Section: Transfusion Medicine

Original Research Article

A STUDY ON ACUTE ADVERSE EFFECTS OF BLOOD TRANSFUSION IN A TERTIARY CARE CENTRE

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Abstract

Background: Blood transfusion is a life-saving procedure in the clinical scenario and considered as safe when it is done appropriately. Sometimes, however, blood transfusion is associated with significant clinical risks. This study was designed to analyse the frequency of acute transfusion reactions and nature of transfusion reactions reported to the blood bank in the kilpauk Medical College and hospital and the Department of transfusion Medicine, Tamil nadu Dr MGR medical university. **Materials and Methods:** The present study was conducted to find out the incidence of acute transfusion reactions in blood transfusion recipients during the period of May 2018- April 2019. **Result:** A total of 16592 units of whole blood and component transfusions were carried out of which a total of 46 (0.3%) ATRs were encountered. Packed red blood cells (PRBCs) (n = 38, P = 0.075) and whole blood (WB) (n = 4, P = 0.535) were most commonly implicated. FNHTR was the most frequent transfusion reaction encountered (72%), seen most commonly with PRBC (risk of0.47%), and WB (risk of 0.12%,) transfusions. This was followed by allergic reaction reactions (24%), which were seen more commonly with PRBCs (risk of 0.13%,). No reactions were observed with cryoprecipitate. **Conclusion:** In our study, we observed acute transfusion reactions in 0.3% of transfusions with 54.5% definite attribution to the components transfused. The majority of the reactions observed were FNHTR and Allergic Transfusion Reactions. In the severity level most of the reactions were mild. Since transfusion reactions likely to happen even after several precautions, it is imperative to strengthen further the hemovigilance system for better outcome.

INTRODUCTION

Prior to the discovery of blood group antigens, approximately one third of human transfusions resulted in adverse outcome, oftendeath.[1] With the discovery of blood group antigens in 1901, by Karl Landsteiner, transfusion therapy changed from a hazardous proposition to a relatively safe procedure. Safety from transfusion transmitted diseases improved with advancement of technology. The recent testing facilities have lowered the incidence of transfusion-transmitted diseases to minimum. However, the incidence of adverse effects due to human errors, ABO incompatibility, alloimmunization, bacterial contamination, and immunomodulation phenomena remain a matter of concern.[2]

Access to adequate and safe blood transfusion facilities is integral to any basic health care delivery infrastructure. They are often lifesaving in critically ill patients. On the flipside, blood transfusions are also inherently embedded with risks ranging in severity from minor to life threatening.

Judicious patient selection with pragmatic pre transfusion assessments of risk versus benefit to the potential recipient combined with stringent quality control is an effective mode of reducing transfusion related adverse events. In addition, continuous monitoring of transfusion related complications can promote patient care and safety.

The goal of hemovigilance was to observe, identify, and prevent the occurrence or recurrence of transfusion related unwanted events of as to increase the safety, efficacy, and efficiency of the blood

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transfusion process, covering the entire blood transfusion chain of donors to recipients.

On the basis of this core principle, The Haemovigilance Programme of India (HvPI) was launched by the Indian Pharmacopoeia Commission in collaboration with the National Institute of Biologicals on December 10, 2012.[3]

The HvPI that comes under the Pharmacovigilance Programme of India (PvPI), tracks adverse reactions related to blood transfusions and blood product administration in affiliated blood banks across India. This study was aimed to recognize the pattern of ATR in our centers from established standards under HvPI, to enable us take necessary measures to minimize the transfusion related adverse effects in the hospital and improve the overall transfusion safety in the institute.

MATERIALS AND METHODS

This Cross sectional study was conducted among Patients who had been develop acute transfusion reactions with blood and blood components during the study period between MAY 2018 – April 2019 in the Department of Transfusion Medicine, Kilpauk Medical College and Hospital

Sample size: All patients admitted to the wards of various specialty departments who were transfused with blood components issued by Kilpauk Medical College Hospital and The Tamil Nadu Dr MGR Medical University blood bank and reported to have transfusion reaction during or after transfusion of blood components. (Purposive Sampling)

Inclusion criteria

All patients admitted to the wards of various specialty departments who were transfused with blood components issued By Kilpauk Medical College Hospital and The Tamil Nadu Dr MGR Medical University blood bank and reported to have transfusion reaction during or after transfusion of blood components were included in this study.

