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Blood transfusion reactions; evaluation of 462 transfusions at a tertiary hospital in Nigeria.

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Summary

The immuno-haematological safety of blood remains an important and recurring issue in blood transfusion practice. Data concerning morbidity and mortality from blood transfusion is sparse in Nigeria however and while the current efforts at reduction in the incidence of adverse consequence of blood transfusion is encapsulated in the concept of Haemovigilance, the Nigerian blood transfusion service is yet to institute the practice. A prospective study of 462 transfusions at the Obafemi Awolowo University Teaching Hospital was done to evaluate the incidence and pattern of transfusion reactions in the hospital. The overall incidence of transfusion reactions is 8.7% (40 cases), with febrile non-haemolytic transfusion reactions (FNHTR) constituting 65% of these. The incidence of adverse reaction is significantly related to a positive history of previous transfusion (p=0.0039). Efforts must be sustained at evolving a system to minimize the incidence and consequences. The development of a haemovigilance system in which data regarding all transfusions carried out in Nigerian hospitals is collated and analyzed is necessary. The advent of the National Blood Transfusion Service (N.B.T.S) in Nigeria with Zonal centres in the six geopolitical zones of the country offers an opportunity for setting up a national haemovigilance programme.

Keywords: *Transfusion reactions; haemovigilance.*

Résumé

La sécurité immuno-hématologiques du sang demeure un issu important et courant en transfusion sanguine. Les données concernant la morbidité et la mortalité due a la transfusion sanguine sont rare au Nigeria alors que les efforts courant de réduire l'incident des effets indésirables sont incorporée dans le concept d'hemovigilence, le service national de transfusion sanguine au Nigeria n'a pas encore institue cette pratique. Cette étude prospective sur 426 cas de transfusion au centre universitaire hospitalier Obafemi Awolowo était faite pour évaluer l'incidence et la fréquence de réaction transfusionaire a l'hôpital. L'incidence totale des réactions était de 8.7%(40 cases), avec des réaction transfusionaire non-hémolytique d'état fébrile de 65 % . L'incidence des réactions indésirables est significativement lie a l'histoire d'allergie des transfusions précédentes (p=0.0039). Les efforts doivent être soutenus en déploiement au système pour minimiser l'incidence et les conséquences. Le développement du système hemovigilance afin de collecter et d'analyser tous les cas de transfusion dans les hôpitaux nigérian est nécessaire. L'installation dans les zones centrale dans les six zones géo politique d'unité du service national de la transfusion sanguine, offre une immense opportunité pour le programme d'hemovigilence.

Introduction

Blood transfusion has remarkably evolved since its introduction into clinical practice, to become an indispensable life saving measure in patient care. The first transfusion attempts were reported in the 17th century and they involved transfusion of animal blood to human beings. This continued sporadically up to the 19th century [1]. James Blundell is generally credited with the introduction of blood transfusion into the clinical practice of medicine in 1818. However John Henry Leacock had reported earlier, in 1816, of systematic experiments in Edinburgh on dogs and cats that established that donor and recipient must be of the same species [1]. Morbidity and mortality attending blood transfusion practice remained very high until the discovery 100 years afterwards by Karl Landsteiner, of the ABO blood group system, making transfusion routinely practicable. However, the issue of safety has remained a considerable burden of concern in clinical practice due to the occurrence of adverse events or complications. One major category

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of such adverse events is transfusion reactions. Other complications of blood transfusion include transmission of infectious agents (including viral, protozoan, bacterial agents and prions), circulatory overload and iron overload. Transfusion reactions refer to immunologically mediated adverse signs and symptoms occurring in a patient receiving a unit of blood or blood component with no other explanation other than the unit received [2,3]. There is paucity of literature on the study of transfusion reactions in Africa and most of the available data relate to studies done among the western population. Febrile reactions are generally believed to be the commonest transfusion reactions [4]. They could accompany a haemolytic episode i.e. a febrile haemolytic transfusion reaction (FHTR), or as a febrile non-haemolytic transfusion reaction (FNHTR). Reported incidence of allergic, or urticarial transfusion reactions differs significantly [4-7].

