

Descriptions of acute transfusion reactions in the teaching hospitals of Kermanshah University of Medical Sciences, Iran

Mehrdad Payandeh¹, Mohammad Erfan Zare^{1, 2}, Atefeh Nasir Kansestani², Shirin Falah Pakdel¹, Firuzeh Jahanpour¹, Hoshang Yousefi³, Farzaneh Soleimani¹

¹Medical Biology Research Center, Kermanshah University of Medical Science, Kermanshah, Iran.

²Student Research Committee, Kermanshah University of Medical Science, Kermanshah, Iran.

³Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Kermanshah, Iran.

Corresponding Author: Mohammad Erfan Zare, BSC student of Medical Lab Science.

Medical Biology Research Center, Kermanshah University of Medical Science, Kermanshah, Iran.

E-mail: mezarelab@yahoo.com

Tel: +98 831 4276473

Fax: +98 831 4276471

Abstract

Background: Transfusion services rely on transfusion reaction reporting to provide patient care and protect the blood supply. Unnecessary discontinuation of blood is a major wastage of scarce blood, as well as man, hours and funds. The aim of the present study was to describe the main characteristics of acute transfusion reactions reported in the 4 hospital of Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran.

Material and Methods: The study was carried out at 4 teaching hospital of Kermanshah University of Medical Sciences, Kermanshah, Iran over 18 months from April 2010. All adult patients on admission in the hospitals who required blood transfusion and had established diagnosis and consented were included in the study.

Results: In the year 2010 until 2012, a total of 6238 units of blood components were transfused. A total of 59 (0.94%) cases of transfusion reaction were reported within this 3 years period. The commonest were allergic reactions which presented with various skin manifestations such as urticarial, rashes and pruritus (49.2%), followed by increase in body temperature of $> 1^{\circ}\text{C}$ from baseline which was reported as febrile non-hemolytic transfusion reaction (37.2%). pain at the transfusion site (6.8%) and hypotension (6.8%).

Conclusion: It is important that each transfusion of blood components to be monitored carefully. Many transfusion reactions are not recognized, because signs and symptoms mimic other clinical conditions. Any unexpected symptoms in a transfusion recipient should at least be considered as a possible transfusion reaction and be evaluated. Prompt recognition and treatment of acute transfusion reaction are crucial and would help in decreasing transfusion related morbidity and mortality, but prevention is preferable.

Key Words: Acute transfusion reactions, Febrile non-hemolytic transfusion reaction, Transfusion-related acute lung injury

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Introduction

The transfusion of blood components is usually a temporarily effective means of correcting red cell, platelet and coagulation factor deficits. Unfortunately, blood components are occasionally unsafe, which results in a spectrum of adverse reactions following transfusion^{1, 2}. Complications associated with blood transfusion therapy may be classified based on time of onset as acute and late

transfusion reactions or based on etiology as immunological and non-immunological³⁻⁵. Acute transfusion reactions (ATRs) have been found to occur during or within 24 hours of transfusion and include acute hemolytic transfusion reaction (AHTR), allergic, febrile non-hemolytic transfusion reaction (FNHTR), fluid overload, transfusion-related acute lung injury (TRALI), anaphylactic and metabolic reactions. ATRs in practice are associated with

an immune response to antigens on red cells, white cells, or platelet and plasma proteins. These types of reactions may vary in severity from mild to fatal. Manifestation of the type of ATR may vary with the blood product transfused, the clinical condition, and past medical history of the recipient. The rate of reaction with whole blood transfusion was about two and a half times greater than with packed red blood cells, and there is also a significant relationship between reactions and increased storage time of blood components. Most type of reactions occurs when patients require more than one unit or large volume of blood. It has also been reported that FNHTRs associated with red cell transfusions occurred more in patients who have had previous pregnancies and/or previous blood transfusions. The aim of the present study was to describe the main characteristics of acute transfusion reactions reported in the 4 hospital of Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran.

