Surgical Considerations in the Use of Platelet-Rich Plasma

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Abstract: Platelet-rich plasma is an autologous source of platelet-derived growth factors that enhance surgical soft- and hard-tissue wound healing. Surgeons should be aware of its mechanisms of action and benefits, as well as the controversy regarding its use.

Recent dental literature has showcased a variety of tissue-engineering therapies and growth factor products such as enamel matrix derivative, recombinant bone morphogenetic proteins, recombinant platelet-derived growth factor (PDGF), and platelet-rich plasma (PRP). Of these four biologics, PRP has received significant attention because it is an autologous product with simple in-operatory preparation and purported wide-ranging therapeutic effects. This article will review the basic science behind PRP and its potential applications.

WHAT IS PRP?

Marx first reported on the applications and clinical benefits of platelet-rich plasma in 1998. He noted that PRP is a volume of autologous plasma with a platelet concentration above baseline.[1] The typical range for baseline platelet count averages from 150,000/µL to 440,000/µL. Commercially available PRP preparation systems have been shown to increase platelet concentrations by 160% to 740%.[2-4] Typically, to achieve therapeutic effects, a 400% to 500% increase in platelet concentration is required to reach the recommended PRP platelet count of 1,000,000/µL in a 5-mL volume.[4,5]

HOW IS PRP PREPARED?

Because PRP is an autologous product, preparation is initiated by drawing 20 mL to 60 mL of blood from the patient on whom surgery is to be conducted. The volume of drawn blood is determined by the anticipated size of the surgical field and the requirements of the specific PRP preparation system being used. Blood should be drawn immediately before the initiation of surgery and the infusion of intravenous fluid.[4] Blood cannot be drawn and stored ahead of time. Once obtained, the patient's blood is mixed with anticoagulant and processed according to the preparation system manufacturer's directions.[4,6] PRP will remain stable in

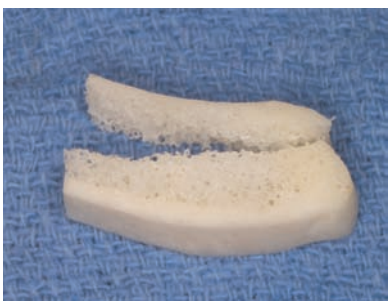

Figure 1 Block allograft that will be prepared for grafting.

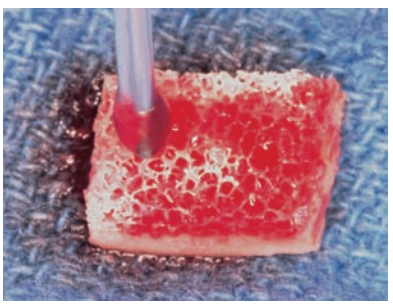

Figure 2 PRP delivered into the block allograft.

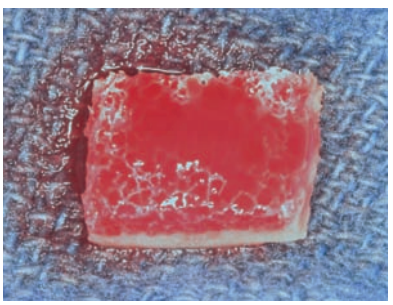

Figure 3 PRP saturation of the block allograft.

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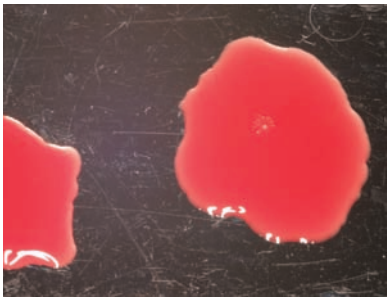

Figure 4 PRP extruded on a mirror demonstrates the immediate clot that is formed from processing and final application.

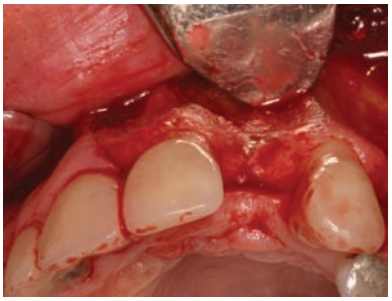

Figure 5 Defect before ramus block grafting.

