Pattern of Adverse Transfusion Reactions in Acute Leukaemia Treated with Different Types of Blood Component Therapy in a Tertiary Care Hospital

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Abstract

Background: Transfusion of blood products is one of the principle components of supportive management in patients with acute leukaemia. **Objective:** The purpose of this study was to observe the pattern of adverse transfusion reactions (ATR) in acute leukaemia patients receiving blood component therapy. **Methodology:** This observational study was conducted in the Department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2018 to December 2018. Total ninety-five diagnosed case of Acute Myeloid Leukaemia (AML) and Acute Lymphoblastic Leukaemia (ALL) patients were selected for the study. **Results:** Four types of transfusion reactions including Febrile Non-Haemolytic Transfusion Reaction (FNHTR), Allergic, Anaphylactic, Delayed Haemolytic Transfusion Reaction (DHTR) were detected by clinical observations and relevant laboratory investigations. In this study, 25 (26.3%) patients showed different types of adverse transfusion reactions. Allergic reactions (48%) found to be the most common followed by FNHTR (32%), anaphylactic reactions (16%) and DHTR (4%). Allergic reactions (58.34%) were predominant in platelet transfusion and febrile reactions (62.5%) observed in red cell concentrate (RCC) transfusion. Urticaria, pruritus, angioedema, breathlessness, stridor, shivering, hypotension were prominent symptoms in allergic and anaphylactic reactions. On the other hand, fever, chills and rigors were prominent symptoms in case of febrile non haemolytic transfusion reaction. In our study no association between transfusion reaction with age, sex, types of donor, types of platelet and unit of transfusion was found. ATRs are mostly non-severe but rarely cause severe transfusion reaction. **Conclusion:** For safe blood transfusion close monitoring of transfusion, early recognition of pattern of reaction and prompt action may decrease transfusion related adverse events.

Key words: Acute leukaemia, blood component therapy, adverse transfusion reactions.

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Introduction

Acute leukaemia including Acute Myeloid Leukaemia (AML) and Acute Lymphoblastic Leukaemia (ALL) are the most prevalent Haematological Malignancy (HM) affecting Bangladeshi population, accounting for 42.4% of all HM cases, while these two constituted 66% of leukaemia cases.¹ The overall incidence of AML is 3.7 cases per 100,000 of the population. The median age at diagnosis is approximately 70 years and 66% is over 60 years of age.² ALL is the most common malignancy in childhood with the majority of cases in the 2-10 years of age group (median 3.5 years) but rare leukaemia in adults, 0.7-1.8/100000 annually. In adults, peak at 15-24 years with further peak in older age (2.3/100000 among > 80 years).³ In the management of acute leukaemia requires cytotoxic chemotherapy, prolonged hospitalization and aggressive

supportive care including transfusion of blood products (red cell cone, platelet cone, Fresh Frozen Plasma).

Despite advances in modern blood banking procedures and all the precaution taken, a small but significant number of blood transfusions are still complicated by various kinds of adverse reactions. Adverse transfusion reactions (ATR) are mostly not severe but rarely cause severe diseases including transfusion related acute lung injury (TRALI), anaphylactic shock and acute haemolytic transfusion reaction (AHTR).

Acute leukaemia patient receiving immunosuppressive drug in chemotherapy schedule which can mask transfusion reaction so these patients need special attention for diagnosis of transfusion reaction. Moreover, transfusion reaction pattern and frequency may vary significantly according to number of different variables. So, this study aimed to early detection of transfusion reaction and its pattern in acute leukaemia patient and which will help to generate better and effective management plan in order to contribute to safe blood transfusion and enhance life expectancy of leukaemia patient.

Materials and Methods

This observational study was conducted in the Department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2018 to December 2018. Total ninety-five diagnosed AML and ALL patients were enrolled who met all inclusion criteria. The study was approved by the Institutional Review Board (IRB) of BSMMU. Only diagnosed case of AML and ALL ≥ 12 years receiving or in need of transfusion during management were included in this study. Written consent was obtained from the acute leukaemia patients or from their guardians. Patients suffering from febrile illness and refused to give informed written consent were excluded from the study. Patient were interviewed, clinically examined and investigated for different types of adverse transfusion reactions if required. Clinical and laboratory information were recorded with a semi-structured data collection sheet. Categorical data was grouped as percent and numbers and mean with standard deviation measured from continuous data. Chi-square test was used to extract p-value. The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) version 24.0 for windows.

