



Platelet Transfusion – Use, Abuse and Misuse

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ABSTRACT

Platelet transfusion is the mainstay therapeutic support of surgical, hematological, oncological, and transplant patients after myeloablative therapy. Platelet refractoriness continues to challenge us in day-to-day practice. The threshold for transfusing these platelets to patients continues to stimulate debate and there is an urgent need to review the current indications and contraindications of platelet transfusion to avoid related complications. Platelets are ABO and Rh typed. ABO identical or compatible units are preferred, but not required.

Random donor platelets (RDP) are dosed at 1 unit per 10 kg of body weight. Stable patients who are not refractory to platelet transfusions can be expected to have a platelet count increase between 5,000-7,000 per unit. Single donor platelets (SDP) is dosed at 1 apheresis unit per transfusion episode, which is generally equivalent to 6-8 units of pooled RDP.

The general guidelines for platelets transfusion with thrombocytopenia include: stable patients with platelet counts $<10,000/\mu\text{L}$, patients with platelet counts $<20,000/\mu\text{L}$ associated with minor bleeding, fever or splenomegaly, patients with platelet counts $<50,000/\mu\text{L}$ with significant bleeding or undergoing an invasive procedure and patients with documented platelet function abnormalities. Patients who have ingested aspirin products 48 hours or longer prior to surgery are not at increased risk for bleeding due to platelet dysfunction. Contraindications to platelets transfusions in thrombocytopenia include: thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), heparin-induced thrombocytopenia, platelet count $>100,000/\mu\text{L}$ without evidence of platelet dysfunction, idiopathic thrombocytopenic purpura unless bleeding is life threatening, prophylactically following routine cardiac surgery.

A febrile non-hemolytic transfusion reaction (FNHTR) is the most common complication of platelet transfusion. Allergic reactions are mild and are observed in approximately 1% of platelet transfusions. Rare reactions to platelets include bacterial sepsis, transfusion related acute lung injury, and transfusion associated graft vs host disease (GVHD).

Patients exposed to foreign platelet antigens may develop alloantibodies that cause platelet immune refractoriness or alloimmunization. Previous exposure occurs through pregnancy or transfusion. Alloimmunization is most often due to patient antibodies against donor HLA class I antigens on the platelet surface. The risk of alloimmunization is greatly reduced by leukoreduction, with no difference in risk between leukoreduced RDP and SDP. To assess platelet response, a one hour post-platelet count is necessary. Patients suspected of alloimmunization should have an HLA antibody screen. If positive, HLA antigen typing should be performed. In patients who do not respond to HLA-matched SDP, a trial of IVIG or aminocaproic acid may be beneficial. These patients may also benefit from ABO identical platelets.

The serious hazards of platelets transfusion include alloimmunization and the induction of refractoriness, GVHD, and the transmission of infections, all of which could be life-threatening. Less risky alternative therapeutic approaches like recombinant human thrombopoietin (rhTPO), lyophilized heat-treated platelet membrane preparations, thrombospheres and infusible platelet membranes (IPM) may become more widely available in future minimizing platelets transfusion to the least.

INTRODUCTION

Modern oncological practice heavily relies on platelets support. Use of platelets is indicated for the prevention and treatment of hemorrhage in patients with thrombocytopenia or platelet function defects. The platelet count is the primary trigger for the use of platelets, with clinical risk factors for bleeding and

the extent of bleeding also influencing the decision to transfuse. Whereas platelet transfusions may be necessary for hemostasis in conditions with inadequate platelet production, platelet transfusions are usually ineffective and may even be harmful in those characterized by peripheral platelet destruction or consumption. A brief outline of the contributing causes of

thrombocytopenia and its effective management would be discussed in this article to minimize platelets transfusion's use, abuse and misuse in general clinical practice.

