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Paper #109

The Effect of Platelet Rich Plasma on Articular Cartilage during the Development of Osteoarthritis in a Anterior Cruciate Ligament Transection Rabbit Model

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Summary:
Platelet rich plasma has protective effect on the joint during the development of osteoarthritis following anterior cruciate ligament transection in a rabbit model.

Abstract:
Introduction:
Development of osteoarthritis is characterized by articular cartilage loss, osteophyte formation, joint effusion, synovial inflammation and so on. Intra-articular injection of agents such as hyaluronan or corticosteroid is used for the symptom management, though the modification of disease progression is not adequate. Platelet rich plasma (PRP) is the fraction of autologous blood including high concentration of platelets which serves as a reservoir for growth factors known to regulate tissue healing process. The clinical use of PRP in orthopedic field is growing fast, but the in vivo studies to support the PRP usage are relatively insufficient. Several osteoarthritis models of rabbit have been developed. Among them, anterior cruciate ligament transection (ACLT) model produces cartilage lesions large enough for evaluating structural effects of specific treatment with reduced animal morbidity. The purpose of this study was to investigate the in vivo effect of intra-articular injection of PRP on the maintenance of the articular cartilage and the gene expression of various inflammatory mediators in a ACLT rabbit model of osteoarthritis.

Methods:
Twenty mature NZW rabbits were divided into four groups; control (normal, left knees of the first ten rabbits), PRP injection to normal (right knees of the first ten rabbits), ACLT (left knees of the second ten rabbits), PRP injection to ACLT (right knees of the second ten rabbits). In ACLT groups, ACL transection was performed by completely excising the ACL. In groups where the rabbit received PRP, intra-articular injection of 500uL PRP was performed at 2,4,6, and 8 weeks after surgery. All rabbits were sacrificed 10 weeks after surgery and evaluated. Gross morphologies were inspected after india ink application. Medial, lateral femoral condyles, medial, lateral tibial plateaus, and medial, lateral menisci were evaluated by ICRS guideline. Amount of joint effusion and osteophyte formation were also checked. Microscopic scoring of cartilage alteration was performed under Safranin-O and H&E staining using grading system by Pritzker and colleagues. Messenger RNA expression levels of typical genes regarding catabolic enzymes, inflammation, and cartilage matrix in synovium, cartilage, and ACL were analyzed using real time polymerase chain reaction. MMP-1,3,9, TIMP-1, TNF-a, IL-1ß, Sox-9, and Type II collagen were the genes evaluated. All the experimental procedures involving the use of animals were in accordance with the NIH Guide for the Care and Use of Laboratory Animals and the procedures were approved by Ethics Committee of our institute.

Results:

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Degenerative changes in articular joints were apparent in ACLT groups compared to non-ACLT groups. In ACLT groups, gross morphologic evaluation showed less severe cartilage damage on medial, lateral femoral condyles and tibial plateaus in a group which received PRP compared to a group without PRP. Evaluation regarding medial and lateral menisci alteration, joint effusion, and osteophyte formation also showed similar results. In non-ACLT groups, a group with PRP showed better results compared to a group without PRP, but the difference was less than that between the two ACLT groups. Histologic evaluation results were similar to gross morphologic evaluations. These results were supported by gene analysis. Messenger RNA expression levels of genes related to inflammation (TNF-a, IL-1ß) and catabolic enzymes (MMP-1,3,9) were elevated in ACLT groups compared to non-ACLT groups and the extent of elevations was less profound in a groups which received PRP. Similarly, mRNA levels of genes related to catabolic enzyme inhibitor (TIMP-1) and cartilage matrix (Sox-9, Type II collagen) were decreased in ACLT groups and the extent of decreases was less in a group with PRP.

Discussion and Conclusion:
Using gross morphologic, histologic, and gene expression analyses, this study demonstrated quantitatively and qualitatively that the exogenously injected PRP has protective effect on the joint during the development of osteoarthritis in a rabbit ACLT model. Although the exact mechanism of PRP on the protection of joint during the development of osteoarthritis is not clear, this study supports the usage of PRP in the clinical orthopedic field.