

Incompatible blood transfusion in children in Burkina Faso

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Published: 23rd January, 2017

Accepted: 23rd January, 2017

Received: 12th December, 2016

Open Journal of Hematology, 2017, 8-1

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Keywords: incompatible blood, alloimmunization, red blood cell, children

ABSTRACT

Background: Transfusion therapy saves lives, but remains complicated by RBC immunization. So, erythrocyte phenotyping in blood donors and recipients is crucial in minimizing alloimmunization.

Objectives: To determine the frequency of Rhesus and Kell incompatible red blood cell transfusions in children.

Methods: A cross-sectional observational study was conducted in two paediatric health centres in Ouagadougou, Burkina Faso. Usually, standard phenotyping, ABO and RhD was determined for transfusion. Extended phenotyping i.e. RhC, RhE, Rhc, and Rhe and Kell antigens, was determined in both the recipients and the donor red blood cell units as well. The samples were analyzed using the LISS-Coombs indirect antiglobulin test to determine if alloimmunization had occurred.

Results: Out of the 474 transfused children, a haemoglobin level under 70g/L was observed in 86% of them, malaria (49%) was the main indication for blood transfusion and incompatible Rhesus /Kell transfusions were demonstrated in 25% of the cases. The red cell alloimmunization was observed in 4.2% of the patients.

Conclusions: Performing erythrocyte phenotyping in donors and recipients will diminish the risk of alloimmunization in children receiving multiple transfusions later in life.

INTRODUCTION

Burkina Faso is a Sub-Saharan African country, in which blood transfusion is an important field in medical therapies. About 7% of deaths during hospitalization were imputed to anaemia and deaths attributable to malarial anaemia in children fewer than five years were

13% [1].

In our context, the decision of red blood cells is both based on the haemoglobin level and each patient's capacity to tolerate anaemia. For haemoglobin above 100g/L blood transfusion is generally not indicated while under 70 g/L it is recommended [2]. In chronic anaemia, blood transfusions are not usually required except in

special circumstances such as an acute symptomatic anaemia which is defined by a haemoglobin between 50 and 60g/L or when the basal haemoglobin drops by 20g/L.

Pre-transfusion phenotype typing in Burkina Faso comprises only the donor's and the recipient's A, B and D antigens. Unfortunately, this typing could be insufficient when repeated transfusions are needed, which is the case for children in whom malaria and sickle cell anaemia are one of the main causes of acute anaemia [2]. If there is likely repeated transfusion, phenotyped A, B, O and the five Rhesus antigens D, C, E, c, e as well as for Kell compatible red cells typing are recommended to minimize alloimmunization [3, 4].

The objective of this study was to describe the frequency of incompatible blood transfusions concerning the antigens C, E, c, e and Kell in children in Burkina Faso. Our aim was also to estimate the impact of these antigens on alloimmunization occurrence.

METHOD AND DESIGN

Subjects

All transfused children in two paediatric health centres in Ouagadougou, Burkina Faso, were included during a period of 6 months from August 2013 to February 2014.

MATERIALS

Oral informed consent was obtained from the parents. Collected parameters were age, sex and the reason for RBC transfusion. All the data were obtained from the patients' medical records. The RBC units were from voluntary blood donors and only the first RBC unit transfused was considered for the study.

PROCEDURES

Recipients' red cells were obtained by venous puncture and by the pilot tube for the RBC unit. The haemoglobin level was determined using the ABX Pentra 60 Haematology Analyzer (Horiba ABX SAS, Montpellier, France). To determine the frequency of incompatible transfusions, after the transfusion process, a blood group Rh/Kell phenotype was determined for the recipients and the transfused RBC units as well. The antigens RhC, RhE, Rhc, and Rhe were detected with the

conventional tube technique (LISS-Coombs indirect antiglobulin test) and Kell antigen was determined by the Coombs LISS technique of the laboratories DiaMed® (LISS/Coombs ID- cards). Two weeks after the blood transfusion, the diagnosis of alloimmunization was conducted by indirect antiglobulin test (ID-Card Coombs Anti-IgG). For the antibody screening, we used test cell reagents ID-DiaCell I-II-III and test cell reagent ID-DiaPanel for antibody identification.

