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Platelet Transfusion in Clinical Practice: A Narrative Literature Review

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ABSTRACT

Platelet transfusion plays a vital role in clinical practice, serving as a cornerstone in the management of various medical conditions. Thrombocytopenia, characterized by a low platelet count, can result from decreased platelet production, increased peripheral platelet destruction, increased splenic sequestration, or dilutional thrombocytopenia. Platelet transfusion is commonly administered for prophylactic purposes to prevent bleeding in patients with hypoproliferative thrombocytopenia and before invasive procedures or surgeries. In cases of bleeding or significant bleeding risk, therapeutic platelet transfusion is employed. This review article aims to provide an understanding of platelet transfusion and its applications in daily clinical practice. The dosage and administration of platelet transfusion, as well as potential complications, are discussed. Understanding the indications, contraindications, and appropriate use of platelet transfusion is crucial for optimizing patient outcomes and ensuring safe and effective clinical practice.

1. Introduction

Platelets are circulating cell fragments characterized by their small size, abundance, and lack of a nucleus. Platelets fulfill various functions in a wide range of physiological processes in the human body, including blood clotting, wound healing, and immune response.¹ Since the first blood transfusion experiment in the 17th century, blood transfusion has evolved from whole blood transfusion to using specific components based on clinical indications, such as red blood cells, platelets, frozen plasma, and plasma derivatives. Platelets play a crucial role in the process of hemostasis through their response to vascular injury. Platelet transfusion was proven to reduce mortality rates from bleeding in patients with acute leukemia in the 1950s, and its usage has continued to expand since then. Platelet transfusion plays a crucial role in the field of clinical practice, serving as a

cornerstone in the management of various medical conditions.²

Platelets are one of the blood components frequently used for blood transfusion. The number of patients receiving platelet transfusions has been increasing in recent years. Platelet transfusion is employed in patients with low platelet count (thrombocytopenia) or platelet function disorders. Platelet transfusion can be administered as prophylaxis to reduce the risk of bleeding and as therapy to control active bleeding. In daily clinical practice, over 70% of platelet transfusions are performed for prophylactic purposes. Platelet transfusion has become an integral part of managing cases involving cancer, hematologic malignancies, bone marrow failure, and bone marrow transplantation.³ This study aimed to provide an understanding of platelet transfusion and its

applications in daily clinical practice. Understanding the indications, contraindications, and appropriate use of platelet transfusion is crucial for optimizing patient outcomes and ensuring safe and effective clinical practice.

Causes of thrombocytopenia

Thrombocytopenia is a hematological condition characterized by a platelet count $<150 \times 10^9/L$, although some literature also uses a cutoff value of $<100 \times 10^9/L$. Based on its pathophysiology, thrombocytopenia can be caused by decreased platelet production, increased peripheral platelet destruction, increased splenic sequestration, and dilutional thrombocytopenia. The investigation of thrombocytopenia should consider the patient's age, baseline platelet values, medical and surgical history, family history, medication history, physical examination to assess signs of bleeding or thrombosis, and laboratory tests.⁴ The following are the causes of thrombocytopenia:

Decreased platelet production

Causes of decreased platelet production include bone marrow failure (such as aplastic anemia), bone marrow suppression due to exposure to certain medications (such as valproic acid, daptomycin, certain chemotherapy agents), chronic alcohol use, congenital thrombocytopenia, viral infections (such as cytomegalovirus, Epstein-Barr virus, and parvovirus), and systemic conditions such as nutrient deficiencies (folate, vitamin B12), sepsis, and myelodysplastic syndromes.⁵

Increased peripheral platelet destruction

The lifespan of platelets is approximately 8-10 days. Increased peripheral platelet destruction can be caused by immune-related or non-immune processes. In immune-mediated thrombocytopenia, antiplatelet autoantibodies bind to platelets and megakaryocytes, leading to increased platelet destruction by the reticuloendothelial system and reduced platelet production. Antiplatelet antibodies can be found in

conditions such as primary immune thrombocytopenia (ITP), drug-induced ITP, lymphoproliferative disorders, autoimmune conditions like systemic lupus erythematosus (SLE), and chronic infections such as hepatitis C, human immunodeficiency virus (HIV), and *Helicobacter pylori* infection. Non-immune causes of increased platelet destruction can be observed in patients with prosthetic heart valves, preeclampsia, HELLP syndrome, disseminated intravascular coagulation (DIC), and thrombotic microangiopathies.⁵

