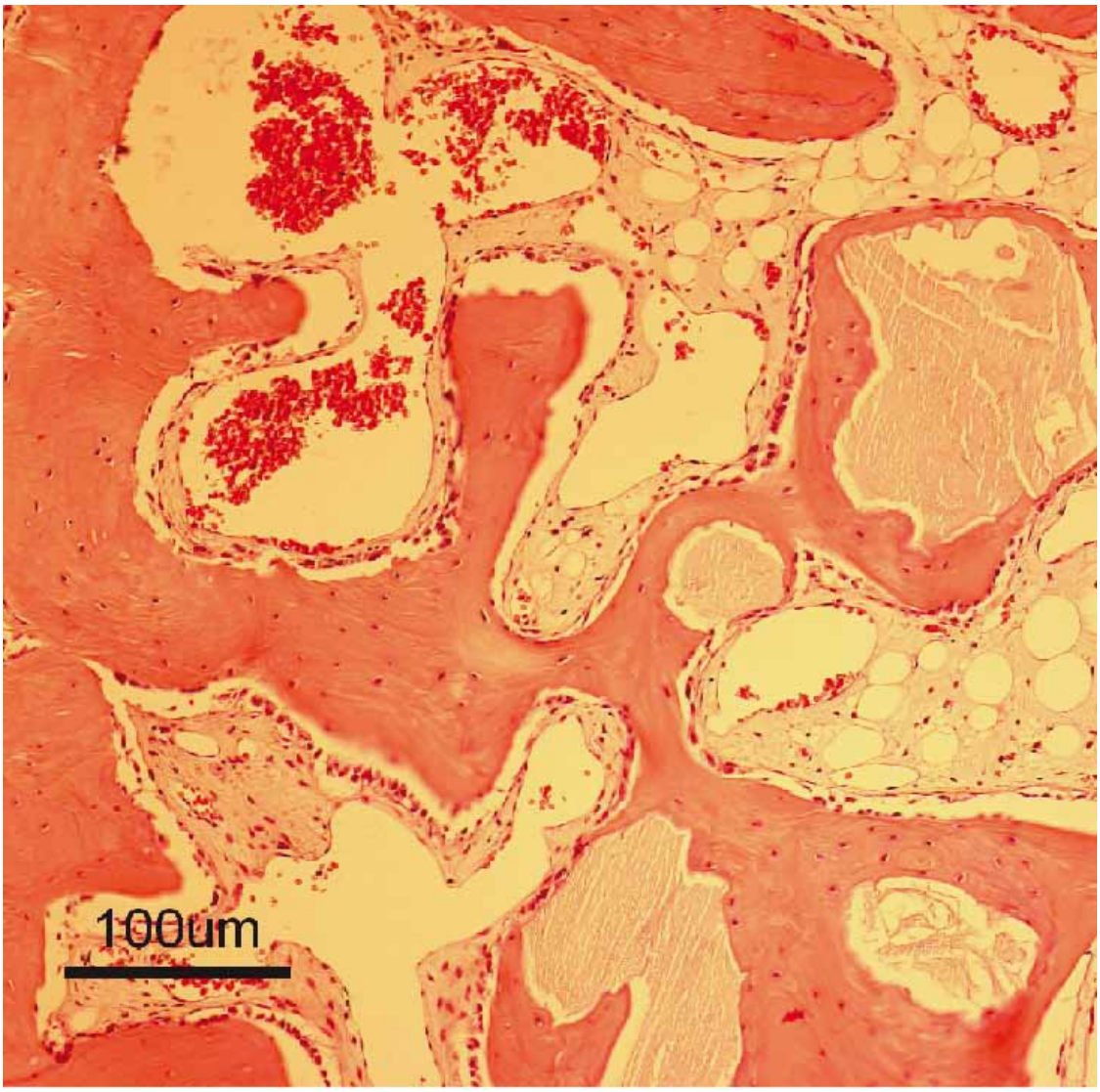
Experimental studies



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EXPERIMENTAL STUDIES

019

The bone tissue responses to prehydrated and collagenated cortico-cancellous porcine bone grafts: a study in rabbit maxillary defects

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ORIGINAL ARTICLE
Clinical Implant Dentistry and Related Research
2008 Dec;10(4):264-70

ABSTRACT

Bone substitutes of xenogeneic origin are frequently used as grafting materials for filling bone defects and maxillary sinus floor augmentation procedures. To be effective, bone substitutes must have osteoconductive properties and be completely replaced with new bone with time. In order to improve the clinical handling, it is possible to add collagen gel to prehydrated and collagenated porcine bone (PCPB) particles, with the result of a sticky and moldable material which facilitates its application in the site to be filled.

