

## ORIGINAL ARTICLE

# An audit of reported acute transfusion reactions in Universiti Kebangsaan Malaysia Medical Centre

Y RABEYA MBBS, DBS&T, AH ABDUL-KAHAR Dip MLT, and C-F LEONG FRCPA, FRCP(Edin)

Department of Diagnostic Laboratory Services, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur.

### Abstract

Transfusion is an irreversible event which carries potential benefits as well as risk to the recipient. The objective of this study was to analyse all reported transfusion reactions of the year 2008 in the Blood Bank Unit of Universiti Kebangsaan Malaysia Medical Centre (UKMMC). This is a retrospective study that was carried out by retrieving data from the laboratory information system. A total of 27842 transfusions were documented and the total reported transfusion reactions were 149. The incidence of transfusion reaction was 1 in 187 of all transfusions (0.54%); in which 69 (0.25%) were allergic in nature and 61 (0.22%) were febrile non-haemolytic transfusion reactions (FNHTR). Hypotensive reactions were identified in 6 (0.02%) patients. There were 9 (0.03%) cases reported with haemoglobinuria where no serological evidence of haemolytic transfusion reaction (HTR) was found. One HTR (0.003%) was identified and this was due to an error in patient identification in the ward. Other specified reactions like transfusion-related acute lung injury (TRALI), bacterial infections, Graft versus host disease (GVHD) were not reported. The highest frequency of the reactions occurred in the red cell transfusions which accounted for 111 cases. In conclusion, the incidences of transfusion reactions are low when compared to those reported by other centres.

*Key words:* audit, blood transfusion, blood components, transfusion reactions.

### INTRODUCTION

In modern clinical practice, blood transfusion has an important role for patient care. Although the blood supply has become increasingly safer through improved donor selection and infectious disease testing, there are still a variety of transfusion reactions encountered. These transfusion reactions are mainly non-infectious in nature and may be acute or delayed in onset. In acute transfusion reactions, clinical signs and symptoms occur during or within a few hours after completion of the transfusion. These reactions are haemolytic transfusion reactions (HTR), febrile non-haemolytic transfusion reactions (FNHTR), allergic reactions, anaphylactic reactions, transfusion-related acute lung injuries (TRALI), and transfusion-associated sepsis. A number of metabolic complications may also occur such as hyperkalaemia especially in newborn and infant. Delayed transfusion reaction may not be evident for days, weeks, months or even years

after the transfusion and these delayed transfusion reactions are commonly under-diagnosed.<sup>1,2</sup>

Transfusion reactions are serious complications of the haemotherapy. The objective of this study was to audit and identify the types of transfusion reactions documented in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) for the year 2008. The results would serve as a guide for education and strategic planning to reduce the adverse reactions of blood transfusions in the future.

### MATERIALS AND METHODS

#### *Evaluation of transfusion reaction*

In UKMMC, a standard transfusion reaction investigation protocol is followed to investigate the transfusion reactions. All recognized transfusion reactions are routinely reported to the blood bank on a standard reporting form. The transfusion reaction form includes patient details (name, age, sex, registration number,

*Address for correspondence and reprint requests:* Associate Professor Dr Leong Chooi Fun, Head of Blood Bank Unit, Department of Diagnostic Laboratory Services, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, Cheras, 56000 Kuala Lumpur, Malaysia. Tel: +6 0193210370, e mail: ctleong@ ppukm.ukm.my

ward and diagnosis), signs and symptoms noted during the reaction (e.g. fever, chills, urticaria, haematuria, etc), time of occurrence, amount of blood transfused, previous history of transfusion or transfusion reaction, and obstetric history for female patients. Immediately following any suspected transfusion reaction, the blood bag together with the infusion set and a post transfusion blood sample from the patient were sent to the blood bank for investigation. Other investigations such as post transfusion full blood picture, urine haemoglobin, and serum bilirubin were also performed.

In the blood bank, a clerical check was done. The patient's (pre- and post-transfusion samples) and the donor's blood group were reconfirmed. The patient's pre and post-transfusion samples were then checked for Direct and Indirect Coombs Test. Recheck cross match was done on patient's pre and post transfusion sample with donor red cell from the blood bag. A sample from the blood bag and segment tube respectively was sent for sterility check to rule out bacterial contamination. Once the investigations were completed, all the results were reviewed by the blood bank physician. If necessary, further consultation with the ward staff was performed to resolve any ambiguities. Transfusion reactions are classified according to standard AABB definitions.<sup>3</sup> The final evaluation and recommendations were then recorded in a hard copy as well as into the laboratory information system.

