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Original Research Article

Effectiveness of buffy coat leucoreduced packed red blood cells in decreasing febrile non-hemolytic transfusion reactions in thalassemic patients

Neeti Dutt[1]*, Meena Sidhu[1], Sushil Sharma[2], Ravi Parihar[2], Dinesh Kumar[3]

[1]Department of Blood Transfusion Medicine and Immunohaematology, Government Medical College, Jammu, Jammu and Kashmir, India
[2]Department of Paediatrics, Government Medical College, Jammu, Jammu and Kashmir, India
[3]Department of Preventive and Social Medicine, Government Medical College, Jammu, Jammu and Kashmir, India

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***Correspondence:**
Dr. Neeti Dutt,
E-mail: drneetidutt@gmail.com

ABSTRACT

Background: Blood transfusions have always been associated with a number of adverse outcomes which have steadily decreased over years owing to new discoveries and technical advancements. Thalassemic patients are more prone to transfusions related complications owing to repeated transfusions. Study of these reactions and correlating them with the leucodepletion status of the transfused packed red blood cells (PRBCs) reduces transfusion complications due to the transfused leukocytes.
Methods: This is a prospective study carried out on 1750 transfusions in 138 thalassemic patients at our institute between August 2015 and March 2016. The total transfusions were classified into four categories depending on the leucodepletion status of the PRBC's. The clinical records and the reaction workup done to rule out the hemolytic reactions were recorded.
Results: Reactions were recorded in 17 (0.97%) out of a total of 1750 transfusions. 14 (4.1%) reactions were recorded on transfusions of non-leukoreduced PRBCs whereas only 2 (0.16%) reactions were recorded in leucoreduced (buffy coat) PRBCs. 1 (0.8%) reaction was recorded on transfusion of leucodepleted PRBCs done by bedside filter. No reaction was documented when buffy coat leucoreduced PRBCs were used along bedside filter.
Conclusions: Elimination of WBCs from donor packed cells results in reduction of adverse reactions following blood transfusion. Various methods of leucoreduction have been successfully employed in the past and shown to reduce transfusion reactions in multi transfused thalassemic patients. In resource limited settings, leukoreduction using the buffy-coat method is an effective intervention in reducing the transfusion reactions.

Keywords: Febrile non-hemolytic transfusion reaction, Leucoreduction, Thalassemia

INTRODUCTION

Blood transfusions have always been associated with a number of adverse outcomes which have steadily decreased over years owing to new discoveries and technical advancements. The discovery of blood group antigens in 1901 by Karl Landsteiner dramatically reduced adverse outcomes including deaths resulting from blood transfusions.[1] Screening of donor blood for infectious diseases reduced the chances of transfusion transmitted infections. Despite these advancements, a variety of adverse effects like alloimmunization, hemolytic reactions, and allergic phenomena due to transfusions remain a concern especially in thalassemia

patients requiring repeated transfusions. Febrile nonhemolytic transfusion reactions (FNHTRs) are the most common of these reactions estimated to be 0.5 to 6.8 percent of all units transfused.[2,3] Patients with a history of FNHTRs are at a 15-percent risk of recurrence of this type of reaction.[4] The presence of white blood cells (WBCs) in the blood is primarily thought to be responsible for most of these reactions. FNHTRs are believed to be WBC-mediated by interaction between the recipient's cytotoxic antibodies and HLA and/or WBC-specific antigens located on donor WBCs. Formation of antigen-antibody complexes leads to complement binding and release of endogenous pyrogens.[3] Therefore, leukoreduction of RBCs should reduce the incidence of FNHTRs and associated clinical costs. Leucoreduction has also been shown to reduce human leukocyte antigen alloimunization and platelet refractoriness. It is also reported to prevent the transmission of leukotropic viruses, such as cytomegalovirus, human T-cell leukemia virus, and Epstein Barr virus.[5] In view of these findings, a study was carried out to compare adverse outcomes in patients of thallassemia receiving non leucoreduced blood to those receiving leucoreduced blood.

