A PROSPECTIVE STUDY ON THE USE OF LEUCOCYTE - FILTERS IN REDUCING BLOOD TRANSFUSION REACTIONS IN MULTI-TRANSFUSED THALASSEMIC CHILDREN

K K Tan, W S Lee, L C T Liaw, A Oh

ABSTRACT

Two hundred and eleven blood transfusions were administered to 26 multi-transfused thalassemic children (aged 9 months-13 years) over a 6-month period. Eighteen children were receiving buffy coat-poor packed red cells (PRC) prepared by centrifuge while 8 children received filtered blood through a leucocyte - filter (Sepacell R-500A). Transfusion reactions occurred in 8.5% (n=18) of transfusions and in 42.3% (n=11) of patients. 11.9% (n=16) and 2.6% (n=2) of reactions occurred in 50% (n=9) and 25% (n=2) of patients receiving buffy coat-poor PRC and filtered blood respectively.

Transfusion reactions in toto were significantly reduced in the group receiving filtered blood ($p<0.05$). However, febrile reaction alone was not significantly reduced ($p>0.1$). The median onset and duration of reaction were 2 hours (range 10 minutes - 18 hours) and 4 hours (range $\frac{1}{2}$ - 24 hours) respectively. 72.2% (n=13) of the reactions occurred during transfusion. 88.8% (n=16) of the reactions caused only one symptom. 19.2% (n=5) of all patients had recurrent reactions, all of them receiving buffy coat-poor PRC.

The commonest clinical manifestation was fever (n=7), followed by urticaria (n=5) and petechial rash (n=2). The outcome was good, with no patient experiencing symptoms exceeding 24 hours. Only 0.9% (n=2) of the transfusions were discontinued.

Keywords: *prospective study, blood transfusion, thalassemia.*

SINGAPORE MED J 1993; Vol 34: 109-111

INTRODUCTION

The transfusion-dependent thalassemia syndromes constitute one of the most serious public health problems in the Mediterranean, Middle and Far East[1,2]. Regular blood transfusion is a major component in the modern management of homozygous beta thalassemia[3,4]. Transfusion therapy may be complicated by allosensitization and transmission of viral infection[5]. However, a vast majority of complications arising from blood transfusion are non-haemolytic, non-infectious processes[6]. The most frequent cause of general paediatric admission in Penang General Hospital is blood transfusion for thalassemia[7]. The objectives of this study were to determine whether the use of leucocyte-filters reduce the frequency of transfusion reactions and to establish the clinical manifestations of transfusion reactions in local thalassemic children.

PATIENTS AND METHODS

All children who were admitted to the Paediatric Unit of the Penang General Hospital between July to December 1991 and who fulfilled the following criteria were included into the study:

i) Regular admissions for blood transfusion as part of the management.
ii) Fever of at least 38°C within 24 hours of transfusion in a previously apyrexial child.
iii) Unexplained urticaria within 24 hours of transfusion.

The temperature, pulse, respiratory rate, blood pressure and presence of any skin rash were carefully recorded before, during and after transfusion. Eight children were using a bedside leucocyte removal filter (Sepacell R-500A, Asahi Medical Co, Tokyo, Japan) and this was only available to patients who could afford to purchase it, as the hospital does not provide filters to thalassemic patients currently. The number of transfusions were not equal among the patients due to the reduced transfusion requirements in 4 splenectomised patients and an Iranian patient who left midway through the study.

As of July 1991, all the blood transfusions consist of buffy coat-poor PRC prepared by centrifugation. The donor blood is collected in a primary bag (containing the anticoagulant citrate-phosphate-dextrose-adenine) of a triple pack (Fenwal Laboratories, Deerfield, Illinois) and then centrifuged at 1740g for 5 minutes in a refrigerated centrifuge Sorvall RC3C (Du Pont Medical Products, Wilmington, Delaware). The supernatant platelet rich plasma, including the buffy coat and top layer of the red cells is then expressed into the first satellite bag intended for platelet storage. The additive solution (100ml of ADSOL ie Adenine, Dextrose, Saline and Mannitol) in the second satellite bag is allowed to flow into the primary bag containing the PRC. Blood of less than 7 days were administered whenever possible. Investigations for haemolytic transfusion reactions were performed only when clinically indicated. Red cell antibodies were screened qualitatively by using the Selectogen test (Ortho Diagnostic Systems, NJ, USA) when indicated by initial cross matching. Serological tests for hepatitis C virus and leucocyte antibodies were not available in this hospital. The residual leucocyte counts were analysed by using Sysmex k-1000 automated counter (TOA Medical, Kobe, Japan) and manually.

