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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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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 ant 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"*.

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