ANALYSIS

The data were collected and analyzed through using the Epi info. The statistical test used was the chi-square test; a 95% confidence interval was used in the statistical analysis.

RESULTS

A total of 948 samples (474 recipients and 474 RBC transfusion units) were tested. In the population having been screened, the mean age was 3.5 ± 3.1 years old (range: 6 months - 15 years old). The haemoglobin levels and main indications for transfusion are presented in [tables 1](#) and [table 2](#).

Table 1: Frequency of transfusions in children and their age according to the level of haemoglobin

| Hemoglobinlevel (g/L) | Number of patients | Frequency |
|-----------------------|--------------------|-------------|
| ≤ 70 | 408 | 86% |
| 70 - 100 | 60 | 12.5% |
| > 100 | 06 | 1.5% |
| Total | 474 | 100% |

Table 2: Haemoglobin level and indications for RBC transfusion

| Indications for RBC transfusion | Mean hemoglobin level (g/L) (range) | Number of children | Frequency |
|---------------------------------------|-------------------------------------|--------------------|------------|
| Malaria | 53g/L (25 -70) | 233 | 49% |
| Bacterial and viral infections | 77g/L (55 - 90) | 81 | 17% |
| Haemolytic anemia | 54g/L (35 -75) | 75 | 16% |
| Vaso-occlusive crisis | 76g/L (50 -85) | 60 | 12% |
| Malignant haemopathies | 71g/L (30 - 90) | 14 | 3% |
| Others | 79g/L (60 -115) | 11 | 2% |
| Total | - | 474 | 100 |

The distribution of the Rhesus phenotype presented in [table 3](#) shows that the main phenotypes were Rh Dccee; Rh DCcee and RhDccEe. The frequency of Kell antigen was ≤ 1.0 % in both groups.

Table 3: Distribution of the phenotype Rhesus of the RBC units and the recipient

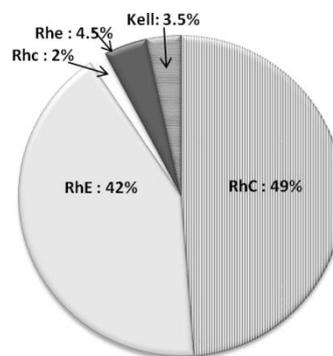
| Phenotype Rhesus | RBC units Number (%) | Patients Number (%) | p |
|------------------|----------------------|---------------------|----|
| Rh Dccee | 293 (61.8%) | 299 (63.1%) | NS |
| Rh DCcee | 67 (14.2%) | 61 (12.9%) | NS |
| Rh DccEe | 64 (13.5%) | 63 (13.3%) | NS |
| Rh dccee | 33 (6.7%) | 27 (5.7%) | NS |
| Rh DCcEe | 6 (1.3%) | 7 (1.5%) | NS |
| Rh DccEE | 6 (1.3%) | 5 (1.0%) | NS |
| Rh dCcee | 4 (1.0%) | 9 (1.9%) | NS |
| Rh DCCee | 1 (0.2%) | 3 (0.6%) | NS |
| Number | 474 (100%) | 474 (100%) | |

P significance level: 0.05; P NS: No significant

A total of 119 out of 474 (25% of transfusions) were incompatible for the Rhesus C, E, c, e and/or Kell antigens. For those children who received incompatible blood, 73% (87/119)

were under five. RhC and RhE antigens were the most frequent incompatible transfusions with 49% (58/119) and 42 % (50/119) of the cases respectively ([Figure 1](#)).

Figure 1: Frequency of Rhesus and Kell antigens involved in incompatible transfusions



The alloimmunization was 4.2% (5/119) and the anti-C and anti- E antibodies were observed ([table 4](#)).