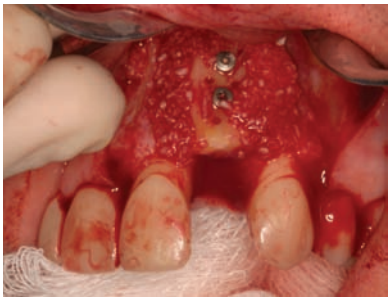

Figure 6 Ramus block graft mixed with particulate FDBA graft and PRP in place before membrane placement.

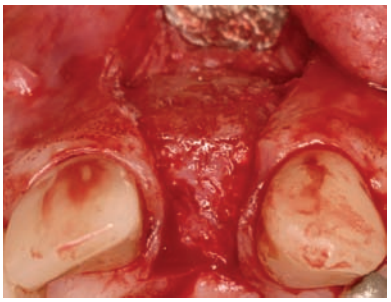

Figure 7 Four months after grafting. Note graft incorporation.

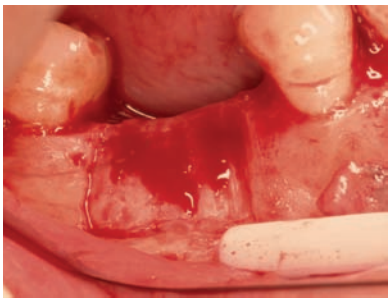

Figure 8 Prepared recipient site that will receive the block allograft.

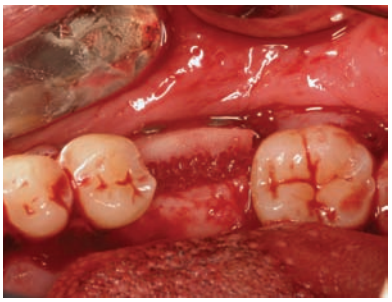

Figure 9 Block allograft with PRP is fixated into the recipient site with screws.

an anticoagulated state for up to 8 hours after processing.[4,5] To activate the platelets within PRP, the prepared product typically is combined with topical thrombin and delivered to the surgical site in an automixing device.[1,7,8] Another option is to prepare the block allograft before placement into the surgical site (Figure 1 through Figure 3).

HOW DOES PRP WORK?

PRP is an autologous concentration of eight growth factors: PDGF-AA, PDGF-BB, PDGF-AB, transforming growth factor-beta 1 (TGF-β1), TGF-β2, vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor (ILGF-I). These growth factors are stored within platelet alpha granules, and initiation of their release begins within 10 minutes of blood clotting (Figure 4).[3-5,7,9,10] After 1 hour, 95% of these factors are released, and the platelets then continue to synthesize and release additional growth factors over the next 7 to 8 days.[4,5]

When examined individually, the growth factors within PRP produce a multitude of effects. PDGF is a potent mitogenic and chemotactic factor for both fibroblasts and osteoblasts. In vivo studies have shown PDGF to stimulate bone formation and consistently enhance wound fill.[9,11] TGF stimulates the proliferation of osteoblast precursor cells, has a direct stimulatory effect on bone collagen synthesis, and also decreases bone resorption by inducing apoptosis of osteoclasts.[9] ILGF-I has been shown to enhance the differentiation of osteoblasts by increasing the expression of type I collagen as well as the rate of bone matrix apposition.[12,13] VEGF is a potent angiogenic cytokine that promotes endothelial cell proliferation and migration, leading to increased vascular ingrowth.[4,14] Finally, EGF has demonstrated the ability to speed wound epithelialization and reduce scar formation.[4,15,16]

CLINICAL APPLICATIONS FOR PRP

Initial clinical applications for PRP focused on large bone grafts for the repair of craniofacial defects, such as the traditional ramus block graft (Figure 5 through Figure 7) and, more recently, the block allograft (Figure 8 and Figure 9). The results of these studies suggested that PRP accelerated the rate of bone formation and produced greater trabecular bone density.[1] As such, early PRP studies focused on bone grafting procedures. Hanna[8] found that periodontal intrabony defects treated with bovine-derived xenograft and PRP

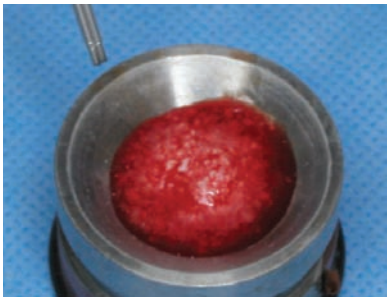

Figure 10 PRP applied to bovine bone matrix.

