

Criteria for Indication of Blood Products for Transfusion

Criteria for the use of blood products

[Summary] Red cell concentrates – Appropriate indication/use

Objective

The main objective of red cell replacement is the adequate oxygenation of peripheral tissues.

Indication criteria

1) Indication in chronic anemia (mainly indication for non-surgical cases)

[Anemia in hematological diseases]

In severe anemia, in general, transfusion of 1-2 units/day is recommended.

In chronic anemia, hemoglobin (Hb) level = 7g/dL is considered a criteria for use of red cells, but the necessary volume must be decided based on factors such as the level (speed) of progression of anemia and the period of disease progression and, thus, can not be uniformized.

* Keeping Hb at >10g/dL is not necessary

* Conditions such as iron-deficiency, vitamin B12-deficiency, folate-deficiency, or autoimmune hemolytic anemia, for which other treatment modalities are available, should essentially be treated without transfusion.

[Anemia in chronic bleeding]

In severe anemia due to chronic bleeding from the intestinal tract or the genitourinary system, transfusion is essentially not indicated. In case clinical cardiovascular symptoms (palpitation or short-of-breath at efforts, edema, etc.), affecting the patient's routine life, are present, 2 units of red cells should be transfused, and the patient observed for the improvement of clinical symptoms. When the patient's general condition is good, Hb<6g/dL is a criteria for indication of transfusion.

2) Indication in acute bleeding (mainly indication for surgical cases)

Transfusion is not necessary with Hb>10g/dL, but almost indispensable with Hb<6g/dL.

* Indication of transfusion based solely on Hb level is not appropriate.

3) Transfusion in the perioperative period

(1) Pre-operative transfusion

The patient's general conditions must be evaluated by checking factors such as the cardio-pulmonary function, diagnosis (benign or malignant disease), age, body weight or the presence of other special morbid condition (state) when deciding the need of transfusion.

* The previous habitual 10/30 rule, which suggests Hb level <10g/dL and hematocrit (Ht) level <30% as the criteria for the decision of pre-operative transfusion, is presently considered without reliable evidence.

(2) Intra-operative transfusion

For blood loss of 20-50% of the circulating blood volume, infusion of artificial colloid solution (hydroxyl-ethyl starch (HES), dextran, etc.) is recommended. When there is risk of tissue oxygen debt dependent on red cell deficit, red cell concentrate is indicated. At this level of bleeding, rarely use of isotonic albumin product (5% human albumin or heat-inactivated human plasma protein) is required.

For blood loss of 50-100% of circulating blood volume, isotonic albumin is administered when suitable. Additionally, when administration of more than 1,000ml of artificial colloid solution is needed, the use of isotonic albumin product should be considered.

In case of massive bleeding of volume exceeding the circulating blood volume (more than 100% within 24-h) or rapid infusion of blood (>100mL/min) is necessary, the use of fresh frozen plasma and platelet concentrate should be considered.

Usually, Hb level of 7-8g/dL suffices for adequate oxygen delivery to the tissues, but in cases of cardiac diseases, such as coronary heart disease, keeping Hb level around 10g/dL is recommended.

(3) Post-operative transfusion

At the 1st to 2nd postoperative days, the reductions of the extracellular volume fraction and of albumin level are common, but if vital signs are stable, the use of crystalloid fluid solution may be necessary, but not of red cell concentrates, isotonic albumin preparation or fresh frozen plasma.

Dosage (Volume of transfusion)

The improvement of Hb level achieved by red cell concentrate transfusion can be estimated by the following formula:

Estimated Hb level improvement (g/dL) = Transfused Hb volume (g) / Circulatory volume (dL)

Circulatory volume: 70mL/kg [Circulatory volume (g) = Body weight (kg) x 70mL/kg/100]

For example, when 2 units (400mL-derived red cell concentrates contain approximately 280mL volume. Thus, the Hb volume in each product is approximately 53g (19g/dL x 280/100dL)) when red cells with Hb=19g/dL are transfused into an adult patient with BW=50kg (Circulatory volume=35dL), and the estimated Hb increase will be 1.5g/dL.

