AUTOLOGOUS PLATELET GEL (APG) STUDY PROPOSAL

INTRODUCTION

Elective knee and hip surgeries are common and confer a major burden on society and the healthcare industry. Approximately 300,000 elective knee or hip surgeries occur in the United States every year with elective knee and hip surgeries comprising up to 5% of the national healthcare expenditure. Much of this cost may be associated indirectly with the significant amount of post-operative bleeding that occurs with elective knee or hip replacement. While a very small amount of bleeding (<100 ml) occurs during surgery itself, the most significant amount of blood loss occurs post-operatively (1000-1500ml).

Postoperative blood loss in general is closely associated with increased morbidity and mortality, delayed healing, elevated levels of infections, and an increased need for red blood cell transfusions. Concurrently, patients who require red blood cell transfusions are exposed to the gamut of risks associated with transfusions: infections, transfusion reactions, immunosuppression, delayed wound healing, and transfusion related infection. Minimizing post-operative blood loss may drastically reduce the rate of blood transfusion and associated risks, overall length of stay in the hospital, and risk of post-operative wound infections with potential for significant improvements in pain control and recovery time.

A novel innovative procedure that may offer a significant reduction in post-operative bleeding is that of using autologous platelet gel (APG) applied directly to surgical wounds. While APG seems easy to use and offers several tangible advantages, it remains poorly researched in the setting of orthopedic surgery, with only 5 studies published supporting use in the past 10 years.

APG is convenient and safe, in that it is made from the patient's blood that has been collected prior to surgery. APG is easily prepared during the preoperative period. APG is easy to use, by direct application to the surgical wound including cut bone surface, synovia, tendons and other soft tissue prior to closure of the surgical wound site. Other benefits associated with APG use in orthopedic surgical settings in addition to ease of preparation and use and bleeding reduction are a reduction in post-operative pain, and improvements in post-operative recovery duration.

The advantages of using APG in orthopedic settings should warrant further study by medical researchers in this field. The use of APG could potentially lead to a reduction in the need for red blood cell transfusions and pain medication, plus a reduction in recovery and rehabilitation time, not to mention that it could produce significant and tangible improvements in the quality of care.

As promising as it seems, the technique of using APG in post operative orthopedic settings remains poorly studied. New research is needed before widespread use can naturally be expected. Studies that improve the knowledge base surrounding the effect of using APG on various types of patients, and studies that follow their clinical outcomes are essential. Itemization of cost savings realized as a result of a reduction in post-operative care and the significant cost savings realized by the minimization of the need for medications and extended hospital stays following the use of APG is important as well.

PURPOSE

1. To measure the effect of autologous platelet gel therapy on post-operative bleeding rates
2. To measure the effect of autologous platelet gel therapy on blood transfusion rates
3. Report the effect of autologous platelet gel on post-operative pain
4. Measure the effect of APG on recovery time
5. Assess the cost effectiveness of using autologous platelet gel

STUDY DESIGN

This study is a prospective, randomized control trial. All patients undergoing elective hip or knee surgery by Dr. X will be screened for eligibility. All patients found to be eligible will be approached for entry into the trial. Patients providing informed consent will then be randomized to one of two groups. Group A will be

patients undergoing surgery that will have APG applied during surgery. Group B will be patients undergoing surgery and given the standard care without the use of APG. Approximately 25 patients will be randomized to each of the two groups for a total of 50 patients in the entire study.

SUBJECT POPULATION

Inclusion Criteria:

1. **Patients undergoing elective total knee or hip replacement surgery at X Hospital**
2. 18 years of age or older and must be able to sign informed consent for participation in the study
3. Hemoglobin of greater than or equal to 12 gm/dl
4. Platelet count greater than or equal to 30,000 prior to enrollment.

Exclusion Criteria:

1. use of erythropoietin therapy in the month prior to enrollment
2. hemodynamic instability
3. history of platelet dysfunction syndrome or hypofibrinogenemia
4. known sensitivity to bovine thrombin

SUBJECT SELECTION CRITERIA

All potential subjects scheduled for total knee or hip replacement surgery by Dr X, MD, are eligible and will be contacted by the study coordinator by phone after surgery is scheduled. If a patient is qualified and interested, the informed consent will be obtained and pre-op laboratory studies will be drawn less than one month but greater than 1 week prior to surgery. Initial laboratory studies will include: complete blood count (CBC), platelet count, prothrombin time (PT), partial thromboplastin time (PTT) and international normalization ratio (INR). Other information collected from subjects: pain tolerance using a questionnaire for that purpose, global health status information using a specific assessment for that purpose current prescription and over the counter medications usage. Patients will be instructed to discontinue any aspirin or non-steroidal medications at least two weeks prior to surgery.

