자 씀

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Abstract

Transforming Growth Factor-ß$_1$ Accelerates Resorption of a Calcium Carbonate Biomaterial in Periodontal Defects

Background: In a previous study, recombinant human TGF-ß$_1$ (rhTGF-ß$_1$) in a calcium carbonate carrier was implanted into critical-size, supraalveolar periodontal defects under conditions for guided tissue regeneration (GTR) to study whether rhTGF-ß$_1$ would enhance or accelerate periodontal regeneration. The results showed minimal benefits of rhTGF-ß$_1$ and a clear account for this could not be offered. One potential cause may be that the rhTGF-ß$_1$ formulation was biologically inactive. Several growth or differentiation factors have been suggested to accelerate degradation of biomaterials used as carriers. The objective of this study was to evaluate possible activity of rhTGF-ß$_1$ on biodegradation of the calcium carbonate carrier.

Methods: rhTGF-ß$_1$ in a putty-formulated particulate calcium carbonate carrier was implanted into critical-size, supraalveolar periodontal defects under conditions for GTR in five Beagle dogs. Contralateral defects received the calcium carbonate carrier combined with GTR without rhTGF-ß$_1$ (control). The animals were euthanized at week 4 week postsurgery when block-biopsies of the defect sites were collected for histologic and histometric analysis. Radiographs were obtained at defect creation, week 2 and week 4.

Results: No statistically significant differences were observed in new bone formation (bone height and area) among the treatments. However, total residual carrier was significantly reduced in sites receiving rhTGF-ß$_1$ compared to control (p=0.04). Similarly, carrier density was considerably reduced in sites receiving rhTGF-ß$_1$ compared to control, the difference being borderline statistically significant (p=0.06).

Conclusions: Within the limitations of the study, it may be concluded that rhTGF-ß$_1$ accelerates biodegradation of a particulate calcium carbonate biomaterial indicating a biologic activity of the rhTGF-ß$_1$ formulation apparently not encompassing enhanced or accelerated periodontal regeneration.

KEY WORDS

Transforming growth factor- ß$_1$, calcium carbonate carrier, biodegradation, periodontal regeneration.

Transforming Growth Factor-ß$_1$ Accelerates Resorption of a Calcium Carbonate Biomaterial in Periodontal Defects

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I. Introduction

Transforming growth factor-ß (TGF-ß) is a homodimeric peptide with multifunctional actions controlling growth, differentiation, and function of a broad range of target cells.[1] Tissue-specific and developmentally dependent expression strongly suggests a significant role in specific morphogenetic and histogenetic events. Thus far, five distinct TGF-ßs with 65-80% homology have been identified.[1] Currently thought to consist of at least 26 different proteins, TGF-ß$_1$ supports wound healing by augmenting angiogenesis and fibroblast collagen formation.[2,3] In addition, TGF-ß$_1$ is thought to be involved in regulating cell proliferation and differentiation and the production of extracellular matrix.[4] Also, a role of TGF-ß$_1$ in recruiting and stimulating osteoprogenitor cells to proliferate, providing a pool of early osteoblasts has been suggested.[5] In perspective, TGF-ß$_1$ technologies appear attractive candidate therapies to support periodontal wound healing/regeneration.

In a previous study, recombinant human TGF-ß$_1$ (rhTGF-ß$_1$) in a putty-formulated particulate calcium carbonate carrier was implanted into critical-size, supraalveolar periodontal defects under conditions for guided tissue regeneration (GTR) to study whether rhTGF-ß$_1$[*] would enhance or accelerate periodontal wound healing/regeneration.[6] Control sites received the calcium carbonate carrier combined with GTR without rhTGF-ß$_1$. The histometric analysis could not discern significant benefits of the rhTGF-ß$_1$ formulation. Overall, sites receiving rhTGF-ß$_1$ and control treatments exhibited limited bone formation and regeneration of the periodontal attachment suggesting marginal, if any, effects of rhTGF-ß$_1$. Although the results failed to discern a significant benefit of rhTGF-ß$_1$, an obvious account of the results could not be offered. Could possibly the putty-formulated particulate calcium carbonate carrier or the GTR device rendered the growth factor ineffective or biologically inactive? Parallel studies evaluating rhTGF-ß$_1$ using the supraalveolar periodontal defect model without GTR showed similar limited effects ruling out an inhibitory effect of the GTR device.[7] Other studies suggest that biomaterials implanted into periodontal sites indeed may obstruct bone formation and periodontal regeneration.[8] Still other studies may be interpreted to suggest that growth or differentiation factors may accelerate biodegradation/biotransformation of a biomaterial used as a carrier.[9,10]

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[*] Genentech Inc., San Francisco, CA, USA

A re-examination of the study by Wikesjö et al.[6] using additional parameters was thus deemed necessary to discern possible effects of rhTGF-ß$_1$ on biodegradation of the putty-formulated particulate calcium carbonate carrier.