Inappropriate indication/use

Combination with fresh frozen plasma indicated by reason other than reposition of coagulation factors;

Use in terminal patients.

Precautions

- 1) Transmission of infectious agents
- 2) Iron overload
- 3) Prevention against graft-versus host disease (GVHD)
- 4) Use of leukocyte-reduction filter

5) Hemolytic transfusion reaction

[Summary] Platelet concentrate – Appropriate indication/use

Objective

Platelet transfusion aims to control or prevent hemorrhage by reposition of platelets.

Indication criteria

The below criteria is merely an aim and, is not necessarily suitable to all cases.

Platelet count between $2-5 \times 10^4/\mu\text{L}$: platelet transfusion is necessary if hemorrhage control is difficult.

Platelet count between $1-2 \times 10^4/\mu\text{L}$: sometimes severe hemorrhage may occur, and platelet transfusion may be necessary. With platelet count $<1 \times 10^4/\mu\text{L}$, severe hemorrhage occurs quite frequently, and platelet transfusion is often necessary.

* In general, with platelet count $>5 \times 10^4/\mu\text{L}$, platelet transfusion is rarely necessary.

* In chronic thrombocytopenia (such as aplastic anemia), platelet transfusion should be avoided even with platelet count as low as $0.5-1 \times 10^4/\mu\text{L}$.

1) Active hemorrhage

In cases of severe active hemorrhage (especially retinal, central nervous system, lungs, gastrointestinal tract) due to thrombocytopenia, platelet transfusion must be indicated to keep platelet levels $>5 \times 10^4/\mu\text{L}$.

2) Pre-operative state

When platelet count is $<5 \times 10^4/\mu\text{L}$, depending on the type of operation, the need of platelet concentrate preparation or pre-operative transfusion must be decided.

* In elective surgery patients, or patients receiving lumbar puncture, extradural anesthesia, transbronchial biopsy, or liver biopsy, if pre-operative platelet count is $>5 \times 10^4/\mu\text{L}$, platelet transfusion is not necessary.

3) Perioperative care in patients receiving extracorporeal circulation (artificial heart lung)-assisted operation

Platelet count $<3 \times 10^4/\mu\text{L}$ in the intra or post-operative period is an indication for platelet transfusion. However, after protamine sulfate injection at the time of removal of extracorporeal circulation, coagulation tests should be appropriately performed, analyzed, and platelet transfusion must be considered to keep platelet levels at $>50 \times 10^4/\mu\text{L}$.

For cases receiving complex cardio-vascular surgical procedures, with need of long-time ($>3\text{hs}$) extracorporeal cardio-ventilatory support, or those receiving re-operation with need of large synechia detachments, or those with bleeding tendency due to chronic renal or hepatic disorders, in which refractory bleeding tendency (such as oozing) without coagulation factor deficiency is observed, platelets should be transfused to keep values between $5-10 \times 10^4/\mu\text{L}$.

4) Massive hemorrhage

When rapid blood loss needing transfusion of volumes higher than the body circulatory

volume occurs, and bleeding tendency symptoms are due to difficult hemostasis as well as thrombocytopenia, platelet transfusion is indicated.

5) Disseminated intravascular coagulation

In cases of DIC (the underlying diseases such as leukemia, cancer, obstetric disorders, or severe infection) with strong bleeding tendency, in which platelet count decreases to levels $<0.5 \times 10^4/\mu\text{L}$ in a short period of time, and bleeding symptoms are present, platelet transfusion is indicated.

*Platelet transfusion is not indicated in chronic DIC.

6) Hematological disorders

(1) Hematologic malignancy

During the remission induction chemotherapy of acute leukemia and malignant lymphomas, if platelet count decrease to values $<1-2 \times 10^4/\mu\text{L}$, platelet transfusion must be planned to keep platelet count at $>1-2 \times 10^4/\mu\text{L}$.

(2) Aplastic anemia/Myelodysplastic syndrome

Platelet count of $0.5 \times 10^4/\mu\text{L}$ or less is indication of platelet transfusion.

Platelet transfusion must be planned to keep platelet count $> 1 \times 10^4/\mu\text{L}$.

