Evaluation of Autologous Platelet Concentrate for Intertransverse Process Lumbar Fusion

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Abstract

Data on the role of platelet concentrate (PC) in spinal fusion are limited. Using the New Zealand white rabbit model, we compared fusion rates at L5–L6 using 2 different volumes (1.5 cm^3, 3.0 cm^3) of iliac crest autograft with and without PC (4 groups total, 10 animals in each). PC was collected from donor rabbits and adjusted to a concentration of 1×10^6 platelets/mL. Bone growth and fusion were evaluated using biomechanical, radiographic, and histologic testing.

At 1.5 cm^3, autograft alone had a 29% fusion rate, compared with autograft plus PC, which had a 57% fusion rate (P = .06). At 3.0 cm^3, the fusion rate approached 90% in both groups. Radiologic fusion had a 70% correlation with biomechanical test results. Huo/Friedlaender scores were 4.3 (SD, 2.9) for 1.5-cm^3 autograft alone; 5.0 (SD, 3.5) for 1.5-cm^3 autograft plus PC; 4.7 (SD, 2.5) for 3.0-cm^3 autograft alone; and 7.7 (SD, 0.6) for 3.0-cm^3 autograft plus PC.

For 1.5-cm^3 autograft, a trend toward improvement in biomechanically defined fusion was found when PC was added, which suggests that, when the amount of bone graft is limited, PC may function as a graft extender in posterolateral fusion. At higher volumes of bone graft, no appreciable difference was noted between groups. Although radiography revealed fusion masses, the technique was not useful in identifying pseudarthrosis. On histologic analysis, adding PC seemed to result in more mature bone at both volumes, with the most mature bone in the group with 3.0-cm^3 autograft plus PC.

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In the United States, 180,000 to 250,000 spinal fusions are performed each year.[1] Of the numerous types of procedures performed, posterolateral lumbar intertransverse process arthrodesis with use of iliac crest autograft is still commonly performed.[1] As is well documented, use of autograft has its limitations and complications, including limited quantity of available bone, poor bone graft quality, and chronic donor site pain.[2,3] Despite significant advances in the field, not all fusions of the lumbar spine are successful; estimated rates of pseudarthrosis range from 5% to 35%.[4,5] Given the imperfect results of spinal fusion and the morbidity associated with use of autogenous iliac crest bone graft, there has been much interest in developing alternatives that will increase the union rate in spinal fusion and decrease the need for autologous graft.[6-8]

Mechanical enhancements using rigid internal fixation devices have been shown to increase fusion rates and are thought to promote fusion by limiting motion.[9,10] Devices using electrical stimulation and low-intensity ultrasound have also been demonstrated to increase the rate of fusion, but the mechanism of action is less clear.[11-14] Although the aforementioned alternatives may affect the molecular biology of spinal fusion, they fail to directly provide the osteoconductive or osteoinductive properties necessary for adequate bone formation and healing.

Since Urist discovered bone morphogenic proteins (BMPs) in 1965, many polypeptides have been identified as bone growth factors.[15] Growth factors that promote bone formation are desired for use with osteoconductive, biodegradable scaffolds because they have the potential to enhance proliferation and differentiation of osteogenic cells at the site of interest.[16] Recent approaches to spinal fusion have used these osteoinductive agents as potential bone graft alternatives. Preliminary results with use of BMPs are very promising. Extracted and purified protein from cadaveric bone has been used clinically to help heal

femur and tibial nonunions,[15,17] and its efficacy has also been demonstrated in animal models of intertransverse process fusions.[1,7,8,18] In contrast, limited work has been conducted on use of autologous growth factors, platelet concentrate (PC) in particular, and their role in enhancing spinal fusion.[19]

Use of PC has a sound basic science foundation. After bone graft implantation and during initial hematoma formation, cytokines and growth factors are released. Occurring next are cellular recruitment, osteoconduction, osteoinduction, and, finally, remodeling.[20] In healing responses, platelets quickly adhere to the injury site or bone graft surfaces and degranulate, releasing many polypeptide growth factors. The best-studied growth factors in bone healing and graft incorporation are platelet-derived growth factor (PDGF), transforming growth factor (TGF-β), and insulinlike growth factors 1 and 2 (IGF-1, IGF-2).