METHODS

This study was carried over a period of 8 months from August 2015 to march 2016, on patients with thalassemia major who were on regular transfusion regime and who were transfused with packed red cells at our institute. All these patients were divided into four categories according to the status of leucoreduction of the transfusion:

- Leucodepletion by bedside filter
- Leucoreduction by buffy-coat method
- Leucoreduced blood with bedside filter
- Non-Leucoreduced blood

All transfusions were meticulously monitored and the transfusion records as well as clinical charts were reviewed for evidence of any transfusion reactions that occurred within one hour of the commencement of the transfusion. In patients who had transfusion reactions, the reaction workup was checked to rule out the hemolytic reactions.

RESULTS

The outcome of 1750 transfusions given during the study period were analysed as under.

Transfusions using only bedside filters

A total of 125 transfusions were given using bed side filter, i.e. 7.1% of the total 1750 transfusions. Twenty-four patients used bed side filter. About 16.6% patients used (n=4) bedside filters regularly without any prior transfusion reactions. About 50% (n = 12) patients used bedside filters irregularly. About 33.3% patients (n = 8) started using bedside filter after experiencing transfusion reactions. Of the twelve patients who used bedside filter irregularly, one patient developed febrile non-hemolytic transfusion reaction. Therefore, only one reaction was recorded in patients receiving bedside filtered PRBCs during the study period (Table1).

Table 1: Various categories of leucoreduced blood transfusions and frequency of FNHTR'S caused due to them and its statistical significance.

Categories	Total no. of transfusions	Percent of total transfusions	Number of reactions (FNHTR)	Reaction rate	95 C- I for proportion	Statistical inference
Bedside filter	125	7.1%	1	0.8%	0.04-3.8	Between bedside filter and non-leucoreduced P = 0.06
Buffy coat-leucoreduced	1223	69.8%	2	0.16%	0.02-0.53	
Buffy coat-leucoreduced with filter	62	3.5%	0	0%	0.0-4.7	Between leucoreduced and non-leucoreduced P < 0.0001
Non-leucoreduced	340	19.4%	14	4.1%	2.36-6.65	
Total	1750	100%	17	0.97%	0.58-1.52	

Z test for proportion (between leucoreduced and non-leucoreduced) is 6.9 p<0.0001 (Highly Significant).
Z test for proportion (between bedside filter and non leucoreduced) is 1.8 p = 0.06 (Not Significant)

Transfusion using buffy-coat leukoreduced packed red blood cell

A total of 1223 transfusions were performed using buffy-coat leukoreduced PRBCs; that is 69.8% of the total 1750 transfusions. Transfusion reactions occurred in 0.97% (n = 17) of total 1750 transfusions and 8.2% (n = 12) of 146 patients. 0.16% (n = 2) reactions occurred in patients receiving buffy-coat leukoreduced PRBCs (Table 1).

Transfusion using buffy coat leucoreduced blood with filter

A total 62 transfusions were performed using buffy coat leucoreduced blood with filter i.e. 3.5% of the total transfusions (1750). No transfusion reaction occurred in this group (Table1).

Transfusions using nonleukoreduced blood

A total of 340 transfusions were done by nonleukoreduced PRBCs; that is 19.4% of the total 1750 transfusions. 4.1% (n=14) reactions occurred in patients recieving nonleukoreduced PRBCs (Table 1).

DISCUSSION

With the advent of transfusion therapy, thalassemia is no more a rapidly fatal disease of childhood but a chronic illness compatible with a prolonged life. On the other hand, frequent blood transfusions leading to transfusion reactions, transfusion transmitted infections, iron overload and the chronic nature of the disease have contributed to a whole new spectrum of complications. Some of these complications arise due to immune mediated mechanisms involving donor WBCs. Thus, elimination of WBCs from donor packed cells result in reduction of such adverse reactions. Various methods of leucoreduction have been successfully employed in the past and shown to reduce febrile non-haemolytic transfusion reactions.