* Usually thrombocytopenia is of chronic evolution, thus, if platelet count is $> 0.5 \times 10^4/\mu\text{L}$ and the hemorrhagic symptoms are mild (such as subcutaneous petechia), platelet transfusion is not indicated.

(3) Immunologic thrombocytopenias

Cases of idiopathic thrombocytopenic purpura (ITP) receiving surgical procedure should be pre-treated by immunosuppressants such as corticosteroids, and in case of ineffectiveness of this treatment, platelet transfusion may be considered.

* In general, ITP is not indication of platelet transfusion.

When severe thrombocytopenia is observed in newborns from mothers with ITP, in addition to plasmapheresis, use of corticosteroids or immune globulins as well as platelet transfusion may be required.

Neonatal alloimmune thrombocytopenia (NAIT), which occurs due to materno-fetal incompatibility of platelet alloantigens, may cause severe thrombocytopenia, and these cases should receive transfusion of antigen-specific platelets.

(4) Thrombotic thrombocytopenia (TTP) and hemolytic uremic syndrome (HUS)

* Essentially, platelet transfusion is not indicated.

(5) Platelet functional disorders

Platelet transfusion indicated solely in cases of severe or refractory hemorrhage.

(6) Others: Heparin-induced thrombocytopenia (HIT)

Platelet transfusion is contraindicated.

7) Solid tumors

Patients with solid tumors receiving strong chemotherapy should have the platelet count checked.

Platelet count $<2 \times 10^4/\mu\text{L}$ and presence of hemorrhage tendency, platelet should be transfused to keep values $>1-2 \times 10^4/\mu\text{L}$.

8) Hematopoietic stem cell transplantation (such as bone marrow transplantation)

In the post hematopoietic stem cell transplantation period, until hematopoietic function recovers, platelet transfusion must be planned to keep values $>1-2 \times 10^4/\mu\text{L}$.

In general, when platelet count is $<1-2 \times 10^4/\mu\text{L}$, platelet transplantation is indicated for prevention of hemorrhage.

Dosage (volume of transfusion)

$$\text{Estimated platelet count increase post-transfusion } (/ \mu\text{L}) = \frac{\text{Transfused platelet count} \times 2}{\text{Circulatory volume (mL)} \times 10^3}$$

(Circulatory volume is calculated as 70mL/kg)

For example, when 5 units of platelet concentrate (include $>1 \times 10^{11}$ platelets) is transfused to a patient with 71kg (circulatory volume = 5,000mL), the estimated platelet count increase will be $>13,500/\mu\text{L}$.

Essentially, the volume of each transfusion is calculated by the above formula, but in routine practice, 10-unit platelet concentrate is often used. In children with body weight $<25\text{kg}$, the 10-unit platelet concentrate must be transfused slowly (3-4 h).

Inappropriate use

As a principle, platelet transfusion in terminal patients as a prolonging-life measure must be avoided.

Precautions

- 1) Transmission of infectious agents
- 2) General transfusion method
- 3) Use of leukocyte-reduction filters
- 4) Irradiation
- 5) Cytomegalovirus (CMV) antibody-negative platelet concentrates
- 6) HLA-matched platelet concentrates
- 7) ABO and Rh blood typing and crossmatching
- 8) ABO group-incompatible transfusion

[Summary] Fresh frozen plasma (FFP) – Appropriate indication/use

Objective

The therapeutic reposition of coagulation factors is the main objective. The preventive transfusion of FFP is meaningless, except for cases receiving invasive procedures.

Indication criteria

Transfusion of FFP is indicated only in case another safe and effective plasma-derived product or an alternative product (such as recombinant drugs) is not available. Prothrombin time (PT) and activated partial thromboplastin time (APTT) values must be measured prior to transfusion, and in cases of massive hemorrhage, fibrinogen must also be tested.

1) Reposition of coagulation factors

- (1) Prolonged PT and/or APTT (PT of (i) $\text{INR} > 2.0$, (ii) $< 30\%$; APTT of (i) more than twice the standard upper limit value of each institution, (ii) $< 25\%$)

Hepatic failure: indicated in case of hepatic failure leading to deficiency of multiple coagulation factors, and consequent hemorrhage tendency.