Haemolytic reactions could be immediate or delayed, depending on whether signs and symptoms occur within or after 24hours. Immediate haemolytic transfusion reactions usually result from ABO incompatibility. It is believed to be the most dangerous type of transfusion reaction and highly avoidable; they are usually due to clerical or administrative error [4]. Haemolytic antibodies are generally IgM or rarely complement binding IgG.

There have been reported cases in which rapid destruction of transfused red cell was observed although no blood group antibodies could be detected [8,9]. Even autologous blood transfusion surprisingly was not free from the hazards of transfusion reactions [10]. Other blood transfusion reactions of importance due to the attendant morbidity and mortality include transfusion related acute lung injury (TRALI) and post-tranfusion purpura. Data concerning morbidity and mortality from blood transfusion is sparse in Nigeria and even though there have been few studies and anecdotal reports of adverse transfusion reactions, prospective studies evaluating the burden of transfusion reactions in Nigerian hospitals are few if any.

Currently, global efforts at reducing the incidence and adverse effects of transfusion are encapsulated in the concept of Haemovigilance. The objective of this system is to collate data on every adverse event related to the use of blood products, with evaluation and analysis leading to decisions being made to ensure the immuno-haematological safety of blood products [11]. The aim of this study was to evaluate the incidence and pattern of blood transfusion reactions among transfusion recipients at the Obafemi Awolowo University Teaching Hospital Ile-Ife Nigeria as a first step towards setting up a haemovigilance programme for the blood transfusion service of the Hospital.

Methods

The study is a prospective study including all cases of blood transfusions carried out in the hospital within a study period of one year (January 2004 to December 2005). Approval for the study was secured from the Ethics Committee of the Hospital. All Wards and units in the Hospital were notified about the study. Patients were identified by transfusion requests processed in the blood bank and followed up to the ward. Informed (oral) consent was obtained from all patients included in the study.

A questionnaire prepared for the study, was administered within twenty-four (24) hours of the transfusion episode and patients were further assessed clinically within two weeks of the transfusion. Transfusion recipients ≤15 years were classified as children while those >15 years were classified adults. The blood transfusion logbook on the ward was reviewed with every transfusion. Patients requiring investigations were investigated according to the approved protocol for the specific reactions. Transfusion recipients recently transfused within two weeks prior to admission were excluded from this study. The temperature charts were reviewed to exclude the possibility that a febrile event was one in a series of intermittent febrile episodes.

Data obtained from the study was collated, cross-checked for errors and omissions. Data analysis was done using descriptive and inferential statistics (SPSS 11.0 for windows 2001 version). A p value <0.05 was significant.

Results

Total of 462 transfusions in 258 patients were studied, consisting of 157 (60.9%) adults and 101(39.1%) children. There were 92 (35.6%) female and 65 (25.2%) male adults, and 29 (11.2%) female and 72 (28%) male children. Red cell component use constituted 71.8%, whole blood transfusions accounted for 8.6%, and platelet transfusion accounted for 6.5% of the total component use while fresh frozen plasma transfusion accounted for the remaining 13.1% of the transfusions carried out within the study period. A total number of 40 cases of adverse transfusion reactions were observed out of 462 transfusions giving an overall incidence of 8.7%. The reactions seen were; febrile reaction, allergic reaction and haemolytic transfusion reaction (delayed type). The incidence of the various types of reactions seen is shown in Table 1. The overall incidence of transfusion reactions was higher in the adult

Table 1: Incidence of types of blood transfusion reactions.

	Frequency (% of total transfusion reactions)
Allergic reaction alone	6 (15%)
Isolated Febrile Non-Haemolytic Reaction (FNHTR)	26 (65%)
FNHTR And Allergic Reaction	7 (17.5%)
Haemolytic Transfusion Reaction	2 (5%)
No Adverse Reaction	422
Total	462

was transfused with a Group O, RH- D positive blood, and developed fever, jaundice and haemoglobinuria a day after the transfusion. In the second case, a multiply transfused cancer patient, a 5 year old girl, developed fever hyperbilirubinaemia and progressive anaemia three days after blood transfusion. The offending antigen was not identified.