#### Study Design

In this retrospective study, all cases of reported suspected transfusion reaction for the year 2008 were evaluated. The data were retrieved from the laboratory information system and also the hard copies of transfusion reaction reports. Data were collected and recorded in a worksheet and analyzed to find out the incidence of various

types of transfusion reactions and the types of blood components involved.

## RESULTS

In the year 2008, a total of 27842 units of blood components were transfused, of which 15563 (55.9%) were red cell products, 5355 (19.2%) platelet concentrates, 4907 (17.6%) fresh frozen plasma (FFP) and 2017 (7.2%) cryoprecipitates.

A total of 149 cases were reported to have suspected transfusion reactions. The incidence of clinically suspected transfusion reactions was 1 in 187 units transfused or 0.54% of total blood components transfused. According to the Standard AABB definition of transfusion reactions, the incidences (Table 1) and the correlation of clinically suspected and laboratory investigations reported cases were shown in Table 2. Of these, 69 cases (0.25%) were reported to have allergic reactions which presented with various forms of skin manifestations such as rashes, urticaria, pruritus, maculopapular rashes and flushing, followed by 62 cases (0.223%) of increase in body temperature of  $\geq 1^{\circ}\text{C}$  from the baseline, of which 61 cases (0.22%) were reported as febrile non-haemolytic transfusion reaction and 1 case (0.003%) was confirmed to be haemolytic transfusion reaction. This case of haemolytic transfusion reaction was due to ABO mismatch as a result of failure to identify the patient correctly in the ward. There were 6 cases (0.02%) with low blood pressure. All these patients were critically ill with the following diagnosis: Stage IV cervical cancer complicated with pleural effusion, chronic myeloid leukaemia with blast crisis, myelodysplastic syndrome with septicaemia, a premature baby with respiratory distress syndrome and another 2 patients with septicaemia. The investigations showed no evidence of haemolytic transfusion reaction, bacteraemia or shock secondary to

**TABLE 1: Incidence of clinically suspected transfusion reactions  
(Total blood transfusion = 27842)**

Types of reaction	No. of cases	Incidence
Total	149	1 in 187 (0.54%)
Allergic reaction	69	1 in 403(0.25%)
FNHTR	61	1 in 456(0.22%)
HTR	1	1 in 27842(0.003%)
Hypotension	6	1 in 4640 (0.02%)
Haemoglobinuria	9	1 in 3093 (0.03%)

**TABLE 2: Results of the transfusion reaction investigation in relation to clinical presentation (n=149)**

Clinical presentation	Laboratory investigation report	No. of cases
♦ Skin rashes	• Most probably allergic reaction	69
♦ Increase in 1°C base line body temperature	• Most probably FNHTR	61
	• HTR	1
♦ Red Urine	• Haemoglobinuria	9
♦ Hypotension	• Likely to be related to underlying disease	6
♦ Others		
♦ Tachycardia	• Likely to be related to underlying disease	1
♦ Rigour 5-6 hrs post transfusion	• Likely to be related to underlying disease	1
♦ Dyspnoea	• Most probably due to fluid overload	1

bacterial contamination of blood component products, or anaphylactic shock. Therefore, the hypotension could most likely be related to the underlying diseases. There was also 1 case each (0.003%) with tachycardia, rigours and dyspnoea respectively due to causes not specified.

In our audit, there were 9 cases (0.03%) of unexplained passing of red urine during or post completion of packed red cells transfusions. However, these episodes were short-lived, mostly resolved spontaneously within 24 hours to 48 hours with no other clinical evidence to suggest haemolytic transfusion reaction. All the blood components that were involved in these reactions were packed red cells. These 9 patients were transfused with a total of 12 units packed cells with a range of 1-2 units per patient. Analysis of the packed red cells units involved showed that they were all about 20 – 25 days in storage. 4 of 12 units were re-issued more than one time; while the other units were released for the first time for the patients.

When we analysed the types of blood components involved in these 149 cases of suspected transfusion reactions, the frequencies of transfusion reactions for various blood components were as follows: packed red cell, 111/15563 units (0.71%), FFP, 25/4907 units (0.51%) and platelet concentrate, 13/5355 units (0.24%). Cryoprecipitate was not reported to be involved in any of the transfusion reactions in 2008 (Table 3).

## DISCUSSION

Blood component therapy is an essential part of management for modern day clinical practice. As with any medical or technical procedure, the therapy has the potential for both benefit and risk to the patient as illustrated by our audit.

