Transfusion and Apheresis Science 54 (2016) 296–302

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Review

Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
RBC alloantibodies
Haemolytic transfusion reactions
Blood transfusion
Sub-Saharan Africa

ABSTRACT

Background and objectives: Previous studies of Sub-Saharan Africans show significant alloimmunization to red blood cell (RBC) antigens, but country-specific data are limited. Thus, the aim of this study was to estimate, by meta-analysis, the overall proportion of red blood cell alloantibodies among transfused patients.
Methods: We systematically searched Medline, Embase, and the Africa-Wide Information database to identify relevant studies in any language. Case reports, comments, letters, conference abstracts, editorials, and review articles were excluded. Of the 269 potentially relevant articles, 11 studies fulfilled our selection criteria.
Results: Overall proportions of alloimmunization were 6.7 (95% CI: 5.7, 7.8) per 100 transfused patients. With regard to antibody specificity, among clinically significant antibodies, anti-E ranked as the most common, followed by anti-K, anti-C and anti-D.
Conclusion: Meta-analysis of available literature quantifies and qualifies the clinical challenge of RBC alloimmunization among transfused patients in Sub-Saharan Africa. These results should drive policy decisions in favour of routine testing of RBC antigens and irregular antibodies for transfused patients as a standard of care throughout Sub-Saharan Africa.

Contents

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http://dx.doi.org/10.1016/j.transci.2015.10.017
1473-0502/

1. Background

Red blood cell (RBC) alloantibodies in transfused patients can result in significant morbidity and mortality [1], especially where healthcare resources are limited. Alloimmunization to clinically significant RBC antigens such as those in the Rh, Kell, Kidd and Duffy blood group systems can create formidable challenges in multiply transfused patients by making it difficult or impossible to find compatible units and, thus, jeopardize patient safety [1–3]. Alloantibodies can cause a number of serious transfusion reactions including acute intravascular haemolysis, delayed haemolytic transfusion reactions (DHTRs), and haemolytic disease of foetus and newborn (HDFN) [4]. For instance, in the United States of America (USA), 15% of transfusion-related fatalities are caused by non-ABO HTR [5]. Moreover, it has been reported that single-antibody haemolytic transfusion reactions are among the leading causes of transfusion-related mortality in the USA [5]. Thus, routine RBC antibody screening should be a public health imperative integrated into any system of blood banking and transfusion medicine.

Africa is the second-largest and second most populous continent on the planet. Based on forecast, by 2050, Africa will record the world's largest population growth and Sub-Saharan Africa will account for the majority of the increase [6]. This population growth will impact health care delivery, which has already been facing enormous difficulties, including the provision of adequate and safe blood. In 2010, the prevalence of anaemia in Sub-Saharan Africa has been estimated to be 60%, much of this due to malaria and malnutrition. Perinatal haemorrhage persists as a cause of death and is a leading indication for RBC transfusion [7]. Accessing safe blood products represents one of the biggest challenges in Sub-Saharan Africa. Over the past decades, much effort has been dedicated to preventing transfusion-transmitted infections (TTIs) and many African blood services routinely screen blood components to mitigate the risk of TTIs [8,9]. However, RBC alloantibodies outside the ABO blood group system are not routinely screened in most healthcare institutions, thus increasing the risk of immune haemolysis and its significant morbidity and mortality [10–12]. Furthermore, management of patients with alloantibodies and the associated complications, such as DHTRs and HDFN, imposes enormous medical and economic challenges. Studies reporting the prevalence of RBC alloantibodies in Sub-Saharan Africa are scanty and a previous narrative review that included three studies conducted in two countries revealed that 1–6% of transfused patients displayed clinically relevant RBC antibodies [12]. In this context, it is critical to integrate previous estimates and ascertain the actual burden of RBC alloantibodies in patients in Sub-Saharan Africa. We believe that this is the first comprehensive meta-analysis on RBC alloimmunization in Sub-Saharan Africa and we hope it will drive changes in pre-transfusion immunohaematologic testing that will advance patient safety.

2. Methods

2.1. Search strategy and study selection

This review was prepared and conducted in accordance with PRISMA guidelines [13]. Medline, Embase, and the Africa-Wide Information databases were searched for studies in any language published up to July 1st, 2015. Key search themes were "blood transfusion", "isoimmunisation", and "Africa" and were described by medical subject heading terms and keywords. The search strategy is shown in Table 1. Duplicates were removed using Endnote X7 software and two authors (A.M.N. and P.B.M.) carefully examined all articles independently. Studies were included if they report on the frequency of red cell alloantibodies in transfused patients in sub-Saharan Africa. Complete articles that met inclusion criteria were downloaded. The bibliographies of selected articles were examined to identify additional relevant literature that had not been identified during the screening of databases. These two authors then read the full-text articles and screened them according to pre-defined inclusion and exclusion criteria. We also included one grey literature source, a master's thesis. Case reports, comments, letters, conference abstracts, editorials, or narrative review articles were excluded.

2.2. Data extraction

Data extraction was conducted independently by two investigators (A.M.N. and P.B.M.) and disagreements were resolved by consensus. Extracted data included study design, population under study, study size, number of alloimmunized patients, and types of alloantibodies detected.

2.3. Statistical analysis

Data were analysed using the statistical software package R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria) with the command "Metaprop" (R package: meta; Schwarzer 2014) [14]. Proportions were logit transformed and pooled within the DerSimonian and Laird

Table 1
Systematic review search strategy.

1.	exp Isoantibodies/
2.	(alloantibodies or irregular antibodies or red cell antibodies or rbc antibodies or irregular erythrocyte antibodies or allo immunization or alloimmunization or alloimmunisation).tw.
3.	exp africa/
4.	exp blood transfusion/
5.	blood transfusion*.tw.
6.	1 or 2
7.	4 or 5
8.	3 and 6 and 7