A brief account of platelets transfusion history may help within the context of past and current platelet transfusion practices. The value of platelets transfusions for thrombocytopenia was first reported in 1910, when Duke described three patients with bleeding due to thrombocytopenia, each of whom showed improvement with transfusions of platelet containing fresh, whole blood. The discovery was followed by the development of new techniques to prepare platelets components. Before the 1950s, fresh whole blood or platelet rich plasma transfusions were only therapeutic agents available for thrombocytopenic states and related bleeding disorders. These treatments were cumbersome and their effectiveness was limited by the risk of volume overload. Methods of platelets pheresis using centrifugation were developed in the 1950s and 1960s, allowing platelets concentrate to be given, though the platelet shelf life of early platelets concentrate was used to be few hours only. Unsuccessful attempts were carried out to prolong the storage of platelets by freezing and lyophilization methods during this era. An attempt to store platelets at 4°C could result to a maximum of 24 hours shelf life of functionally effective platelets. In 1970, platelets stored at room temperature were shown to have greater hemostatic efficacy than the stored one at 4°C. With the improvement of storage conditions and containers by mid 1980s, it was possible to store platelets up to 5 days at 22°C. In 1985, storage at room temperature was extended to 7 days; however concerns about high reaction rate and potential extent of bacterial proliferation during 7 days storage forced regulators to curtail the shelf life to 5 days only.

Platelet transfusion therapy must be individualized based on the patient's requirements and the clinical diagnosis of the thrombocytopenic or dysfunctional state. Pseudothrombocytopenia due to in vitro platelet clumping on automated instrument counts should be excluded prior to any consideration of therapy. It should be crosschecked by manual counting, if deemed necessary.

At present, platelet for therapeutic use is prepared from either unit of whole blood or by apheresis. Whole blood derived platelets can be prepared using platelet rich plasma (PRP) where whole blood is collected into anticoagulant nutrient solution and subsequently centrifuged to separate out PRP. The PRP is centrifuged to separate out platelet concentrate (PC), which contains 60-75% of platelets present in whole blood unit from which it has been derived. A single unit of random donor platelets -platelets concentrate (RDP/PC) contains approximately $0.5-0.7 \times 10^{11}$ platelets suspended in 50 mL of plasma. The same may be obtained from buffy coat technique where leucocytes are removed and discarded from buffy coat aliquot. Both methods use differential centrifugation of whole blood to prepare a concentrate of platelets suspended in the donor's plasma. Platelet concentrates are nearly free of red cells; the number of white cells varies with the technique used in preparation. Presently PRP-derived platelet concentrates are stored in approximately 40-50 ml plasma for up to 5 days at 22°C in specialized plastic bags that are permeable to oxygen and carbon dioxide, with gentle continuous agitation on platelet agitators. The number of platelets in single bag is too small for

an adequate therapeutic effect in adult with thrombocytopenia; therefore platelets concentrate for 4 to 10 donors are customarily combined (pooled concentrate). Once pooled, platelets outdate in 4 hours. Unused platelets must be returned to the blood bank within 30 minutes of issue. Alternatively, apheresis can be used to collect more platelets from single donor.

The use of apheresis platelets is growing popularity. In this method whole blood is drawn from a donor, is mixed with anticoagulant nutrient mixture and centrifuged to segregate according to their density. The various components (buffy coat, platelets) are recognized by optical sensors, which subsequently direct them into separate containers. The undesired components are returned to the donor. Single donor platelets (SDP) collected by apheresis contain approximately $3.0-4.0 \times 10^{11}$ platelets suspended in 200-600 mL of plasma. It is not pooled before transfusion as they contain approximately the equivalent of 5 units of whole blood PRP derived PC.

