Original Article

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Study of the Frequency and Specifcity of Red Cell Antibodies in Patients with Hemoglobinopathies.

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ABSTRACT

Blood transfusions are necessary for patients with sickle cell disease (SCD) and thalassemia as part of their supportive care. Red cell alloimmunization is one of the treatment's most dangerous adverse effects, though. This study set out to determine the frequency and specificity of red cell alloimmunization in Egyptian individuals with sickle cell anemia and thalassemia. In this study, 200 Egyptian patients who had received several transfusions, 140 patients with transfusion-dependent thalassaemia, and 60 patients with sickle cell anemia who were receiving care at the Pediatric Children Hospital at Cairo University between March and October of 2019 were included. The Diamed-ID microtyping system was used to identify alloantibodies. Among the studied populations were sickle cell and thalassemia patients. In 22/200 patients, or 11%, alloimmunization was prevalent. The two most common types of alloantibodies were those against the E antigen (30%) and the Kell antigen (37%).

The investigational patient group's antibody presence was not influenced by age, gender, age of transfusion onset, or splenectomy. Extended red blood cell plating is an important step to consider prior to obtaining blood transfusions for individuals with hemoglobinopathies who will probably require many transfusions. Patients with hemoglobinopathies in Egypt are encouraged to have their RBC units phenotyped for Kell and all Rh antigens before beginning transfusion therapy; this is currently the standard of treatment for these patients.

Keywords : Multitransfused · Alloimmunization · Antibodies · Blood transfusion · sickle cell disease · Thalassaemia.

INTRODUCTION

The most common and clinically significant single gene illnesses in the world are called hemoglobinopathies. With a carrier incidence of 6–10%, β-thalassemia is the most common haemoglobinopathy in Egypt. Out of 1.5 million live births nationwide, an estimated 1000 babies are born with β-thalassaemia major each year [1]. Appropriate and frequent red cell transfusions continue to be the cornerstone of treatment for severe instances of thalassemia; however, transfusion-related problems such as viral infections.

Its benefits are limited by hemosiderosis and RBC antigen immunization [2]. One of the transfusion-related issues that can complicate transfusion therapy is the development of alloantibodies and autoantibodies. Research has shown that some alloantibodies are hemolytic, resulting in hemolytic transfusion responses, while others are not clinically significant [3]. The development of alloantibodies may not only decrease RBC post-transfusion survival but also increase the difficulty of obtaining appropriate cross-match compatible blood [2]. Patients with hemoglobinopathies may require more blood transfusions as a result of these antibodies. Effective factors for alloimmunization include the recipient's immune status, the immunomodulatory effect of isogenic blood transfusion on the recipient's defense system, and the variance in erythrocyte antigenicity between the donor and recipient. It results in a range of hemolytic transfusion reactions, precludes safe blood transfusions, and causes infantile hemolytic diseases [4].

Patients with thalassemia have reported global alloimmunization frequencies ranging from 1.13 to 40.4%. Antibodies against the RBC antigens of Kidd (Jka & Jkb), Dufy (Fya & Fyb), Kell (K), and Rh (C, c, & E) were the most frequently identified alloantibodies [5].

In patients with thalassemia, the cause of alloimmunization is unknown. However, other studies found that the occurrence is probably caused even more by the recipient's immunological system, lack of a spleen, and different red cell phenotype between donors and recipients [6].

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Aim of Work

Both beta-thalassemia and sickle cell disease (SCD) are prevalent in Egypt, but the former is more common. The country does not have a national screening program, and carrier detection by premarital and/or early antenatal screening for both thalassemia and SCD is not required nor commonly used. SCD and β-thalassemia put a financial and social strain on the Egyptian government as well as the family of the afflicted. There is a pressing need to investigate any element that may impact the health of individuals with β-thalassemia, given the high frequency of carriers and rising incidence of newly diagnosed cases. Thus, we made the decision to investigate the types, frequency, and risk factors associated with the development of alloantibodies in hemoglobinopathies caused by multiple transfusions. And provide these individuals with the specific alloantibodies they possess in order to facilitate safe blood transfusions in the future.

PATIENTS AND METHODS

Patients

This investigation was carried out in compliance with Egypt's research code, the Helsinki Declaration of 1964, and any subsequent revisions. The Cairo University Department of Clinical and Chemical Pathology's Research Ethics Committee gave it its blessing. For every participant, informed written consent was obtained from the patients or legal guardians. Each patient received an explanation that any information collected for this study would remain strictly onfidential and would not be used for any other reason. In the Paediatric Children Hospital at Cairo University, a cross-sectional study was carried out for 200 previously identified emoglobinopathies that were regularly transfused between March and October 2019. Individuals requiring blood transfusions due to systemic or other hemolytic.

Transfusion Protocol

Target Hb levels of 9–11.5 g/dl were maintained by transfusioning nonleukodepleted packed red blood cells that were compatible with ABO and Rh (D). Clinical information was gathered from each patient, including age, sex, age at which transfusion began, frequency of transfusions, and splenectomy.

Methods

Every patient underwent a full blood count as well as blood grouping utilizing DiaMed Cassetes and a centrifuge (ABO, RH typing, and reversed grouping system). Using screening and identification methods, autoantibodies and alloantibodies were looked for in each patient. A Diamed three-rBC panel was used for the antibody screening test, and the manufacturer's recommendations were followed for interpretation of the data. Antibody identification was performed on cases that tested positive for antibodies utilizing Diamed's 11 RBC panel, which is based on column agglutination technology. Concurrently, an auto control was conducted to ascertain the existence of autoantibody.