Results

Among total patient 67.4% belongs to AML and 32.6% belongs to ALL group. Mean age for AML and ALL was 34 ± 15 years and 30 ± 14 years respectively. Female sex was predominance (53.1 %) in AML and male sex was predominance (67.7%) in ALL. We did not find any significant relationship between age and sex with transfusion reaction. 31.37% male and 20.45% female subjects showed transfusion reaction (p: 0.228). Maximum reactions (36%) were observed in 12- 21 years age group (P-value is 0.600). Out of 95 subjects receiving blood component, red cell concentrate (RCC) was highest 48.4 %, Fresh Frozen Plasma (FFP) was lowest 11.6% and platelet concentrate having second 40%. During study period 7.4 % blood components were collected from blood relatives and 92.6% from unrelated donor. Among them 14% patient developed transfusion reaction with related donor and 27% with unrelated donor (p:0.453). In platelet cone transfusion maximum subjects (65%) transfused random donor platelet while 35% subjects transfused single donor aphaeretic platelet. Frequency of transfusion reactions in aphaeretic platelet and random donor platelet transfusion was 34.61 % and 42.85% respectively (p: 0.608).

Table 1: Pattern of transfusion reaction

Pattern of reaction	n (%)
FNHTR	8 (32.0)
Allergic	12 (48.0)
Anaphylactic	4 (16.0)
DHTR	1 (4.0)

Among the (26.3%) transfusion reactions 8 (32%) were Febrile Non-Haemolytic Transfusion Reaction (FNHTR), 12 (48%) were allergic reactions, 4(16%) were anaphylactic reactions and 1(4%) were Delayed Haemolytic Transfusion Reaction (DHTR). (Table 1) Male subjects were predominant (75%) in allergic reaction but equal sex distribution (50% male & 50% female) in case of febrile and anaphylactic reaction.

Table 2: Distribution of transfusion reaction in different blood component

Types of reaction	RCC (%)	Platelet conc. (%)	FFP (%)	P-value
FNHTR	62.5	37.5	0.0	0.208ns
Allergic	33.33	50.0	16.67	
Anaphylactic	0.0	100	0.0	

The frequency of FNHTRs to RCC (62.5%) was significantly higher than those to platelet concentrate (37.5%). In contrast, the frequency of allergic

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reactions to platelet components (50%) was significantly higher than RCC (33.33%) and FFP (16.67%). However, about 100 % anaphylactic reactions were observed in case of platelet transfusion. (Table 2)

Table 3: Symptoms of transfusion reaction

Symptoms	n (%)
Fever	8 (16.3)
Urticaria	12 (24.5)
Breathlessness	4 (8.2)
Stridor	2 (4.0)
Hypotension	4 (8.2)
Angioedema	4 (8.2)
Shivering	3 (6.1)
Pruritus	12 (24.5)

Urticaria, pruritus, angioedema, breathlessness, stridor, shivering, hypotension were prominent symptoms in allergic & anaphylactic reactions. Fever, chills & rigors were prominent symptoms in case of febrile non haemolytic transfusion reaction. (Table 3) In our study we found that mean transfusion requirement of AML was more than ALL (p: 0.001) and no relationship between transfusion reaction and unit of transfusion was found (p: 0.123). (Table 4)

Table 4: Distribution of transfusion reaction by unit of transfusion.