It is generally accepted that prophylactic platelet transfusions reduce the risk of hemorrhage in patients undergoing chemotherapy for leukemia or cancer. Platelet transfusion is a cornerstone of supportive therapy for patients undergoing cytotoxic chemotherapy. However, the degree of thrombocytopenia that should trigger the use of prophylactic platelet transfusions -the platelet-transfusion trigger is still debated. The definition of the platelet-transfusion trigger is important because of increasingly aggressive anticancer treatment, the need to avoid transfusion-associated risks, and costs. These prophylactic transfusions are usually given when the platelet count falls below 20,000 / μ L. However, the risk of bleeding depends not only on the platelet count, but also on the underlying disease, the use of drugs that interfere with platelet function, and complications such as fever and infection. Moreover, platelet concentrates are a limited and expensive resource, and they carry a low but nevertheless measurable risk of untoward effects. These points were considered at the National Institutes of Health Platelet Transfusion Consensus Conference, whose results were published in 1987. The safety of decreasing the usual prophylactic platelet-transfusion threshold to an automated platelet count of 10,000 / μ L should be viewed as a general reference value rather than an absolute one. Expert clinical judgment and careful monitoring of the patient remain the cornerstones of platelet-transfusion practice.

Despite improvement in production of PC the conventional platelet transfusion has many drawbacks. A febrile non-hemolytic transfusion reaction (FNHTR) is the most common complication of platelet transfusion. FNHT reactions occur in approximately 1% of all transfusion reactions. This increases to as much as 30% in patients who have multiple transfusions. This is due to either recipient antibodies to donor WBCs or cytokines, i.e., IL-1, IL-6 and TNF in the platelet components that are released from the WBCs during storage. Symptoms include an increase in temperature, chills/rigors, tachycardia, and dyspnea. The reaction generally subsides within 30 minutes of stopping the transfusion. Most FNHTR do not recur. Patients with recurrent FNHTR may benefit from leukoreduced platelet components, particularly those leukoreduced prior to storage. A preexisting fever is not a contraindication for platelet transfusion. Allergic reactions occur in approximately 1% of platelet transfusions. These reactions are generally mild and respond to antihistamines. Rare reactions to

platelets include bacterial sepsis, transfusion related acute lung injury, and transfusion associated GVHD. Fever and chills may be the presenting symptoms of acute hemolysis, bacterial sepsis, or FNHTR. Therefore, it is important to stop the transfusion and follow hospital policy for reporting transfusion reactions to the blood bank so that an investigation can determine the cause of the reaction.

Transfusion associated GVHD is specifically eliminated by irradiation of platelets. Filtration does not prevent GVHD since lymphocytes are of similar size to RBC and therefore transmitted through filter. Indications for irradiated platelets include the period after stem cell transplantation, Hodgkin's disease, fetal transfusion, neonatal exchange transfusion and congenital defects of cell-mediated immunity. Platelets from partially or fully matched donors (either selected or by default, such as those from first degree relatives) should always be irradiated for any recipient because the viable lymphocytes they contain may not be efficiently eliminated by the host immune system.

Though transmission of infection is minimized by careful screening procedures and by excluding high-risk individuals from the donor pool, the dwindling risk of transmission of hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) despite of screening procedures still occasionally may contaminate blood products and an advent of hepatitis G and a new variant of Creutzfeldt-Jacob disease adding to the list also bring new fears. In recent years, the recognition that leucocyte found in PC may result in undesirable biological and clinical effects (Bordin et al, 1994) has led to pre-storage leukoreduction in many jurisdictions. Leukoreduction (filtration) of platelets is frequently performed to remove the white blood cells responsible for alloimmunization and CMV transmission.

Donor requirements and infectious disease screening for apheresis platelet donation are the same as for whole blood donation, except that recent ingestion of aspirin is not permitted for apheresis donation since the product may be the sole source of platelets for a recipient.

Whenever possible the plasma of a platelet component should be ABO compatible with the recipient's red cells, particularly if the recipient is a child. Platelets are ABO and Rh typed. ABO identical or compatible units are preferred, but not required. Ideally, transfused platelets should be Rh (D) compatible with the recipient. Although not present on platelets, the Rh (D) antigen is present on Rh (D) positive red cells. Since platelet concentrates contain a few red cells, Rh (D) negative patients must receive from Rh (D) negative donors. Rh (D) positive patients can receive platelets from either Rh (D) positive or Rh (D) negative donors. In adults, ABO incompatible platelets may be used because the volume of plasma in the product is usually not clinically significant. Apheresis units may contain approximately 350 mL of plasma, but passive transfer of antibodies rarely results in hemolysis. Cross-matching is not necessary because the volume of RBCs is <2 mL in each platelet component. However, 1 mL of RBCs is capable of causing alloimmunization to the D antigen. Rh compatibility is therefore recommended in women of childbearing age and children to prevent D antibody formation and potential hemolytic disease of the newborn. When Rh incompatible transfusions are necessary,