The distribution of the various types of adverse reactions seen according to the specialty wards where transfusions are carried out is as shown in the Table 2. There was no significant relationship between the forms of adverse transfusion reactions seen and the various wards where blood/ blood components

Table 2: Incidence of types of transfusion reaction seen in different wards

Reaction type	No of reactions per ward (%) Children wards	Medical wards	Surgical wards	Obst. and Gynae. wards	Total n (%)
Allergic reaction alone	2 (5%)	3 (7.5%)	-	1 (2.5%)	6 (15%)
Febrile non- haemolytic transfusion reaction alone	12 (30%)	5 (12.5%)	6 (15%)	3 (7.5%)	26(65%)
Febrile non-haemolytic transfusion and allergic reaction	2 (5%)	2 (5%)	1 (2.5%)	2 (5%)	7 (17.5%)
Haemolytic transfusion reaction	1 (2.5%)*	-	-	1 (2.5%)	2 (5%)
Total	17 (42.5%)	10 (22.5%)	7 (17.5%)	7(17.5%)	40(100%)

P=0.58

population, 25 out of 157 than for the children 15 out of 101 (15.9% to 14.8%), however, there was no statistical difference in the occurrence of adverse reactions between children and adults (χ^2=0.05, *P*=0.82). Febrile non-haemolytic reactions (FNHTRs) constituted 65% of cases of total incidence of transfusion reactions and accounted for 72.2% of adverse reactions noticed in children as compared to 59.1% in adults. Patients receiving multiple transfusions (i.e. more than one unit) within an interval of two weeks duration, had a higher risk of experiencing an adverse transfusion than patients receiving single units. (*P*=0.0064). Allergic reactions occurring alone and the occurrence of allergy and FNHTR together in the same transfusion recipient had incidences of 1.2% and 1.5% respectively (Total incidence of allergy was 2.7%). Haemolytic transfusion reactions accounted for 5% of all adverse reactions and an overall incidence of 0.4% in the study population. No case of the immediate haemolytic transfusion reaction was seen. In one case, a 40 year old Group O, RH D negative lady

Table 3: Effect of previous transfusion on incidence of adverse reaction

Previous transfusion	Incidence of reaction		
	Yes	No	Total
Yes	15 (21.3%)	40 (73%)	55
No	23 (11.3%)	180 (88.7%)	203
Total	38	220	258

P=0.0039

were used (*P*=0.58). For the adult population, women had an overall higher incidence of adverse transfusion reactions than the male population (15% as against 11%). This was not statistically significant; p=0.40. FNHTR accounted for 72% of all adverse transfusion reactions in adult males while it accounted for 59.1% in females. Allergic reactions were slightly more common in the females (39%) than the males (28%). The incidence of adverse reaction was significantly related to a positive history of previous transfusion. A total of 55 patients had a history of previous

transfusion. Fifteen of these (27%) experienced an adverse reaction as against 23 of 203 of transfusion naïve recipients; (11.3%, P= 0.0039). Table 3.