Lowery and colleagues[19] recently reported on the clinical use of autologous growth factor (AGF) prepared by ultraconcentrating autologous platelets. Their hypothesis was that platelets are a rich source of multiple growth factors that may have a mitogenic effect on mesenchymal cells and osteoblasts. Supporting their predictions, they reported that 100% (19/19) of single-level spine fusions were successful when AGF was used.

We hypothesized that PC could be used to increase the success rate of intertransverse process fusion in the presence of a decreased amount of bone graft. The study reported here was designed to define the functional, radiographic, and histologic outcomes of PC-enhanced intertransverse process fusion in an established New Zealand white rabbit model.[21] To our knowledge, this study is the first to examine the role of autologous PC in spinal fusions in this model.

Methods and Materials

Platelet Concentrate: Preparation and Use

Approximately 100 mL of whole blood was collected from each rabbit using 10 mL of acid citrate dextrose as an anticoagulant. This collected blood was then centrifuged at 300g for 12 minutes to separate the various constituents. Plasma layer and buffy coat were transferred to a new tube and centrifuged for another 12 minutes at 1200g to pellet out the platelets. Excess plasma was then removed, and the platelets were resuspended in the residual plasma to generate PC. PC concentration was adjusted to approximately 1×10^6 platelets/mL.

PC and a thrombin/$CaCl_2$ mixture (1000 units thrombin in 10% $CaCl_2$) were mixed at a ratio of 9:1 and immediately added to the bone graft. The result was a PC clot encasing the autograft. For 1.5-cm^3 autograft, 4.5 cm^3 of PC mixture was added; for 3.0-cm^3 autograft, 3.0 cm^3 of PC mixture was used.

Intertransverse Process Fusion: Surgical Procedure

Adult female New Zealand white rabbits weighing 4.5 to 5 kg were housed in an approved animal facility for a minimum of 1 week before surgery. Single-level intertransverse process fusions were performed at the L5–L6 level, as described by Boden and colleagues.[8,21,22] Preoperative spine x-rays were obtained to rule out underlying bone pathology. Anesthesia was achieved with acepromazine (0.75 mg/kg subcutaneous) followed by ketamine (15 mg/kg) and xylazine (2.5 mg/kg). The rabbits were then intubated, and isoflurane inhalation was used to maintain anesthesia. Enrofloxacin (5-10 mg/kg subcutaneous) was injected immediately before surgery.

The rabbits were shaved, positioned, and prepped in a standard surgical fashion. Either one or both iliac crests were exposed through separate fascial incisions, and approximately 1.5 cm^3 of corticocancellous graft was obtained from each crest. The appropriate levels were identified intraoperatively by referencing from the sacrum with manual palpation.

A dorsal midline incision was made, and then 2 paramedian fascial incisions, and the L5–L6 levels were identified using manual palpation. The L5–L6 transverse processes were decorticated with a power burr, and the shavings were left in the lateral gutters in all cases. One of the 4 grafting options (1.5-cm^3 bone graft alone, 3.0-cm^3 bone graft alone, 1.5-cm^3 bone graft plus PC, 3.0-cm^3 bone graft plus PC) was selected before surgery for each rabbit in a randomized order.

After the grafting material was placed, incisions were closed, and the rabbit was extubated. Postoperative posteroanterior (PA) and lateral spine x-rays were obtained to confirm the level of fusion. A follow-up period of 5 weeks was chosen because fusions have been shown to be distinguishable from nonunions by this time.[22,23] Rabbits were given calcein (10 mg/kg subcutaneous) 1 and 11 days before sacrifice as a fluorescent marker of mineralization for later histologic examination.

Evaluation of Fusion Masses

PA and lateral x-rays obtained after sacrifice were reviewed by 2 independent blinded readers, with fusion defined as continuous bridging of bone from one transverse process to the next. Biomechanical testing was then performed on 7 of 10 specimens. At time of necropsy, the remaining 3 specimens were immediately preserved for histology. All evaluations were accomplished in a blinded fashion. In contrast to the pull-apart testing used by Boden and colleagues,[8,21,22] our laboratory has established functional multidirectional flexibility testing as a more kinematically relevant methodology to evaluate rabbit lumbar spine stability.[24,25] This methodology was thus used for specimen analysis in the present study.