II. Materials and Methods

A. Animals

Five male Beagle dogs (age 18-24 months, weight 12-15 kg) were used. Animal selection, management, surgery protocol, and periodontal defect preparation followed routines approved by the local Institutional Animal Care and Use Committee. The animals were fed a soft-consistency laboratory diet supplemented with vitamins throughout the study. A soft diet was chosen to alleviate potential mechanical interference with wound healing during food intake.

B. Surgical Protocol

Surgical procedures were performed under sodium pentobarbital anesthesia[†] (20-30 mg/kg, IV) preceded by acepromazine[‡].(1 mg/kg, IM) Routine dental infiltration anesthesia was used at the surgical sites. During surgery, the animals received lactated Ringer's solution[§]. (300-500 mL, IV)

Bilateral, critical-size, supraalveolar periodontal defects were created at the 3rd and 4th mandibular premolar teeth in each animal.[11] Briefly, following sulcular incisions and elevation of buccal and lingual mucoperiosteal flaps, the alveolar bone was resected around the circumference of the teeth using chisels and water-cooled rotating burs.

[†] Nembutal® Sodium Solution, Abbott Laboratories, North Chicago, IL, USA

[‡] PromAce®, Aveco Co Inc., Fort Dodge, IA, USA

[§] Lactated Ringer's Inj., USP, Abbott Laboratories

The exposed root surfaces were instrumented with curettes, chisels, and water-cooled rotating diamonds to remove the cementum. The resulting clinical defect approximated 5 mm from the cemento-enamel junction (CEJ) to the reduced alveolar crest. The 1st and 2nd mandibular premolar teeth were extracted and the crown of the 1st molar amputated level with the reduced alveolar crest.

The maxillary 1st, 2nd, and 3rd premolar teeth were surgically extracted and the maxillary 4th premolars reduced in height and exposed pulpal tissues were sealed with Cavit®‖ in order to alleviate potential trauma from the maxillary teeth to the experimental mandibular sites.

C. Experimental Protocols

Using a split-mouth design, contralateral, supraalveolar periodontal defects were implanted with rhTGF-ß$_1$ in a carrier or carrier alone (control). Experimental treatments were alternated between left and right jaw quadrants in consecutive animals. Both treatments were combined with GTR. The carrier comprised medical grade, natural, porous, particulate calcium carbonate¶ and medical grade hydroxyethyl starch providing putty-like handling characteristics; 0.5% gelatin and 20 µM sodium acetate solution was mixed with hydroxyethyl starch to form a visco-elastic gel to contain the calcium carbonate particles in a manageable mass.

‖ Cavit®, ESPE, Seefeld/Oberbayern, Germany

¶ Biocoral® 1000, Inoteb, Saint-Gonnery, France

For each defect scheduled to receive rhTGF-ß$_1$, 0.25 mL buffer containing 20 µg rhTGF-ß$_1$ was added to approximately 0.7 g calcium carbonate particles, the hydroxyethyl starch gel was then added to produce a homogenous putty-like mass. Final implant volume/defect approximated 0.8 mL. rhTGF-ß$_1$ and control constructs were prepared under aseptic conditions.

D. Wound Management

Defects receiving rhTGF-ß$_1$ or control treatments had the putty-like material shaped around the premolar teeth to the contour of the resected alveolar bone. The teeth were then fitted with an expanded polytetrafluoroethylene (ePTFE) barrier[#] secured with an ePTFE suture[**] at the CEJ (Figure 1). Periostea were fenestrated at the base of the mucoperiosteal flaps and the flaps were advanced, adapted, and sutured using horizontal mattress sutures approximately 2 mm coronal to the CEJ.

E. Postsurgery Protocol

A long-acting opioid[††] (0.015 mg/kg IM, BID, 2 days) was used for immediate pain control.

[#] GORE-TEX Regenerative Material Transgingival Configuration, W.L. Gore & Associates Inc., Flagstaff, AZ, USA

[**] GORE-TEX Suture CV5, W.L. Gore & Associates Inc.