In the present study, febrile non-haemolytic transfusion reactions occurred in 0.97% of the total transfusions and in 8.69% (n=12) of the total patients. When bedside filter was used, reaction rate was 0.8% and when buffy-coat leucoreduced blood was used, reaction rate came out to be 0.16%. When both bedside filter and leucoreduced blood were used, no reactions were documented. On the other hand, use of non leucoreduced blood resulted in the occurrence of febrile non-haemolytic transfusion reactions with a reaction rate of 4.1%. This shows that a highly significant reduction occurs in febrile non-haemolytic transfusion reactions when buffy-coat leucoreduced blood is transfused as compared to non leucoreduced blood ($p<0.0001$). However, there is no significant reduction ($p=0.06$) in febrile non-haemolytic transfusion reaction between bedside filter and non leucoreduced blood. In our study, majority of the febrile non-haemolytic transfusion reactions occurred in patients recieving non-leucoreduced blood i.e 82.3% (n=14) and there is significant reduction in these transfusion reactions in patients receiving leucodepleted blood i.e 17.6% (n=3) with $p<0.0001$.

Table 2: Comparison with other studies.

Name of study	Reaction rate with leucoreduction	Reaction rate without leucoredution	Result
Devi AMS et al[6]	0.22%	0.58%	Significant reduction
Tan KK et al[8]	2.5%	11.9%	Significant reduction
Kumar H et al[7]	1%	4%	Significant reduction
Present study	0.16%	0.97%	Significant reduction

According to Devi AMS et al transfusion reaction rate was 0.22% when leucoreduced blood was used and 0.58% when non leucoreduced blood was used. Reaction rate was nil when bedside filter was used in their study.[6] Similarly in Tan et al reported reaction rates in 26 thalassemic children who had recieved 211 blood transfusions over a 6-month period. Transfusion reactions occurred in 8.5% (n = 18) of transfusions in 2.3% (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 PRBC and filtered blood, respectively. Transfusion reactions were significantly reduced in the group receiving filtered blood ($P<0.05$).[8] In another study carried by Karen E et al who compared the results of incidence of FNHTRs over two time periods after introduction of universal leucoreduced PRBCs found that there was a significant difference in the incidence of FNHTRs seen between the two-time periods (0.37% in 1994 vs. 0.19% in 2001, $p = 0.0008$).[9] Kumar H et al also showed that after the introduction of leucodepletion of blood for thalassemics at their center, the incidence of non-haemolytic febrile transfusion reactions (NHFTR) fell from 4% in 2002 to 1% in 2003.[7] On comparing our study with the above mentioned studies we get the similar results which indicate that prestorage leukoreduction of RBCs is beneficial in reducing the incidence of FNHTRs. This reduction of FNHTRs is one of several arguments supporting the use of universal leukoreduction of blood components. Comparison between various studies have been shown in Table 2.

CONCLUSION

Regular blood transfusion forms the lifeline of Thalassemic patients thereby increasing the life span of thalassemic patients, that is usually accompanied by many transfusion complications. Febrile non-hemolytic

reactions are the most common type of reactions reported in these patients and cause a lot of discomfort to the patients. Therefore, it is necessary to supply blood components that carry reduced risks of transfusion reactions in these patients. Although leukocyte depletion by using integral in-line built filters is the most effective method of preventing febrile non-hemolytic transfusion reactions but due to cost restraints it is not being practised in all blood transfusion centres.

In present study, buffy coat leucoreduced blood along with bedside filters has proved to be the most effective among the three categories, with no reaction recorded.

However, the cost factor prevents all patients from using bedside filters. A simple buffy-coat method of leukoreduction, which is a cost-effective method reduces transfusion reactions significantly when compared to nonleukoreduced PRBC. In this way, it remains a good alternative to using bedside blood filters in a resource limited setups.

This study has many limitations including small sample size and did not look at the rate of under reported transfusion reactions, which is commonly seen in clinical practice. There is also the possibility that some reactions went unnoticed and therefore were not recorded.

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