prophylaxis with Rh immune globulin should be considered. Use of anti-D for Rh-negative recipients of Rh-positive platelets is essential. If Rh D positive platelets have to be given to an Rh D negative patient who may become pregnant in the future, anti-Rh (D) immunoglobulin (50mcg/250 IU) should be given to avoid the 5% risk of the patient developing Rh D antibodies. Similarly both male and female Rh-negative persons who could be potential recipients of Rh-positive bone marrow transplant. One dose of anti-D (120mcg/600IU) is sufficient to cover up to 10 standard doses of platelets given over a 28 day period. It should be administered via intravenous or subcutaneous route to prevent the possibility of a hematoma developing. ABO incompatibility can reduce the expected count increment (CI) by 10-30%. Group 'O' PCs are tested for high titer anti-A and anti-B and if positive should only be transfused to group 'O' recipients. This is to avoid hemolysing the patient's red cells by anti-A or anti-B in the donor's plasma.

DOSAGE

On an average RDP-platelet concentrate is dosed at 1 unit per 10 kg of body weight. Stable patients who are not refractory to platelet transfusions can be expected to have a platelet count increase between 5,000-7,000 per unit.

SDP is dosed at 1 apheresis unit per transfusion episode, which is generally equivalent to 6-8 units of pooled RDP-platelet concentrate.

Platelets should be rapidly transfused over 30 to 40 mins. A dose is usually sufficed to stop hemorrhage; transfusion may be repeated every 24 to 48 hours till bleeding ceases, and/or bone marrow recovery is evident. In the presence of severe infection or DIC, a higher dose or more frequent transfusion may be required.

MANAGEMENT OF PLATELET REFRACTORINESS

Patients exposed to foreign platelet antigens may develop alloantibodies that cause platelet immune refractoriness or alloimmunization. Previous exposure occurs through pregnancy or transfusion. Alloimmunization is most often due to patient antibodies against donor HLA class I antigens on the platelet surface. The risk of alloimmunization is greatly reduced by leukoreduction, with no difference in risk between leukoreduced RDP-platelet concentrate and SDP. To assess platelet response, a one-hour post-platelet count is necessary.

A corrected count increment (CCI)* of >7,500 indicates an acceptable response. If the CCI is <7,500 in the absence of infection, splenomegaly or other circumstances causing platelet destruction, alloimmunization may be present. About one-third multiply transfused patients could develop platelets alloimmunization. The demonstration in such patients of a poor post-transfusion platelet increment on two occasions suggests the diagnosis of a platelet-refractory state. There are multiple possible causes of the platelet refractory state. Nonimmune causes include hypersplenism, disseminated intravascular coagulation (DIC), sepsis and medications. Immune causes include alloantibodies, such as HLA and platelet-specific antibodies; autoantibodies, such as those found in patients with ITP; and drug-related antibodies, such as those associated with administration of quinidine. In acutely ill, multiply transfused hematology/oncology patients, the cause(s) of the platelet refractory state are often difficult to

define. A multiple linear regression analysis identified above-mentioned factors associated with platelet refractoriness. In vitro demonstration of platelet antibodies (HLA antibodies or platelet-specific antibodies) confirms the diagnosis. Once the platelet-refractory state occurs, controlling bleeding may be difficult. It is important to reserve platelet transfusions for appropriate clinical circumstances in which an effective increment is anticipated.