After potting the L4 and L7 vertebrae in resin mounts, L5 and L6 were fitted with Plexiglas motion-detection flags attached to the vertebral bodies by pairs of 0.062-in Kirschner wires. These flags were designed for detection by an optoelectronic motion-measurement system (Optotrak, Northern Digital, Waterloo, Canada). Mean error of this system was previously determined to be 0.014°.[26]

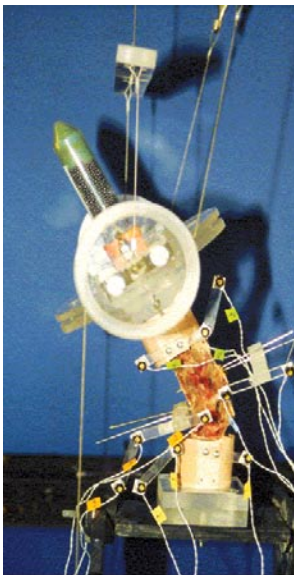

Figure 1. Biomechanical testing apparatus.

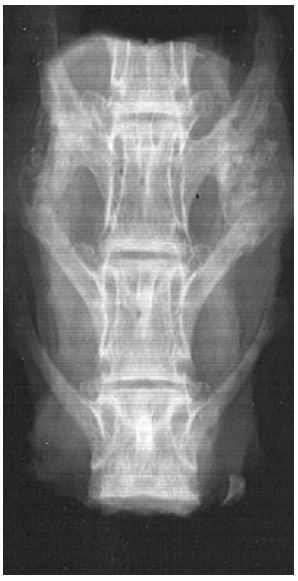

Figure 2. X-ray of postmortem specimen shows radiographic fusion.

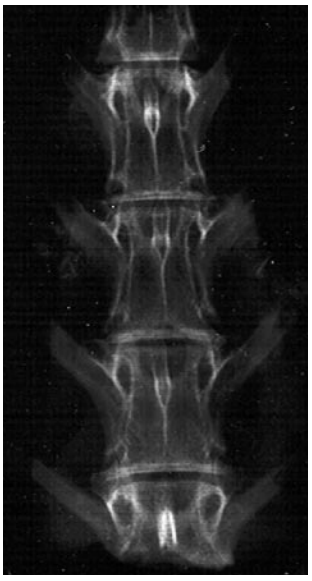

Figure 3. X-ray of postmortem specimen shows radiographic nonunion.

Six pure moments (flexion and extension, right and left lateral bending, right and left torsion) were then applied to the top mount. The maximum moment applied in each direction was 0.27 Nm, which is body mass proportional to the moment applied in human studies.[25] Range of motion (ROM) was measured for each motion tested. Specimens were kept moist with normal saline throughout the testing protocol. Figure 1 depicts the testing apparatus.

Histologic Analysis

Histologic analysis was performed on 3 randomly designated animals in each of the 4 study groups in order to evaluate the maturity of bone induced by autograft plus PC versus autograft alone. This evaluation included assessment of callus constituents (bone, cartilage, fibrous tissue).

Specimens for decalcified sectioning were placed in buffered 10% formalin. After fixation, these specimens were decalcified in EDTA/HCL (ethylenediaminetetraacetic acid/hydrochloric acid) and embedded in paraffin. Six-micron sections were stained with hematoxylin and eosin (H&E). Specimens for undecalcified sectioning were dehydrated through graded ethanols, and cleared in toluene under vacuum and pressure on a Tissue Tek VIP 2000 tissue processor (Global Medical Instrumentation [GMI], Ramsey, Minn). These specimens were then infiltrated with increasing concentrations of methylmethacrylate (MMA) and embedded in MMA. Five-micron-thick sections were stained with toluidine blue, pH 3.7. In addition, unstained 9-micron-thick sections were obtained for analysis of fluorescent labeling. Specimens from the decalcified and the undecalcified groups were then graded in blinded fashion according to the Huo/Friedlaender classification scheme,[27] which histologically scores callus maturation on a 1-to-10 scale based on the presence of fibrous tissue, cartilage, bone, and their respective intermediates.

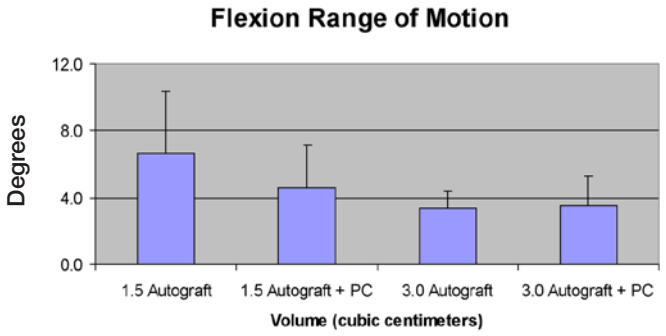

Figure 4. Mean range of motion in flexion for explanted motion segments in each tested group shows a trend toward decreased motion both as the amount of bone graft is increased and, in particular, as platelet concentrate gel is added to the 1.5-cm^3 autograft group.