* Prophylactic use of FFP is not indicated, except for cases with PT of $\text{INR} > 2.0$ ($< 30\%$) ongoing invasive procedures.

Association with L-asparaginase administration: in case production of inhibitors of blood coagulation and fibrinolytic factors is deficient and, in addition, there is decreased production of coagulation factors in the liver, FFP transfusion is indicated for the simultaneous reposition of these factors.

Disseminated intravascular coagulation (DIC): generally, prolonged PT and APTT as well as fibrinogen $< 100\text{mg/dL}$ as described in (1) (Refer to the “Diagnostic criteria of DIC”) are indications for use of fresh frozen plasma.

Massive hemorrhage: bleeding tendency due to dilution of coagulation factors is an indication of fresh frozen plasma transfusion. In emergency patients, such as trauma, presence of consumptive coagulopathy must be investigated, and only in case bleeding tendency due to coagulation factor deficiency is observed, FFP should be indicated.

Deficiency of a coagulation factor without available concentrated product: deficiency of coagulation factors V, XI, or of multiple factors including these, FFP transfusion is indicated in case bleeding tendency is present or invasive procedure is indicated.

Urgent correction of Coumarin anticoagulant (such as Warfarin) effect (PT $\text{INR} > 2.0$ ($> 30\%$)): in general, improvement is achieved within 1 hour after administration of vitamin K. Rarely, use of FFP for a more urgent correction may be necessary, but even in this case, concentrated prothrombin conjugate product should be the first choice, if available.

- (2) Hypofibrinogenemia ($< 100\text{mg/dL}$)

Disseminated intravascular coagulation (DIC)

Post-administration of L-asparaginase

2) Reposition of inhibitors of blood coagulation or fibrinolytic factors

In case of thrombosis due to deficiency of protein C or protein S, FFP should be indicated

for reposition of the deficient factor, when appropriate. For bleeding tendency dependent on deficiency of plasmin inhibitor, antifibrinolytic agent should be used, and in case improvement is not achieved, FFP transfusion is indicated.

3) Reposition of plasma factors (cases with normal PT and APTT)

Thrombotic thrombocytopenic purpura (TTP): plasmapheresis using FFP as the replacement solution is indicated in case of acquired TTP. In congenital TTP, sole administration of FFP is usually effective.

* Plasmapheresis using FFP as the replacement solution is not necessarily effective in cases of acquired hemolytic uremic syndrome (HUS)

Dosage (volume of transfusion)

The minimum plasma activity of coagulation factors necessary for the physiologic hemostasis is 20-30% of the normal values.

The recovery rate of replaced coagulation factors varies among the various factors, but setting the recovery rate to 100%, and the circulatory plasma volume at 40mL/kg (70mL/kg (1-Ht/100)), the necessary volume of FFP to achieve a 20-30% increase of plasma coagulation factors is, theoretically, 8-12mL/kg (20-30% of 40mL/kg).

Inappropriate use

- 1) Improvement and reposition of plasma circulatory volume
- 2) Nutritional support as the source of protein
- 3) Improvement of wound healing
- 4) Use in terminal patients
- 5) Others

Use of FFP should also be not indicated for the treatment of severe infections or burn injury without DIC, prevention of hemorrhage during extracorporeal circulation (artificial heart lung) or uncompensated hepatic cirrhosis.

Precautions

- 1) Melting procedures
- 2) Transmission of infectious agents
- 3) Citrate toxicosis (Hypocalcemia)
- 4) Sodium overload
- 5) Allergic reactions
- 6) Use of transfusion set

[Summary] Albumin preparation – Appropriate indication/use

Objective

The objective of albumin preparation use is the maintenance of colloid osmotic pressure to keep the circulatory plasma volume and to transfer body cavity and intercellular fluid to the intravascular space for the treatment of refractory severe edema.

Indication criteria

1) Hemorrhagic shock

In case of hemorrhage of more than 30% of the circulating blood volume, crystalloid fluid solution is the first choice, but combination of artificial colloid solution is also suggested. However, use of albumin preparation is essentially not necessary.

In case of severe hemorrhage of more than 50% of circulating blood volume is suspected, or when plasma albumin level is less than 3.0g/dL, use of isotonic albumin should be considered.