Exclusion Criteria

- Adverse effects occurring 24 hours after blood transfusion
- The acute transfusion reactions were categorised based on the following Criteria:
- Classification of Acute Transfusion Reactions (<24 hrs) 4
- Immunological Reactions:
- Acute Haemolytic Transfusion Reaction (AHTR)
- Febrile, nonhemolytic transfusion reaction (FNHTR)
- Urticarial transfusion reaction
- Anaphylactic transfusion reaction
- Transfusion Related Acute Lung Injury (TRALI)

Non immunological Reactions

- Transfusion associated sepsis
- Hypotension associated with ACE inhibitiors
- Transfusion associated circulatory overload
- Nonimmune hemolysis
- Air embolism
- Hypocalcaemia (ionized calcium/citrate toxicity)
- Hypothermia
- Delayed ([24 h) transfusion reactions—immunologic
- Alloimmunization, RBC antigens
- Alloimmunization, HLA antigens
- Delayed Hemolytic
- Graft-vs-host disease
- Posttransfusion purpura
- Delayed (24h) transfusion reactions—nonimmunologic
- Iron overload
- Those who are not willing to participate in this study.

The study was conducted in Government kilpauk medical college and hospital.ATRs reported to the Department of Transfusion Medicine between May 2018 to April 2019 were worked up in the study by using standard operating procedures. In our centre, coombs cross-matched ABO & Rh compatible PRBCs and Whole blood, ABO Group compatible FFP and Platelets were issued. During issue of blood/blood component, a Transfusion Reaction Reporting Form (TRRF) was attached.

The clinicians were trained about the transfusion protocol i.e.the Whole Blood (WB) and Packed Red Blood Cells(PRBC) transfusion should be started within half an hour and completed within 4 h after issue while Platelet concentrate (PC) and Fresh Frozen Plasma (FFP) should be transfused immediately after issue and completed with in15–20 min. There was no premedication protocol before the start of transfusion. Clinicians from Department of Medicine, Surgery, Gynaecology and Obstetrics, Paediatrics and Orthopaedics, burns,surgical gastroenterology were trained to have a uniform reporting of data to the Department of Transfusion Medicine.

The duly filled TRRF along with used blood bag and attached blood transfusion (BT) set, 2 blood samples (EDTA and plain vial) taken from the opposite limb and 1st post transfusion urine specimen after reaction were received.

Statistical Analysis: Data analysis was done using SPSS software. Demographic details were given in descriptive statistics. Quantitative data was given in summary statistics. P< 0.05 was considered significant.

RESULTS

During the study period, 16592 units of blood and blood components were transfused to patients admitted in various clinical specialties. Out of 16592 units transfused, 46 patients (0.3%) had ATRs during or after transfusion within 24 hours.

The incidence of FNHTR was maximum observed in 33 (72%) patients, followed by Allergic Transfusion Reaction in 11(24%) patients, TRALI

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and TACO in 1(2%) patient each. All patients were managed successfully and no casualty due to transfusion reactions was reported.

Of all the reported ATRs, 38 (83%) occurred with PRBC ,4 (9%) with WB, while FFP transfusions were responsible for 3 (7%) and platelet concentrates with 1(2%) reaction.

Maximum cases of ATRs were from Department of Obstetrics and Gynaecology 30 (65%) reactions. Of the 46 patients who had ATRs, 6 were males and 40 were females. The mean volume of blood or its component transfused, when reactions were noted was 117.33 ml (range 10–250 ml).

Transfusion with Packed Red Blood Cell (PRBC) was most commonly associated with adverse reactions (38 reactions out of 6129 transfusions; P = 0.075, Ƶ2 = 6.916), followed by whole blood (WB) transfusions (4 reactions out of 1688 transfusions; P = 0.535, Ƶ2 =2.184).

A total of 7078 units of fresh frozen plasma (FFP) transfusions were carried out that finally resulted in 3 reactions (P =.002, Ƶ2 = 15.182). A total of 1652 units of platelets transfusions were carried out that finally resulted in 1 reaction. (P =0.298 Ƶ2 = 3.680)

In our study, out of 16592 components ,46 patients developed ATR. Among the 46 ATRs reported 32% were O positive,28% were B positive, 22 % were A positive, 6% were AB positive , 2 were O negative, 2% were B negative, 2% AB negative Out of 46 patients,31 patients had previous history of sensitization.