As the possible influence of the gel on the bone tissue response is not known, the objective of the study was to histologically evaluate the bone tissue responses to PCPB graft with or without collagen gel and to evaluate the resorption/degradation properties of the biomaterials.

For these study, bilateral bone defects (dimensions: 5x8x3 mm) were created in the maxilla of 14 rabbits. The defects were filled with prehydrated and collagenated cortico-cancellous porcine bone (PCPB) particles (OsteoBiol® *Gen-Os*®, Tecnoss®, Giaveno, Italy - granulometry: 250-1000 μm) as control material, or PCPB particles mixed with collagen gel (OsteoBiol® *mp3*®, Tecnoss®, granulometry: 600-1000 μm) as test material. A collagen membrane (OsteoBiol® *Evolution*, Tecnoss®) was used to cover the defect and to prevent migration of the particles and the wounds were closed with resorbable sutures. Animals were killed after 2 (n=3), 4 (n=3), and 8 weeks (n=8) for histological and morphometrical evaluations.

According to the results of these evaluations, there was no obvious difference between the test and control materials. There were no signs of adverse reactions, and both osteogenesis and angiogenesis followed ordinary time frames. Both materials showed bone formation directly on the particles by typical osteoblastic seams. The bone area increased with time (2-8 weeks) for both sides, from 16,2% (control) and 19,2% (test) to 42,7 and 43,8%, respectively. The PCPB, whether mixed with collagen gel or not, was resorbed by osteoclasts as well as part of remodeling with the formation of osteons within the particles. Morphometry showed a decrease of PCPB area from 19,4% (control) and 23,8% (test) after 2 weeks to 3,7 and 9,3% after 8 weeks, respectively. The histology showed that the membrane had fulfilled its function and was well integrated with the overlaying soft tissues.

CONCLUSIONS

From the findings of this study, it is possible to conclude that mixing collagen gel and PCPB to facilitate the clinical handling does not influence the bone tissue responses to the material, which exhibited osteoconductive properties and was resorbed with time. Both graft materials exhibited osteoconductive properties as bone formation with typical osteoblastic seams observed directly on the surface of the grafted particles. The morphometric measurements showed increased bone area with time in parallel with a decrease of the graft area. The Authors concluded that *"collagenated porcine bone exhibits good biocompatibility and osteoconductive properties, whether mixed with collagen gel or not. In this model, the material was resorbed by surface osteoclasts as well as part of remodeling with the formation of osteons"*.

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EXPERIMENTAL STUDIES

066

Comparison of a xenogeneic and an alloplastic material used in dental implants in terms of physico-chemical characteristics and in vivo inflammatory response

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ORIGINAL ARTICLE
Materials Science and Engineering C, Materials for biological applications
2013 Aug 1; 33(6):3506-13

ABSTRACT

When the bone volume available is not sufficient for the proper rehabilitation of the patient, it is possible to use bone grafts of different types (autogenous bone, allografts xenografts and synthetic materials), all with specific advantages and disadvantages. In most cases, because of the lack of reliable information on their indications and effectiveness, as well as of comparative studies, the choice of the grafting material is left to the surgeon's preferences.
In this study, the Authors evaluated two commercial bone grafts used in dentistry: OsteoBiol® *Gen-Os*® (Tecnoss®, Giaveno, Italy) a xenograft of porcine origin, formed by hydroxyapatite (HA) and collagen type I, having 80% of cancellous bone and 20% of cortical bone; and Bonelike® (Medmat Innovation, Porto, Portugal) a synthetic bone substitute, formed by a patented glass-reinforced hydroxyapatite.
These two biomaterials were evaluated in terms of chemical composition, crystallinity, particle size and size distribution, porosity, surface area and density. Moreover, they were tested *in vivo* with reference to their inflammatory response after intramuscular injection in rats.
The evaluation revealed that Bonelike® and OsteoBiol®, although used in the clinical practice for the same purposes, possess markedly different chemical and physical properties and that they induce different inflammatory responses after their implantation.