Material and Methods

The study was carried out at 4 teaching hospital of Kermanshah University of Medical Sciences, Kermanshah, Iran over 18 months from April 2010. All adult patients on admission in the hospitals who required blood transfusion and had established diagnosis and consented were included in the study. We used leukocyte filtration for preparing of blood component. Each consenting blood transfusion recipient who met the inclusion criteria was administered a questionnaire to obtain bio-data, relevant social, and past medical history including transfusion history. A general physical examination was also carried out on each of them before commencing the transfusion. During transfusion, vital signs were monitored half an hour after the commencement of the transfusion and then subsequently hourly to the end of the transfusion. At the same time, patients were observed for feature of transfusion reaction, which included chills/rigors, itching, urticaria, nausea, vomiting, and dyspnea. The monitoring was continued 4 hourly up to 24 hours after transfusion. Data on the date of blood donation, blood group of donor blood, type of donation, and type of blood component were also

recorded. Blood and urine samples were collected from each patient before and after transfusion, which were used to investigate for ATR in suspected cases. All the patients had pre-transfusion packed cell volume (PCV), urinalysis done and post-transfusion urine sample was visually checked for hemoglobinuria in addition to urinalysis. Acute transfusion reactions were defined as those occurring at any time up to 24 hours following a transfusion of blood components with excluding cases of acute reactions due to incorrect blood component transfusion. According to these signs and symptoms transfusions reactions were recognized as febrile nonhemolytic, allergic, fluid overload, transfusion-related acute lung injury (TRALI), anaphylactic and metabolic reactions. Subjects suspected to have ATR sent for microscopy and culture, regrouping, cross match and direct Coombs test. The SPSS software package version 16 (SPSS Inc., Chicago, Illinois, USA) was used for the statistical analysis.

Results

In the year 2010 until 2012, a total of 6238 units of blood components were transfused, of which red cell products were 2944 (47.1%), fresh frozen plasma 1437 (23%), platelet concentrates 1349 (21.6%) and cryoprecipitate 508 (8.1%). According to specialties, blood components were used in hematology (2023 units), adult intensive care unit (1124 units), surgery (728 units), emergency (521 units), oncology (467 units) and Internal medicine (425 units) departments. Overall, 3680 (58.9%) of the recipients were males and 2558 (41%) were females. The median age of these recipients was 45 years old ranging from 3 months to 79 years. The number of recipients aged from 50 to 60 years old was higher in both female 325 (12.7%) and male 576 (15.6%) recipients. A total of 59 (0.94%) cases of transfusion reaction were reported within this 3 years period. The incidence of clinically suspected transfusion reactions was 0.94% of total blood components transfused. The majority of symptoms reported were mild and transient. The commonest were allergic reactions which presented with various skin manifestations such as urticarial, rashes and pruritus (49.2%), followed by increase in body

temperature of $> 1^{\circ}\text{C}$ from baseline which was reported as febrile non-hemolytic transfusion reaction (37.2%). pain at the transfusion site (6.8%) and hypotension (6.8%). TRALI and metabolic reactions were not detected during the period study. The highest reporting rate for ATR was observed with packed cells (27/59),

followed by fresh frozen plasma (18/59), platelet (12/59) and Cryoprecipitate (2/59). 54.2% of the transfusion reactions were observed in male and 45.7% in female recipients (table1). The characteristics of the recipients with recognized transfusion reactions are shown in table 2.

Table 1. Acute transfusion reactions according to blood components

	Number of units transfused	Allergic reactions	FNHTR	pain at the transfusion site	hypotension	Total
RBCs	2944	13	9	3	2	27
FFP	1437	8	8	1	1	18
Platelet concentrates	1349	7	4	0	1	12
Cryoprecipitate	508	1	1	0	0	2
Total	6238	29	22	4	4	59

Table 2. Characteristics of recipients with recognized transfusion reaction

Age (years)	
Median (min. and max. values)	45 (3 month – 79 years)
Sex	
Male	32 (54.2)
Female	27 (45.7)
Number and percentage of transfusion reactions according to specialties	
Hematology	21 (35.5%)
ICU	8 (13.5%)
Surgery	4 (6.7%)
Emergency	4 (6.7%)
Oncology	13 (22%)
Internal medicine	9 (15.2%)
Number and percentage of blood components involved	
RBCs	27 (45.7%)
FFP	18 (30.5%)
Platelet	12 (20.3%)
Cryoprecipitate	2 (3.3%)

