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Research Progress of Platelet Transfusion in China

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ABSTRACT

Platelet products have been increasingly used for more than 50 years. Platelet transfusion is effective for correcting bleeding caused by thrombocytopenia and platelet function defects. In this review, we will outline research on platelet transfusion in China including platelet biosafety, cryopreservation of platelets, the assessment of the effectiveness of platelet transfusion, the causes of platelet transfusion refractoriness including immunization against CD36, and neonatal alloimmune thrombocytopenia.

Contents

Worldwide utilization of platelet transfusions has steadily increased since the introduction of modern platelet component therapy. There are many factors affecting the efficacy of platelet transfusion, and platelet-associated antigens vary among different races. In this article, we review platelet transfusion-related studies conducted in China in the recent years, including those related to platelet products, the efficacy of platelet transfusion, platelet blood groups and antibodies, and blood management during blood loss.

Overview of Platelet Products Used in China

At present, clinical platelet products in China include platelets prepared from whole blood, apheresis platelets, and frozen platelets. Apheresis platelets are widely used in China. They are collected with automated blood collection systems and stored in agitators for 5 days. As for the production of whole blood platelets, generally 400 mL of whole blood is collected from the donor and preserved at 20 to 24°C, separated in 24 hours, and used within 24 hours. Frozen platelets are preserved at −80°C using 5% dimethyl sulfoxide as cryoprotectant and used within 1 year. At present, all 3 types of platelet products are used in different regions in China. The precise proportion of usage for the 3

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types of platelet product is not available, but research on apheresis platelets is much greater than for the other 2 [1-5].

Cryopreserved platelets prolong the storage time of platelets. They can quickly meet patients' needs in emergencies. Xing et al [6] compared platelet counts, mean platelet volume, bacterial culture, and other blood safety indicators before and after freezing. They found that the recovery rate of platelets after freezing and thawing was 96.78% ± 1.34%, mean platelet volume was increased by 13.56% ± 3.04% on average, and bacterial culture and biological safety indicators met the clinical application standards. Zhao et al [7] evaluated platelet activation and the hemostatic effect for emergent bleeding after freezing apheresis platelets for 9 months, and found that CD41 and CD62p fluorescence intensity did not change significantly before and after freezing; effective hemostasis was found in 126 cases of acute blood loss.

Li et al [8] retrospectively analyzed the efficacy of cryopreserved platelets in 1900 cases over an 8-year period. They found that 96% of the patients achieved hemostasis within 2 hours after the transfusion of cryopreserved platelets, and the platelet count in 72% of the patients was significantly increased. The main adverse effects were allergic reactions and fever. In the study by Zhu et al [9] using frozen apheresis platelets and cryoprecipitate to treat patients with postpartum hemorrhage, coagulation and fibrinogen levels in the patients were significantly increased after the combined transfusion, and hemostasis was achieved in 96.15% of patients.

Because of the increased chance of bacterial contamination for platelets compared with other blood products, there has been much research to find a sensitive and quick way to detect bacteria. Wang et al [10] used the polymerase chain reaction (PCR) detection technique for amplification of the bacteria-conservative fragment 16S rRNA, and detected 7 bacterial fragments with no cross-reactivity to normal human DNA by combining fluorescent and biotin-labeled probes, as well as 5 colony-forming units (CFUs)/mL or higher *Pneumococcus*, 6.5×10^4 CFUs/mL *Staphylococcus*, and 35 CFUs/mL *Pseudomonas aeruginosa*.

In addition to bacterial contamination, changes in platelet shape, function, and apoptosis during storage are important factors causing platelet storage injury. Yu et al [11] used a PCR technique to detect changes in 49 types of microRNA during platelet storage and found that among 10 types of microRNA, hsa-miR-326, hsa-miR-96, hsa-miR-16, hsa-miR-155, and hsa-miR-150 were up-regulated, whereas hsa-miR-7, hsa-miR-145, hsa-miR-24, hsa-miR-25, and hsa-miR-15a were down-regulated, and the increased expression of hsa-miR-326 was an important indicator of platelet apoptosis. The findings suggest that hsa-miR-326 may be involved in platelet apoptosis during storage.

Assessment of the Effectiveness of Platelet Transfusion

There are various ways to assess the effectiveness of platelet transfusions. In a bleeding patient, this should include a clinical assessment for the cessation of bleeding.