CONCLUSIONS

The results of this study show that these two biomaterials have quite distinct properties and the tissue response elicited by Bonelike® granules was consistently more intense than that triggered by OsteoBiol® granules, particularly in terms of collagen production and formation of fibrous capsule.
Consequently, the Author concluded that *"the thorough characterization of these materials revealed substantial differences in their physico-chemical properties that seem to explain, at least partly, the more intense inflammatory response of Bonelike®"*.

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EXPERIMENTAL STUDIES

080

Influence of local administration of pamidronate on extraction socket healing – a histomorphometric proof-of-principle pre-clinical in vivo evaluation

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ORIGINAL ARTICLE
Clinical Oral Implants Research
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ABSTRACT

After tooth extraction, the physiological socket remodelling results in marked volumetric changes in both the hard and soft tissue of the alveolar ridge. The possibility to mantain hard and soft tissue volume after tooth extraction is important in order to avoid a more complex treatment, as augmentation procedures.
To reduce hard tissue loss after tooth extraction it has been suggested to interfere pharmacologically with bone remodelling with, for example, a systemic administration of bisphosphonates.
The aim of this study was to evaluate the influence on extraction socket healing of local administration of pamidronate, adsorbed on a collagenated porcine bone substitute. Two American Fox-hound dogs were subjected to tooth extraction and the sockets were then loosely filled, in a split-mouth fashion, with a collagenated porcine bone substitute (OsteoBiol® *Gen-Os*®, Tecnoss®, Giaveno, Italy; CPB), rehydrated either with 90 mg/ml pamidronate (Aredia®; test) or with sterile saline (control). After 4 months of healing, the Authors proceeded with the histological evaluation revealing substantial differences in healing patterns: control sites presented with various amounts of newly formed bone and no evidence of CPB inside the socket; in contrast, limited amounts of bone were observed at test sites, which were filled with CPB mainly embedded in connective tissue.

CONCLUSIONS

Based on the results of the histological evaluation, the Authors conclusion is that *"local administration of pamidronate adsorbed on a collagenated porcine bone substitute in particulate form appeared to delay extraction socket healing, but may also reduce post-extraction dimensional changes in terms of horizontal bone width. Additionally, pamidronate appears to obstruct resorption of the porcine bone substitute"*.

Abstract author: Cristina Rodighiero, dental journalist, free publication, not for resale. Printed by Tecnoss® Dental s.r.l.

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EXPERIMENTAL STUDIES

098

Bone regeneration in iliac crestal defects: an experimental study on sheep

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ORIGINAL ARTICLE
Hindawi Publishing Corporation
BioMed Research International
2016;2016:4086870