In case use of artificial colloid solution is unsuitable due to presence of conditions such as renal failure, isotonic albumin is indicated. Moreover, when infusion of more than 1,000mL of artificial colloid solution is necessary, the use of isotonic albumin preparation should be considered.

2) Extracorporeal circulation (artificial heart lung)-assisted cardiac surgery

In general, crystalloid fluid solution is mainly used as the filling solution of extracorporeal circulation (artificial heart lung) in cardiac surgery. The transitory hypoalbuminemia due to hemodilution caused by extracorporeal circulation (artificial heart lung) does not need correction. However, when severe hypoalbuminemia or low oncotic pressure is observed since the pre-operative period, or in case of infants with body weight <10kg, the use of isotonic albumin preparation may be indicated.

3) Treatment of refractory ascites of liver cirrhosis

For the maintenance of plasma circulatory volume at the time of peritoneal puncture for aspiration of large volume ascites, use of hypertonic albumin preparation should be considered. Additionally, for the treatment of refractory ascites, the short-time (up to 1 week) combination of hypertonic albumin preparation may be indicated.

* Hypoalbuminemia due to chronic pathologic conditions such as liver cirrhosis is not necessarily an indication for use of albumin preparation.

4) Treatment of nephrotic syndrome with refractory peripheral edema and pulmonary edema.

* In chronic pathological conditions such as nephrotic syndrome, albumin preparation is generally not indicated, but acute severe peripheral or lung edema may require short-time (up to 1 week) administration of hypertonic albumin preparation in addition to diuretics.

5) Extracorporeal circulation, such as hemodialysis, in unstable circulatory dynamics

● In hemodialysis of patients with unstable blood pressure, especially those complicated by diabetes or by hypoalbuminemia, prophylactic administration of albumin may be indicated in an attempt to increase plasma circulatory volume.

6) Therapeutic plasmapheresis without need of coagulation factor reposition

* In cases without need of coagulation factor reposition, such as Guillain-Barre syndrome and myasthenia gravis, isotonic albumin preparation is indicated.

* Although rare, heat-inactivated human plasma protein may cause hypotension, and is essentially contraindicated.

7) Severe burn injury

When burn surface area exceeds 50% of body surface area, and the correction of plasma circulatory volume by infusion of crystalloid fluid solution (extracellular fluid-reposition solution) is quite difficult, use of artificial colloid solution or isotonic albumin preparation is indicated.

* In general, within 18 hours from burn injury, use of crystalloid fluid solution (extracellular fluid-reposition solution) is essentially indicated, but if albumin level is $>1.5\text{g/dL}$ in this phase, the use of albumin preparation should be considered.

8) Pulmonary edema or evident peripheral edema due to hypoproteinemia

• For hypoalbuminemia in pre-operative or post-operative period or cases with hypoalbuminemia due to symptoms such as diarrhea in poor-intake patients, or those with refractory lung edema or evident peripheral edema, the use of hypertonic albumin preparation should be considered.

9) Conditions such as acute pancreatitis with evident reduction of plasma circulatory volume

For hypovolemic shock due to significant decrease of plasma circulatory volume caused by pathological conditions such as acute pancreatitis or ileus, use of isotonic albumin preparation is indicated.

Dosage (volume of transfusion)

The dose of albumin preparation to be used is calculated by the following formula. The total dose of albumin obtained by this formula is administered divided into fractions, according to the patient's symptoms, in 2-3 days period.

Necessary dose (g) = Estimated increase dose (g/dL) x circulating plasma volume (dL) x 2.5

The following points need consideration. There is discrepancy between the estimated increase dose and the measured increase value; the plasma circulating volume is calculated as 0.4dL/kg ; and the intravascular albumin recovery rate is set at 40% (4/10).

Inappropriate use

- 1) Nutritional support as the source of protein
- 2) Cerebral ischemia
- 3) Merely the maintenance of albumin level
- 4) Use in terminal patients

Precautions

- 1) Sodium content
- 2) Lung edema, heart failure
- 3) Hypotension
- 4) Diuresis
- 5) Impaired albumin synthesis