Results

Radiographic Analysis

Radiographically, 3 (7.5%) of 40 x-ray studies generated interobserver disagreement regarding presence of fusion.

In the 1.5-cm^3 autograft-alone group, 4 animals were found to be radiographically fused, and 5 were found to be unfused; there was interobserver disagreement about 1 animal. In the 3.0-cm^3 autograft-alone group, 9 animals had a radiographic fusion, and 1 had a failure of fusion. In the 1.5-cm^3 autograft-plus-PC group, 4 animals had a radiographic fusion, 4 had failure of fusion, and 1 was the subject of disagreement. In the 3.0-cm^3 autograft-plus-PC group, 6 animals had a radiographic fusion, 3 had a failure of fusion, and 1 was the subject of interobserver disagreement. Figures 2 and 3 depict a radiographically fused specimen and an unfused specimen, respectively.

Biomechanical Testing

Results from biomechanical testing further characterized the fusion masses. Flexion, the direction of greatest motion for the rabbit lumbar spine, has been shown to be the best marker for fusion in our laboratory.[24,25]

Flexion ROM at the L5–L6 segment was characterized to be 12.38° (SD, 2.70°) by Grauer and colleagues,[24] who later determined that fusion with autograft at this level decreased mean ROM to 2.34° (SD, 0.66°),[25] with pseudarthrotic spines having mean flexion ROM of 6.28° (SD,

Table. Radiographic, Biomechanical, and Histologic Characterization of Fusion Site

Autograft	Fusion Rate		Histologic Fusion (Huo/Friedlaender[27] Score)
	Radiographic	Biomechanical	
1.5 cm^3	4/10 (40%)	2/7 (29%)	4.3 ± 2.9
1.5 cm^3 + platelet concentrate	4/10 (40%)	4/7 (58%)	5.0 ± 3.5
3.0 cm^3	9/10 (90%)	6/7 (86%)	4.7 ± 2.5
3.0 cm^3 + platelet concentrate	6/10 (60%)	6/7 (86%)	7.7 ± 0.6

1.23°). With these baseline parameters defined in the rabbit model, fusion in our study was defined a priori as 4° or less of flexion. Fusion ROM for flexion is shown graphically averaged for each group in the Table. For 1.5-cm^3 autograft alone, 2 (29%) of 7 animals were biomechanically fused (mean flexion, 6.7°; SD, 3.7°); for 3.0-cm^3 autograft alone, 6 (86%) of 7 animals were fused (mean flexion, 3.4°; SD, 1.0°); for 1.5-cm^3 autograft plus PC, 4 (57%) of 7 animals were fused (mean flexion, 4.6°; SD, 2.6°); and, for 3.0-cm^3 autograft plus PC, 6 (86%) of 7 animals were fused (mean flexion, 3.5°; SD, 1.8°) (Figure 4).

There were no statistically significant differences between the groups. However, the 1.5-cm^3 autograft-plus-PC group appeared to have a fusion rate twice that of the 1.5-cm^3 autograft-alone group (57% vs 29%, $P = .06$). Both 3.0-cm^3 autograft groups had biomechanical fusion rates of almost 90%, making any possible differences nearly impossible to detect, and the magnitude of these differences of little clinical importance.

There was a 70% correlation between radiographic and biomechanical fusion rates—consistent with previous studies in which plain x-rays were found to have a limited role in defining fusion.[28]

Histologic Testing

Histologic sections were analyzed with several staining preparations. Toluidine blue staining highlighted the regions of calcification. Calcified islands were seen in the autograft fusion masses corresponding to the original grafting material. Low-magnification images are shown in Figures 5 and 6. Higher magnification toluidine blue and H&E staining further defined the fusion masses (Figure 6). Autograft fusion masses were characterized predominantly by cartilaginous tissue and small amounts of fibrous tissue between bone graft fragments. High magnification also revealed multinucleated cells around the bone graft fragments.