Table 1: Frequency of transfusion reactionwith respect to associated WB/component transfusions

Type of transfusion reaction	PRBC (N=6129)	FFP (N=7078)	WB (N=1688)	Platelet (N=1652)	Total (N=16592)
FNHTR	29(0.47)	2(0.03)	2(0.12)	NR	33(0.2%)
ALLERGIC	8(0.13)	NR	2(0.12)	1(0.06)	11(0.06%)
TRALI	NR	1(0.01)	NR	NR	1(0.006%)
TACO	1(0.016%)	NR	NR	NR	1(0.006%)
Total	38(0.62%)	3 (0.04%)	4 (0.24%)	1 (0.06%)	

- The incidence of FNHTR with 1000 components transfused 2
- The incidence of allergic reaction with 1000 components 0.6
- The incidence of TRALI with 1000 components transfused 0.6
- The incidence of TACO with 1000 components transfused 0.6

Out 46 transfusion reaction reported 72%were FNHTR,11%were allergic reaction,2% were TRALI, 2% were TACO

Table 2: Type of transfusion reaction with respect to associated WB/component transfusions:

Type of transfusion reaction	TOTAL(N=46)	Percentage
FNHTR	33	72%
ALLERGIC	11	24%
TRALI	1	2%
TACO	1	2%

Among the 46 reported most of the reactions are due to PRBC 82%, whole blood implicated in 4% of the cases, FFP implicated in 6% and platelets implicated in 2%, no reaction reported with cryoprecipitate.

Table 3: Implicated components

Implicated component	Total no reactions (n=46)	Percentage
PRBC	38	82%
WB	4	9%
FFP	3	7%
Platelets	1	2%

The highest number of reaction was reported from O&G department(62.5%).In medicine 13% , surgery 6.5%,burns and plastic surgery6.5%, surgical gastroenterology 4.3%, orthopedics 4.3% were reported

Table 4: Relative frequency of departments reporting acute transfusion reactions

Department	No of reaction (n=46)	Percentage
O&G	30	65
BURNS&PLASTIC SURGERY	3	7
MEDICINE	6	13
ORTHOPEDICS	2	4
SURGERY	3	7
SURGICAL GASTRO	2	4

FNHTR most commonly associated with PRBC 88%,whole blood implicated in 6%,FFP implicated in 6%

Table 5: Days of storage versus FNHTR reaction units

No. of days stored in blood bank	No. of W/B, PRBCN=31	Percentage (%)
0-7	6	19.35%

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8-14	8	25.80%
>14	17	54.83%

Allergic reactions

Allergic reactions were observed in 11 patients (8 females and 3 males). Age ranged from 18 months to 80 years. Of the 11 patients, 8 patients had PRBCs transfusion and 2 were transfused with whole blood, 1were transfused with platelet concentrate.

PRBC is most is most commonly implicated in allergic reaction 73%,whole blood implicated in 18%, platelet implicated in 9% of allergic reactions, no allergic reactions reported with FFP.

Severity of the reaction was classified based on "Common Terminology Criteria for Adverse Events (CTCAE) classification"92

Table 6: Severity of the reaction

Type of reaction	Mild	Moderate	Severe	Life threatening	Death
FNHTR	29	4	-	-	-
ALLERGIC	1	9	1	-	-
TRALI	-		1	-	-
TACO		1	-	-	-
TOTAL	30(65%)	14(30%)	2(5%)	-	-

The imputability of the reaction is categorized by using "National Health care Safety Network Biovigilance Component Hemovigilance Module Surveillance Protocol"99

Table 7: Imputability

Imputability	FNHTR (n=33)	Allergic (n=11)	TRALI (n=1)	TACO (n=1)	Total
Definite	20	5			25 (54.34%)
Probable	4	6		1	11(23.91%)
Possible	4	-	1		5 (10.86%)
Doubtful	5	-			5 (10.86%)
Ruled out	-	-			-
Not determined	-	-			-

DISCUSSION

During the study period, 16,592 blood components were transfused; among these 46 (0.30%) cases of acute transfusion, reactions were reported. In a similar study done by Rajni Bassi et al, they reported 100 (0.40%) acute transfusion reactions out of 25,099 transfusions of various components in a Medical College Hospital at Patiala.[5]

Sharma et al., in their study reported 0.92% of ATRs among 3,455 whole blood and components transfused in a tertiary care hospital at Sikkim.[6] Khalid et al, in their study reported only 0.082% ATRs among 2,25,662 transfusions of various components at a tertiary care hospital in Saudi Arabia.[7] The higher percentage of reactions is attributed due to multiple transfusions.

The frequency of ATRs was more in females (86%) than in males (14%). A similar skewed incidence of transfusion reactions toward females was seen in studies done by khalid et al (54.3%) and sharma et al (59.4%).[6,7]

However, studies done in India by Kumar et al. and Bhattacharya et al, show a lower incidence of transfusion reactions in females, 45.7% and 34.2%, respectively.[2,8] The higher percentage of ATRs among females in our study is due to relatively higher number (65%) of reports received from Obstetrics & Gynaecology department.