Patients will be randomized to one of two groups: Group A patients undergoing surgery that will have APG applied during surgery; Group B patients undergoing surgery followed by no APG. Groups A and B will be further subdivided into patients having total knee A(1) or B(1) or total hip replacement surgeries A(2) or B(2) .

RISKS

Use of APG has no known significant side effects. Maintaining sterility of the blood is integral to preventing postoperative complications such as infection or delayed wound healing. It has been used extensively by several institutions for many years in thousands of patients with no reported adverse events attributed to its use. It is currently being used at X Hospital in maxillo-facial surgery department with excellent results. Contraindications for use of platelet gel include: platelet dysfunction syndrome, critical thrombocytopenia, hypofibrinogenemia, hemodynamic instability, sensitivity to bovine thrombin. It should be noted that the thrombin used in forming the APG will be derived from bovines. Any patients with a known sensitivity to bovine thrombin will be excluded from the trial.

STUDY PROCEDURES

SURGERY

The same surgeon, X, MD, will perform all surgeries to minimize surgical technique variables. All total knee replacement surgeries will be performed using the same approach as will all the total hip replacement surgeries. Surgical drains will be placed in the same approximate anatomical position for each respective type of surgery.

EQUIPMENT FOR APG DEVELOPMENT

A platelet centrifuge for collecting is required for this study. The *Angel* platelet centrifuge collecting system manufactured by Cobe Cardiovascular is one example and is the brand and type used for this study. The

Angel centrifuge system allows for a smaller amount of blood to be drawn initially (120ml vs. 300ml) as opposed to other brands, and offers the feature of standardization of the amount of APG used for each subject.

DEVELOPING APG

Platelet gel is made by drawing a 120 ml sample of whole blood from a patient approximately ½ to 1 hour prior to the initial incision. The blood sample is drawn into syringes containing 5cc of anticoagulant citrate dextrose solution A (ACD-A) to prevent clotting. The blood sample is placed in a centrifuge collecting system to separate the platelets from the other blood components. This yields approximately 6-10 ml of platelet rich plasma which is then mixed with 5,000 units of topical thrombin and 5 ml of 10% calcium chloride. The thrombin and calcium chloride activate growth factors which promote and accelerate bone and soft tissue healing. This activation occurs by the initiation of the clotting cascade whereby fibrinogen is converted to fibrin and platelet degranulation occurs.

Making APG from the patient's own blood requires minimal nursing time and takes approximately an hour with minimal intervention by the technician.

APG APPLICATION

The prepared APG is applied directly to the surgical wound including cut bone surface, synovia, tendons and other soft tissue prior to closure of the surgical wound site.

DATA COLLECTION

For the first three days post-op period, all patients will have their surgical site inspected at each shift. Surgical drainage will be recorded until drain is discontinued. Daily measurements beginning on post-op day 1 until discharged from acute care (anticipated day 4): CBC, platelet count, PT, PTT, INR measured daily.

All patients will have the following measures recorded per shift: perceived pain assessment; use of oral and intravenous pain medication both narcotic and non-narcotic; type of medication; route of delivery; total dose (number of pills or number of milliliters used).

All patients will have complete perceived pain scale and global health assessment completed prior to surgery and at 6 weeks, 3 months and after surgery.

All patients will be monitored for evidence of infection, receiving transfusion or any other adverse event thought to be related to surgery. Patients will be questioned regarding any known complications since their time of discharge such as infection, transfusion, etc. Patients' knee flexion, extension and general ambulation for patients that had total knee replacement surgery and general ambulation, hip abduction and adduction for patients that underwent total hip replacement surgery will also be measured at 6 weeks post op.

All patients will receive the same physical and rehabilitation therapy for their respective type of surgery (total knee vs. total hip replacement). Daily measurements until discharge for total knee replacement patients: amount of flexion and extension; general ambulation ability. Daily measurements for total hip replacement patients: ability of hip abduction and adduction; general ambulation assessment.

OUTCOME VARIABLES

The primary endpoint of this study is to compare the amount of post-op bleeding in platelet gel patients versus no platelet gel used during total knee and hip replacement surgeries. Secondary endpoints will include the effect of platelet gel on transfusion requirements, pain associated with surgery, rehabilitation progress and length of stay.