Increased splenic sequestration

In normal individuals, approximately one-third of the platelet mass is located within the spleen. However, when conditions such as splenomegaly and increased congestion in the spleen occur, platelets tend to accumulate within the spleen, leading to a reduction in the circulating platelet count.⁵

Dilutional thrombocytopenia

Dilutional thrombocytopenia can be found in patients who receive massive blood transfusions or massive fluid resuscitation.⁵

Indication of platelet transfusion

Platelets can be transfused with the aim of preventing bleeding (prophylactic indication) or stopping bleeding (therapeutic indication) in patients with thrombocytopenia.⁶

Prophylactic platelet transfusion

Prophylactic platelet transfusion to prevent bleeding is indicated based on the following threshold values:

Hypoproliferative thrombocytopenia

Thrombocytopenia is a common issue encountered in hematologic and oncologic patients. Platelet transfusion is commonly administered as prophylaxis to prevent bleeding in cases of hypoproliferative thrombocytopenia caused by malignancy or chemotherapy effects. The American Association of

Blood Banks (AABB) recommends platelet transfusion to prevent spontaneous bleeding when the platelet count is $\leq 10,000/\mu\text{l}$. This threshold increases to $\leq 15,000\text{-}20,000/\mu\text{l}$ if the patient has an increased bleeding risk, such as fever, infection, or inflammation.⁶

Disseminated intravascular coagulation (DIC)

In cases of DIC, prophylactic platelet transfusion is administered when the platelet count is $< 50,000/\mu\text{l}$.⁶

Before invasive procedure or surgery, including 1) Neurosurgery or ophthalmic surgery: $< 100,000/\mu\text{l}$. 2) Major surgery: $< 50,000/\mu\text{l}$. 3) Central line placement: $< 20,000/\mu\text{l}$. 4) Epidural anesthesia: $< 80,000/\mu\text{l}$. 5) Bronchoalveolar lavage (BAL): $< 20,000\text{-}30,000/\mu\text{l}$. 6) Endoscopy: $< 50,000/\mu\text{l}$ for therapeutic procedures,

$< 20,000/\mu\text{l}$ for low-risk diagnostic procedures. 7) Vaginal delivery: $< 30,000/\mu\text{l}$ if uncomplicated, $< 50,000/\mu\text{l}$ if complicated. 8) Lumbar puncture: $< 20,000/\mu\text{l}$ in hematologic malignancies, $< 50,000/\mu\text{l}$ in patients without hematologic malignancies.^{2,6}

Therapeutic platelet transfusion

Bleeding

Clinically significant bleeding typically refers to bleeding that is more severe than skin bleeding or epistaxis lasting > 30 minutes, typically classified according to the World Health Organization (WHO) as grade 2 or higher.⁷ Table 1 presents the modified WHO bleeding scale.

Table 1. Modified WHO bleeding scale.⁷

Bleeding grade	Examples
Grade 1	Petechiae or purpura that is limited to 1 or 2 specific areas or is scattered and not closely grouped Bleeding in the oropharynx or epistaxis lasting less than 30 minutes
Grade 2	Melena, hematemesis, hemoptysis, hematochezia, musculoskeletal bleeding, or soft tissue bleeding that does not require a red blood cell transfusion within 24 hours of onset and without hemodynamic instability Severe oropharynx or epistaxis > 30 minutes Oral blood blisters causing symptoms Multiple bruises, with each bruise larger than 2 cm or at least one bruise larger than 10 cm Diffuse petechiae or purpura Gross hematuria Bleeding from invasive sites Abnormal vaginal bleeding that results in the saturation of more than 2 pads with blood within a 24-hour period Retinal bleeding without visual impairment
Grade 3	Bleeding requiring red blood cell transfusion and without hemodynamic instability Bleeding in body cavity fluids is grossly visible Brain bleeding without neurological signs and symptoms
Grade 4	Fatal bleeding from anywhere Non-fatal brain bleeding with neurological signs and symptoms Debilitating bleeding, including retinal bleeding with visual impairment Bleeding with hemodynamic instability

In severe/significant bleeding (WHO grade ≥ 2), the platelet count is maintained $> 50,000 \mu\text{l}$. Empirical platelet transfusion is considered for the initial management of bleeding. In minor bleeding (WHO grade 1) and without additional risk factors, platelet transfusion is only given if the platelet count is

