Platelet transfusion :indication, ordering and associated risk

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COLLECTION

random donor pooled platelets:A single unit of platelets can be isolated from every unit of donated blood by centrifuging the blood

The number of platelets per unit varies according to the platelet count of the donor; a yield of 7×10^{10}

four to six units are pooled to allow transfusion of 3 to 4×10^{11} platelets per transfusion

Apheresis (single donor) platelets

collected from volunteer donors in a one- to two-hour apheresis procedure

Platelets are selectively removed along with some white blood cells (WBCs) and most RBCs and plasma are returned to the donor

A typical apheresis platelet unit provides the equivalent of six or more units of platelets from whole blood (ie, 3 to 6 x 10^{11} platelets)

Advantages of single donor platelets

exposure of the recipient to a single donor rather than multiple donors, and the ability to match donor and recipient characteristics such as HLA type, cytomegalovirus (CMV) status, and blood type for certain recipients

Both WBD and apheresis platelets contain some WBCs that were collected along with the platelets

These WBCs can cause febrile nonhemolytic transfusion reactions (FNHTR), alloimmunization, or transfusion-associated graft-versus-host disease (TA-GVHD) in some patients

Because of their plasma content, transfused platelets can cause adverse reactions including transfusion-related acute lung injury (TRALI) and anaphylaxis

Platelets concentrates also contain a small number of RBCs that express Rh antigens on their surface (platelets do not express Rh antigens)

The small numbers of RBCs in apheresis platelets pose an extremely low, but non-zero risk of Rh alloimmunization in most patients

transfusion medicine services avoid giving platelets from RhD-positive donors to RhD-negative females of childbearing potential because of the potential risk of RhD alloimmunization and subsequent hemolytic disease of the fetus and newborn (HDFN)

STORAGE

Platelets are routinely stored at room temperature, because cold induces clustering of von Willebrand factor (WVF) receptors on the platelet surface and morphological changes of the platelets, leading to enhanced clearance by hepatic macrophages and reduced platelet survival in the recipient

The risk of bacterial infection from platelets increases with storage duration

The shelf-life of platelets stored at room temperature is generally only five days, which are counted starting from midnight on the day of collection

This short shelf-life contributes to the potential for low platelet inventory and platelet shortages

INDICATIONS FOR PLATELET TRANSFUSION

most authors use the term "therapeutic transfusion" to refer both to transfusion of platelets to treat active bleeding and transfusion of platelets in preparation for an invasive procedure that could cause bleeding

The term "prophylactic transfusion" is used to refer to platelet transfusion given to prevent spontaneous bleeding

Actively bleeding patient

Actively bleeding patients with thrombocytopenia should be transfused with platelets immediately to keep platelet counts above 50,000/microL

in most bleeding situations including disseminated intravascular coagulation (DIC), and above 100,000/microL if there is central nervous system bleeding

Surgical or anatomic defect

Fever

Infection or inflammation

Coagulopathy

Acquired or inherited platelet function defect

Neurosurgery or ocular surgery – <100,000/microL

Most other major surgery – <50,000/microL

Endoscopic procedures – <50,000/microL for therapeutic procedures; 20,000/microL for low risk diagnostic procedures

Bronchoscopy with bronchoalveolar lavage (BAL) – <20,000 to 30,000/microL

Central line placement – <20,000/microL

Lumbar puncture – <10,000 to 20,000/microL in patients with hematologic malignancies and <40,000 to 50,000 in patients without hematologic malignancies; lower thresholds may be used in patients with immune thrombocytopenia (ITP)

Neuraxial analgesia/anesthesia – <80,000/microL

Bone marrow aspiration/biopsy – <20,000/microL

Prevention of spontaneous bleeding

prophylactic platelet transfusion to prevent spontaneous bleeding in most afebrile patients with platelet counts below 10,000/microL due to bone marrow suppression

use higher thresholds (ie, 20,000 to 30,000/microL) in patients who are febrile or septic

acute promyelocytic leukemia (APL) have a coexisting coagulopathy

- use a platelet transfusion threshold of 30,000 to 50,000/microL

SPECIFIC CLINICAL SCENARIOS

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generally use a threshold platelet count of 10,000/microL (transfuse for a platelet count <10,000/microL)

An exception is acute promyelocytic leukemia (APL), for which the threshold is higher (transfuse for a platelet count of <30,000 to 50,000/microL) due to a higher bleeding risk

If fever, sepsis, or coagulopathy is present, or if the patient is not hospitalized and/or cannot be closely monitored, higher thresholds may be needed.

