Combined Use of Platelet-rich Plasma (PRP) and Autologous Bone Grafts for Regeneration of Long Bone Critical-size Defects

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Introduction: Large diaphyseal bone defects represent a therapeutical challenge to orthopedic surgeons and are often associated with a high morbidity. Autologous bone grafting is still considered to be the gold standard in treating large bony defects despite the disadvantages arising from donor site morbidity, limited amount of donor bone, increased operative time and length of hospitalization. Besides this gold standard, the use of platelet-rich plasma (PRP) for improving bone defect healing is discussed controversially. By using PRP with a distinctly higher concentration of platelets compared to native blood, positive effects on bone healing could be shown. Receptors for these growth factors were also found in autologous cancellous bone graft. Therefore a combined use of PRP and autologous cancellous bone graft could represent a successful method to promote bone healing. The aim of this study was to evaluate the treatment of a diaphyseal critical-size defect in a rabbit model with a combination of PRP and autologous cancellous bone. Furthermore, the assumed synergistic effects of combining PRP with autologous bone were investigated.

Methods: A critical-size defect of the radial diaphysis in 24 New Zealand white rabbits was filled either with autologous cancellous graft as control group or with autologous cancellous graft combined with autologous PRP. Six animals of each group were sacrificed after three and six weeks. The quantitative analysis of new bone formation was measured histomorphometrically in the central and cortical area of the defect zone. Furthermore, the extent of bone healing was determined quantitatively by cone-beam computed tomography (CBCT). In addition, the accumulation factor of the platelet count in PRP compared to native blood was measured and the concentrations of the growth factors PDGF and TGF-ß1 were also quantified in serum and in PRP using the ELISA-Technique.

The outcome measures of the radiological and histomorphometrical evaluations were examined by two-way analysis of variance (ANOVA). Differences between the independent variables were checked in post hoc tests [Tuckey's studentized range (HSD) tests for variables]. Significance was defined as a p value < 0.05. For evaluating the outcome measures of the PRP preparations (comparison of 2 groups) the unpaired student's t-test was used, p < 0.05 was considered statistically significant.

Results: The histomorphometrical analysis demonstrated a significantly improved new bone formation in the central as well as the cortical defect zone after 6 weeks compared to 3 weeks (Figure 2 and 3). Furthermore, a significant improvement in bone healing was observed histomorphometrically in the PRP groups concerning the central area of the defect zone as well as the cortical defect zone after 3 and 6 weeks compared to control groups without PRP treatment (Figure 2 and 3). The radiological findings
were in accordance with the histomorphometrical results (Figure 1). Comparing native blood and PRP a significant enrichment of platelets (5.4 fold) was detected in PRP (p < 0.01). In addition, the concentrations of PDGF and TGF-β1 increased significantly compared to serum (p < 0.01).

**Discussion:** Within this animal study the combination of PRP and autologous cancellous bone grafts improved bone healing significantly compared to the sole application of autologous bone. The contradictory results on the effectiveness of PRP in other studies may be related to the use of various and non-standardized methods to obtain PRP. Therefore, further efforts should be initiated to establish a standardized protocol of PRP preparation in order to increase the acceptance of PRP and autologous bone for bone healing disorders in clinical use. The synergistic effects of PRP and autologous bone may reduce the time needed for healing of bone defects and it could lead to a reduction in the needed amount of autologous bone grafts.

**Significance:** We consider this a significant study because all aims are achieved and this may lead to a change in the current concepts.

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**Figure 1 A-D:** CBCT-volumetry of the radial defect in coronal images: A) autograft 3 weeks, B) autograft 6 weeks, C) autograft PRP 3 weeks, D) autograft PRP 6 weeks

**Figure 2 A-D:** Histological sections of the A) autograft group 3 weeks after surgery, B) autograft group 6 weeks after surgery, C) autograft PRP group 3 weeks after surgery, D) autograft PRP group 6 weeks after surgery.
Graph 1: Histomorphometrical analysis of the area of new bone in relation to the total defect area concerning the cortical defect zone.

Graph 2: Histomorphometrical analysis of the area of new bone in relation to the total defect area concerning the central defect zone.

Graph 3: Quantification of the volume of new bone in relation to the total defect area by CBCT-volumetry.

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