Paediatric Unit
Penang General Hospital
Jalan Residensi
10990 Penang
Malaysia

K K Tan, MD, MRCP, DCH
Paediatrician

W S Lee, MBBS
Medical Officer

L C T Liaw, MD
Medical Officer

Haematology Division
Penang General Hospital

A Oh, MBBS
Clinical Specialist

Correspondence to: Dr K K Tan

The frequency of reactions was tested by chi-square with Yates correction. A $p<0.05$ was considered as significant.

RESULT

Two hundred and eleven transfusions were administered to 26 children (aged 9 months-13 years) from July to December 1991. There were 16 male and 10 female patients. Four patients had been splenectomised prior to the study. The median number of transfusions was 8 (range 3-17) and the median age of the patients was 8 years. Reactions occurred in 8.5% (n=18) of transfusions and in 42.3% (n=11) of patients. 11.9% (n=16) and 2.6% (n=2) of patients receiving buffy coat-poor PRC and filtered blood respectively ($x^2= 4.18$, df=1; $p<0.05$). However, febrile reaction alone was not significantly reduced ($x^2 =2.63$, df=1; $p>0.1$). The median onset and duration of reactions were 2 hours (range 10 minutes-18 hours) and 4 hours (range $\frac{1}{2}$ - 24 hours) respectively. 72.2% (n=13) of the reactions occurred during transfusion. 88.8% (n=16) of the reactions caused one symptom, 5.6%(n=1) caused 2 symptoms and 5.6% (n=1) caused 4 symptoms. 19.2% (n=5) of the patients experienced more than one reactions, all of them receiving buffy coat-poor PRC. Three patients had 2 reactions each while 2 patients had 3 reactions. The mean ($\pm$1SD) residual leucocyte counts in the buffy coat-poor PRC and filtered blood were 1.89×10^9 ($\pm 1.05 \times 10^9$) and 0.40×10^9 ($\pm$0.24) respectively. The clinical manifestations are listed in Table I. All the reactions were clinically non-haemolytic. Headaches, chest pain, arthralgia, hypotension and haemoglobinuria were not observed in any patient. In 2 patients with petechial rash, fever and thrombocytopenia were not present.

Table I - Clinical manifestation of blood transfusion reactions in multi-transfused thalassemic children admitted to Penang General Hospital.

Signs and symptoms	Number
fever	7
urticaria	5
petechial rash	2
macular rash	1
eyelid swelling	1
cough	1
dyspnoea	1
sweating	1
cold peripheries	1
Total	20

One patient developed an anaphylactoid reaction 45 minutes after transfusion. He presented with cough and dyspnoea and was sweaty with cold peripheries. There were no fever, rash, hypotension, tachypnoea or wheeze on examination. The symptoms rapidly resolved within an hour with discontinuation of the transfusion and intravenous chlorpheniramine. The frequency of reactions are tabulated in Table II. Most of the reactions were mild in nature. Eight patients required observation alone, 6 were prescribed chlorpheniramine (4 orally and 2 parenterally) and 2 received paracetamol. Only 0.9% (n=2) of transfusions were discontinued; one in a patient with anaphylactoid reaction and the other in a patient with generalised urticaria. None of the reactions persisted for more than 24 hours.

Table II - Frequency of transfusion reactions in multi-transfused thalassemic children.