$< 10,000/\mu\text{l}$, similar to patients without bleeding symptoms. If the bleeding is more significant but not life-threatening, platelet transfusion may be considered if the platelet count is $< 30,000/\mu\text{l}$. The benefits and risks of platelet transfusion in patients with minor bleeding need to be considered.⁶

Trauma

Low platelet count is associated with increased morbidity and mortality in trauma patients requiring massive blood transfusions. In patients with multiple trauma and head trauma, the platelet count is maintained $>100,000/\mu\text{l}$.⁶

DIC

The key management approach for DIC is addressing the underlying cause. Platelet transfusion in DIC is administered to patients with active bleeding or high bleeding risk (e.g., postoperative, undergoing invasive procedures) to maintain a platelet count $>50,000/\mu\text{l}$.⁶

Intracerebral hemorrhage

Many guidelines recommend maintaining a platelet count $>100,000/\mu\text{l}$ in patients with central nervous system bleeding.⁶

Contraindication of platelet transfusion

Platelet transfusion is contraindicated in patients with thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), and heparin-induced thrombocytopenia (HIT). Although significant thrombocytopenia may be present in these cases, they generally involve a prothrombotic state. Therefore, platelet transfusion can further trigger thrombosis and increase mortality if given as prophylaxis in the absence of significant bleeding. Platelet transfusion is not necessary in patients with autoimmune platelet destruction, such as immune thrombocytopenic purpura (ITP), if there is no active bleeding, as the transfused platelets can undergo the same destruction as the patient's own platelets, rendering it less beneficial.⁸

Dosage and administration of platelet transfusion

There are two methods to obtain platelets for transfusion, namely differential centrifugation from whole blood (platelet concentrate/random donor platelets) and donor apheresis. The typical dosage of platelet transfusion for adults is 4-6 units of platelet

concentrate (or 1 unit per 10 kg of body weight), estimated to increase platelet count by 30,000-60,000/ μl . For pediatric patients, the dosage used is 1 unit of platelet concentrate per 10 kg of body weight, estimated to increase platelet count by 50,000/ μl .⁸

The patient needs to have adequate-sized intravenous cannula access. Adults typically use sizes 18G to 22G, while pediatric patients use sizes 24G to 26G. In rare cases where intravenous access is inadequate, intraosseous access can be used for transfusion routes. Pre-transfusion medications such as antihistamines can be given to patients with a history of allergic reactions to previous transfusions. The patient's vital signs need to be checked before starting the transfusion. The rate of platelet transfusion is 2-5 ml/minute, typically completed within 1 to 2 hours. A slower rate may be considered for patients at risk of fluid overload. During the transfusion, the patient's vital signs are monitored every 15 minutes. If a transfusion reaction occurs during the transfusion, the transfusion is stopped, followed by a transfusion reaction management protocol.^{2,9}

Complications of platelet transfusion

Platelet transfusion can potentially lead to a range of complications, like any other blood transfusion. These complications include immune-mediated complications such as febrile non-hemolytic transfusion reaction (FNHTR), allergy/anaphylaxis, transfusion-associated graft-versus-host disease (TA-GVHD), transfusion-related acute lung injury (TRALI), post-transfusion purpura, transfusion-related immunomodulation (TRIM), platelet refractoriness, and non-immune-mediated complications such as transfusion-associated circulatory overload (TACO), physical injury, sepsis, viral infection transmission, and hypotensive reactions.¹⁰

Febrile non-hemolytic transfusion reaction (FNHTR)

FNHTR is a frequently encountered complication with a frequency ranging from 4% to 30%. FNHTR is

characterized by an increase in body temperature of $\geq 1^{\circ}\text{C}$ within the first 4 hours of the transfusion, which can resolve within 48 hours. It may be accompanied by nausea, vomiting, dyspnea, and hypotension.¹⁰

Allergy and anaphylaxis

The frequency of allergic reactions ranges from 0.09% to 21%, manifested as pruritus, urticaria, or bronchoconstriction, and rarely associated with fever. Anaphylaxis can occur in 1 out of 50,000 transfusions. The diagnosis is clinically established and represents a medical emergency.¹⁰

Transfusion-associated graft-versus-host disease (TA-GVHD)