In our study, majority of transfusion reactions (91.30%) were reported following PRBC/WB transfusions. Similar results were observed in studies done by Bhattacharya et al8 (82.8 %) and Rajni Bassi et al,[5] (91%). Kumar et al,[2] reported lower percentage (42.8%) of ATRs. The reason for lower percentage of ATRs in their study is due to the practice of using leukoreduced blood components.

In our study, the highest percentage of reactions was constituted by FNHTR (72%), probably due to the usage of Non leucodepleted PRBCs in our hospital. The present study correlated well with the study done by Chowdhury FS et al,[9] and Rajni Bassi et al5, they reported highest incidence of FNHTR, 62.5% and 73% respectively.

The incidence was low in the study done by kumar et al,[2] which is due to the usage of leukoreduced components in their institution.

In our study, 72% of the patients who developed FNHTR study had a history of prior sensitization in the form of transfusion or pregnancy. It is known that these events lead to the formation of anti-HLA antibodies, which are responsible for the occurrence of FNHTR. Similar results were reported by Vasudev et al.[10] In their study where most of the patients (68%) had a previous history of sensitization. proper inventory management and providing patients with relatively fresh blood will decrease the incidence of FNHTR and allergic reactions.

In our stuy, 31 WB/PRBC units were responsible for FNHTR. Out of these, 17 units (54%) were more than 14 days old; a similar difference in rate of reaction compared with duration of storage in the blood bank was found by vasudevet al.[10] This

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association of increased febrile reaction with increased storage time could be due to the cytokines released during storage of components.

Allergic reaction: Incidence of allergic reactions was found to be the second highest, constituting 24 % in the present study. Some amount of plasma kept in PRBCs to reduce the viscosity may be responsible for enhanced allergic reactions. Incidence of allergic reactions varied greatly in literature (25–55.1 %). The present study correlated well with the literature done by Chowdhury et al, Khalid et al, Bhattacharya et al, which also showed the second highest prevalence as allergic reactions in their studies.

Out of 11 reactions, 8 allergic reactions were due to PRBC transfusion. The incidence of allergic reaction with PRBC is 0.13%.The incidence of allergic reactions with PRBC in kumar et al,[2] is 0.046%. The incidence is very low comparing to our study.

In our study out of 11 patients 6 (55%) had previous history of sensitisation. Similar results were also reported by Vasudev et al.[10] In their study where most of the patients had a previous history of sensitization.

TRALI is a rare, but important cause of transfusion-related mortality. A single case (1 in 7000 FFP) of TRALI was reported in our study. Estimates of the incidence of TRALI include 1 in 5000 units of packed RBC, 1 in 2000 plasma- containing components, and 1 in 400 units of whole blood derived platelet concentrates.[11]

Papovasky and taswell found the incidence of TACO is 1:707 recipients of RBCs, and 20% of the affected patients received a single unit of RBCs.[12]

P. Robillard et al in their study suggested that the incidence was 1:5000 components, and 1.3% of the cases resulted in death. In the critical care setting, 1:356 units transfused resulted in TACO.[13] From 2007 to 2011, 15% of the transfusion associated fatalities reported to the FDA (in 32 patients) were a consequence of TACO.[14]

In a study by Popovsky et al, the incidence of circulatory overload was estimated to be 1 in 3,168 (0.03%) patients transfused with PRBC.12 In our study the incidence of TACO with PRBC transfusion was 0.016%.

In our study, we did not encounter ABO mismatch or bacterial contamination among the cases reported as in the study by Kumar et al.[2] In a study by Bhattacharya et al. bacterial contamination was suspected in 4 cases transfused with packed red cells.

Imputability: The imputability of the reaction is categorized by using "National Healthcare Safety Network Biovigilance Component Hemovigilance Module Surveillance Protocol". Among the the reported reactions in our study, definite was (54.34%), probable was 23.91%, possible was 10.86%, doubtful was 10.86%.the imputability scoring correlates well with similar study conducted by Harvey et al.[10]

Severity of the reaction: Severity of the reaction was classified based on "Common Terminology Criteria for Adverse Events (CTCAE) classification"Among the reported reaction 65% were mild, 30% were moderate, 5% were severe reaction comparing to sanders et al mild allergic reaction was higher in our study, moderate and severe reaction was low. No life-threatening reaction was reported in our study, 7% life threatening reaction were reported in sanders et al.[15]

CONCLUSION

In our study, we observed acute transfusion reactions in 0.3% of transfusions with 54.5% definite attribution to the components transfused. The majority of the reactions observed were FNHTR and Allergic Transfusion Reactions. In the severity level most of the reactions were mild. Since transfusion reactions likely to happen even after several precautions, it is imperative to strengthen further the hemovigilance system for better outcome.

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