Statistical Methods

The Chi square ($\chi 2$) test was used to compare the data, which were statistically defined in terms of frequencies (number of cases) and percentages. When the anticipated frequency is less than five, an exact test was utilized in its place. SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006) was the computer program used for all statistical calculations.

RESULTS

Patient Characteristics

200 haemoglobinopathies individuals with mean ages of 12 years were included in our study; 107 (54%) of them were male and 93 (46%) were female. Thirty-six cases (30%) had sickle cell anemia, forty cases (20%) had thalassemia intermedia, and 100 cases (50%) had thalassemia major. Table 1 summarizes the patient's demographic information, transfusion history, and clinical data.

The majority blood group, 72 (36%), was A positive. Other blood groups that were present were O positive, 42 (21%) and B positive, 19 (9.5%) and AB positive, 3 (1.5%) and O negative, A negative, and B negative, respectively. Of our cases, 5 (2.5%) had RhD negative results.

22 individuals (11%) had alloantibodies found in them; the majority of these patients (19,86.4%) had only one alloantibody, one patient (4.5%) had two antibodies, and two patients (9.1%) had three.

Thirteen out of every hundred thalassemia major cases (13%) and thirty-three out of every hundred thalasemia intermedia cases (7.5%) had these alloantibodies. Alloantibodies were found in 6/60 (10%) of the sickle cell patients in the study group.

In the two examined groups (thalassemia and sickle cell patients), a total of 27 alloantibodies with 9 distinct subtypes were found in our cohort. Anti-K accounted for 37% of all antibodies in 10/27, with anti-E (8/27, 30%), anti-C 2/27, anti-D 2/27, anti-c, 1/27, anti-Kidd 1/27, anti-Cw 1/27, anti-Dufy 1/27, and anti M in subsequent order of frequency.

DISCUSSION

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In our cohort, nine distinct subtypes of 27 alloantibodies were identified in the two investigated groups (thalassemia and sickle cell patients). Anti-K accounted for 37% of all antibodies in 10/27, with anti-E (8/27, 30%), anti-C 2/27, anti-D 2/27, anti-c, 1/27, anti-Kidd 1/27, anti-Cw 1/27, and anti-Kidd 1/27 following closely behind. 1/27 (4%) anti-Dufy and anti-M iRegular blood transfusions and iron chelation significantly increase oxygen patients' quality of life and life expectancy [7]. One of the major risks associated with transfusion (SHOTs) is alloimmunization, which can accelerate tissue iron loading [9], limit RBC survival, complicate RBC cross-matching, and delay the effectiveness of safe transfusion.

The rates of alloimmunization in patients with hemoglobinopathies vary. The frequency of alloimmunization in the current study was 11%. This was comparable to a research by Ahmed et al. (2010) that found 11.3% of Egyptian patients with sickle cell anemia and thalassemia [10].n 1/27 (4%).

Geographical differences may also have a role in the incidence of alloimmunization, as seen by the higher frequencies of 23.1, 23.8, and 26% in Tanta, Menoufia, and Mansoura, respectively. Their research was conducted in Egypt's northern governorates, which have previously been occupied by the Roman and Greek empires, among other civilizations.

This might affect the inhabitants' genetic composition in these northern regions [11–13]. The reduced incidence of alloimmunization in multitransfused thalassemic patients in the Mediterranean basin may provide weight to this observation. Despite routine pretransfusion RBC phenotyping, Politis et al. [14] observed an incidence of 11.6% alloimmunization in their study of Thalassemia and sickle cell patients in Greece.

Five patients in our study group (those with sickle cell anemia and thalassemia) showed a Rh negative phenotype. Remarkably, anti-D alloantibodies, indicating alloimmunization to the D antigen, were seen in three of those patients. One possible reason for this could be an inadvertent transfusion of donor blood containing a weak Rh variation that was mistakenly typed as Rh negative during standard typing. The production of anti-D alloantibodies is attributed to the epitopic diversity of Rh D variations, which can elicit a robust immunological response in recipients with varying variants [17]. This highlights the necessity of using cutting-edge molecular tools to correctly type Rh-negative donors in order to guarantee safe blood transfusions. Alloimmunization to D antigen was much higher in RH negative patients in other studies, which is comparable to this finding.

Alloimmunization was higher in girls than in males in our study, which is consistent with previous research [18, 32–34].

Pregnancy and delivery exposure increase a patient's chance of alloimmunization, making female gender a significant independent risk factor that could have a major effect on the patient's future. Furthermore, because of their prior alloimmunization, these patients may have a higher incidence of hemolytic disease in their newborns.

It has been previously shown that splenectomized patients produce more alloantibody than nonsplenectomized patients. According to Singer et al. [3], this might be the result of changes in the RBC membrane that raise immunomodulation and raise the risk of RBC allosensitization. Aside from that, the spleen's absence.

To maximize the benefits of transfusion while preventing problems, our research and other studies have demonstrated the need for steps to minimize the production of alloantibodies. Phenotyping a newly diagnosed patient, namely looking for Kell and Rh blood type antigens, and transfusion of matched blood components are essential steps in reducing the incidence of RBC alloantibodies and hemolytic transfusion events in individuals with hemoglobinopathies.

Regular testing for the development of alloantibodies in those who have had multiple transfusions and the availability of leukoreduced, Rh and Kell phenotyped, antigen-matched blood may help enhance the care of these individuals.

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