Table 4: Distribution of alloantibodies in incompatible blood transfusion

| Patient N° | Age (years) | Recipient phenotype | RBC Phenotype | Alloantibodies | |
|------------|-------------|---------------------|---------------|----------------|----------|
| | | | | Anti RhC | Anti RhE |
| 1 | 6 | ccee | Ccee | + | |
| 2 | 2 | ccee | Ccee | + | |
| 3 | 4 | Ccee | ccEe | | + |
| 4 | 12 | ccEe | Ccee | + | |
| 5 | 9 | Ccee | ccEe | | + |

DISCUSSION

Indications for red blood cell transfusion

Haemoglobin level

In the context of Burkina Faso, all medical orders for RBC transfusions mention the haemoglobin level. On this basis, blood transfusion was justified for 86% of the children who presented a haemoglobin level lower than 70g/L. The indication for transfusion is traditionally based on haemoglobin thresholds ranging from 70 to 100g/L and they are the same whatever the patients' age [4]. However, taking into account only the haemoglobin level does not usually justify a blood transfusion. There is not a single transfusion threshold for all patients and the decision to transfuse should take account of each patient's age, pathology and comorbidities.

More than the haemoglobin value, it is the haemodynamic tolerance of the anaemia that appears to be the best criterion for estimating the need of a transfusion. A transfusion could be carried out above a haemoglobin concentration of 70g/L if anaemia is poorly tolerated. On the contrary, in chronic anaemia, a haemoglobin level lower than 70 g/L could be well tolerated and blood transfusion might be unnecessary.

Acute anaemia

Malaria

Acute anaemia is common in paediatrics and various clinical situations are likely to be at the origin of a severe anaemia requiring an RBC transfusion. In our study, malaria was one of the key indications for transfusion (49%), probably related to a high parasitic density in a malarial

transmission season. Malaria is a public health problem and, more particularly, in sub-Saharan Africa in which the children who are under five constitute a vulnerable group [5, 6, 7]. Severe malaria caused by the *Plasmodium falciparum* presents clinically most frequently in African children as cerebral malaria or severe anaemia due to malaria. Severe anaemia due to malaria is a leading cause of pediatric hospitalization in sub-Saharan Africa. It represents about 20% to 26% of all anaemia cases [8, 9] and its management often includes a blood transfusion.

Bacterial or viral infections

Bacterial or viral infections are another major healthcare problem in children in Africa. These infections may be responsible for severe sepsis and septic shock [10]. The pathophysiology of sepsis and septic shock is complex. It involves decreased oxygen delivery and myocardial and multiorgan dysfunction. The treatment of septic patients requires optimization of oxygen delivery in order to minimize cellular dysfunction [11]. Red blood cell transfusion is a therapeutic strategy frequently advocated for these patients so as to make sure there is adequate oxygen delivery by optimizing their cardiac output and haemoglobin level.

Acute haemorrhage

Hypovolemia secondary to a sudden and significant loss of blood volume is also responsible for acute anaemia. The main pathophysiological basis of the acute blood loss is due to the rapid decline of haemoglobin level and the increased risk of cellular hypoxia with the deleterious effects of tissue. The haemorrhagic shock involves the vital prognosis and requires a need for immediate treatment. In addition to oxygenation and vascular filling, the transfusion decision is strongly recommended. The goal of this transfusion decision is to increase the red blood cells mass, which helps to improve the oxygen-carrying capacity of blood.

Chronic anaemia

Chronicity of an anaemia is not synonymous with its stability and under different circumstances, blood transfusion might be needed [12]. In sub-Saharan Africa, some chronic pathology will be at the origin of an anaemia, and could require a red blood cell transfusion. Indeed,

severe haemolysis related to Glucose-6-phosphate dehydrogenase (G6PD) deficiency and sickle cell disease contributes to anaemia among children [13]. However, in sickle cell disease, the majority of vaso-occlusive crisis does not require a simple blood transfusion. Blood transfusion would increase the risk of complications in particular with development of acute chest syndrome.