Chemotherapy for solid tumors – Cancer chemotherapy often makes patients thrombocytopenic from bone marrow suppression.

Randomized trials of platelet transfusion threshold in this population have not been performed

Observational studies support a prophylactic platelet transfusion threshold of 10,000/microL ; a higher threshold, such as 20,000/microL, may be appropriate for patients with necrotic tumors

Immune thrombocytopenia (ITP) — Individuals with ITP produce antiplatelet antibodies that destroy circulating platelets and megakaryocytes in the bone marrow

Circulating platelets in patients with ITP tend to be highly functional, and platelet counts tend to be well above 30,000/microL

Bleeding is rare even in patients with severe thrombocytopenia (platelet count <30,000/microL)

TTP or HIT

Platelet transfusions can be helpful or even life-saving in patients with these conditions who are bleeding and/or have anticipated bleeding due to a required invasive procedure (eg, placement of a central venous catheter)

platelet transfusion should **not** be withheld from a bleeding patient due to concerns that platelet transfusion will exacerbate thrombotic risk

platelet transfusions may cause a slightly increased risk of thrombosis in patients with these conditions

thus, we do not use prophylactic platelet transfusions routinely in patients with TTP or HIT

ORDERING PLATELETS

Platelet dose

apheresis versus whole blood derived (WBD) platelets

leukoreduced units (if not routinely provided by the blood collection agency)

Irradiated units

cytomegalovirus (CMV)-negative platelets are required

the ABO type of the donor and the recipient need to be identical

Dose

approximately one WBD unit per 10 kg of body weight, which translates to SIX to EIGHT units of WBD platelets or one apheresis unit, both providing approximately 3 to 4 x 10^{11} platelet

For prophylactic transfusion, there is generally no reason to transfuse platelets more often than once a day

This platelet dosing is expected to raise the platelet count by approximately 30,000/microL within 10 minutes of the infusion

For an average-sized adult, six units of WBD platelets or one unit of apheresis platelets are transfused over approximately 20 to 30 minutes

ABO, Rh, and HLA matching

Platelets express ABO antigens and HLA class I antigens on their surface. They do not express Rh antigens (D, c, C, e, or E) or HLA class II antigens

it is common and acceptable to transfuse non ABO-identical platelets due to inventory constraints

transfusion of ABO-non-identical platelets are associated with lower post-transfusion platelet increments when compared with transfusion of ABO-identical platelets, especially when there is major-ABO incompatibility between the recipient and the platelets (eg, group O recipient receiving group A platelets)

Clinically significant hemolytic transfusion reactions secondary to transfusion of minor ABO-incompatible platelet products with high amounts of plasma and or "high titers" of anti-A or anti-B (eg, group O platelets given to group A patient) are uncommon, but they do occur

To limit such hemolytic reactions, some transfusion services monitor and limit the volume of ABO incompatible plasma given to a patient via platelet transfusions, or they volume-reduce or wash the ABO incompatible platelet products to reduce the plasma content

COMPLICATIONS

Infection — Donor screening procedures and pathogen inactivation do not completely eliminate the risk of bacterial and other bloodborne infections, and transfusion-transmitted bacterial infection from platelets represents a serious hazard of platelet transfusion that may be fatal

Measures that reduce the presence of bacteria include enhancements to skin preparation technique, diversion of the first 15 to 45 mL of collected blood so that it is not transfused, culturing the product, and using pathogen-inactivation technologies

Transfusion reactions

Transfusion-associated circulatory overload (TACO) – Platelet transfusion introduces approximately 200 mL of intravascular volume per transfusion

The incidence of TACO is in the range of 1 percent of transfused recipients. The incidence is higher in patients predisposed to volume overload due to comorbidities such as congestive heart failure, kidney failure, respiratory failure, and positive fluid balance.