[††] Buprenex Injectable, buprenorphine HCl, Reckitt & Colman Pharmaceuticals Inc., Richmond, VA, USA

A broad-spectrum antibiotic[‡‡] (2.5 mg/kg IM, BID, 2 weeks) was used for infection control Plaque control was maintained by twice daily topical application of chlorhexidine[§§]. (40 mL of a 2% solution) Observations of experimental sites with regards to gingival health, flap adaption, edema, and purulence were made daily. The ePTFE devices were not removed.

Gingival sutures were removed at day 10. Photographs were obtained at defect creation, suture removal, and at week 2 and 4. Radiographs were obtained at defect induction, and at week 2 and 4. Thiopental sodium anesthesia[‖‖] (20-25 mg/kg, IV) was used for suture removal and radiographic registrations.

F. Histological Procedures

The animals were euthanized at week 4 postsurgery using an intravenous injection of concentrated thiopental sodium. Tissue blocks including teeth, bone, and soft tissues were removed. The blocks were fixed in 10% buffered formalin for 3-5 days, decalcified in 5% formic acid for 8-10 weeks, trimmed, dehydrated, and embedded in butyl methacrylate-paraffin. Serial sections (7 µm) were cut in a buccal-lingual plane throughout the mesial-distal extension of the teeth.

[‡‡] Baytril® Brand of Enrofloxacin, Mobley Corporation, Shawnee, KS, USA

[§§] Chlorhexidine Gluconate 20%, ICI Pharmaceutical Group, Wilmington, DE, USA

[‖‖] Pentothal®, Abbott Laboratories, North Chicago, IL

Every 14th section was stainedwith Ladewig's connective tissue stain modified by

Mallory allowing for observations at 100-µm intervals.

G. Histological Evaluation

One experienced, calibrated, masked examiner (KTK) performed the histometric analysis using a PC-based image analysis system[¶¶] with a custom application for the supraalveolar periodontal defect model.[11] The most central stained section for each root of the 3rd and 4th premolars, identified by the size of the root canal, was used for the analysis.[12] The following parameters were recorded for buccal and the lingual tooth surfaces for each section:

Defect Height: distance between apical extension of the root planing and the CEJ.

Device Height: distance between apical extension of the root planing and most coronal aspect of the ePTFE device.

Defect Area: area under the ePTFE device circumscribed by the planed root, the width of the alveolar bone at apical extension of the root planing, and the device.

Bone Regeneration (height): distance between apical extension of the root planing and the coronal extension of new alveolar bone formed along the planed root.

Bone Regeneration (area): area represented by new alveolar bone formed along the planed root.

[¶¶] Image-Pro Plus™, Media Cybernetics®, Silver Spring, MD, USA

Total Residual Carrier: combined area of residual calcium carbonate carrier particles within the defect site.

Carrier Density: ratio residual calcium carbonate carrier particles to bone within regenerated bone.

H. Statistical Analysis

Data was collected at tooth level and this was taken into consideration in the analysis. Standard errors of the mean were adjusted for the correlation of the observations within animals. Generalized estimating equations were used to assess the impact of different factors on carrier resorption. Measurements at tooth level were used and estimates were adjusted for the clustering of observations into animals using a robust variance estimator. Wald tests were used for multiple comparisons and the level of significance was set at 5%. A stratified analysis comparing residual carrier and new bone between the experimental groups was carried out using the median (5.1 mm^2) of the wound area as cut off point.

III. Results

A. Clinical Observations

With the exception for one control site exhibiting gingival inflammation, the surgical sites exhibited healthy gingival conditions (Figure 1). There was no specific clinical characteristic differentiating rhTGF-ß$_1$ sites from the control. Two animals demonstrated limited exposure of the ePTFE device.

B. Radiographic Observations

The radiographic appearance of the rhTGF-ß$_1$ and control sites was similar reflecting the particulate nature of the calcium carbonate biomaterial. Radiopacity compatible with the biomaterial was observed in all animals suggesting that significant amounts remained at week 4 postsurgery.

C. Histological Observations

All defect sites were available for analysis with the exception for one root in a control site that was lost in the histotechnical preparation. Generally, the barrier device was located near the CEJ and the epithelium arrested at the CEJ. Three animals exhibited an inflammatory infiltrate, partially or completely occupying the defect site, localized to the buccal and/or lingual aspect of the mesial and/or distal root of the premolar teeth in sites receiving rhTGF-ß$_1$. These animals also exhibited sites without an inflammatory infiltrate. Similarly, two control animals exhibited a bilateral

inflammatory infiltrate occupying the defect site. Defects in remaining animals did not exhibit an inflammatory infiltrate.