ABSTRACT

Successful implant placement requires adequate alveolar ridge dimensions and, if the implant site presents a lack of bone, Guided Bone Regeneration (GBR) is the surgical procedure commonly performed in order to provide an augmentation in terms of volume for the insertion of dental implants. Several types of membranes and biomaterials have been proposed for GBR techniques and the selection of the most appropriate grafting material is one of the key factors in achieving adequate bone formation.
The aim of the present study was to determine the in vivo tissue responses and gap healing patterns around dental implants treated with cortico-cancellous porcine bone blocks, collagenated cortico-cancellous porcine bone versus only membrane in a standardized sheep peri-implant gap-defect model. In the iliac crest of six sheep 4 defects were created for the insertion of an implant and the defects were filled with 1) control, only membrane (OsteoBiol® *Evolution*, Tecnoss®, Giaveno, Italy); 2) 250–1000 μm cortico-cancellous particulate porcine bone mix (OsteoBiol® *Gen-Os*®, Tecnoss®) + resorbable equine pericardium membrane (OsteoBiol® *Evolution*) (test 1); 3) cancellous equine bone blocks (OsteoBiol® *Sp-Block*, Tecnoss®) + resorbable membrane (OsteoBiol® *Evolution*) (test 2); 4) pre-hydrated collagenated cortico-cancellous porcine bone mix (90% granulated mix, 10% collagen gel) (OsteoBiol® *mp3*®, Tecnoss®) + membrane (OsteoBiol® *Evolution*) (test 3). The animals were sacrificed after a 4-month healing period and all specimens were processed and analyzed with histomorphometry, with the result that all experimental groups showed an increase of new bone. From the findings it is evident that particles of cortico-cancellous porcine bone 250–1000 μm particulate mix (CCPB) favour bone formation with a result similar to those obtained with pre-hydrated collagenated cortico-cancellous porcine bone mix (PCCPB). All biomaterials used in the present study were characterized by the presence of bone formation and absence of inflammatory cell infiltrates. However, the defect treated by membrane alone was characterized by the presence of soft tissues and a little immature bone.

CONCLUSIONS

As stated by the Authors, "*the function of the graft is not only to improve the space-making capabilities of the membrane, but also to provide additional points on which osteoblasts can start forming new bone. We have shown that CCPB and PCCPB promote bone regeneration in large defects (7 mm wide and 4 mm deep) around dental implants*".
In conclusion, this study demonstrates that particulate porcine bone mix and porcine cortico-cancellous collagenated pre-hydrated bone mix, used as scaffolds, induce bone regeneration and these findings suggest that these biomaterials are characterized by a high biocompatibility and can induce a faster and greater bone formation.

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Influence of a collagen membrane positioned subjacent the sinus mucosa following the elevation of the maxillary sinus. A histomorphometric study in rabbits

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ABSTRACT

In order to allow implant placement in the posterior maxillary regions, it is necessary to increase bone volume by means of sinus floor elevation. This procedure is widely applied and various biomaterials have been recommended to fill the elevated space. In case of a perforation of the sinus mucosa, it has been suggested to apply resorbable collagen membranes to protect the perforation. In order to have further information about the role of a collagen membrane placed subjacent the sinus mucosa, this study aimed to evaluate the healing after elevation of the sinus mucosa when a collagen membrane was placed between the sinus mucosa and a xenograft used as filler. In this study, 18 rabbits were used. Sinus mucosa elevation was performed bilaterally. After elevation of the sinus mucosa, a small piece of equine collagen membrane (OsteoBiol® *Evolution*, Tecnoss®, Giaveno, Italy) was placed subjacent the sinus mucosa at one site (test site), while no membranes were placed within the sinus at the control sites. At both sites, a collagenated cortico-cancellous porcine bone (OsteoBiol® *Gen-Os*®, Tecnoss®) was placed within the elevated space. The subsequent analysis showed that the elevated area was reduced between 2 and 8 weeks of healing by about 25% at the test and 47% at the control sites. After 8 weeks of healing, the mineralized new bone within the elevated space was 18.2±5.5% at the test and 26.7±7.7% at the control sites. Within the available space at the test site, the percentage was 27.3±7.0% after 8 weeks of healing. At 2 and 8 weeks of healing, within the elevated space, the xenograft proportion was 30.9±4.4% and 6.9±2.8% at the test, and 35.2±7.3% and 9.6±4.9% at the control sites, respectively. When the marrow spaces were counted together with the mineralized bone, the total bone formed within the available space after 8 weeks was 46.71% and 55.14% at the test and control sites, respectively.

CONCLUSIONS

From the results of the present study, new bone appeared to form from the native bone of the sinus walls and then propagated toward the middle and the submucosa regions. The collagen membrane contributed to maintain the available area, but the morphometric analyses of the healing in the elevated region after sinus membrane elevation were very similar when an internal collagenous membrane was placed as without the membrane placement. Likewise, the healing process in the elevated region appeared to be largely unaffected by the application of an internal collagenous membrane.