The clinical difficulty of attaining hemostasis in platelet-refractory states has prompted the development of strategies to try to prevent their occurrence. The use of leuko-reduced blood products is the preventive strategy most commonly employed. This technique reduces exposure to the leukocyte-associated HLA antigens thought to be responsible for inducing HLA alloimmunization. Patients suspected of alloimmunization should have an HLA antibody screen. If positive, HLA antigen typing should be performed. In patients who do not respond to HLA matched SDP, a trial of IVIG or aminocaproic acid may be beneficial. These patients may also benefit from ABO identical platelets.

*Calculation of CCI

$$CCI = \frac{(\text{Post-txn count} - \text{Pre-txn count}) \times \text{Body Surface Area (M}^2\text{)}}{\text{Number of Platelets given (x } 10^{11}\text{)}}$$

Once alloimmunization has occurred, controlling bleeding is a challenge for which compatible single-donor platelets, if available, may be the only effective strategy. In the already alloimmunized patient, the selection of compatible, hemostatically effective platelets requires costly specialized transfusion services. Identification of HLA or platelet-specific antibodies provides the basis for the subsequent selection of HLA-matched and/or cross-match-compatible platelets for transfusion. If platelet alloimmunization is identified, single-donor apheresis platelets from a donor more closely matched for HLA antigens should be tried. Such donors may be family members (who are more likely to be HLA compatible with the patient), or HLA-selected community donors. If fully matched donors are not available, data support the use of partial HLA matching. If the CCI is low following transfusion of HLA-matched PCs check for non-immune causes of refractoriness (fever, splenomegaly, DIC, amphotericin-B treatment) and test for antibodies to Human Platelet Antigens (HPA) if there is no obvious cause for non-immune refractoriness. If refractoriness is due to non-immune causes and if there is significant bleeding, give two or three adult therapeutic doses (ATD) or give one ATD two or three times daily. If no cause for poor responses to HLA-matched platelet transfusions is found, and the patient is not bleeding, withhold prophylactic platelet transfusions.

Unfortunately, neither HLA-compatibility nor platelet cross-match compatibility is a guarantee of a good post-transfusion increment or of platelet hemostatic effectiveness in any given alloimmunized patient. Because of decreased donor exposure to HLA antigens and lower leukocyte content, the use of random-donor apheresis platelets might be expected to delay the onset of alloimmunization compared to pooled random-donor platelets. However, studies on single donor versus pooled random donor platelet transfusions to prevent alloimmunization have given inconsistent results.

RATIONALE FOR PLATELET TRANSFUSION

The major indication for platelet transfusion is the treatment or prevention of bleeding in profoundly thrombocytopenic patients with bone marrow failure due to malignancy and/or myelosuppressive therapy. Within even these clinical circumstances, however, consideration must be given to the overall clinical picture, including the severity of the complications, rather than just the platelet count per se when considering the necessity for a platelet transfusion. Although platelet transfusion therapy has become a mainstay in the support of cancer patients receiving aggressive chemotherapy, the appropriate clinical circumstances for either prophylactic or therapeutic platelet therapy requires considerable clinical judgment.

Platelet transfusions may also be indicated for moderately thrombocytopenic patients at risk for bleeding undergoing major surgical procedures, but this is usually necessary only in cardiothoracic surgery, in which abnormal microvascular bleeding is a consequence not only of thrombocytopenia but of platelet dysfunction induced by the cardiopulmonary bypass machine. In most other circumstances, pathologic (generalized) bleeding due to thrombocytopenia is seldom encountered unexpectedly during surgery, and thrombocytopenia diagnosed pre-operatively is usually amenable to other therapeutic modalities, depending on the underlying cause. Only very rarely is "washout" by massive intraoperative transfusion sufficient in itself to cause pathologic bleeding on the basis of a lowered platelet count and to require platelet replacement therapy.

Platelet transfusions may be useful in the thrombocytopenic, massively bleeding patient with DIC. Because thrombocytopenia usually is a component of the more global hemostatic defect associated with a consumption coagulopathy, replacement of fibrinogen with cryoprecipitate or other clotting factors with fresh frozen plasma (FFP) may also be required. Platelet survival is variably shortened in DIC; this necessitates frequent monitoring of platelet levels and possibly more frequent platelet transfusions to maintain hemostasis.

