

Strategies for Avoiding and Controlling Hemorrhage And Anemia without Blood Transfusion

I. Volume Expanders

Crystalloids

Substances capable of crystallization, which in solution can be diffused through animal membranes. Crystalloid should be given in a ratio of 2-3ml per 1ml blood loss. Adverse effects are marked edema and a decrease in hematocrit with initial hemodilution.

- **Ringers Lactate**
Combined electrolyte solution containing Na⁺, K⁺, Ca⁺⁺, Cl⁻, and Lactate. Osmolarity (mOsm/L) of =273.
- **Normal Saline**
0.9% Sodium Chloride which is isotonic, restores both water and sodium chloride losses. It is also used for extracellular fluid replacement and to initiate and terminate blood transfusions without hemolyzing red blood cells.
- **Hypertonic Saline**
3% or 5% Sodium Chloride; used in hyponatremia and hypochloremia due to electrolyte and fluid loss replaced with sodium-free fluids. It is also used in drastic dilution of body water following excessive water intake and for emergency treatment of severe salt depletion.

Colloids

A glue-like substance such as a protein or starch whose particles when dispersed in a solvent remain uniformly distributed and fail to form a true solution. Particles of colloidal dispersions are too large to pass through cell membranes and such dispersions usually appear cloudy. Colloids should be given in a ratio of 1ml per 1ml blood loss. Adverse effects are prolonged hypervolemia and anemia postoperatively.

- **Dextran**
Modified polysaccharides composed of branched glucose residues. Used as volume expanders and are classified according to their average molecular weight. Dextran is effective as a plasma expander in the treatment of shock due to surgery or trauma, but should be used only if whole blood or blood products are not available.
- **Gelatin**
A derived protein obtained by the hydrolysis of collagen present in the connective tissues of the skin, bones, and joints of animals.
- **Hetastarch**
Plasma volume expander prepared from waxy sorghum starch. The colloidal properties of 6% HES approximate those of human albumin. Useful as a plasma volume expander in management of shock due to hemorrhage, burns, sepsis, trauma, or surgery.

II. Hemostatic Agents for Bleeding/Clotting Problems

Topical

Chemical hemostatics are indicated for use in surgical procedures in the control of hemorrhage from capillaries, veins, and small arteries when ligation or other conventional methods are impractical or ineffective. These products act by application of pressure and provision of a structural meshwork for clotting. Available products are made of gelatin, oxidized cellulose, oxidized regenerated cellulose, and microfibrillar collagen.

- **AviteneR**
Microfibrillar collagen (powder/non-woven web sheet)-Absorbable topical hemostatic agent prepared as a dry, sterile, fibrous, water insoluble, partial hydrochloric acid salt of purified bovine corium collagen. It is more suitable for procedures as an adjunct to hemostasis when control of bleeding by ligation or conventional procedures is ineffective or impractical. It is designed for better absorption and has properties of good wound adherence, but has major disadvantages with ease of handling and increased risk of infection.
- **GelfoamR, GelfilmR**
Gelatin, absorbable (sponge, powder, film)-A sterile, pliable surgical sponge prepared from purified gelatin solution and capable of absorbing and holding many times its weight of whole blood. When implanted into tissues, it is absorbed completely w/in 4-6 weeks without inducing excessive scar formation. Advantageous in controlling bone bleeding and hemorrhaging involving large volumes. Should not be left in the dural space due to risk of compression.
- **OxycelR, HemopakR**
Oxidized cellulose

II. Hemostatic Agents for Bleeding/Clotting Problems (cont.) Injectable

- **Desmopressin**
A synthetic analog of arginine Vasopressin, the naturally occurring human antidiuretic hormone (ADH). Urine volume is reduced and urine osmolality is increased. Useful in increasing plasma levels of factor VIII activity in patients with hemophilia A or Von Willebrand's Disease. Desmopressin will often maintain hemostasis in patients with hemophilia A during surgery and post-op when administered 30 minutes prior to procedure.
- **Aminocaproic Acid**
Hemostatic agent that provides the conversion of plasminogen to plasmin. It is effective anti-fibrinolytic agent for clinical bleeding where fibrinolysis is a contributing factor. The drug should not be used for fibrinolytic hemorrhage (diffuse intravascular coagulation) unless heparin is given concurrently due to substantial risk of clot formation. In the management of amegakaryocytic thrombocytopenia, the need for platelet transfusion may be decreased by use of 8-24g/day for 3 days to 13 months.