Allergic and anaphylactic reactions

Allergic reactions to platelet transfusion are relatively common

They are usually due to IgE directed against proteins in the donor plasma

Common symptoms include urticaria and pruritus in mild cases, and wheezing, shortness of breath and hypotension in more severe cases

Febrile non-hemolytic transfusion reactions (FNHTR) – These reactions are mediated by various inflammatory mediators and leukocytes and may manifest as fevers, chills, and rigors

PLATELET COUNT INCREMENT

Following a platelet transfusion, the platelet count should rise, with a peak at 10 minutes to one hour and a gradual decline over 72 hours

A general rule of thumb is that transfusion of a standard pool of whole blood derived (WBD) platelets or one apheresis unit should increase the platelet count by approximately 30,000/microL in an adult of average size

Platelet count increment is typically measured within 24 hours in patients given prophylactic platelet transfusions

The length of time platelets have been stored has a modest effect on their survival in the recipient

Massive transfusion

BLOOD AND VOLUME REPLACEMENT

The management of the patient who is being rapidly and massively transfused requires careful and ongoing consideration of a number of complex physiological relationships

The primary concerns are maintaining cardiac output, oxygen carrying capacity, and hemostatic potential

Volumes up to 30 liters of crystalloid fluid can be life lifesaving in adults, but correction of the fluid deficit with crystalloid solutions occurs at the expense of increasingly severe tissue swelling, with stiff lungs and abdominal compartment syndrome ultimately being limiting

Along the way, blood dilution becomes an increasing problem and requires treatment with RBCs (oxygen carrying), plasma (osmotic and clotting proteins), and platelets.

Packed RBCs (pRBCs) in additive solution typically have a hematocrit of approximately 60 percent, with the remainder of the volume consisting of 10 percent plasma and 30 percent saline-based anticoagulant and nutrient additive solutions

the fluid portion of pRBCs is 25 percent plasma, with the concentration of all of the plasma coagulation factors at 25 percent of normal (0.25 units/mL)

ALTERATIONS IN HEMOSTASIS

activation and consumption of coagulation factors secondary to tissue trauma, such as massive head injury or muscle damage, or they may have reduced activity of coagulation factors secondary to prolonged shock, hypoxia-induced acidosis, hypothermia, or failure to clear activation peptides that act as competitive inhibitors

The replacement of blood loss with pRBCs and a crystalloid volume expander will result in gradual dilution of plasma clotting proteins leading to prolongation of the PT and aPTT

In an adult, there will be an approximate 10 percent decrease in the concentration of clotting proteins for each 500 mL of blood loss that is replaced

Additional bleeding based solely on dilution can occur when the level of individual coagulation proteins falls to 25 percent of normal. This usually requires 6 to 10 units of red cells in an adult

the PT, aPTT, and fibrinogen should be monitored in patients receiving massive blood transfusions of this magnitude

Two to eight units of fresh frozen plasma (FFP) should be given if the values exceed 1.5 times control

Each unit of FFP might be expected to increase the clotting protein levels by 6 percent in an adult, but because of losses in product preparation, storage, and of transfused factors to the interstitial space, typical increments are of the order of 2.5 percen

Cryoprecipitate or, when available, virus-inactivated fibrinogen concentrate, may be used when fibrinogen levels are critically low (ie, <100 mg/dL)

In an adult, each 10 to 12 units of transfused RBCs are associated with a 50 percent fall in the platelet count

significant thrombocytopenia can be seen after 10 to 20 units of blood, with platelet counts below 50,000/microL

For replacement therapy in this setting, six units of whole blood derived platelets or one apheresis concentrate should be given to an adult

each unit should increase the platelet count by 5000/microL or 30,000/microL for a full six unit

COMPLICATIONS OF MASSIVE TRANSFUSION

Metabolic alkalosis:

the metabolism of each mmol of citrate generates 3 mEq of bicarbonate (for a total of 23 mEq of bicarbonate in each unit of blood)

metabolic alkalosis can occur if the renal ischemia or underlying renal disease prevents the excess bicarbonate from being excreted in the urine

This may be accompanied by hypokalemia as potassium moves into cells in exchange for hydrogen ions that move out of the cells to minimize the degree of extracellular alkalosis

Low ionized calcium level — Citrate binding of ionized calcium can lead to a clinically significant fall in the plasma free calcium (ionized calcium) concentration

significant hypocalcemia should not develop in this setting except under extreme circumstances

the risk is substantially greater in a patient with either preexisting liver disease or ischemia-induced hepatic dysfunction. In such patients, the plasma ionized calcium concentration should be monitored and calcium replaced

10 percent calcium gluconate is used, 10 to 20 mL should be given intravenously (into another vein) for each 500 mL of blood infused

PREVENTION OF HYPERKALEMIA — Infants and patients with renal impairment may develop hyperkalemia because of potassium leakage due to prolonged blood storage

Select only red cells collected less than 10 days prior to transfusion.

Any unit of red cells can be washed immediately before infusion to remove extracellular potassium