Bone regeneration appeared limited to the apical aspect of the defect sites without notable differences between rhTGF-ß$_1$ and control sites (Figure 2). However, one animal exhibited considerably greater bone formation for both the rhTGF-ß$_1$ and control site. New cementum formation and regeneration of a functionally oriented periodontal ligament was limited, if at all appreciable, and thus not included in the histometric analysis. Similarly, root resorption appeared limited. Ankylosis was not observed.

D. Histometric Analysis

The rhTGF-ß$_1$ and control groups did not differ significantly with regards to defect characteristics (defect height, device height and wound area; Table 1). There were also no statistically significant differences in bone formation (height and area) among the treatments. On the other hand, total residual carrier was significantly smaller in sites that received rhTGF-ß$_1$ compared to that in the control ($p=0.04$). Similarly, carrier density was considerably smaller in the rhTGF-ß$_1$ group; this difference however did not reach statistical significance ($p=0.06$). This observation may indicate that rhTGF-ß$_1$ increased the resorption rate of the putty-formulated particulate calcium carbonate carrier, but this effect did not influence bone formation or regeneration of the periodontal attachment.

Table 1. Comparison between experimental groups (mean ± SE)

	rhTGF-ß$_1$	Control	p-value
Defect height (mm)	4.1 ± 0.2	4.3 ± 0.2	0.38
Device height (mm)	4.1 ± 0.4	4.4 ± 0.1	0.89
Wound area (mm^2)	4.8 ± 0.6	5.5 ± 0.4	0.33
Bone height (mm)	2.1 ± 0.2	2.2 ± 0.3	0.36
Bone area (mm^2)	3.2 ± 0.4	3.4 ± 0.5	0.81
Residual carrier (mm^2)	0.9 ± 0.2	1.6 ± 0.4	0.04
Carrier density (%)	10.9 ± 2.2	15.7 ± 2.5	0.06

A stratified analysis for wound area showed that carrier density and residual carrier area were significantly smaller for the rhTGF-ß$_1$ group in smaller wound areas ($p<0.05$) (Figures 3 and 4). No significant differences were observed for these parameters in larger wound areas ($p>0.05$). No significant differences were observed between experimental groups regarding new bone height and area irrespective of wound area (Figures 5 and 6).

In the multivariable model, residual carrier area was significantly smaller for the rhTGF-ß$_1$ group, and this difference remained significant even after adjusting for wound and bone area (Table 2). On the other hand, no significant differences were observed in carrier density between experimental groups after adjusting for wound and bone area. Despite its positive effect on the resorption rate of the carrier, new bone height and area were not statistically different between groups, after adjusting for wound and carrier area (Table 3).

Table 2. Effect of rhTGF-ß$_1$ on biodegradation after adjustment for wound and bone area.

		ß ± SE	p-value
Residual carrier	rhTGF-ß$_1$	-0.51 ± 0.24	0.03
	Wound area	0.24 ± 0.08	0.003
	Bone area	-0.07 ± 0.08	0.36
Carrier density	rhTGF-ß$_1$	-1.16 ± 1.89	0.54
	Wound area	1.79 ± 0.63	0.004
	Bone area	-0.50 ± 0.60	0.41

Table 3. Effect of rhTGF-ß$_1$ on bone formation after adjustment for wound and carrier area.

		ß ± SE	p-value
Bone height	rhTGF-ß$_1$	0.24 ± 0.25	0.33
	Wound area	0.27 ± 0.08	0.0001
	Carrier area	0.05 ± 0.14	0.74
Bone area	rhTGF-ß$_1$	-0.02 ± 0.43	0.96
	Wound area	0.50 ± 0.14	0.0001
	Carrier area	-0.27 ± 0.25	0.29

IV. Discussion

The objective of this study was to evaluate the effect of rhTGF-ß$_1$ on biodegradation of a putty-formulated particulate calcium carbonate biomaterial used as a carrier for rhTGF-ß$_1$ in a well-characterized periodontal defect model. As previously observed, the rhTGF-ß$_1$ construct, alone or combined with GTR, showed no significant effects on periodontal wound healing/regeneration[6,7] potentially indicating the rhTGF-ß$_1$ formulation being biologically inactive. This study, on the other hand, also evaluating biodegradation of the calcium carbonate biomaterial, indicates that the rhTGF-ß$_1$ construct was biologically active accelerating degradation of the calcium carbonate biomaterial while not affecting periodontal wound healing/regeneration.

