The Student Section

Donation Platelet Rich Plasma Use in Cardiac Surgery as a Means to Improve Patient Outcomes

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Cardiovascular disease is the leading cause of death in today's society. According to the Centers for Disease Control and Prevention, "one in every three deaths is from heart disease and stroke, equal to about 2,200 deaths per day."[1] It is approximated that more than half a million heart surgeries are performed in the United States every year in an effort to manage many of these heart complications.[2] While cardiac surgery can be life-saving, the recovery these patients face after a procedure is lengthy with multiple factors contributing to the successfulness of their outcome. Patients may be faced with intraoperative or postoperative bleeding, pain and inflammation, and postoperative wound complications or infections associated with the vein harvesting site and sternal incision. In an attempt to combat these problems, vast amounts of research has been conducted over the past few decades. Platelet Rich Plasma (PRP) or Platelet Gel (PG), has been identified as an adjunct to other therapies in order to decrease the incidence of cardiac patient's intraoperative and postoperative complications.[3]

Platelet Rich Plasma (PRP) is an increased concentration of platelets floating in a small amount of plasma after being processed in a centrifuge. It is obtained by collecting the patient's own blood and placing it in a centrifuge where it is spun at varying speeds until it is separated into three layers. These layers include PRP, Platelet Poor Plasma (PPP), and Red Blood Cells (RBC).[3] PRP has a five-fold increase in concentration of platelets compared to normal blood. It is often derived from the patient's own blood and has been found to have a large number of growth factors and cytokines.[4]

Prior to cardiac procedures, blood from the patient is collected and the PRP is separated and then returned to the patient at the completion of cardiopulmonary bypass (CPB). This is done with the intention of decreasing the patient's need for allogenic platelet transfusions postoperatively.[5] While PRP can be sequestered and directly given back to the patient postoperatively, it is also common to see PRP transformed into Platelet Gel (PG). This process includes mixing the separated PRP with thrombin and calcium chloride.[3,6] These additions to the PRP activates the clotting cascade and produces the PG.[3] PG, whether through donated blood or autologous blood (forming autologous platelet gel (APG), has demonstrated its effectiveness in wound healing as a topical sealant and as an anti-infective.

Although there have been major advancements in cardiac surgery over the past few decades, bleeding continues to be a major complication and the need for blood transfusions still remains a chief concern.[5] According to Stover et al.,[7] patients undergoing coronary artery bypass grafting (CABG) procedures and other combined procedures such as CABG and valve repair or replacement, are at a higher risk for exposure to allogenic blood products. Much of this has to do with the insult on blood once it passes through the CPB circuit. This causes activation of platelets in the blood rendering them dysfunctional at their time of need postoperatively.[7] This platelet dysfunction is said to be the most common cause of nonsurgical bleeding af-

Continued on Page 8

Continued from Page 7

ter CPB, and necessitates the use of allogenic transfusions to replace the platelets that are no longer viable.[7] While substantial advances in blood safety have been made over the past few decades, allogenic transfusions are still associated with risks. These include ABO- transfusion reactions, transfusion-related acute lung injury (TRALI), and bacterial contamination in platelet products, all of which have serious consequences for surgical patients.[8] As demonstrated in a study done by Stover et al.,[7] none of their patients that were in the aphaeresis group were transfused with allogenic platelets postoperatively. This decreased the risk of being exposed to blood products from between 6 to 8 donors for these patients as opposed to the control group who did not receive platelet sequestration.

Not only do blood transfusions have associated risks, but they are also a costly intervention. In a study by Murphy et al.,[9] they found an increase in morbidity associated with transfusions. This translated into longer hospital stays and increased admission costs. They came to the conclusion that if allogenic transfusion was not used as an intervention, well over 50% of all infections and ischemic events would have been prevented in their study population. This would have reduced the non-operative costs of an admission by approximately 40%.[9] In another study by Davies et al.,[10] it was concluded that cell salvage of the patient's blood and reinfusion of the blood postoperatively may be a cost-effective method to reduce exposure to homologous blood transfusions.