Discussion

According to specialties, the highest use of transfusions was observed in the hematology unit followed by adult ICU and surgery units. Patients in the hematology unit including major thalassemia patients which needs to over transfusion for RBCs. Further, the use of blood components in critically ill patients vary and this has been object of discussion. Vincent *et al.*⁶ demonstrated, in a prospective multicenter observational study which included 3534 patients from 146 western European ICUs, the common occurrence of anemia and the great use of blood transfusions (rate of transfusion during the ICU period of 37%). Rao *et al.*⁷, conducted a prospective observational study in order to assess the transfusion practice in 1247 critically ill patients and showed that 666 (53%) were administered red cells, 202 (16%) platelets and 281 (22%) fresh frozen plasma.

The authors considered appropriate use of blood components in these patients and concluded that transfusion practice was consistent and in general, there was not an excessive use of blood components. We demonstrated that the adult ICU accounted for 18% of the units transfused. Our results were similar but it is important to consider the methods we used to collect such data. In our region, emergency, trauma, cardiothoracic and oncology surgical patients are placed and evaluated in the ICU during the postoperative period, increasing the ICU's proportion of blood components transfused when reported by specialties. Further analysis according to procedures or diagnosis instead of specialties might result in different values. The use of blood components in surgery, emergency and oncology departments was also similar with the current literature. Chiavetta *et al.*⁸ carried out a

cross-sectional survey of the transfusion of blood components in teaching and non-teaching hospitals in central Ontario – Canada and demonstrated a high transfusion use in operations and procedures of the digestive and cardiovascular systems. Among the hospitals supplied by the KUMS, three provide a range of surgical services including emergency, Orthopedic Surgery, oncology and cardiothoracic surgery. Additionally, a hospital has oncology services including chemotherapy for hematological diseases. These local characteristics may explain our results regarding the use of blood components in these specialties and It is logical to assume that these differences with the results of other studies depend on the kind of services provided by each hospital.

The incidence of acute transfusion reaction in our study was 0.94% of total blood components transfused, which was similar to University of Puerto Rico, Auckland Regional Blood centre and North India who reported the overall low incidence of immediate transfusion reactions which was 0.2%, 0.34% and 0.35% respectively⁹⁻¹¹. In contrast to our study, the overall incidence of transfusion reactions at the Obafemi Awolowo University Teaching Hospital, Nigeria was higher than our result which was 8.7%¹². Also, Incidence of acute transfusion reactions reported in the pediatric intensive care unit in Montreal and Haemovigilance Unit of Brest University Hospital in France was 1.6% and at 5 in 1000 transfusion respectively^{13, 14}.

In our study, the majority of symptoms were mild and transient. Allergic reactions were the commonest symptom (49.2%) presented with various skin manifestations such as urticarial, rashes and pruritus. More serious reactions were reported such as pain at the transfusion site (6.7%) and hypotension (6.7%), however none of these were severe based on data. Our findings were similar to Handerson *et al*⁹ who reported the majority of symptoms were mild and transient with the commonest symptoms were fever, rigors and rash or urticaria. Study in North India reported FNHTR and allergic reactions were the most common of all types of adverse transfusion reactions¹¹. However, a 9-year study period by Ronald *et al*¹⁵ observed a low rate of allergic transfusion reaction which