Bone regeneration (height and area) was limited without significant differences between the rhTGF-ß$_1$ and control groups. The reason for this may be attributed to obscure effects of rhTGF-ß$_1$ combined with GTR or obstruction to bone formation by the calcium carbonate biomaterial obturating the defect site to migration and proliferation of a regenerate from the periodontal ligament. In previous studies, we also observed limited bone formation due to apparent obstruction of the wound space inflicted by biomaterials.[8,14]

It is difficult to accept the limited effect of rhTGF-ß$_1$ on bone formation in the periodontal model; several studies have confirmed an osteoconductive potential of rhTGF-ß$_1$.[5,15,16] Potentially GTR may compromise osteoconductive properties of rhTGF-ß$_1$ or the 4-week healing interval may have been too short to reveal discernable effects of rhTGF-ß$_1$; the cause may only be speculated upon. Nevertheless,

the amount of residual particulate carrier biomaterial was significantly smaller in the rhTGF-ß$_1$ group compared to control in smaller wound areas. A stratified analysis dichotomizing the defect sites into smaller and larger wound areas showed that while bone formation (height and area) was not influenced by wound area, carrier density and residual carrier were significantly smaller for sites implanted with rhTGF-ß$_1$ while no difference was found in larger wound areas. This observation implies that rhTGF-ß$_1$ increased the degradation rate of the biomaterial. This is in agreement with previous studies where differentiation factors such as bone morphogenetic proteins have been shown to accelerate degradation of the biomaterials used as carrier technologies.[9,10]

Additional statistical analysis was performed to determine if any other factors affected the outcome. When the two treatment groups were compared adjusting for wound and bone area, residual carrier area was significantly smaller for the rhTGF-ß$_1$ group while carrier density was not affected even after adjusting for wound and bone area. New bone height and area were again not affected for both groups even after adjusting for wound and carrier area.

Histometric analysis of new cementum formation, regeneration of a functionally oriented periodontal attachment, root resorption, ankylosis was not included. The histological observations revealed limited, if any, new cementum formation. Root resorption and ankylosis were rare. These observations are in synchrony with previous studies evaluating GTR technologies and using a 4-week healing interval.[17]

Tissue maturation in this defect model apparently commands longer observation intervals that regeneration of the periodontal attachment is clearly distinguishable at least using incandescent and polarized light microscopy.[18]

Within the limitations of the study, it may be concluded that rhTGF-ß$_1$ accelerates biodegradation of the particulate calcium carbonate biomaterial indicating a biologic activity of the rhTGF-ß$_1$ formulation apparently not encompassing enhanced or accelerated periodontal regeneration. This observation corroborates a previous study where recombinant human bone morphogenetic protein-2 accelerated biodegradation of a biomaterial used as a carrier in the supraalveolar periodontal defect model also without affecting regeneration of the periodontal attachment.[9]

V.Conclusion

In a previous study, recombinant human TGF-ß$_1$ (rhTGF-ß$_1$) in a putty-formulated particulate calcium carbonate carrier was implanted into critical-size, supraalveolar periodontal defects under conditions for guided tissue regeneration (GTR) to study whether rhTGF-ß$_1$* would enhance or accelerate periodontal wound healing/regeneration.[6] Control sites received the calcium carbonate carrier combined with GTR without rhTGF-ß$_1$. The histometric analysis could not discern significant benefits of the rhTGF-ß$_1$ formulation. Overall, sites receiving rhTGF-ß$_1$ and control treatments exhibited limited bone formation and regeneration of the periodontal attachment suggesting marginal, if any, effects of rhTGF-ß$_1$. Although the results failed to discern a significant benefit of rhTGF-ß$_1$, an obvious account of the results could not be offered. The present study re-evaluated the previous study utilizing the same parameters to examine if this finding holds true and additional parameters were added to discern any possible effects of rhTGF-ß$_1$ on biodegradation of the putty-formulated particulate calcium carbonate carrier. The following conclustions were made.

1. Bone regeneration (height and area) was limited without significant differences between the rhTGF-ß$_1$ and control groups.

2. The amount of residual particulate carrier biomaterial was significantly smaller in the rhTGF-ß$_1$ group compared to control in smaller wound areas.

