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Bloody Good News

Newfoundland and Labrador Provincial Blood Coordinating Program

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Corticosteroids and IVIG in the treatment of Immune Thrombocytopenia

Immune Thrombocytopenia (ITP) is an autoimmune disease distinguished by a decrease in platelet count. Patients with ITP generally show symptoms of petechiae or pupura, a tendency to bruise easily and a decrease in platelet count upon investigation.

Treatment should be provided with the intention of restoring a safe platelet count (above 20x10^9/L) to avoid life threatening bleeding while considering other important factors. Among these factors are the patient's age, platelet count and whether the patient is actively bleeding.

Corticosteroids and Intravenous Immune Globulin (IVIG) are two treatment options used in the management of ITP. The use of corticosteroids allows the patient to receive treatment while allowing the physician adequate time to determine which patients have acute ITP and which patients will progress to chronic ITP requiring supplementary treatment. Some common corticosteroids used are: Prednisone, Methylprednisolone and Dexamethasone. Unplanned remission occurs in approximately 80% to 90% of children with ITP whereas in adults, remission is limited. ITP in many adults is stable without treatment with approximately 10% advancing to a more serious thrombocytopenia. Care must be taken to divert consequences such as osteoporosis when taking corticosteroids for an extended period of time. Corticosteroids are usually the initial treatment for non-life threatening ITP.

Treatment of ITP with IVIG has been successful for many years. IVIG was first used to treat ITP in 1981 and became an established practice in 1983. IVIG has been efficient in raising platelet counts in approximately 85% of patients and obtaining normal platelet counts in 65% of these patients. Because IVIG infusion usually raises the platelet count between 20 to 50x10^9/L within 24 hours, it is a first line treatment for life threatening ITP when patients present with active bleeding. Guidelines for the use of IVIG for the treatment of ITP have been established for the regional health authorities of Newfoundland and Labrador. Dosing should be followed as recommended to obtain maximum benefit. These guidelines have been adapted from: *Guidelines for the use of IVIG for Hematologic and Neurologic Conditions* found in the *Transfusion Medicine Review Volume 21(2).*
The guidelines are as follows:
Acute Setting – There must be a diagnosis of ITP and one of the following two: 1) major bleeding and platelet count less than 50 x 109/L; or 2) ITP not responding to steroids after a minimum of three days. IVIG may also be used when preparing a thrombocytopenic patient for surgery when there is insufficient time to depend on steroids.
Acute Dose: 1 g/kg per day for 2 consecutive days.

Chronic Setting – There must be a diagnosis of ITP and the following 2 criteria: 1) demonstrated responsiveness to IVIG as shown by administration required no more frequently than every 2 wks. and a platelet increase greater than 20 x 109/L; and 2) use in conjunction with other agents. There must be a record of the treatments used and platelet counts for review by a specialist with expertise in the management of ITP. Review is to occur every 3 months for the first year then every 6 months thereafter.
Chronic Dose: 0.5 to 1 g/kg per day, no more frequently than every 2 wks.

Because of the cost of IVIG, it is usually used to treat ITP in life threatening situations where the patient is actively bleeding, the patient has not responded well to corticosteroids or to raise platelet count before surgery where time does not permit the use of corticosteroid therapy.

James Blundell (1790-1878) graduated with his medical degree in 1813 with expertise in midwifery and physiology. Upon graduation from the University of Edinburgh, Scotland, he returned to his birthplace, London. In 1818, his article "Experiments on the Transfusion of Blood by the Syringe" was published. Through conducting a series of animal experiments, he discovered the benefits of executing transfusion in a timely manner to prevent coagulation; the importance of expelling the air from the syringe prior to transfusion; and the incompatibility of heterologous donors. He also invented multiple instruments for the transfusion of blood including the impellor and the gravitator. Some of his inventions are still in use today.

He was an innovator and pioneer and was one of the first physicians to practice blood transfusions in humans. There is some controversy as to whether his first human to human transfusion, from a husband to his wife suffering postpartum hemorrhage, occurred in 1818 or 1829. Over a five year period, he performed ten transfusions of which five were successful and published those results. He became a fellow of the Royal College of Physicians in 1838 and retired in 1847.

Single Unit Transfusion: More is not always better

How many times have you seen an order for "transfuse 2 units of RBCs over 3-4 hours each"? It appears frequently as a standing order. The patient's hemoglobin may be hovering in the "low 70's" for several days with no change in clinical status but as soon as it drops below 70 g/L, they receive two units. They are "topped up" with 2 units of RBCs. The question begs to be asked – transfuse one, reevaluate, and if necessary, transfuse the second?