Firestone mentioned that as many as 10% of recipients may experience an adverse effects of blood transfusion.<sup>1</sup> In our analysis, a total of 149 transfusion reactions were suspected and investigated. This gave the overall incidence of suspected transfusion reactions of 1 in 187 (0.54%). The incidence of allergic reactions was 1 in 403 (0.25%) of all blood component transfusions and FNHTR was 1 in 456 (0.22%). These incidences were lower than that of the previously reported of 1-3% for allergic reaction.<sup>1, 4</sup> and 1 in 200 for FNHTR.<sup>1</sup> This lower incidence in our study could be due to the under reporting of the transfusion reaction or pre-transfusion prophylactic use of antipyretic and anti-histamine in some patients.

Of the total 149 transfusion reactions, 69 cases were due to allergic reaction. Red cell transfusion was most commonly associated with these allergic reactions, followed by the FFP and the platelet concentrates with rates of 0.71%, 0.51% and 0.24% respectively. For the 61 cases of suspected FNHTR, 56 cases (91.8%) occurred following red cell transfusion but only 8.2% were associated with platelet transfusion.

**TABLE 3: Frequencies of transfusion reactions in relationship to total blood components transfused**

Components	No. of units with transfusion reactions	Total unit transfused	% of transfusion reaction
<b>Packed cell</b>	111	15563	0.71
<b>FFP</b>	25	4907	0.51
<b>Platelet</b>	13	4941 (random platelets) 414 (apheresis platelets)	0.24
<b>Cryoprecipitate</b>	0	2017	0
<b>Total</b>	149	27842	

This differs from other studies which showed that platelet transfusions are more often the cause of FNHTR.<sup>5,6,7</sup> Parrotta and Snyder<sup>8</sup> reported that frequency of FNHTR was higher with platelet transfusions (4% -30%) than that of red cell transfusions (0.5%). This could be due to the fact that the platelet concentrates that we received from the National Blood Centre were usually 2 days in storage. Previous studies showed that FNHTR rates were much higher for platelets of 3-5 days in storage than those of 1-2 days in storage. This could be due to the continuous release of cytokines by residual white cells in the platelet concentrate which then causes transfusion reaction.<sup>7,8,9,10</sup> Furthermore, majority of the red cell products that were transfused to our patients were packed red cells, and only a small percentage of the products were leuco-depleted red cells. This may explain the higher incidence of FNHTR due to packed red cells than platelets concentrate in our centre. According to the AABB standard guideline, to minimise FNHTR, pre-medication with antipyretic and/or transfusion with leuco-depleted packed cell is recommended for patients with 2 consecutive episodes of FNHTR.<sup>3,6,11,12,13</sup> Leucocyte filters may also be effective in removal of leucocytes from the blood products, thus reducing the incidence of FNHTR following blood transfusions.<sup>14,15</sup>

There was one reported case of acute haemolytic transfusion reaction which occurred in a patient with 'O' type blood group. He received a unit of packed red cells transfusion for anaemia secondary to his underlying condition. This patient was inadvertently transfused with about 10 ml of 'B' positive blood which was cross-matched for another patient in the same

ward. He developed fever upon transfusion and the transfusion was stopped immediately. Investigation revealed a procedure error caused by improper identification of the patient for transfusion. Fortunately, the patient recovered without further complications. According to previous studies, the frequency of acute HTR was approximately 1 in 76000 transfusions.<sup>16,17</sup> Caspari and Greinacher<sup>18</sup> documented that the estimated risk of transfusing blood to a wrong patient varies from 1 in 400 in Belgium, 1 in 19,000 in UK to 1 in 27,007 in Scotland. Although the ABO-related fatal reactions are very few, they are preventable by strict adherence to standard operating procedures and good knowledge of the adverse effects following the transfusion errors. This emphasizes the importance of continuous medical education on blood transfusion in helping to minimize the complications or adverse effects of blood transfusion.

There were 9 cases of unexplained passing of red urine reported following red cell transfusion without any other clinical signs and symptoms of HTR. All these patients were ≤ 10 year of age, of which five were diagnosed with acute lymphoblastic leukaemia (ALL), 3 with neuroblastoma and 1 with non-Hodgkin's lymphoma. These 9 patients were transfused with a total of 12 units leucocyte-poor red blood cell concentrates, with a range of 1-2 units per patient. Investigations done on these patients with post transfusion urine showed that the red urine was due to haemoglobin which cleared off within 24 hours. Urine urobilinogen were negative. Other laboratory investigations for transfusion reactions were negative. All these cases showed post transfusion increment of

haemoglobin levels with normal serum bilirubin levels. The majority of the packed red cells that were given to these patients were 20-25 days in storage. 8 of the 12 units given to these patients were released for the first time, while the other 4 units had been released more than once. These post transfusion haemoglobinuria could likely be due to the storage changes (non-immune haemolysis in the blood bag). Red cells could also be damaged due to mixing with inappropriate intravenous fluid infusions such as dextrose, before or during the transfusion; or the small branula size. Therefore, strict adherence to proper handling, storage and administration of blood products are important to minimize the possibility of non-immune haemolysis.