3. Histological observations revealed limited, if any, new cementum formation.

Root resorption and ankylosis were rare findings.

4. It may be concluded that rhTGF-ß$_1$ accelerates biodegradation of the particulate calcium carbonate biomaterial indicating a biologic activity of the rhTGF-ß$_1$ formulation apparently not encompassing enhanced or acclerated periodontal regeneration.

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Figure Legends

Figure 1. Critical-size, supraalveolar periodontal defect implanted with rhTGF-ß$_1$ in a putty-formulated particulate calcium carbonate carrier before and after application of an ePTFE-barrier for GTR and at 4 weeks postsurgery (left).

Figure 2. Photomicrographs showing the critical-size, supraalveolar periodontal defects at 4 weeks postsurgery. The left photomicrograph shows a defect site implanted with rhTGF-ß$_1$ in the calcium carbonate carrier under conditions for GTR and the right photomicrographs shows a control defect without rhTGF-ß$_1$. The green arrows delineate the base of the approximately 5-mm defects; the ePTFE-barriers adapted to the teeth at the CEJ.

Figure 3. Carrier density by wound area (* $p<0.05$). Note significantly smaller carrier density for the rhTGF-ß$_1$ group in the smaller wound areas.

Figure 4. Residual carrier area by wound area (* $p<0.05$). Note significantly smaller carrier area for the rhTGF-ß$_1$ group in the smaller wound areas.

Figure 5. Bone height by wound area. No significant differences were observed between the two groups regarding new bone height irrespective of the wound areas.

Figure 6. Bone area by wound area. No significant differences were observed between the two groups regarding new bone area irrespective of the wound areas.

Figures

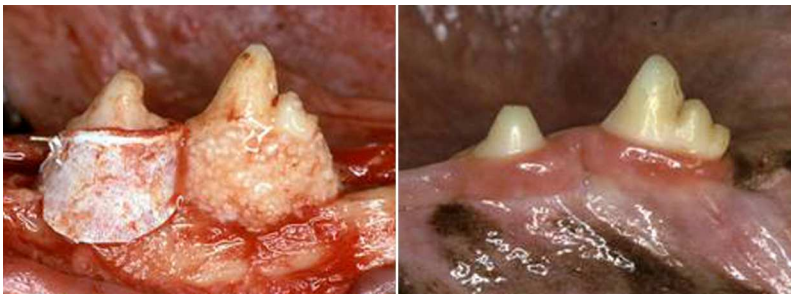

Figure 1. Critical-size, supraalveolar periodontal defect implanted with rhTGF-ß$_1$ in a putty-formulated particulate calcium carbonate carrier before and after application of an ePTFE-barrier for GTR and at 4 weeks postsurgery (left).

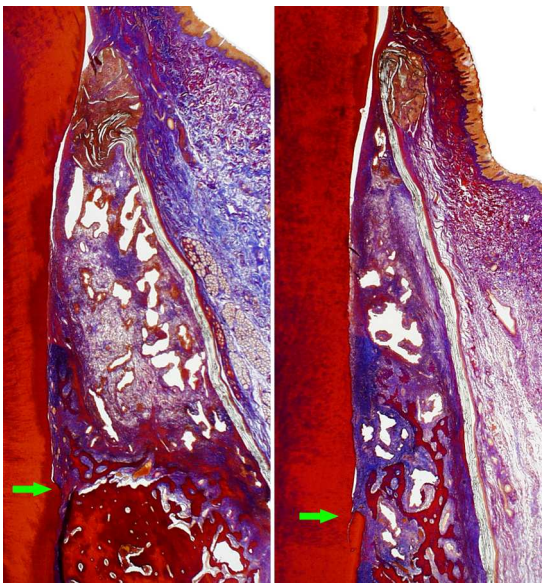

Figure 2. Photomicrographs showing the critical-size, supraalveolar periodontal defects at 4 weeks postsurgery. The left photomicrograph shows a defect site implanted with rhTGF-ß$_1$ in the calcium carbonate carrier under conditions for GTR and the right photomicrographs shows a control defect without rhTGF-ß$_1$. The green arrows delineate the base of the approximately 5-mm defects; the ePTFE-barriers adapted to the teeth at the CEJ.