In life-threatening bleeding in patients with an immune type of thrombocytopenia and in patients with either congenital or acquired thrombocytopathies, other therapies are usually more appropriate, although platelet transfusions may be indicated for serious bleeding. Many patients with ITP have a decreased risk of bleeding compared to patients with an identical platelet count caused by bone marrow failure. The presumed mechanism is that platelets newly released from the bone marrow are more hemostatically functional than older platelets. Therefore, patients with immune thrombocytopenia are not usually candidates for platelet transfusion even in the presence of severe thrombocytopenia (less than 5,000/ μ l). In addition, the survival of transfused platelets in patients with ITP is measured in hours, making it impossible to effectively maintain a target platelet count. Platelet transfusions should be used only for significant or life-threatening bleeds (e.g. CNS), or to treat bleeding during a required major surgical procedure. Platelet transfusion usually is not required to control bleeding during splenectomy. However, if necessary, the transfusion is most effective if administered after clamping the splenic artery to prevent the transfused platelets from being removed by the spleen.

Platelet transfusions conventionally are thought to be contraindicated in patients with TTP/HUS. The administration of platelets to patients with TTP has been reported to be associated with cerebral thrombotic events (Gordon et al, 1987). Thus, platelets probably should be administered only in the setting of life-threatening hemorrhage or perhaps prior to surgical procedures.

INDICATIONS FOR PLATELET TRANSFUSION

Platelet count <10,000/ μ L due to bone marrow infiltration or suppression, for prophylaxis or bleeding

Patients with platelet counts $>5,000/\mu\text{L}$ who are not bleeding and who are otherwise stable may not require transfusion. Between $10,000/\mu\text{L}$ and $20,000/\mu\text{L}$, clinical judgment must be exercised with consideration to the risk of serious bleeding and to the presence of infection, coagulopathy, splenomegaly or other clinical circumstances which increase that risk by compromising platelet function or survival. Aplastic anemia patients are not usually transfused in the absence of serious bleeding.

Platelet transfusions should be avoided in immune thrombocytopenia (ITP, PTP), and in thrombotic microangiopathies such as TTP, HUS and HELLP syndrome, even when the thrombocytopenia is very severe. Other therapeutic strategies, such as steroids, intravenous gamma globulin, or plasma exchange, are usually more appropriate, depending on the clinical diagnosis.

In cases of life-threatening hemorrhage, platelet transfusions in the immune thrombocytopenias may on rare occasions be necessary when other therapies have either failed or not had time to become effective. Platelet transfusion therapy in such patients with increased platelet destruction may require more intensive therapy than in patients with marrow failure.

Platelet transfusions are contraindicated in heparin-induced thrombocytopenia, as this may precipitate extensive intravascular coagulation.

Platelet count <50,000/ μ L with microvascular bleeding, or pre-operatively

If surgery cannot be postponed or there is traumatic bleeding, patients with a platelet count of $< 50,000/\mu\text{L}$ may require a platelet transfusion. For elective surgery, it is preferable to wait for the platelet count to rise spontaneously, or with appropriate treatment. In the case of drug-induced or alcohol-induced thrombocytopenia, the platelet count usually returns to normal spontaneously within 1-2 weeks after the offending agent has been withdrawn.

Occasionally, massive transfusion may result in dilutional thrombocytopenia to $<50,000/\mu\text{L}$ associated with abnormal microvascular bleeding and requires platelet replacement therapy. Prophylactic platelet administration after the transfusion of a fixed number of red cell units is not indicated. For neurosurgical procedures, a platelet count of $>100,000/\mu\text{L}$ is recommended.

Platelet count <50,000/ μ L with microvascular bleeding in cardiac surgery off CPB

This includes thrombocytopenic cardiac surgery patients with on-going abnormal microvascular bleeding in whom no surgical

cause can be identified. Such patients usually have qualitative as well as quantitative platelet abnormalities, which are felt to contribute to the bleeding tendency. However, prophylactic platelet transfusion is not recommended in view of the lack of evidence that this is helpful in preventing bleeding in cardiac surgery patients. The indications for autologous platelets do not differ from the indications for allogeneic platelets.