Individual Huo/Friedlaender histologic scores for tested specimens are listed in Figure 7. Mean scores were 4.3 (SD, 2.9) for 1.5-cm^3 autograft alone; 4.7 (SD, 2.5) for 3.0-cm^3 autograft alone; 5 (SD, 3.5) for 1.5-cm^3 autograft plus PC; and 7.7 (SD, 0.6) for 3.0-cm^3 autograft plus PC.

The intertransverse region of the 1.5-cm^3 autograft-alone specimens demonstrated moderate fibrous tissue. Despite endochondral bone formation around the decorticated surfaces of the transverse processes, no bridging intertransverse callus was seen. This group had the lowest mean score on H&E stains (4.3; SD, 2.9). The 1.5-cm^3 autograft-plus-PC group (mean score, 5; SD, 3.5) had calcified islands of bone and larger amounts of new bone formation resulting in qualitative differences in this group as compared with the 1.5-cm^3 autograft-alone group.

Calcified islands and bridging calcification were seen in both 3.0-cm^3 autograft groups, but mean histologic scores on H&E stain were higher for the autograft-plus-PC group (7.7; SD, 0.6) than the autograft-alone group (4.7; SD, 2.5). Low- and high-power images are shown in Figures 5 and 6.

There were no significant inflammatory reactions appreciated in any of the groups.

Calcein fluorescent staining confirmed active mineralization fronts in the PC specimens. Active mineralization fronts were present to a lesser extent in the autograft-alone specimens.

There were no statistically significant differences in the groups' histologic scores. However, there was a trend for mean scores to be higher for the autograft-plus-PC groups than for the autograft-alone groups, irrespective of volume of autograft used. In addition, qualitative review of the calcein-labeled sections revealed a trend toward more osteoblastic activity, vascular ingrowth, and a more robust front of calcification.

Statistical Analysis

One-way ANOVA was used to compare the 4 treatment groups' flexibility ROM data, and the Wilcoxon test was used for correlations between radiographic fusion and biomechanical fusion. For all tests, significance was set at $P<.05$.

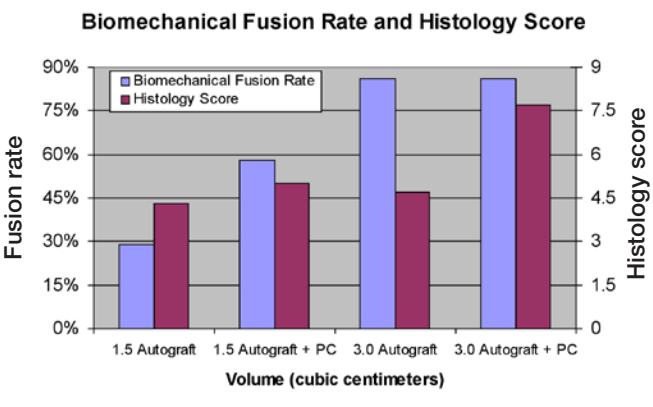

Figure 7. Biomechanical and histologic characterization of fusion site. Graph shows the general trend toward a higher fusion rate as the amount of bone graft is added and toward higher histologic scores as platelet concentrate is added, irrespective of amount of bone graft.

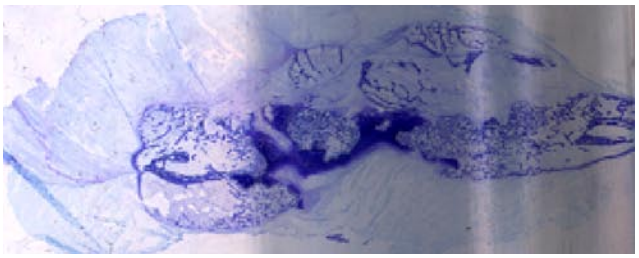

Figure 5. Low-power histologic results show bony ingrowth toward solid intertransverse fusion in 1.5-cm^3 autograft plus platelet concentrate. Outlined segments represent transverse processes.

Figure 6. Low-power histologic results show bony ingrowth toward solid intertransverse fusion in fibrous bridge without bony fusion mass. Outlined segments represent transverse processes.

Discussion

As our understanding of the molecular biology of bone homeostasis and repair increases, our ability to favorably manipulate the healing response continues to improve. The goal is to provide the right factors in the ideal concentrations at the appropriate time, using the best medium or carrier. PC use is of molecular, clinical, and practical appeal. We now briefly examine each of these rationales.