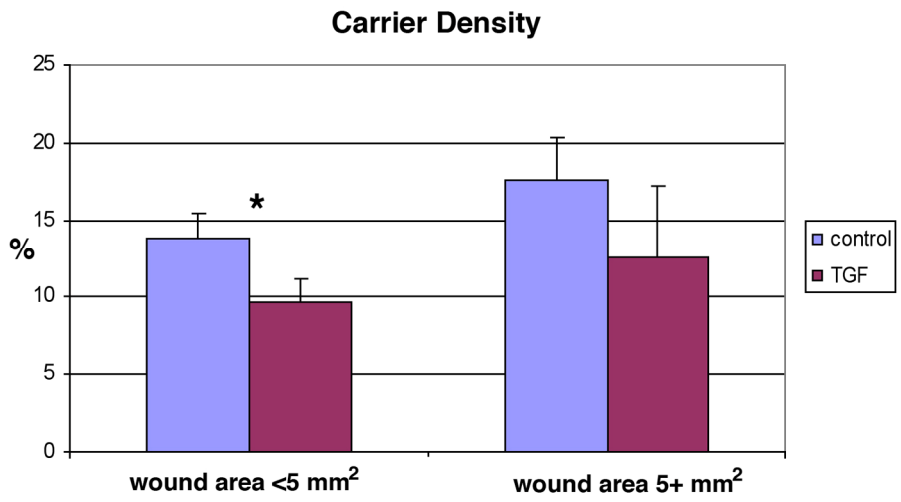

Figure 3. Carrier density by wound area (* $p<0.05$). Note significantly smaller carrier density for the rhTGF-ß$_1$ group in the smaller wound areas.

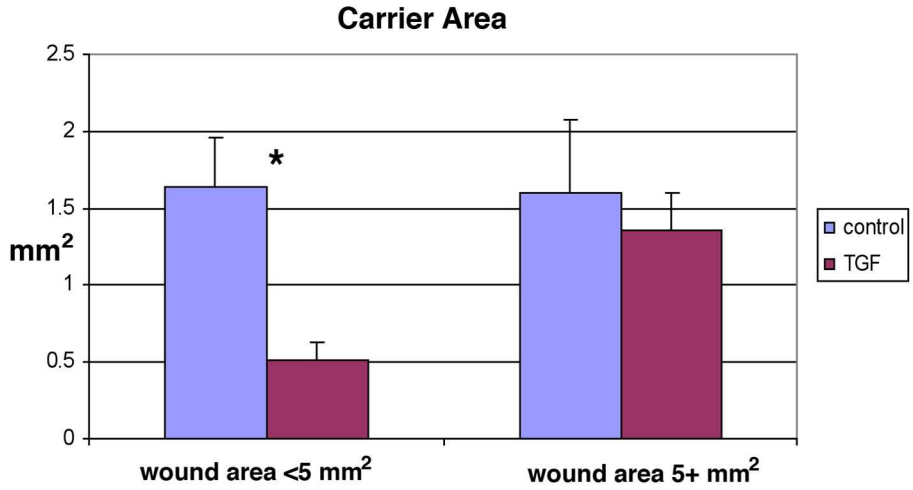

Figure 4. Residual carrier area by wound area (* $p<0.05$). Note significantly smaller carrier area for the rhTGF-ß$_1$ group in the smaller wound areas.

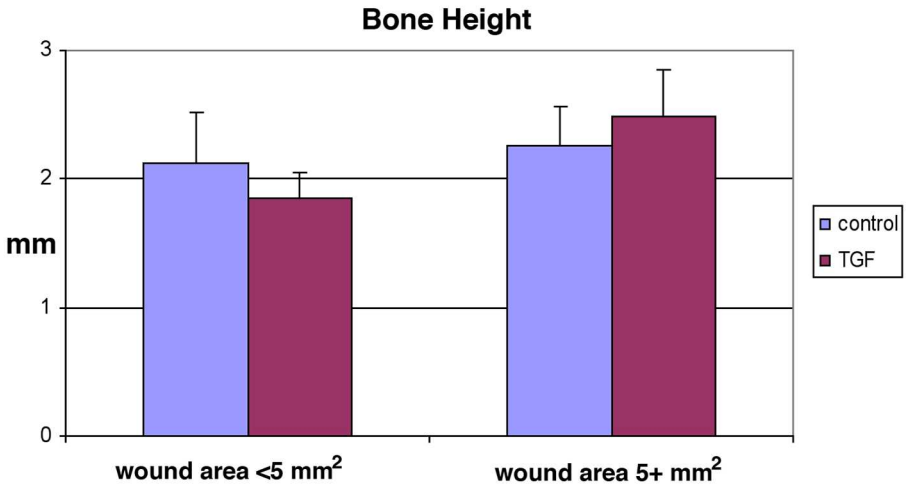

Figure 5. Bone height by wound area. No significant differences were observed between the two groups regarding new bone height irrespective of the wound areas.

