BONE MARROW ASPIRATE WITH OR WITHOUT PLATELET CONCENTRATES AS A BONE GRAFT SUBSTITUTE FOR POSTEROLATERAL SPINAL FUSION: A RANDOMIZED, CONTROLLED STUDY USING AN ANIMAL MODEL

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Introduction

Attempts are under way to develop biologic alternatives that can improve union rates in spinal fusions without complications (30%) associated with the gold standard iliac crest autograft. Bone marrow, a rich source of osteoprogenitor cells, was shown to effectively increase healing rates in both, spinal and long bone applications, in both preclinical and clinical cases. Platelet-rich plasma (PRP) is a 4-5x concentrate of native platelets that enhance spinal fusions by releasing a wide range of local autologous growth factors, including TGF-β and PDGF, which are known to stimulate vascular ingrowth, and cell migration. In this study, a well-established rabbit posterolateral fusion model was used to evaluate the role of PRP in bone fusion. A randomized, controlled study was undertaken to compare bone formation using either bone marrow and calcium phosphates (TCP) alone, or bone marrow and calcium phosphates enriched with PRP and compared with autograft controls.

Materials and Methods

Study Design Thirty-three New Zealand White rabbits randomly divided into three groups underwent a well-established posterolateral intertransverse process spinal fusion model. (*Group 1)*, the control group, consisted of rabbits that underwent a posterolateral fusion between L5-6 with autologous iliac crest bone graft harvested from both iliac crests. (*Group 2)* rabbits underwent a L5-6 posterolateral fusion with TCP Conduit©, BM aspirate harvested from the femur and tibia, and the PRP concentrate. Blood was collected from the ear vein and processed using the Symphony II system (DePuy Spine) to obtain the platelet concentrate. (*Group 3)* rabbits received a L5-6 posterolateral fusion with TCP soaked in BM aspirate without the PRP concentrate.

Manual Palpation At the six weeks postoperative period, the L5 and L6 vertebral segments of the rabbit lumbar spine were harvested en bloc and the soft tissue carefully removed making sure not to disrupt the bony architecture of the posterolateral fusion mass. Three examiners blinded to the treatment groups evaluated the specimens independently. Forces small enough not to produce gross trauma, but great enough to evaluate for gross intervertebral motion were used. The results were graded on a 3 point scale. ***(Table 1)***

Serial *radiographic images* were scanned and stored in digital form immediately post-op, at 4 and 8 weeks. Using *micro-CT imaging*, each specimen was assessed as fused or non-fused, to provide for overall fusion rates. All samples were decalcified, 50 µm sections prepared and stained with hematoxylin and eosin. *Histological* assessments were performed on all samples.

Table 1. **Manual Palpation Grading Scale**	
3	**No motion. Very firm.**
2	**Some movement, noticeably less malleable than surrounding tissue or fused on one side, but not on the other.**
1	**No palpable difference from surrounding tissue and adjacent segments.**

Results

Utilizing a score of either 2 or 3, there was an obvious increase in the segmental stability in 100% and 92% of the autograft and +PRP specimens, while the -PRP group demonstrated good results in 75% of specimens ***(Figure 1).*** Similarly, *average palpation scores* ***(Table 2)*** in all four groups showed evidence of increased spinal stability was seen with all fusion techniques. Autologous bone graft demonstrated the highest average manual palpation score (2.50 ± 0.55) with +PRP next at (2.17 ± 0.54). The groups that underwent a posterolateral fusion without PRP had an average score of 2.06 ± 0.71. X-ray analyses confirmed placement of the grafts. At 4 and 8 weeks, radio-opacity was visible in all cases, most likely because of the presence of either TCP or because of implanted bone grafts (autograft) ***(Figure 2).*** Micro-CT scans ***(Figure 3a and 3b)*** of the harvested spines at 8 weeks from the +PRP group revealed the presence of posterolateral spine fusion. Analysis of histological sections from the +PRP group shows evidence of bone formation in the intertransverse process spinal fusion ***(Figure 4).***

Table 2		
Group	**AVG**	**STD**
Autograft	**2.50**	**0.55**
+PRP	**2.17**	**0.54**
-PRP	**2.06**	**0.71**

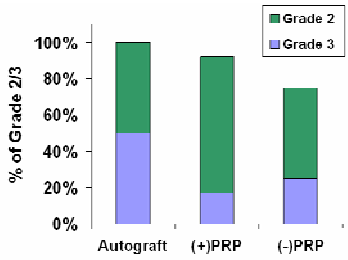

Figure 1

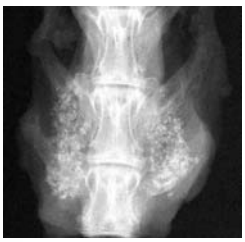

Figure 2: +PRP @ 8 wks

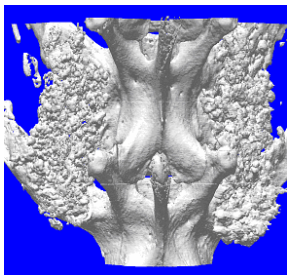

Figure 3a: Dorsal

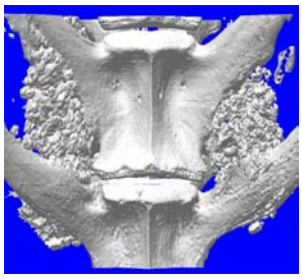

Figure 3b: Ventral

Figure 4: Histology of the Transverse Process (TP)

Discussion

In this randomized controlled animal study we investigated the use of BM aspirate with a TCP osteoconductive scaffold for use as a bone graft substitute for spinal fusions. Furthermore, we investigated the addition of platelet rich growth factors to explore their effect on the quality of the fusion. Platelet rich plasma contains concentrated levels of a variety of osteoinductive factors including platelet derived growth factor (PDGF), a protein found to enhance bone healing by providing stimulatory signals at various stages of osteogenesis. Our study showed that while the autograft group had the highest percentage of fusions the use of BM aspirate on a TCP scaffold was capable of producing a clinically significant result. This was confirmed by imaging and histological evaluation, and more importantly by direct manual inspection. Interestingly, the addition of PRP provided fusion, as well as higher average manual palpation score on direct inspection than did BM aspirate and TCP alone. Addition of PRP, which contains a wide variety of osteogenic signaling proteins, provides the initial cascade necessary to initiate the osteogenic process. The data suggests that selected cases may be amenable to the use of PRP, which can serve to augment traditional methods for posterolateral spinal fusions.

Acknowledgment: Grant Support from DePuy Spine and NIH (NIAMS) T32 AR 050960
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