- **Tranexamic Acid**
Antifibrinolytic agent with actions similar to those of aminocaproic acid, and is about 10x more potent than aminocaproic acid. It is a competitive inhibitor of plasminogen activation, at much higher concentrations, a noncompetitive inhibitor of plasmin. Effective in prevention of excessive bleeding following surgery or trauma.
- **Vitamin K**
Fat-soluble vitamin known as phytonadione. Promotes the hepatic synthesis of active prothrombin (factor II), proconvertin (factor VII), plasma thromboplastin component (factor IX) and Stuart factor (factor X). Administered parenterally it is indicated for the prophylaxis and therapy of hemorrhagic disease of the newborn.

Recombinant Antihemophilic Factors

Recombinant antihemophilic (clotting) factors are biosynthetic forms of endogenous (naturally occurring) human blood coagulations factors. They are prepared using recombinant DNA technology (genetically engineered) and produce the same biological effects as the corresponding plasma-derived clotting products. Biosynthetic antihemophilic preparations are associated with a substantially reduced risk of contamination compared to products manufactured from pooled human plasma.

- **Recombinant Factor VIIa.** Recombinant factor VIIa prevents or controls bleeding in patients with hemophilia. Recombinant factor VIIa is now in clinical trials. (Niasase; NovoSeven)
- **Recombinant Factor VIII.** Factor VIII is essential for blood clotting and the maintenance of effective hemostasis. Recombinant factor VIII provides a means of temporarily replacing missing or dysfunctional factor VIII in order to prevent or control bleeding episodes or to perform emergency or elective surgery in patients with hemophilia A. (Kogenate; Recombinate; ReFacto)
- **Recombinant Factor IX.** This recombinant product provides a means of temporarily replacing missing factor IX in order to prevent or control excessive bleeding in patients with hemophilia B (Christmas disease), including those who require surgery. (Benefix)

Other Drugs

- **Vasopressin**
Antidiuretic hormone used to increase water reabsorption. Exhibits its most marked activity on the renal tubular epithelium, where it promotes the reabsorption of water (ADH effect), and the contraction of smooth muscles throughout the vascular bed (vasopressor effects). Vasopressin infusions are effective in the treatment of bleeding esophageal varices and other types of hemorrhage using a dosage of 0.2 units/min initially, increased to 0.4 units/min if bleeding continues.
- **Conjugated Estrogens**
Contain a mixture of 50-65% sodium estrone sulfate and 20-35% sodium equilin obtained from the urine of pregnant mares. IV (preferred) or IM for rapid cessation of dysfunctional uterine bleeding; usual dose is one 25mg injection. IV for bleeding from uremia.

III. Therapeutic Agents and Techniques for Managing Anemia

Stop the bleeding!

Oxygen Support

Maintain intravascular volume

Iron Dextran (Imferon)

A hematinic agent which is complex of ferric hydroxide and dextran for IM or IV use. Used in treatment of microcytic hypochromic anemia resulting from iron deficiency. Iron Dextran used intravenously replenishes depleted iron stores in the bone marrow to potentiate hemoglobin levels. Iron supplementation may be required by most patients receiving epoetin therapy. Failure to administer iron during epoetin therapy can impair the hematologic response to epoetin.

Folic Acid

Exogenous folate is necessary for nucleoprotein synthesis and maintenance for normal erythropoiesis. Folic acid stimulates production of red and white blood cells and platelets in certain megaloblastic anemias. Used in treatment of megaloblastic and macrocytic anemias due to folate deficiency.

Vitamin B-12

Cyanocobalamin and hydroxocobalamin; Essential to growth, cell reproduction, hematopoiesis and nucleoprotein, and myelin synthesis, and is a coenzyme for various metabolic functions including hematopoiesis. Used for treatment of pernicious anemia, Vitamin B-12 deficiency, increased B-12 requirements due to hemorrhage, malignancy, liver or kidney disease. Increased requirements associated with pregnancy, thyrotoxicosis, hemolytic anemia, hemorrhage, malignancy, hepatic and renal disease.

Erythropoietin

EpogenR, ProcritR, is a synthetic hormone produced by recombinant DNA techniques, which stimulates red blood cell production. Stimulates erythropoiesis in anemic patients with chronic renal failure, and may decrease the need for maintenance transfusions in these patients. It is not beneficial in the acute treatment of anemia as onset of reticulocyte response does not appear until 7-10 days and hemoglobin rise appears over 2-6 weeks of therapy. It is also effective in increasing the procurement of autologous blood in patients about to undergo elective surgery. Dose of 600U/kg IV twice per week for 21 days, 25-35 days before surgery increased volume of red blood cells by 41% compared to placebo in one study. Increasing the amount of autologous blood pre-op decreases the need for homologous blood transfusion.