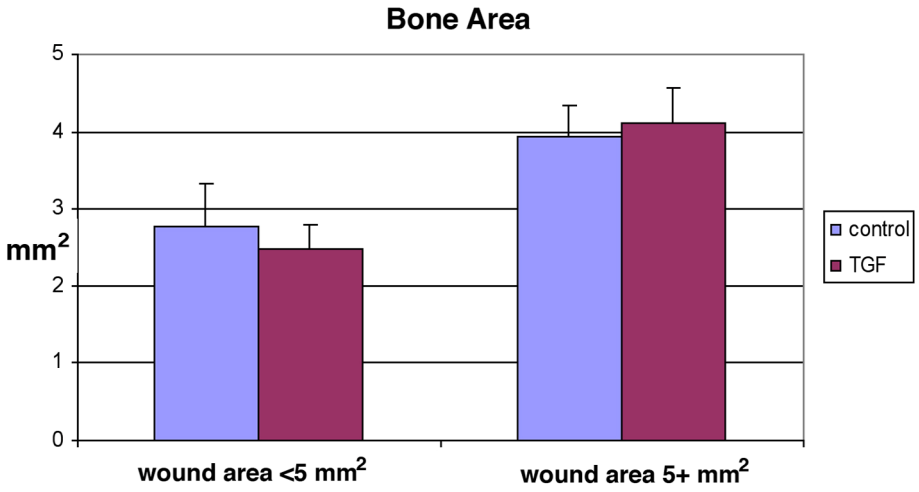

Figure 6. Bone area by wound area. No significant differences were observed between the two groups regarding new bone area irrespective of the wound areas.

국문 요약

변환 성장 유도 단백질인 Tranforming growth factor-ß$_1$은 다양한 종류의 세포들의 성장, 분화, 및 세포 기질의 생성에 관여한다고 알려져 왔다. 또, 골모 세포들의 초기 생성에도 Tranforming growth factor-ß$_1$ 단백질이 활발하게 관여한다고 보고된 바 있어 TGF- ß$_1$을 사용한 치주조직치유나 재생 실험들이 많이 진행되고 있다. 예전의 실험에서, Tranforming growth factor- ß$_1$을 calcium carbonate 운반체를 이용하여 상치조 결손부에 적용한 후 차폐막으로 덮고 골 형성에 어떤 영향을 미치는지 실험하였다. 대조군(control group)에서는 TGF-ß$_1$을 적용하지 않은 채 Biocoral 운반체와 차폐막만 사용하였다. 결과를 살펴보면 두 실험 군 간에 새롭게 생성된 골의 양이나 수직적인 높이에 있어서 유의성 있는 차이가 없었다. 이는 TGF- ß$_1$이 본 상치조 결손부에서 치주조직재생에 부가적인 영향이 없는 것으로 해석될 수 있으나 몇 가지 의문점을 남기게 되었다. 본 연구에서는 이러한 의문점 중 TGF-ß$_1$이 운반체로서 사용된 calcium carbonate (Biocoral)이라는 재료에 미치는 영향에 대하여 조사하기 위해 새로운 조직계측학적 기준들을 첨가하여 실험을 재실시 하였다.

새롭게 생성된 골의 양 (area)과 수직적인 높이 (height)는 두 실험 군 간에 유의성 있는 차이가 없었고, 새로 생성된 백악질은 극히 제한적이었다. 잔존하는 운반체 (calcium carbonate)의 양을 비교해보았을 때, rhTFG-ß$_1$ 군에서 운반체의 양이 현저히 감소됨을 관찰할 수 있었다. 결론적으로 rhTFG-ß$_1$이 calcium carbonate 운반체를 일련의 생물학적인 반응을 통하여 흡수시킬 수 있다는 사실이 입증되었고, 이를 더 넓은 의미로 해석한다면 치주조직재생에 사용되는 여러 성장인자들이 운반체로 사용되는 생물학적 물질들에 영향을 미칠 수 있다는 결론을 내릴 수 있겠다.

핵심되는 말

변환성장유도 단백질 (Transforming growth factor Beta-1); 운반체 (calcium carbonate carrier); 생물학적 흡수 (biodegradation).