ORIGINAL ARTICLE
Clinical Oral Implants Research
2017 Dec;28(12):1567-1576

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EXPERIMENTAL STUDIES

138

Reposition of the bone plate over the antrostomy in maxillary sinus augmentation: a histomorphometric study in rabbits

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ORIGINAL ARTICLE
Clinical Oral Implants Research
2018 Aug;29(8):821-834

ABSTRACT

After sinus floor elevation, it is common to use membranes in order to cover the lateral access window and this approach showed better results than leaving the antrostomy uncovered. In literature different results have been reported following the two approaches and so the Authors of the present study evidenced the need of further data to describe the influence on healing of the closure of the bone window on the lateral antrostomy and on the integration of the bone window plate to the adjacent bone when ethyl-2-cyanoacrylate is used as fixative. Therefore, the aim of this experimental study was to test if the repositioning of the bony plate secured with a cyanoacrylate (test site) over the antrostomy in maxillary sinus augmentation was superior to the coverage of the antrostomy with a collagen membrane (control site) in terms of bone augmentation area and bone density. Moreover, the Authors assess tissue composition and healing processes 2, 4 and 8 weeks after sinus mucosa elevation within the elevated area and in the antrostomy. Eighteen male New Zealand white rabbits were selected and divided in three groups of different periods of healing, i.e., 2, 4, and 8 weeks, of six animals each. After the exposure of the nasal bone, a rectangular access window was prepared, removing the bony plate. A bilateral sinus mucosa elevation was performed, and the space filled with a collagenated cortico-cancellous porcine bone (OsteoBiol® *Gen-Os*®; Tecnoss®, Giaveno, Italy). At the test site, the bone plate was repositioned and secured to the walls of the antrostomy with drops of ethyl-2-cyanoacrylate adhesive. At the contra-lateral control sites, an equine collagen membrane (OsteoBiol® *Evolution*, Tecnoss®) was used to cover the antrostomy. Per group, 6 animals were sacrificed after 2, 4, and 8 weeks of healing, respectively. The histological evaluation showed that the augmented area after elevation decreased between 2 and 8 weeks from 9.4 ± 1.8 to 4.8 ± 2.8 mm^2 at the test and from 9.5 ± 2.6 and 5.1 ± 1.6 mm^2 at the control sites. Small amounts of new bone were seen after 2 weeks in both groups forming from the bony sinus walls and the area of the remaining defects decreased over time at both test and control sites. New bone density increased over time in both groups, with no statistically significant differences. Small residual defects were present both at the test sites in the margin of the bone plate, and at the control sites in the center of the antrostomy.

CONCLUSIONS

The bone healing in the elevated sinus space was similar irrespective of the coverage of the antrostomy. Even if the inference of the results from the present animal study to similar clinical situations in humans has to be considered with care, the Authors concluded that *"the protection of the antrostomy by either repositioning the bony plate or covering the window with a collagen membrane resulted in similar outcomes in terms of new bone formation and xenograft resorption inside the available area. After 8 weeks, the bony plate was well incorporated into the subjacent new bone, while at the control sites, the healing was still incomplete. Residual defects were present in both groups"*.

Abstract author: Cristina Rodighiero, dental journalist, free publication, not for resale. Printed by Tecnoss® Dental s.r.l.

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Histological and micro-computed tomography evaluations of newly formed bone after maxillary sinus augmentation using a xenograft with similar density and mineral content of bone: an experimental study in rabbits

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ABSTRACT

It has been demonstrated that new bone forms after sinus floor elevation, but the tendency of the maxillary sinus to regain the lost space after sinus floor elevation has been documented as well. To counteract the physiological shrinkage of the elevated space, the use of bone fillers has been suggested.