was 17% as compared to our findings. Nigerian Hospital reported higher rate FNHTR which constituting 65% of acute transfusion reaction¹². In Serbia, out of reported transfusion reactions, 54.4% were febrile non-haemolytic transfusion reactions, 38.3% allergic reactions and 1.11% haemolytic reactions¹⁶. In the present study, we did not register any case of TRALI. Wallis *et al*¹⁷ carried out an observational study from 1991 to 2002 in the Freeman Hospital, UK. This facility has 787 beds and includes a regional cardiothoracic surgical unit and the regional liver and liver transplant units. Over 12 years, eleven cases of TRALI were recognized. In order to examine the epidemiology of TRALI a nested case-control study was performed of the first 46 patients with TRALI compared with 226 controls who had received transfusion. The authors suggested that TRALI may be more frequent than previously recognized and demonstrated an overall prevalence of 1 case in 1120 cellular components transfused. Data from Sunita Saxena & Ira Shulman¹⁹ did not demonstrate any case of TRALI. Based on these studies, our findings seem to be consistent but it is important to consider that many clinicians and transfusionists remain unaware of TRALI reactions.

We observed that red cell transfusion was most commonly associated with these acute transfusion reactions, followed by the FFP and platelet concentrates with the rates of 45.7%, 34% and 20.3% respectively. Also, we observed another reaction (but not acute reaction) in thalassemic patients that was alloimmunization against RBCs antigen. According to previous study of thalassemic patients in Kermanshah²⁰, 9.2% patients had alloimmunization against RBCs antigen. Most frequent alloantibody in these patients were reported Anti-LUa (61.5%) followed by Anti-P1 (23.1%). Also, we used single donor platelets system for our patients and so reaction of platelets transfusion were decrease in compare to our previous system of transfusion (Random Donor Platelets). Our finding was similar with Grujic *et al*¹⁶, who reported blood components that caused most of transfusion reactions were erythrocytes followed by fresh frozen plasma and platelets. Further, other study reported that almost half acute transfusion

reactions (but not severe reactions) were related to red blood cell transfusions. On the other hand, two thirds of the most severe reactions were associated with FFP or platelet components¹⁵. It is estimated that the incidence of adverse outcome is 18:100,000 red blood cells issued for children aged less than 18 years²¹. The reaction incidence per unit transfused for plasma was 0.1%, for stable plasma protein solution 0.01%, and for platelets 0.04 %⁹.

It was reported that the most frequent potentially severe outcomes for red cell transfusion were hemolytic reactions and volume overload and for platelet transfusion were major allergic reactions and bacterial contamination²². The incidence of FNHTR but not allergic reactions appears to be related to the duration of platelet storage²³. Limiting transfusion of pooled random donor platelets to those stored ≤ 3 days is an effective strategy in reducing the rate of FNHTR²⁴. Leucocyte-poor red cell was observed to prevent recurrence of FNHTR²⁵. It was suggested that blood components containing larger amounts of plasma may be associated with more severe reactions¹⁵. Various blood-conservation strategies and modalities such as acute normovolemic hemodilution, hypervolemic hemodilution, deliberate hypotension, antifibrinolytics, intraoperative blood salvage and autologous blood donation can be utilised in order to decrease the risks associated with transfusion²¹.

One way of reducing the number of adverse reactions is by limiting the number of transfusions given to patients whom the procedure will achieve some clearly defined clinical goal²⁶. When transfusion is to be carried out, great care should be taken in correctly identifying both patient and blood to avoid ABO mix-ups, and thorough pretransfusion laboratory testing should be done. During and after transfusion the patient should be closely observed for complications²⁶. The incidence of FNHTRs and alloimmunization was low after exclusive transfusion white blood cell-reduced red blood cells and single donor apheresis platelets²⁷. Current treatment of acute transfusion reactions remains largely supportive²⁸. Greater understanding of the blood component and patient risk factors for transfusion reactions will

lead to novel treatment and preventive strategies for reducing the risk of transfusion reactions. Many of these complications of transfusion therapy can be prevented by adhering to well-established practice guidelines²⁹.

In conclusion, It is important that each transfusion of blood components to be monitor carefully. Many transfusion reactions are not recognized, because signs and symptoms mimic other clinical conditions. Any unexpected symptoms in a transfusion recipient should at least be considered as a possible transfusion reaction and be evaluated. Prompt recognition and treatment of acute transfusion reaction are crucial and would help in decreasing transfusion related morbidity and mortality, but prevention is preferable.

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