Methods have been put in place to harvest autologous PRP from patients before a bypass procedure and then transfuse this sequestered PRP to the patient at the completion of surgery.[5] "The concept of removing platelets from a patient immediately before CPB, thereby potentially sparing platelets many of the insults associated with CPB, followed by post-CPB platelet reinfusion, seems a reasonable approach to the problem of post-bypass platelet dysfunction and bleeding."[7] Ideally, the collection of the patient's blood should not be performed immediately preoperatively as it needs time to process and could decrease the patient's hemoglobin level just prior to the procedure. This is considered a limitation in emergency cases; however, sequestration can be done successfully in non-emergent instances and reinfusion of PRP can provide better patient outcomes after cardiac surgery.

As mentioned previously, platelet gel is an activated form of PRP and is formed by combining the platelet concentrate with bovine thrombin and Calcium Chloride (approximately 10 parts PRP mixed with 1 part thrombin/10% CaCl2).[3,11] It is especially useful as a topical sealant and for wound healing with infection prevention/treatment characteristics. In clinical studies, patients undergoing either CABG or aortic surgery receiving APG application on their anastamosis sites had better hemostasis of those sites than the control group (not receiving APG).[11] These results support the use of PG as a topical sealant in cardiac procedures.

Also, through multiple studies and research it has been discovered that PRP contains heightened concentrations of growth factors, which are involved in the key stages of wound healing and tissue regeneration.[3,4] Once the PRP is activated to form the PG, these growth factors are released and take action on the desired site they are applied to. The multiple cytokines and mediators such as platelet-derived growth factor (PDGF) that are present in PG promote angiogenesis and collagen synthesis, which enhances soft tissue would healing.[11] The increased growth factor concentrations are largely responsible for the accelerated soft tissue wound healing that is about 2-3 times faster than normal healing.[3] PDGF is "an activator of collagenase within the later stages of wound healing, allowing for remodeling of collagen to promote wound strength. These function in attracting additional platelets to the developing clot, thus, enhancing the hemostatic response."[11]

In addition to a more rapid patient healing response after surgical procedures, the application of PG in cardiovascular surgical closure could result in reduction of post-operative wound complications.[12] In a retrospective case series, a significant reduction in wound healing disturbances of the chest and leg were demonstrated when PG was applied during cardiothoracic procedures. "In over 1000 patients having saphenous vein harvest, postoperative drainage of the leg wound was seen in 10.2% of the PRP cases and 46.1% of the controls (P< .001)."[12, 13] Platelet-rich gel has also been found to have an antimicrobial effect against various strains of bacteria. These include Escherichia coli and two strains of Staphylococcus aureus (MSSA and MRSA), which are major causes of hospital acquired infections in surgical wounds.[14] Deep Sternal Wound Infections (DSWI) are just one of the many debilitating and life-

threatening complications that patients may face if they acquire an infection in their surgical wound after a cardiac procedure.[15] The use of PG to accelerate wound healing, epithelialization, and formation of tissue granulation has been demonstrated to be beneficial for those patient's that have compromised healing ability.[15] In a study by Kachel et al.,[15] a four week long, non-healing DSWI after cardiac surgery was treated by injecting platelet gel into viable tissue at the wound site. After two weeks time and with only PG treatment, tissue granulation indicating healing was visible. PG releases growth factors over the next 7-10 days continuing it's antimicrobial and healing activities.[11]

So how can perfusionists get involved? As perfusion is a critical part of any open-heart team, there are many opportunities to advocate the use of PRP or PG. This includes on anastamosis sites,[11] conduit harvesting sites,[12,13] sternal incision site, and in the postoperative environment of the Cardiac Care Unit (CCU) as a means of preventing infection or treating infected surgical wounds.[14,15] It is crucial that perfusionists educate practitioners on the benefits and ease of PRP and PG use. The processing time of the autologous blood can take as little as 30 minutes and provides anesthesia with the option of returning the remaining PPP and RBC's to the patient.[11] The resulting PRP that is obtained is stable in the anticoagulated state for approximately 8 hours. At this time the surgeon can determine whether it should be activated to produce PG, and this gel is simply applied to the desired site by the surgical team. The advantages range from antimicrobial effects on surgical sites to increased healing time with decreased scarring and inflammation and therefore better overall patient outcomes.[3,11]

While there have been many successes with the use of PRP and PG, there are still some studies that show inconsistencies. With the many benefits that PG offers (superior patient outcomes, cost benefit for patient and hospital, etc.), it is without question that it should be researched further in hopes that it will one day become the new standard of practice for cardiac procedures.

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