In conclusion, the overall incidence of acute transfusion reaction in UKMMC in the year 2008 was low. No fatal outcome was reported due to transfusion reactions. Other reactions like TRALI, bacterial sepsis and GVHD were not reported. Allergic reactions were the most frequent followed by FNHTR. The highest frequency of reaction was reported in the red cell transfusions.

#### ACKNOWLEDGEMENTS

We would like to thank all the staff of the Blood Bank Unit of UKMMC for their assistance in data collection.

#### REFERENCES

1. Firestone DT. Adverse effects of blood transfusion. In: Rudmann, SV, editor. Text Book of Blood Banking and Transfusion Medicine. Philadelphia: W.B. Saunders Company; 1995. p. 406-33.
2. Cook LO, Wise SC, Larison PJ. Adverse effects of blood transfusion. In: Harmening DM, editor. Modern Blood Banking and Transfusion Practices. 5<sup>th</sup> edition. Philadelphia: FA Davis Company; 2005. p. 336-58.
3. Mazzei CA, Popovsky MA, Kopko PM. Non-infectious complications of blood transfusion. In: Roback JD, chief editor. Technical Manual. 16<sup>th</sup> edition. Bethesda, Maryland: AABB; 2008. p. 715-49.
4. Domen RE, Hoeltge GA. Allergic transfusion reactions. An evaluation of 273 consecutive reactions. Arch Pathol Lab Med. 2003; 127: 316-20.
5. Eder AF, Chambers LA. Non-infectious complications of blood transfusion. Arch Pathol Lab Med. 2007; 131: 708-18.
6. Bakdash S, Yazer MH. What every physician should know about transfusion reactions. CMAJ. 2007; 177: 141-5.
7. Yazer MH, Podlosky L, Clarke GC, Nahirniak SM. The effect of pre-storage reduction on the rates of febrile non-haemolytic transfusion reactions to platelet concentrates and RBCs. Transfusion. 2004; 44: 10-5.
8. Perrotta PL, Snyder EL. Non-infectious complications of transfusion therapy. Blood Reviews. 2001. 15: 69-83.
9. Heddle NM. Universal leukoreduction and acute transfusion reactions: Putting the puzzle together. Transfusion. 2004; 44: 1-4.
10. Heddle NM, Klama LN, Griffith L, Roberts R, Shukla G, Kelton JG. A prospective study to identify the risk factors associated with acute reactions to platelet and red cell transfusions. Transfusion. 2003; 33: 794-7.
11. Sazama K, DeChristopher PJ, Dodd R, Harrison CR, Shulman IA, Shannon C, et al. Practice parameter for the recognition, management and prevention of adverse consequences of blood transfusion. Arch Pathol Lab Med. 2000; 124: 61-70
12. King KE, Shirey RS, Thoman SK, Kennedy DB, Tranz WS, Ness PM. Universal leukoreduction decreases the incidence of febrile non-haemolytic transfusion reactions to RBCs. Transfusion. 2004; 44: 25-9.
13. Paglino JC, Pomper GJ, Fisch GS, Champion MH, Snyder EL. Reduction of febrile but not allergic reactions to RBCs and platelets after conversion to universal pre-storage leukoreduction. Transfusion. 2004; 44:16-24.
14. Norfolk DR, Williamson LM. Leucodepletion of blood products by filtration. Blood Reviews. 1995; 9: 7-14.
15. Jamal R, Mazeni NR, Hussin NH. Evaluation of two types of leucocyte removal filters on transfusion dependent thalassaemics. Malays J Pathol. 2000; 22: 79-83.
16. Alter HJ, Klein HG. The hazards of blood transfusion in historical perspective. Blood. 2008; 112: 2617-25.
17. Linden JV, Wagner K, Voytovich AE, Sheehan J. Transfusion error in New York State: an analysis of 10 years experience. Transfusion. 2000; 40: 1207-13.
18. Caspari G, Greinacher A. The risk of transfusion to the wrong patient in Germany. Transfusion. 2002; 42: 1238-39.