Platelet Concentrate: Molecular Basis

The evidence to use PC is very encouraging on a molecular level. In all wound-healing responses, platelets quickly adhere to wound surfaces and degranulate, releasing many peptide growth factors, including PDGF, TGF-β, vascular endothelial growth factor (VEGF), fibroblast growth factor 2 (FGF-2), and others, into the fibrin network during coagulation in the wound.[29] This entire process, through which an inflammatory response initiates vascular proliferation, is necessary to provide the graft with access to nutrients and cells involved in repair. Therefore, it follows that modifiers of the inflammatory response might alter bone graft incorporation.[30]

Growth Factors

PDGF is released from platelet degranulation during wound healing and is concentrated in PC.[19] The effects of the PDGF class of molecules on bone formation have been described in many in vitro studies.[31,32] PDGF has been found to be a powerful chemotactic factor for osteoblasts in both rat and human tissue.[33,34] PDGF has further been shown to be chemotactic to fibroblasts as well as monocytes and primitive mesenchymal cells, and it has mitogenic activity through stimulation of DNA synthesis and cell replication.[19] Collagen synthesis and protein synthesis are also stimulated by PDGF, but IGF-1 is likely needed to moderate the effects.[31] PDGF also seems to enhance the activity of BMPs in promoting cartilage and bone formation. Finally, demineralized bone matrix treated with PDGF and implanted in rat muscle showed an increase in calcium content and alkaline phosphatase activity.[35]

TGF-β is one of the growth factors initially released at wound sites. The TGF-β superfamily of polypeptides itself has been shown in vivo to stimulate bone formation and healing and collagen synthesis and increase the activity of osteoblasts, chondrocytes, and osteoclasts.[16,31] TGF-β has been extensively studied, particularly with regard to its influence on bone formation and the response of osteogenic cells to growth factor in vitro.[16,36,37] TGF-β enhances bone formation when placed orthopically but is not osteoinductive and does not induce bone formation at heterotopic sites.[38] More likely, TGF-β potentiates the effects of BMPs in bone formation.[39] Systemic application of TGF-β was shown to stimulate osteoblast proliferation and increase bone matrix formation and bone remodeling in rabbit bone defects, and locally applied TGF-β has been shown to accelerate fracture healing in a dose-dependent manner.[32] Both PDGF and TGF-β have mitogenic activity through stimulation of DNA synthesis and cell replication. TGF-β further promotes proliferation of mesenchymal cells,[40,41] potentially increasing the pool of osteochondral progenitor cells. TGF-β also enhances the early stages of differentiation of both osteogenic cells[40] and cartilage cells[42] and thus may increase new bone formation through increased osteogenesis by committed osteoblasts, increased endochondral ossification by committed chondrocytes, or both. Finally, TGF-β may work in concert with other regulatory factors to enhance differentiation of chondrocytes in the endochondral pathway.[16,43] More rapid osteogenesis would result in earlier bone remodeling and, ultimately, more lamellar bone.

Platelet Concentrate: Basic Science Evidence

Although there is a wealth of data supporting the notion that individual growth factors within platelets influence bone healing, there is limited (but convincing) evidence that PC brings these factors to the wound in a bioactive state. Kevy and colleagues[44] characterized growth factor levels in PC using the same preparation technique used in our study. PDGF, TGF-β, and VEGF levels were all linearly correlated with PC. PC and assayed growth factors had a 3- to 6.5-fold increase in absolute levels when compared with a similar preparation of whole blood.

Using the same PC preparation used in our study, Haynesworth and colleagues[45] found a direct effect of platelet-rich plasma releasate on purified human mesenchymal stem cells (hMSCs) and demonstrated that local application of PC causes migration of hMSCs to the wound site, followed by their massive replication. As the bioactive factors diffuse away from the fibrin scaffold, densely populated by hMSCs, the cells cease dividing and are primed

to respond to the endogenous inductive cues that stimulate differentiation. The local and transient activities of PC in this model of tissue repair were responsible for initiating and accelerating the natural healing cascade.