For prophylactic platelet transfusions, the most common formulas include the posttransfusion increment, the percentage platelet recovery, and the corrected count increment (CCI). A posttransfusion increment of greater than 10×10^9/L at 1 or 24 hours is considered a successful transfusion to be consistent with the previous formulas [12,13]. A CCI of greater than 7.5×10^9/L at 1 hour and of greater than 4.5×10^9/L at 20 to 24 hours are considered to be a successful transfusion. A platelet recovery of about 67% in a stable patient indicates a successful transfusion, but the minimum platelet recovery to define a successful transfusion is considered as greater than 30% at 1 hour posttransfusion and greater than 20% at 20 to 24 hours [13].

Platelet transfusion refractoriness (PTR) is defined as the repeated failure to achieve satisfactory responses to platelet transfusions from random donors. It is associated with a number of adverse outcomes including longer hospital stays, increased risk of bleeding, and decreased survival [14-17]. Currently in China, 1- and 24-hours CCI and percent platelet recovery are commonly used to assess the efficacy of platelet transfusion [7-9,18-31].

Wang et al [18] analyzed the efficacy of transfusion in 972 cases of patients with hematologic disease. They found that when using 24-hour CCI as an indicator for assessing the efficacy of platelet transfusion, the effectiveness of apheresis platelets without leukocyte filtration transfusion in hematologic patients was 58.73%. Guo et al [19] used 1- and 24-hour CCI as indicators for the efficacy of platelet transfusion in hematologic disease, and found that the transfusion efficacy of apheresis platelets was better than platelet concentrates; the rate of PTR was 50.0% in the leukemia with infection group, and 18.5% in the leukemia without infection group. The rate of PTR was 15.1% and 46.2% for acute leukemia and aplastic anemia (AA), respectively.

Chen et al [5] found that in AA patients, low fever (body temperature of 37.5-38.5°C) reduced the effective rate of filtered apheresis platelet transfusion; the effective rate was 51.0% in the fever group and 79.7% in the nonfever group. They suggested avoiding platelet transfusion in patients with a low fever. Wang et al [20] examined the efficacy of transfusion of ABO-incompatible apheresis platelets in pediatric patients under emergent circumstances and found that the effective rate of minor matched platelet transfusion (plasma compatible; 87.8%) was higher than that of major matched platelet transfusion (red blood cell compatible; 77.4%). They suggested to focus on plasma compatibility for platelet transfusion under emergent circumstances.

Patients undergoing hematopoietic stem cell transplantation rely on blood component transfusion before and during treatment. Li et al [21] retrospectively observed 69 patients with blood disease undergoing hematopoietic stem cell transplantation. They used 24-hour CCI as an observational indicator, and found that ABO compatibility or incompatibility did not affect the dose of platelet transfusion and timing of transplantation. They reported 32.7% of the patients experienced PTR; infection, fever, and bleeding were the main causes. ABO-incompatible transplantation and myelodysplastic syndrome were also associated with PTR. Another study [22] found that the length of stay in the laminar flow room, the source of hematopoietic stem cells, and ABO compatibility or incompatibility were related to the efficacy of transfusion.

You et al [23] investigated leukocyte filtration in preventing PTR; they counted peripheral platelets 1 hour before and 24 hours after each platelet transfusion, and the CCI was calculated in 759 hematologic patients. They found that leukocyte filtration was effective in preventing PTR. Zhang and Yang [24] studied Gy 137 Cs-irradiated apheresis platelets and found that irradiated apheresis platelets reduced adverse reactions (fever, chill, and other adverse reactions) of blood transfusion in patients receiving platelet transfusion repeatedly and improved the efficacy of platelet transfusion (56.1% vs 84.9%).

Whether immune thrombocytopenia (ITP) patients undergoing laparoscopic splenectomy need perioperative platelet transfusion is a question of great clinical concern in China. Chen et al [25] and Cai et al [26] explored whether ITP patients with severe thrombocytopenia needed platelet transfusion. They determined that low platelet counts should not be a contraindication to surgery in ITP patients before splenectomy, and such patients did not need to receive preventive platelet transfusion.

Study of Immune PTR

Factors affecting the efficacy of platelet transfusion include infection, fever, hypersplenism, other nonimmune factors, as well as human leukocyte antigen (HLA) and human platelet antigen (HPA) antibodies. Other factors affecting the efficacy of platelet transfusion include the age of patients, the number of transfusions, and disease factor. HLA alloimmunization is believed to be the primary cause of immune refractoriness [32,33]. Both recipient and donor/product factors contribute to development of HLA alloimmunization. Immunosuppression appears to reduce the risk of developing antibodies, whereas presensitization (such as pregnancy) increases the risk [34].