Nutritional Support

Immunosuppressive agents if indicated

Oxygen-Carrying Blood Substitutes

Perfluorochemicals, recombinant hemoglobin as well as products derived from human or animal sources are in clinical trials. These intravenous fluids provide volume expansion and have the ability to carry oxygen. (Please refer to the accompanying table, "Status of Oxygen Therapeutics.") Blood substitute products promise significant benefits for patient treatment, including universal compatibility, extended shelf life, and a high degree of safety from infectious agents. Blood substitutes are not essential to the practice of bloodless medicine and surgery.

Granulocyte-Colony Stimulating Factor

Filgrastim is a hematopoietic growth factor produced by recombinant DNA technology which promotes proliferation and maturation of neutrophil granulocytes. It is effective in decreasing the incidence infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever. Therapy is discontinued when ANC was $> 10,000/\text{mm}^3$.

Hyperbaric Oxygen Therapy

10/30 rule for minimum red cell level has no scientific basis.

Techniques

- **Meticulous Hemostasis:** A technique of occluding every bleeding vessel that is encountered in the operating field and exercising great care to avoid inadvertent dissection. This is mainly a matter of skill and caution, and does not require any major surgical equipment. It is applicable to nearly all surgical procedures.
- **Hemodilution:** A procedure whereby blood is removed from a patient immediately before surgery and replaced with a non-blood volume expander. This reduces the loss of red blood cells during surgery. After surgery the collected blood is returned to the patient.
- **Arterial Embolization:** A procedure that uses either a mechanical or chemical agent to close off arteries that are actively bleeding. A special catheter is placed into the lacerated artery ahead of the bleeding and then a substance is injected that closes off the artery. The medical literature states that this procedure is helpful when there is heavy bleeding in the pelvic, gynecological, and abdominal areas.
- **Mechanical Occlusion of Bleeding Vessels:** A surgical technique using a clip, clamp or other similar device to occlude vessels, mainly during surgery. This technique can be used to stop bleeding from small and large vessels.
- **Hypotensive Anesthesia:** A technique of lowering the blood pressure of a patient during surgery to decrease the amount of blood loss. It is most effective in orthopedic procedures, but can be used in a wide range of surgery.
- **Hypothermia:** A technique of lowering an anemic patient's body temperature in order to decrease metabolic activity, heart rate and oxygen consumption. The objective is to lessen the load on decreased numbers of red blood cells.
- **Preoperative Planning:** A technique that requires the surgical team to prepare in advance for any expected or unexpected needs, during the pre-, intra- and postoperative period. Advance planning includes thorough patient assessment to identify clotting deficiencies, consideration of the need for any equipment or procedures such as an intraoperative blood salvage, hemodilution, hypothermia, hypotension, etc. Furthermore, in the postoperative period there is a need for vigilance and early recognition of bleeding, as well as prompt intervention to control hemorrhage.

Devices

- **Electrocautery:** Used during surgery to control bleeding that employs a scalpel-like device using and electric current to cauterize tissues as it cuts. Such devices are widely available in hospital operating rooms.
- **Endoscope:** A tube-like device that can allow physicians to view the internal structures of the digestive tract without surgery. Some can perform limited surgical procedures. Its greatest use involves quickly finding and controlling internal bleeding in the stomach and intestines, a common kind of bleeding managed by emergency room staff.
- **Intraoperative Blood Salvage ("Cell Saver"):** Used to recover blood shed into body cavities as a result of trauma or surgical incision. Shed blood from the surgical wound is aspirated filtered and washed, the RBC's are then returned to the circulatory system of the patient.
- **Hemobag:** An Ultrafiltration reservoir used to concentrate Whole Blood collected from anticoagulated extracorporeal circuits and reservoirs to promote autologous cell fractions, proteins and clotting factors that limit blood loss and donor exposure.
- **Argon Beam Coagulator:** A surgical tool that uses argon gas in addition to electrocautery to promote clotting and limit blood loss during surgery.
- **Gamma Knife Radio surgery:** A machine that employs high energy radiation to "burn" tumors and aneurysms non-invasively. Used mainly for procedures involving the brain.
- **Blood Microsampling Equipment:** Promotes blood conservation by restricting the quantity and frequency of blood sampling for lab tests. Using electrochemistry, analyzers can perform a complete range of common blood tests from only 3-5 drops of blood.
- **Laser:** A device similar in principal to an electrocautery device, but employing light instead of electricity. Used for specific types of surgery, and reported to be very effective in limiting blood loss.