Discussion

The overall incidence of transfusion reactions in this study was 8.7%. This is much higher than the value of 0.2% reported by Climent-Peris *et al.* for the incidence of acute transfusion reactions in Puerto Rico [12]. Underreporting was cited as a possible reason for the very low incidence recorded for the Puerto Rico study. The transfusion reactions reported in this study are febrile non-haemolytic transfusion reaction (FNHTR), allergic reactions and haemolytic transfusion reaction occurring as isolated events or in combination. Febrile non-haemolytic transfusion reaction (FNHTR) is a well-characterized, common adverse reaction to the transfusion of blood products. It constituted the highest proportion of adverse reaction in this study with an overall incidence of 7.1% (33 out of 462) and constituted 82.5% (33 of 40) of all adverse events reported. Although not usually associated with mortality, identification of FNHTR is important because its main manifestation, namely, fever, is a feature that is shared by other more dangerous complications of blood transfusions, such as acute red cell haemolysis, sepsis from a contaminated product, or transfusion-related acute lung injury (TRALI), (no case of TRALI was seen in this series). The earliest studies of FNHTR implicated anti-leucocyte antibodies (leucoagglutinins) in the pathogenesis of this condition [13,14], however, Heddle *et al* in more recent studies have shown that accumulation of cytokines in stored blood products is largely responsible for this adverse transfusion reaction [15,16]. It may be that the relative differences in the concentrations of the cytokines in the units transfused could explain the observed differences in the two groups of patients presenting with FNHTR. A proportion of the febrile non-haemolytic reaction cases 6 out of 26 (23.1%) was a sub-clinical FNHTR event; i.e. had elevation of body temperature ≥1°C within 24 hours of the transfusion, without any other identifiable risk factor other than the transfusion received but had no overt clinical sign/symptom of chills, rigors or headaches. Such cases were only identifiable on review of the temperature chart of such recipient. Febrile non-haemolytic transfusions is of great clinical significance as its occurrence often leads to unnecessary discontinuation of blood transfusion and thus wastage of scarce blood/blood products [17]. In addition, its occurrence is an independent factor that predicts platelet recovery, increment or survival in transfusion recipients [18]. The overall incidence of allergic reactions of in this study is 2.8% (13 out of 462) and accounts for 32.5% (13 out of 40) total cases of adverse transfusion reaction. This is similar to results quoted for some studies, which reported equal incidence of 2-3% for both FNHTR and allergic reactions [5,6]. Hoxworth and Skinner [19] found the overall incidence of allergic reactions to be 1.82% of all transfusions and 30.6% of all transfusion reactions. Ahmed *et al* [7] reported an incidence of 12.6% in Northeast Nigeria. The rather high incidence reported is most likely to be due to the pregnant women population in which the study was done. The present study confirms that the burden of allergic transfusion reaction in relation to total incidence of adverse reactions was more in adult females (39%) compared with male population (28%), this was however not statistically significant. Allergic reactions are known to be more common in relation to plasma transfusion than red cell transfusion[20]. The symptoms manifested vary from mild pruritus to moderately severe forms presenting with periorbital oedema. The use of specific blood component transfusion as against transfusion of whole blood will reduce incidence of allergic reactions. The association of allergic reaction with a febrile episode is not uncommon [21], it was 53.8% of the total incidence of allergy in this study. The incidence was higher in the adult population (19%) as compared with the children (11.1%). This was not statistically significant. In one case, it was necessary to give antihistamine therapy as a premedication due to recurrence of the allergic episode. It was noted that the patient, an eight-year-old girl had a history of allergy (bronchial asthma), with a positive family history. Wilhelm *et al*, [22] showed that atopic patients have a higher risk of suffering from allergic (Type I hypersensitivity) reaction than non-atopic patients.

Haemolytic transfusion reaction was seen in two cases; both were of the delayed type. The incidence of delayed type haemolytic transfusion reaction was 0.4% of all transfusions and constituted 5% of all adverse transfusion reactions seen. The first case was avoidable and its occurrence lends much credence to the fact that there is need for continuous medical education to promote standard practices. The second case was not unusual, occurring in a multiply transfused five-year-old retinoblastoma patient. Awareness of DHTR can limit wastage of scarce resources in "septic work-up" by the clinicians for patients at risk, as was the case in this patient [4]. The offending antigen however could

not be identified. This is not unusual and there had been reports of cases of haemolytic transfusion reactions occurring in apparently compatible red cell transfusions in which antibodies were not demonstrable [8,9]. Direct Coombs' test was positive in both cases of DHTR in this study. No case of Post-transfusion purpura was seen. Post-transfusion purpura has been reported as "very rare" [4] and it was not surprising that no case was recorded in this study. Similarly, no case of transfusion related acute lung injury was seen.

In conclusion, blood transfusion reactions remain a challenge to clinicians and efforts must be sustained at evolving a system to minimize the incidence and consequences. The development of a haemovigilance system in which data regarding all transfusions carried out in Nigerian hospitals is collated and analyzed is long overdue. The advent of the National Blood Transfusion Service (N.B.T.S) in Nigeria with Zonal centres in the six geopolitical zones of the country offers an opportunity for setting up a national haemovigilance programme with the aim of continuous evaluation of transfusion service in order to attain better level of care for transfusion recipients.

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