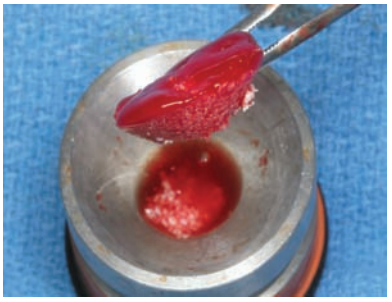

Figure 11 PRP improves the handling properties of the graft material.

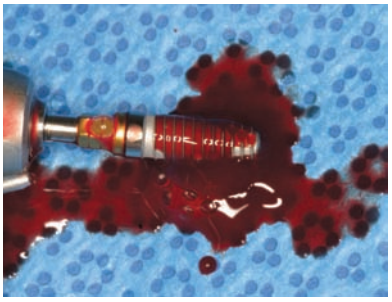

Figure 12 PRP is applied to saturate an implant before placement.

had significant reductions in pocket depth and increased clinical attachment levels when compared with defects treated only with bovine-derived xenograft. Kassolis and Reynolds[17] found that the combination of freeze-dried bone allograft (FDBA) and PRP enhanced the rate of bone formation compared with FDBA and membrane in subantral augmentation grafts (Figure 10 and Figure 11). Since these early studies, a multitude of new clinical applications for PRP have been examined. Dermilap[10] discovered endodontic applications for PRP when successfully treating periapical inflammatory lesions with a combination of PRP and tricalcium phosphate. Studies by Mancuso[3] and Sammartino[18] demonstrated that PRP has the potential to improve healing of third molar extraction sites via decreased residual pocket depth formation and accelerated bony healing. Separate studies by Huang[19] and Cheung[20] showed applications for PRP in periodontal mucogingival procedures. Finally, Fuerst and colleagues[21] recently documented that dental implants placed in conjunction with PRP achieve accelerated bone-to-implant contact during the early stages of implant healing. PRP can be extruded onto the implant fixture before placement of the implant within the bone (Figure 12). This finding may hold promising benefits for immediately loaded implants. While most of these results were statistically significant, further studies are needed to determine whether such enhancements ultimately affect clinical outcomes.

Although the potential clinical applications for PRP are numerous and have shown promising benefits, a number of studies question the efficacy of this growth factor product. Raghoebar,[22] for example, found no beneficial effect on wound healing or bone remodeling when PRP was added to subantral augmentation grafts. Likewise, a systematic review by Wallace and Froum[23] evaluating the effect of maxillary sinus augmentation on implant survival found insufficient data to recommend use of this application. Sanchez[24] found that the addition of PRP to xenografts in the treatment of peri-implant defects demonstrated low regenerative potential. While recent studies indicated that PRP produces no additional long-term benefits, these same studies indicated that PRP enhances osseous regeneration within the initial 12 weeks after surgery.[25,26]

WHY THE CONTROVERSY?

One explanation for the discrepancies in many recent PRP studies is that all PRP preparation systems are not created equal. The PRP preparation systems studied ranged from simple centrifuges to sophisticated dual-spin units with variable revolutions per minute. Kevy and Jacobson[27] compared the efficacy of a number of PRP preparation systems and found that the SmartPReP® (Harvest Technologies Corp, Plymouth, MA), a dual-spin, variable revolutions per minute PRP preparation system, produced both the greatest percentage of platelet yield and the least coefficient of variability. Marx[4] suggested that PRP systems failing to use dual-spin technology do not produce the necessary platelet concentration to achieve therapeutic effects. His comparison of dual-spin with single-spin PRP preparation systems may substantiate the claim that dual-spin systems routinely had more than twice the platelet concentration, three times the PDGF-AB concentration, and three times the TGF-β1 concentration of single-spin systems.[2] When reviewing PRP-associated literature, readers should pay particular attention to the materials and methods for each study and consider if variable results are the consequence of inadequate preparation systems.

CONCLUSION

In an age when many patients are concerned with transmissible diseases, such as HIV and hepatitis, PRP affords clinicians

an opportunity to offer patients growth factors through relatively simple, low-cost, autologous means. With proper preparation, current literature indicates that PRP enhances soft-tissue healing and may stimulate early bone formation. The long-term benefits and ultimate surgical outcomes associated with PRP application, however, remain controversial. Additional randomized, controlled clinical studies evaluating PRP's long-term effects are certainly warranted and may someday put this question to rest.

DISCLOSURE

The opinions and assertions contained in this article are the private ones of the authors and are not to be construed as official or reflecting the views of the Department of the Navy.

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