Intrinsic or acquired platelet dysfunction with bleeding or pre-operatively

The template bleeding time, frequently included as part of the clinical assessment of bleeding risk, is now felt to be of limited usefulness except as an adjunct in the diagnosis of inherited disorders of platelet function. The bleeding time is not a specific indicator of *in vivo* platelet function. Recent meta-analysis of published articles has shown that there is no evidence that the bleeding time is a predictor of the risk of hemorrhage, nor is it a reliable predictor of intraoperative bleeding. A prolonged bleeding time per se is certainly not an adequate justification for the use of platelet transfusion prior to or during invasive procedures.

When the clinical presentation suggests an inherited disorder of platelet dysfunction, or von Willebrand's disease, a prolonged bleeding time may be useful in helping to identify a patient with such a thrombocytopathy. On the other hand, a normal bleeding time under these circumstances should not deter one from pursuing more specific hemostatic tests, such as platelet aggregation with ristocetin, to make a specific diagnosis. Patients with documented disorders of platelet dysfunction (other than von Willebrand's Type II disorders) may benefit from DDAVP prior to invasive procedures or surgery.

Acquired reversible platelet dysfunction occurs most commonly in patients with renal insufficiency. In such patients, therapy with dialysis (in the case of frank uremia), DDAVP, estrogen or cryoprecipitate should be employed as the primary therapeutic strategies for abnormal uremic bleeding; platelet transfusion is seldom indicated. Rarely, platelet transfusions may be required in patients unresponsive to other therapies who have serious bleeding, in which case larger doses may be necessary than in patients with marrow failure.

In patients with other reversible causes of platelet dysfunction, usually due to medication, these drugs should be discontinued prior to elective surgery for as many days as is necessary to clear the drug's effect on the platelets. Prior to emergency surgery in patients with drug-induced platelet dysfunction, DDAVP should be given in preference to platelet transfusion. Exogenous platelets may also be rendered dysfunctional by the drug if it is still circulating. Platelets acetylated by aspirin are dysfunctional and require six to eight hours for recovery of normal function following transfusion.

In patients with irreversible platelet dysfunction associated with myeloproliferative disorders, effective treatment of the underlying disease usually helps to correct the bleeding diathesis, but DDAVP and/or platelet transfusions may be necessary in acute surgical situations or when the patient is bleeding despite other therapies.

Patients with congenial platelet dysfunction, such as Glanzmann's thrombasthenia, Bernard-Soulier syndrome, and storage pool

disease, to name but a few, often have a bleeding diathesis from early age and usually require platelet transfusions for severe bleeding. For many cases of von Willebrand's disease, DDAVP, rather than platelet transfusion is appropriate.

FUTURE CONSIDERATIONS

Platelet substitutes include thrombospheres and infusible platelet membranes (IPM). These products improve bleeding times, albeit transiently (48 hours). Their clinical utility seems to be in patients with thrombocytopenia and active bleeding. These products augment the function of normal circulating platelets. They are not thrombogenic. Heat inactivated human plasma is used in the manufacturing process of these products. Therefore, they could theoretically transmit pathogens. However, the potential advantages to these products include minimal viral and bacterial contamination as a result of heat treatment, reduced alloimmunization, prolonged shelf life (36 months), and reduced FNHTR.

The rational use of transfusions should be considered not only for each thrombocytopenic patient but also on a population basis. Platelets are precious and scarce resource, mostly the result of an altruistic gesture from an unpaid donor. To ensure the adequate supply in the face of increasing demand, an efficient ordering procedure should be put in place so that platelets are not wasted, although it is likely that future demand of routine platelets transfusion support for chemotherapy will be alleviated by the advent of newer techniques and novel molecules. The indiscriminate use of the platelets should be deplored because this increases the risk of platelets refractoriness, developing HLA antibodies, and also acquiring transfusion transmitted infections or GVHD.

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