Siebrecht and colleagues[46] added PC gel to a hydroxyapatite-coated bone chamber, found that the gel significantly increased bony ingrowth into the chamber (vs the same chamber without PC gel), and suggested that PC enhances and may extend the applicability of bone graft substitutes. Our histology results support these claims. Although our scoring system did not reach statistical significance, the qualitative findings suggest there was an increased number of observable mature elements in specimens with PC versus same-volume specimens without PC (Figure 7), suggesting that PC may have a role in advancing the healing process.

That an autologous source of concentrated growth factors has chemotactic and mitogenic activity lends further credence to the therapeutic role of PC in clinical orthopedics.

Platelet Concentrate: Clinical Experience

PC was first used as an autologous fibrin sealant in dural tears and burns as an alternative to allogeneic cryoprecipitate.[47] Oral and maxillofacial surgeons reported on using PC to minimize graft migration and shape in maxillary reconstruction. Marx[48] reported that patients in whom PC gel was used had 25% more bone in oral reconstructive surgery in comparison with patients in whom PC gel was not used.

In the only reported study of PC use in human spinal fusion, 19 patients underwent L5–S1 fusion with instrumentation.[19] The investigators found a 100% fusion rate at 6 months. However, 5 patients underwent repeat surgery, and the heterogeneous population lacked a control group.

The results of our study do not provide any statistically significant data to suggest that PC increases fusion rates in rabbits. We did find a trend toward higher fusion rates when the amount of bone graft was limited; the fusion rate of the 1.5-cm^3 autograft-alone group appeared to double, from 29% to 57%, with the addition of PC (P = .06). As the fusion rate approached 90% in both 3.0-cm^3 autograft groups, it became virtually impossible to detect any difference in fusion rates with and without PC.

Platelet Concentrate: Practical Rationale

There are several advantages in using PC over other bone graft substitutes. Platelets are readily available from the patient's own blood. In addition, use of PC virtually eliminates problems with immunogenicity or transmission of infection, as well as local or systemic side effects, because the source of the graft is the patient's own blood.

Mechanical stability of the graft also has important implications for union rates. In 1993, investigators demonstrated that a flexible sheet or putty of the same demineralized bone matrix, as compared with the gel, resulted in a higher rate of bony union in the rabbit spine.[47] Our findings at time of surgery confirmed that PC gel use decreased the migration potential of the graft and allowed for a more uniform distribution of graft.

Study Limitations

As we did not achieve statistical significance in demonstrating a benefit of adding PC gel to autologous bone graft, additional studies are needed before human application. With more animals being used in such studies, we suspect that a more powerful and valid result will be generated.

Another study limitation is that our use of flexibility testing contrasts with the well-described and popular use of pull-apart testing at certain centers. The rationale for pull-apart testing was based on long-bone fractures[49]; in the spine, however, pull-apart testing determines the stiffness and physical strength of the masses but provides no information about physiologic motion.[25] Grauer and colleagues[24,25] established the baseline physiologic motions of multidirectional flexibility testing and found kinematic characteristics approximating those of the human lumbar spine and supporting use of this testing in evaluating changes in physiologic motion after posterolateral fusion. We believe that multidirectional flexibility testing more closely approximates the physiologic motions of the spine. In the literature, however, neither well-established method has emerged as superior to the other.

Conclusions

PC is a readily available, nonrecombinant, nonimmunogenic source of bioactive and concentrated autologous growth factors. Previous studies have demonstrated that these growth factors directly affect bone growth and healing and enhance bone formation when applied independently or in combination in a PC. In this study, the 1.5-cm^3 autograft-alone group had a 29% fusion rate by biomechanical testing, with an improving trend to 57% fusion when PC was added (P = .06). No appreciable difference was found between the 3.0-cm^3 groups (autograft only, autograft plus PC) with respect to the biomechanical parameters of fusion. Radiography was not useful in predicting fusion, as there was only a 70% correlation between radiographically determined and biomechanically determined fusions. Histologic evaluation of the fusion masses in all groups showed a trend toward increase osteoblastic activity, higher histologic scores, and a more robust active front of mineralization in the groups with PC added. This study provides preliminary evidence that PC directly affects the biology of spinal fusion, and consequently further study is warranted to determine the clinical utility of PC in the setting of lumbar arthrodesis.

Authors' Disclosure Statement

Funding for this study was provided by DePuy AcroMed. Sudha Kadiyala, PhD, wishes to note that he is an employee of DePuy Spine, a Johnson & Johnson Company, and he owns stock in Johnson & Johnson. The other authors report no actual or potential conflict of interest in relation to this article.

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