Original Article

Prevalence of platelet reactive antibodies in patient's refractory to platelet transfusions

Nitin Agarwal[1], Kabita Chatterjee[1], Alok Sen[3], Praveen Kumar[2]

[1]Departments of Transfusion Medicine and [2]Laboratory Medicine, All India Institute of Medical Sciences, [3]Armed Force Transfusion Centre, New Delhi, India

Abstract

Introduction & Aims: Though platelet transfusions have greatly reduced the incidence of major haemorrhagic complications associated with the management of haematological and oncological disorders, refractoriness to infused platelets becomes a major clinical problem for many of these patients. **Materials and methods:** The present study was done to determine the percentage of platelet alloimmunisation due to platelet-reactive antibodies in 340 patients with hematologic or oncologic diseases who had received multiple transfusions (> 10) of blood and blood components and showed platelet refractoriness in 1-hour post transfusion sample. **Results:** Platelet-reactive antibodies were detected in the sera of 127 out of 340 patients (37.35%) who received multiple transfusions (> 10) and showed platelet refractoriness. **Conclusion:** Platelet-reactive antibodies appear to be an important cause of platelet refractoriness in patients of acute leukaemia, aplastic anaemia, NHL, MDS and multiple myeloma receiving multiple platelet transfusions. Platelet refractoriness in patients of ITP and chronic leukaemia appears to be due to other causes and not due to platelet-reactive antibodies.

Key words: Platelet alloimmunization, platelet immunofluorescent test, refractoriness

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Correspondence to:
Dr. Nitin Agarwal,
Department of Transfusion Medicine, All India Institute of Medical Sciences, New Delhi – 110 029, India.
E-mail: nuts_medico@rediffmail.com

Introduction

Platelet transfusion remains the main line of treatment for the prevention of hemorrhagic manifestations in hematology and oncology patients, who suffer from thrombocytopenia and hemorrhagic manifestations, as a result of bone marrow failure either due to disease itself or the treatment (radiotherapy/chemotherapy).[1] Though platelet transfusions have greatly reduced the incidence of major hemorrhagic complications associated with the management of hematological and oncological disorders, refractoriness to infused platelets becomes a major clinical problem for many of these patients. Most of the studies from all over the world have reported an incidence of 15%-25% platelet refractoriness in hemato-oncological patients utilizing leukocyte-reduced blood products.[2-4] The incidence is even higher in patients receiving nonleuko-reduced blood products as is the case in many developing countries.

Inadequate post-transfusion platelet count increments can be due to a number of nonimmunological factors such as splenomegaly, severe sepsis, disseminated intravascular coagulation, drug-induced thrombocytopenia, and so on and immunological factors like alloimmunization with antihuman leukocyte antigen (HLA) or platelet-reactive antibodies, and so on.[3,5] A patient with alloimmunization becomes a challenge for the clinicians and transfusion medicine specialists because of the accelerated destruction of transfused platelets by the respective alloantibodies.[6]

Materials and Methods

The present study was done to determine the percentage of platelet alloimmunization due to platelet-reactive antibodies in 340 patients with hematologic or oncologic diseases, who had received multiple transfusions (>10) of blood components (buffy coat removed) and showed platelet refractoriness in 1 hour post-transfusion sample (1 h corrected count increment less than $< 10 \times 10^9$/L or a percentage platelet recovery less than 20%), using indirect platelet immunofluorescent test (PIFT). PIFT detects antibodies to both human platelet antigens (HPAs) and HLAs. Further, specificity of platelet alloantibodies into HLA and HPA type was not done due to paucity of technique and expertise.

PIFT reagent platelets were prepared by the platelets collected from 10 healthy blood donors with no history of transfusion. These platelets were fixed with paraformaldehyde after washing in PBS-EDTA. The patients' sera were incubated with pooled platelets followed by incubation with fluorescein isothiocyanate-labelled F(ab)2 fragment anti-immunoglobulin G. The platelets were then examined under ultraviolet illumination for the presence of fluorescence.[7]

Results

Out of 340 patients, 255 were males and 85 were females. The mean number of transfusions

Table 1: Rate of alloimmunization to platelet antigens according to diagnosis of patients

Diagnosis	Total number of patients	Patients alloimmunized (*n*)	Patients' alloimmunized (%)
Acute leukemia	132	71	53.7
Aplastic anemia	62	30	48.3
Non Hodgkins lymphoma (NHL)	28	12	42.8
Multiple myeloma	10	4	40
Myelodysplastic syndrome (MDS)	6	3	50
Idiopathic thrombocytopenic purpura (ITP)	52	3	5.7
Chronic leukemia	50	4	8
Total	340	127	37.35

of blood components received by the patients was 33 (range: 10-72). In our study, platelet-reactive antibodies were detected in the sera of 127 out of 340 patients (37.35%), who received multiple transfusions (>10) and showed platelet refractoriness. The incidence of alloimmunization for platelet antigens according to patient diagnosis have been shown in Table 1.

Discussion

Platelet-reactive antibodies, directed against the HLAs and HPA present on the platelet surface, are frequently associated with accelerated platelet destruction and transfusion failure. Platelet-specific antibodies are generally infrequent and are not associated with a statistically significant reduction in corrected count increment. The recognition and determination of platelet-reactive antibodies is extremely important as their presence alters the subsequent management of the patient.

We found in our study that about 37% of the patients were alloimmunized. It shows that major chunk of patients showing refractoriness to platelet transfusion have nonimmunological reasons responsible for early destruction of transfused platelets. In patients showing alloimunization to platelet antigens, nonimmunological factors can also be present further adding to the misery of these patients. Alloimmunization to HLA antigens is more common than to the HPA system and is believed to be the primary cause of immune-mediated platelet refractoriness.[8] Previous reviews have shown incidence of HLA alloimmunization to be 30%-70% in patients receiving nonleukocyte-reduced blood components.[9] The incidence of alloimmunization for platelet antigens according to patient diagnosis have been shown in Table 1. Platelet-reactive antibodies appear to be an important cause of platelet refractoriness in patients of acute leukemia, aplastic anemia, Non Hodgkin's Lymphoma (NHL), Myelodysplastic syndrome (MDS), and multiple myeloma receiving multiple platelet transfusions. Platelet refractoriness in patients of Immune Thrombocytopenic Purpura (ITP) and chronic leukemia appears to be due to other causes and not due to platelet-reactive antibodies. We found patients of acute leukemia to be alloimmunized more frequently than any other diagnosis, whereas Holohan *et al.*[10] found a higher frequency of HLA alloimmunization (80%-90%) in patients with aplastic anemia compared to those with hematological malignancies (40%-60%).

Various strategies to overcome platelet refractoriness are suggested such as HLA-matched or crossmatched platelets for transfusion to avoid crossreactive HLA or platelet antigens. Other therapies like immunosuppressive, rituximab, intravenous immunoglobulin (IVIG), plasma exchange, immunoadsorption, and so on have also been tried with little success. However, developing countries like India are still lagging behind in providing such kind of processes to curb refractoriness to platelet transfusions. Most of the centers in India are still providing ABO and HLA unmatched, nonleukoreduced platelets to the patients. This is high time that this strategy of testing for platelet antibodies and providing crossmatched platelets be started at centers across the country.

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