As health professionals, we have to outweigh the risks versus benefits of any treatment that is provided. Transfusion of blood components and products is not without risk. Transfusion is a liquid tissue transplant that can potentially cause adverse events ranging in severity from minor to severe to life threatening, and in rare cases even death. There are multiple classifications of adverse events that may occur such as minor or severe allergic, febrile non-hemolytic, acute or delayed hemolytic reactions, hypotensive or hypertensive reactions, transfusion associated circulatory overload (TACO), transfusion related acute lung injury (TRALI), transfusion associated dyspnea (TAD), post transfusion purpura (PTP) and transfusion-associated graft versus host disease (TA-GVHD).

The decision to transfuse should occur only after alternative treatments have been considered. Has the patient with chronic anemia been properly assessed to determine the root cause? What alternative treatments are available to minimize their exposure to blood components? Other treatment options should be considered prior to administration of red blood cells.

When transfusion is determined to be the best treatment, the volume and rate of infusion should be determined based on multiple factors including the client's status, presence of co-morbidities, age, and the time of day of the scheduled transfusion. Assessment of the client and not just laboratory results alone should determine the time and amount to transfuse. Questions to be asked include: is the patient actively bleeding; has their clinical status changed; do they have respiratory issues or history of congestive heart failure; can we transfuse one unit today and, if needed, the second unit the next day?

Patient safety should be of utmost importance. With two unit transfusions, the second unit is often infused over the night shift. Research has shown that there is a higher incidence of transfusion errors and adverse events during night time transfusions. The issues with circulatory overload, especially with at risk population such as the elderly, may be minimized by administering the two units over a two day period. It may be determined on day two of the transfusion period that it is not necessary to give the second unit because the patient's symptoms have subsided or resolved. A single unit transfusion on average increases the hemoglobin by 10 g/L.

Single unit transfusions are beneficial to those patients who have a decreased hemoglobin, are clinically stable, with no active bleeding.

In Australia's patient blood management plan, optimizing patient tolerance of anemia is one of the key points. It has been suggested that the ideal population to study to see if there truly is a need to transfuse as quickly as we do would be the Jehovah's Witness, as they refuse transfusion of RBCs. Some initial research with this group has supported that in otherwise healthy individuals there is an ability to adapt to hemoglobin levels at 50 g/L or even lower. This might be beneficial in areas such as surgical procedures in otherwise healthy individuals or even in those with chronic anemia and no other comorbidities. This further supports that we treat the client and not the hemoglobin value; that we assess for alternative therapies; if transfusion is required then start with one; and then proceed if more is required.

The key concepts of single unit transfusion are to transfuse one unit at a time as clinically indicated; to base this decision on assessment of the patient clinical status and

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Upcoming Events:
Canadian Society for Transfusion Medicine Annual Conference – May 1-4, 2014

Effective in 2014, Bloody Good News shall be published twice yearly, in April and October.

Antifibrinolytics and Transfusion

Transfusion of blood components and blood products is not without risk. Preventing or mitigating the risk of bleeding through the use of pharmacologics such as Tranexamic acid (TXA) can support patient care by reducing the likelihood of transfusion of blood components.

A review of the coagulation cascade will take us back a few years, but it is important to understand the principles of hemostasis in the treatment of the bleeding patient or patients scheduled for surgery where bleeding is more likely and frequently does occur.

There are four phases in the hemostasis process. Phase I involves vasoconstriction of the injured blood vessel and the formation of a platelet plug. Phase II results in activation of the coagulation factors with the release of tissue factor and subsequent activation of coagulation pathway and generation of thrombin. Phase III elicits formation of a fibrin clot and stabilization of the clot. Simultaneously in Phase IV, as clot formation begins, the process is regulated to limit the amount of thrombus formation and breakdown of the clot, commonly referred to as fibrinolysis.

Fibrinolysis begins with the conversion of plasminogen by plasminogen activators to create plasmin to break down fibrin. Antifibrinolytic agents such as TXA, an amino acid lysine analogue, blocks the plasminogen lysine binding sites, preventing conversion to plasmin, resulting in fibrinolysis inhibition.

Antifibrinolytic agents target fibrinolytic activity and shuts down the process to mitigate further bleeding. Prophylactic treatment of patients at risk of bleeding during surgical procedures has demonstrated that transfusion of blood components can be reduced and that hemorrhage can be controlled to some degree.

Systematic reviews, randomized controlled trials and recent publications, (Transfusion 2014;54:26-30 and Transfusion 2014;54:31-41) further support the use of TXA in total knee arthroplasty and primary total hip and knee arthroplasty. Tranexamic acid is frequently used in cardiac, spinal, liver surgical procedures. TXA is also used to treat trauma patients, with the most favorable results occurring when patients are treated within 3 hours of injury. The CRASH-2 trial (2010), which evaluated trauma patients with or at risk of bleeding , identified that early administration of TXA followed by a later infusion resulted in a significant reduction of all-cause mortality (in hospital) within hospital one month post injury. The Consensus Conference on Massive Transfusion, led by the National Advisory Committee on Blood and Blood Component and Canadian Blood Services in June 2011, agreed that TXA has positive effects in trauma situations. http://www.nacblood.ca/resources/guidelines/massive-transfusion.html

Literature supports that the use of tranexamic acid reduces the risk of bleeding, and in turn, can reduce the amount of blood components transfused in certain patient populations.