TA-GVHD is an uncommon yet highly dangerous complication that is identifiable by fever and multiple systemic manifestations affecting various organs such as the skin, gastrointestinal tract, and liver. It is caused by T lymphocytes from the donor triggering an immune response and attacking the recipient's tissues. This can occur between 1 to 6 weeks after the transfusion and is observed in individuals with immunocompromised conditions, congenital T-cell defects, populations with low genetic diversity (HLA homozygotes), or first-degree relatives. Manifestations involve various organs such as the skin, intestines, liver, and bone marrow suppression.¹¹

Transfusion-related acute lung injury (TRALI)

TRALI is a rare complication characterized by post-transfusion respiratory failure after ruling out other causes. TRALI can occur within 6 hours after the transfusion. Patients experience acute respiratory deterioration characterized by hypoxemia: $\text{PaO}_2/\text{FiO}_2 \leq 300$ mmHg with oxygen saturation $< 90\%$.¹⁰

Post-transfusion purpura

Post-transfusion purpura is a rare syndrome characterized by a sudden decrease in platelets within 1-21 days after platelet transfusion. It is self-limiting and associated with wet purpura. It is believed to be caused by the formation of autoantibodies as a

complication of platelet transfusion.¹²

Transfusion-related immunomodulation (TRIM)

TRIM is a temporary suppression of the immune system after a patient receives a blood transfusion, leading to an increased risk of infection and longer recovery time for the patient.¹⁰

Platelet refractoriness

Platelet refractoriness is the recurrent failure to achieve the desired platelet count in patients following platelet transfusion. The causes can be immune or non-immune in nature. Human platelet antigens (HPA) play a significant role in the immune-mediated refractoriness of platelets. Patients who receive repeated blood transfusions may develop antibodies against specific HPA. These antibodies can cause destruction of platelets in the immune system. In such patients, cross-matching of platelets can reduce the incidence of platelet refractoriness. Non-immune causes include fever, splenomegaly, and sepsis.¹³

Transfusion-associated circulatory overload (TACO)

TACO is more commonly encountered in pediatric patients and patients with heart insufficiency. In this group, it is recommended to administer blood transfusions at a slower rate with close monitoring.¹⁰

Physical injury

Physical injury can include hematoma, vascular injury, or nerve injury at the intravenous access site.¹⁰

Sepsis and bacterial infection

Platelet concentrates are stored for up to 5 days at a temperature of $22\text{-}24^{\circ}\text{C}$. This temperature range is suitable for bacterial growth, such as *Staphylococcus aureus* and gram-negative bacteria. The risk of platelet transfusion-associated infection varies between 0.14% - 1.41%.¹⁰

Transmission of viral infections

All blood products need to undergo screening for

HIV, HCV, HBV, and other viruses according to the policies of each region. However, there is still a risk of viral transmission because not all viruses can be detected if they are still within the window period. Frequent blood transfusions can put certain populations at a higher risk of transfusion-transmitted infections (TTI). Patients with blood disorders like sickle cell anemia, thalassemia, and hemophilia, as well as cancer patients receiving chemotherapy, are particularly vulnerable to TTI due to their need for multiple donor units. Therefore, it is important to pay special attention and be vigilant for the possibility of TTI in these individuals.^{10,14}

Hypotensive reactions

Bradykinin is believed to play a significant role in hypotensive reactions during blood transfusion. Patients undergoing ACE inhibitor treatment are at higher risk of experiencing hypotension during blood transfusion, with an incidence of approximately 3%. Therefore, inquiring about the patient's medication history prior to transfusion is important.¹⁵

2. Conclusion

Thrombocytopenia can be caused by decreased platelet production, increased platelet destruction, increased splenic sequestration, and dilutional thrombocytopenia. Platelet transfusion can be given to thrombocytopenic patients as prophylaxis to prevent bleeding or as a therapy to control active bleeding. As prophylaxis, platelet transfusion is administered in cases of proliferative thrombocytopenia and prior to invasive procedures/surgery. As therapy, platelet transfusion is given to thrombocytopenic patients with significant active bleeding. The cutoff threshold for blood transfusion varies for each patient, depending on their clinical condition. Platelet transfusion is contraindicated in patients with TTP, HUS, HIT, and non-bleeding ITP. Clinical conditions and vital signs need to be monitored before, during, and after transfusion to assess potential complications that may arise.

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