The aim of the present study was to evaluate possible differences in the assessment of bone formation between histological and micro-computed tomography (CT) analyses in maxillary sinuses augmented with a xenograft with similar density and mineral content of bone. Eighteen male New Zealand white rabbits were randomly divided into three groups. After the sinus mucosa elevation, in the test sites an equine collagen membrane (OsteoBiol® Evolution 0.3 mm, Tecnoss®, Giaveno, Italy) was placed subjacent the sinus mucosa and both sinuses were subsequently filled with similar amounts of collagenated cortico-cancellous porcine bone (OsteoBiol® *Gen-Os*®, Tecnoss®; 250–1,000 μm). Six rabbits per group were sacrificed after 2, 4, and 8 weeks of healing. Biopsies were retrieved, scanned in a high-resolution micro-CT, and subsequently subjected to histological assessments. The histological analyses showed that bone increased over time, from 7.5 ± 2.4% to 27.0 ± 5.3%, between 2 and 8 weeks of healing. After 2 weeks, higher content of xenograft was found at the histological compared with the micro-CT analyses, especially in the middle regions of the sinus. After 8 weeks of healing, higher percentages of bone were found at the histological compared with the micro-CT analyses, being the differences statistically significant.

CONCLUSIONS

Within the limitation of this study, the Authors concluded that *"the outcomes of a micro-CT analysis performed in an early phase of healing may be altered when a resorbable bone substitute with similar density and mineral content of bone is applied"*.

ORIGINAL ARTICLE
Clinical and Experimental Dental Research
2018;1–7

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EXPERIMENTAL STUDIES

Effects of systemic erythropoietin treatment and heterogeneous xenograft in combination on bone regeneration of a critical-size defect in an experimental model

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ORIGINAL ARTICLE
Journal of Cranio-maxillo-facial Surgery
2018 Nov;46(11):1919-1923

ABSTRACT

In order to fill bone defects, different biomaterials like autogenous, homogenous (allograft) and heterogeneous (xenograft) bone grafts, and synthetic (alloplastic) substitutes can be used, as they all present fundamental osteogenic, osteoinductive and osteoconductive properties.
As it has been demonstrated that impaired bone vascularity results in inadequate osteogenesis in bone repair with decreased bone formation, researchers have focused their attention on the possibilities to enhance angiogenesis for proper bone regeneration. In this context, EPO, a physiologic hormone whose essential role is erythrocyte production, has gained more and more interest. Anyway, besides its osteogenic and angiogenic effects in different bone defect models, little is known about potential regenerative effects of EPO on the grafting of defects. Consequently, the aim of the present study was to evaluate the effects of systemic EPO treatment alone or in combination with xenogenic bone graft augmentation on bone regeneration. In this study, 11 adult male rats were subjected to bilateral 5 mm critical size bone defects on the parietal bones under general anaesthesia. Right parietal bone defects were augmented with cortico- cancellous heterologous xenograft bone particles (Osteobiol® *Gen-Os*®, Tecnoss®, Giaveno, Italy) and bone defects of left parietal bones were left empty. The 11 rats were randomly divided in two groups. One group of rats received (i) vehicle (n 1⁄4 6) and other group received (ii) EPO (500IU kg/day) (n 1⁄4 5). EPO treatment was continued for 28 days. After that period, animals were sacrificed and their calvaria were harvested for histomorphometric evaluation. Xenogenic graft augmentation enhanced bone formation and vascularization significantly in either vehicle or EPO treated groups ($p < 0.05$). Histomorphometric analysis of new bone formation revealed that bone formation in the graft group was significantly higher than in the control (p 1⁄4 0.036) group. Histomorphometric results show that angiogenesis was similar in the EPO treated group and the control group. However, angiogenesis was significantly higher in the group treated with a combination of systemic EPO treatment with graft augmentation than graft augmentation alone ($P < 0.01$).

CONCLUSIONS

Within the limitations of the present study, The Authors concluded that *"systemic EPO has no effect on angiogenesis and bone formation of critical-size calvarial bone defects at the end of four weeks. Xenograft augmentation for the treatment of bone defects enhances both angiogenesis and bone formation essential for the physiological function of bone. The present findings corroborate the idea that critical size bone defects require a graft for proper bone healing. Furthermore, the present study indicates that xenograft augmentation potentiates the angiogenic effect of the EPO treatment and systemic EPO treatment may be a promising agent for adjuvant therapy during xenograft augmented bone healing"*.