Required Transfusion	Subjects	n (%)	P-value
0-10 unit	51	10 (19.6)	0.203ns
11-20 unit	23	9 (39.13)	
21-30 unit	6	3 (50.0)	
31-40unit	12	3 (25.0)	
41-50 unit	3	0 (0.0)	

Discussion

In this study mean age for AML and ALL was 34.44 and 30.42 respectively. Tallman and Juliusson et al. showed much higher mean age for AML.^{2,4} The reason for this difference may be due to geographic/ethnic influence. Gender distribution of subjects showed female sex predominance (53.1 %) in AML and male sex predominance (67.7%) in ALL but Jackson et al and Li et al described acute leukaemia is more common in males at almost every age and gender ration of male to female patients was 1.84:1.^{5,6} Among total patients transfusion reactions were observed in 26.3% subjects. These findings are inconsistent with the results of several other studies conducted by Cho J et al and Bhattacharya et al which may be due to increased transfusion requirement in acute leukaemia patient in contrast to other non haematological

patients.⁷⁻⁹ In our study we did not found any significant relationship between age and sex with transfusion reaction. Oakley FD et al found that transfusion reaction incidence was same between sexes in adult patients but in paediatric patients (age < 21 years), showed reactions were more common in males than female.¹⁰ They also reported that incidence of transfusion reaction was more in paediatric patients than adult patients. In another study, Sidhu et al reported among total transfusion reaction 47.8% were seen in males and 52.1% in females.¹¹ In our study we didn't found any relationship between transfusion reaction with types of platelet and donor. Tormey et al also showed that no relationship exists between transfusion reaction with types of platelet transfusion.¹² During our study period we didn't found any relationship between transfusion reactions with unit of transfusion. In contrast, Chowdhury et al found that there was a strongly positive relationship between transfusion reaction and unit on transfusion.¹³ Among the transfusion reactions 8 (32%) were FNHTR, 12 (48%) were allergic reactions, 4 (16%) were anaphylactic reactions and 1 (4%) were DHTR. The frequency of FNHTRs to RCC (62.5%) was significantly higher than those to platelet concentrate (37.5%). In contrast, the frequency of allergic reactions to platelet components (50%) was significantly higher than RCC (33.33%) and FFP (16.67%). However, the nearly 100 % anaphylactic reactions were observed in case of platelet transfusion. Cho J et al found that FNHTR to RCC, platelet cone, FFP were 0.9 %, 0.3% and 0.2% respectively.⁵ Hirayama found that allergic reactions with platelet and RCC have an incidence rate 3.7 % and 0.15% respectively.¹⁴ We observed significant symptoms for individual's pattern of transfusion reaction during our study period. Fever, urticaria, pruritus, shivering, angioedema, breathlessness, stridor, hypotension were the most common sign and symptoms reported in transfusion reactions. Allergic transfusion reactions were the commonest acute transfusion reactions reported and comprised 48% (n:12) of all reactions. Commonest sign and symptoms were urticaria, pruritus and rigors which were treated by simple oral antihistamine. Anaphylactic reactions were found in 16% (n:4) patients. The most common sign and symptoms were urticaria, breathlessness, angioedema, stridor and hypotension. Sidhu et al found that commonest acute transfusion reactions were allergic which comprised 41.5% of all reactions, the most common sign and symptoms were rash,

pruritus and urticaria.¹¹ Dyspnoea and hypotension was the prominent symptoms for anaphylactoid reactions. Similarly, Chavan et al found that allergic reactions were commonest and clinical signs and symptoms were chills and rigors and pruritus.¹⁵ FNHTR were found in 32 % (n:8) patients. The most common sign and symptoms were fever, chills and rigors. Sidhu et al found that 35.1% patients developed FNHTR and most common sign and symptoms were fever, chills and rigors, hypotension and myalgia. Delayed haemolytic transfusion reactions 4% (n: 1) developed in one acute leukaemia patients 5 days after transfusion. There was history of yellowish discoloration of skin and urine, fall in posttransfusion haemoglobin. Peripheral blood film shows features of haemolysis and antibody screening was positive after transfusion. Patient did not recover and died later due to disease process. The overall risk estimates of DHTR cited in various studies vary from 0.007 to 0.6907 per 1000 red cell units transfused.¹⁶⁻¹⁸ DHTR is difficult to diagnose and most often, it is asymptomatic or may even be similar to the clinical signs and symptoms of the patient so that it remains under diagnosed and underreported.

Conclusion

Significant number of patients showed different transfusion reaction in acute leukaemia patient. Therefore, acute leukaemia patient should be monitored closely during transfusion for early detection adverse transfusion reaction.

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