Educational Video – Safe Transfusion Practice and Lanyard Card

The Provincial Blood Coordinating Program has developed an educational video titled "*Safe Transfusion Practice Education – Adverse Transfusion Events*". This video is also supported by a lanyard card.

The purpose of the video and lanyard card is to: provide an educational toll to build on initial competencies and maintain continuing education and certification requirements; provide assessment tool to address accreditation requirements; and also provide quick access to information presented on a lanyard card.

The video depicts two dverse transfusion event cenarios demonstrating an allergic reaction and an acute hemolytic reaction.

Throughout the video the three **R**'s of adverse transfusion events are emphasized: **R**ecognition of signs and symptoms, **R**esponse – initial actions and treatment, and **R**eporting at the facility, regional, provincial and national levels. There is repetition of key messages in both scenarios to reinforce the critical points in the administration of blood components.

The key messages focus on informed consent, the patient being informed of the signs and symptoms of an adverse event; appropriate patient monitoring; patient identification; physician notification and timely action and patient safety.

The competency assessment consists of 20 multiple choice questions that test entry level competencies, pose critical thinking questions as well as questions directly linked to the video. A user is provided three attempts to complete the test.

There are three levels of access to the program; User level, Administrator level and Super User level. The transfusion safety officers and clinical educators have administrator status and will provide additional support to the user if the test cannot be completed in three attempts. The user will be provided with one more attempt after review of the questions and responses. Users will also be able to print the competency test and complete it manually if they choose. A certificate of completion may be printed for continuing education purposes.

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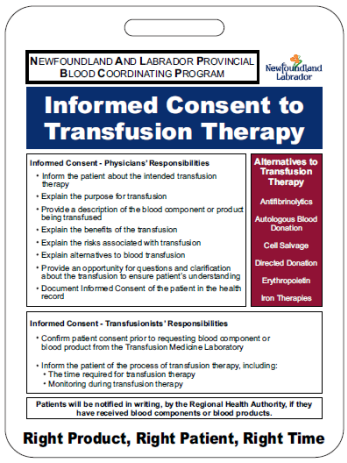
Administrators will be able to track competency within their respective region by user name and clinical area of practice.

The lanyard card provides information on informed consent, lists the signs and symptoms of a transfusion reaction and immediate action required when an adverse event occurs.

The Provincial Blood Coordinating Program through the transfusion safety officers within the regional health authorities will distribute copies of the video. They will be placed on intranets for availability to all staff, nursing and medical students, and laboratory technologists to avail of the competency.



We hope this educational tool will serve well as we continue to support safer patient care.

The Public Health Agency of Canada provided funding for this project.

Single Unit Transfusion - Cont'd from page 2

not on laboratory results alone with the benefits of transfusion outweighing the risks; and to minimize the risks to the patient as those associated with transfusion are often dose dependent. This approach is obtaining recognition worldwide with Australia's development of a "Single Unit Transfusion Guide", and the studies performed in North America, the United Kingdom, Switzerland, and Asia on the evaluation and effectiveness of single unit transfusions in specific populations, both medical and surgical. There is significant evidence to support this change in practice. Finally, it is important to remember that blood is not an endless resource and with the current population trends with the aging population and the number of potential donors decreasing, we must be cognizant of our use of this precious resource and ensure that it is used sparingly, if possible, and appropriately.

Case Study # 19

A 36 year old prima gravida by caesarean section experienced postpartum hemorrhage. Oxytocin was administered IV. No further sources of bleeding were identified. Hemoglobin decreased from 130g/L to 80 g/L. All other bloodwork was normal. 2 units RBC's were transfused increasing the Hgb to 104 g/L. Patient was discharged on day 4 post-partum with Hgb 106 g/L. One week later she complained of extreme weakness, right flank pain, with slightly darkened urine.

CBC results noted Hgb of 78 g/L. BUN, creatinine, bilirubin, and LDH were slightly elevated. Post transfusion IDAT revealed 2+ reactions and DAT 1+ reactions. Review of clerical checks and ABO grouping were accurate.

1. Classify type of reaction.

2. What was the relationship of the adverse event to the transfusion?

3. What was the severity of the reaction?

4. What was the outcome of the adverse event?

Case Study # 18 Interpretation

1. *Type of Reaction – FNH Febrile Non-Hemolytic*
2. *Relationship of adverse event to transfusion – Possible*
3. *Severity of the reaction – Grade 1*
4. *Outcome – Minor-no sequelae*

The whole of science is nothing more than a refinement of everyday thinking.

Albert Einstein (1879-1955) German Theoretical-Physicist

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For reference documents including policies visit:
http://www.health.gov.nl.ca/health/bloodservices/index.html

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