Mode of transfusion	Transfusion reactions	
	Present	Absent
Leucocyte-poor blood	16	119
Filtered blood via Sepacell	2	74

DISCUSSION

Estimates of the overall incidence of transfusion reactions vary widely, due to factors such as the care taken in monitoring patients during and after blood transfusions and the criteria adopted for diagnosing a reaction[8]. Complications occur in 2-5% of transfusions[9]. Barton quoted 7% of all blood product recipients develop non-haemolytic non-infectious reactions. The frequency of complications is inversely proportional to the care exercised in preparing for and supervising the transfusion[9]. The incidence of transfusion reactions also vary widely with different types of leucocyte filters, ranging from 3-36%[10]. Transfusion reactions were noted in 42% of our patients, much higher when compared to 17% of Italian and Greek patients under the Cooleycare programme and 6.6% of Walker's patients[3,8]. In practice, severe reactions such as haemolytic transfusion reactions are rare whereas mild reactions such as fever and urticaria are common[11]. Our study was consistent with the latter observation as severe reactions that require discontinuation of transfusion occurred in only 2 transfusions. Fever and urticaria are among the most frequently encountered transfusion reactions[12]. Febrile reactions were the commonest in our series, as was similarly reported by others[3,10]. Febrile reactions are relatively common with repeated transfusions and the tendency to develop reactions increases as the number of previous transfusions increase[9]. Although transfusion reactions in toto were significantly reduced with leucocyte-filters, this was not the case with febrile reactions in our study. A relatively small sample may have contributed to this effect. Urticarial reactions were more common in our series compared to others[3,10]. Headaches, chest and joint pain were not reported in our series, in contrast to other series[3,10].

Leucocyte-free red cells should be the treatment of choice for prospective recipients of multiple transfusions, as leucocytes are the cause of important transfusion complications[13]. Transfusion reactions, once a serious problem for multi-transfused patients, are now largely controlled by the routine use of leucocyte filters[3]. This may apply to developed countries where resources are more readily available compared to developing countries where priorities in health care may be different. A selective approach as to which patient should receive leucocyte filters offers a more practical compromise. Previous criteria adopted by the Italians required at least 3 reactions, consecutively or very close in time, before filtered red cells are used although currently more than 90% of their thalassemics received filtered red cells[10]. Another suggested approach is to use filters on patients who have had at least 2 severe febrile reactions[11]. Although the outcome of transfusion reactions are generally good in our series, the use of leucocyte filters will help in reducing the discomfort of transfusion reactions which patients may continue to experience with multiple transfusions.

ACKNOWLEDGEMENT

We would like to thank the Director General, Ministry of

Health, for permission to publish this paper; Dr Pyar Kaur for her helpful comments and Dr PG Wong for statistical assistance.

References

1. Fosburg MT, Nathan DG. Treatment of Cooley's Anemia. Blood 1990;76:435-44.
2. WHO Working Group. Hereditary anaemias: genetic basis, clinical features, diagnosis, and treatment. Bull WHO 1982;60:643-60.
3. Rebulla P, Modell B. Transfusion requirements and effects in patients with thalassemia major. Lancet 1991;337:277-80.
4. Modell B, Petrou M. Management of thalassaemia major. Arch Dis Child 1983;58:1026-30.
5. Sekiguchi S, Takahashi TA. Leukocyte-depleted blood products and their clinical usefulness. In: Brozovic B. ed. The role of leukocyte depletion in blood transfusion practice. Proceedings of the international workshop (London 1988). Oxford: Blackwell Scientific Publications 1988:26-34.
6. Barton TC. Nonhemolytic, noninfectious transfusion reactions. Semin Hematol 1981;18:95-121.
7. Annual Report 1991, Penang General Hospital (In press).
8. Mollison PL. Blood transfusion in clinical medicine. 6th rev. ed. Oxford: Blackwell Scientific Publications, 1979.
9. Penington D, Rush B, Castaldi P. Blood groups. Blood Transfusion. In: De Gruchy GC. ed. Clinical Hematology in medical practice. 4th rev. ed. Oxford: Blackwell Scientific Publications. 1978:780-99.
10. Reverberi R, Menini C. Clinical efficacy of five filters specific for leukocyte removal. Vox Sang 1990;58:188-91.
11. Contreras M, Mollison PL. Immunological complications of transfusion. Br Med J 1990;330:173-6.
12. Goldfinger D. Adverse reactions to blood transfusions. In: Gellis SS, Kagan BM. eds. Current Pediatric Therapy 10. Philadelphia: Saunders;1982:243-7.
13. Sirchia G, Rebulla P, Mascaretti L et al. The clinical importance of leukocyte depletion in regular erythrocyte transfusions. Vox Sang 1986;51(Suppl 1):2-8.