The slower the anaemia develops, the easier it is tolerated. Even severe, but well tolerated anaemia due to iron deficiency, can be treated by iron therapy only. In anaemia due to medullary insufficiency, haematopoiesis is easily depressed by the transfusion, therefore, its indication must also remain restrictive [14]. An improvement in the management of this type of anaemia is the use of erythropoiesis stimulating agent like EPO.

Transfusion compatibility

Blood grouping, phenotype Rhesus and Kell

In Africa, transfusion practice is based routinely on standard phenotyping A, B and D antigens in blood donors and patients. Antigens A, B and RhD are of the greatest clinical importance because of their involvement in immediate and delayed haemolytic transfusion reactions and haemolytic disease of newborns. In Burkina Faso, the Rh and Kell antigen distribution between recipients and donors were similar. According to the ethnicity, the following frequencies were observed respectively in blacks and in caucasians: RhD antigen: 92% and 85%; RhC antigen: 27% and 68%; RHE antigen: 22% and 29%; Rhc antigen: 96% and 80% and Kell antigen: 3.5% and 8.8% [14, 15]. The frequency of antigen Rhe is identical in both groups [15]. The immunogenic capacity of the red blood cell antigens varies and the consequences of incompatible antigen transfusion are not similar. The immunogenic antigens are in order of decreasing frequency: the antigens D, E, C and Kell and the most frequent alloantibodies are anti D, anti-E anti-C and anti-K [16, 17, 18]. In the study, about 77% and 76% of the patients were the phenotype Rh cc and Rh ee respectively. The most frequent antigens implied in incompatible transfusions were the antigens C (49%) and E (42%). Such a result suggests the need for extended blood phenotyping in addition to ABO and Rh D.

Alloimmunization

The red cell alloimmunization was observed in 4.2% of the patients. Similar result was noticed in Africa [19]. In the African population, a lower incidence of alloimmunization was reported if the transfusion is carried out in the country of origin [20, 21] compared to transfusion performed in countries where the majority of donors are Caucasians [22]. In sub-Saharan Africa, there is minimal disparity between donor and recipient antigen profiles; this "ethnic matching" [23] explained a lower risk of red cell alloimmunization. These results which reflect the homogeneity of red blood cell antigens in the Africans should not ignore the risk of occurrence of alloimmunization. Although the immunogenicity of the antigen is the key factor, the occurrence of immune alloantibodies also depends on other factors. Indeed, the rate of alloimmunization is known to increase with the multiple RBC units and incompatible transfusion intensity. The recipient's phenotype is important; the homozygous immunize more than the heterozygous. Finally, the immunologic recipient's response is fundamental. Very young children are characterized by an immature humoral immunity. Moreover, more African children are immunosuppressed subjects from repeated infections, the effects of malnutrition and hyposplenism, due to sickle cell disease.

CONCLUSION

Performing extended phenotyping in donors and recipients will reduce exposing children who will receive multiple transfusions in their life to

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the risk of alloimmunization. In particular, efforts should focus mainly on the female patients and on patients with some chronic diseases and thus prone to chronic transfusions. However, this should not conceal a simple recommendation which consists of the right prescription for this type of blood products.

ACKNOWLEDGEMENTS

The authors wish to thank the Director General of National Blood Transfusion Centre Dr Honorine Dahourou and her staff of the Immuno-haematology Laboratory. We also wish to thank those parents and children who have accepted to cooperate with us.

COMPETING INTERESTS

The authors declare that they have no financial or personal relationship(s) which may have inappropriately influenced them in writing this paper.

AUTHORS' CONTRIBUTIONS

KE. (Hôpital Universitaire Pédiatrique Charles de Gaulle) supervised activities, contributed to the scientific data and wrote the manuscript; WNLR. (Hôpital Universitaire Pédiatrique Charles de Gaulle) collected data; DY. (National Blood Transfusion Centre) responsible for the project design NY. (National Blood Transfusion Centre) performed the tests and data management; JS. (CERBA) contributed to this manuscript, English correction and the paper review.

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