



# Indication and Outcomes of Paediatric Blood Transfusion at Three Hospitals in Gabon, Africa

# Indication et Résultats de la Transfusion Sanguine Pédiatrique Dans Trois Hôpitaux au Gabon, en Afrique

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**Keywords**: Blood transfusion, malaria, children, Gabon *Mots-clés:* transfusion sanguine, paludisme, enfants, Gabon

# **ABSTRACT**

**Introduction:** Blood transfusion is a life-saving treatment for severely anaemic children both in developed and developing countries. In this study we describe transfusions in paediatric settings of Gabon, Africa including clinical indications and subsequent outcomes.

**Methods:** This prospective descriptive study was conducted in the cities of Libreville and Lambaréné from 1 January to 30 September 2016. Children between the ages of 1 month and 15 years, who were hospitalised and transfused were included in the study.

Results: We included 287 children who represented 17.1% of all hospitalised children. The male:female ratio was 0.95 and the average age was 3.7 years. Packed red blood cells (PRBC) were administered to 99.3% of anaemic patients. World Health Organization (WHO) defined severe anaemia (haemoglobin (Haemoglobin) <7 g/dL) was the main indication (95.1%) with the mean haemoglobin (Hb) level pretransfusion being 5.1 g/dL  $\pm$  2.7 g/dL, and post-transfusion haemoglobin gain being 2.9 g/dL  $\pm$  1.2 g/dL. Malaria was present in 79% of transfused patients and 46.9% of children screened were homozygous for sickle cell disease. No post-transfusion incident was reported although reporting may have been incomplete.

Conclusion: Blood transfusion is frequent in our context; the clinical outcome is mostly favourable.

## RÉSUMÉ

*Introduction:* La transfusion sanguine est un traitement salvateur pour les enfants gravement anémiés dans les pays développés ou en développement. Dans cette étude, nous décrivons les transfusions en milieu pédiatrique du Gabon, en Afrique, y compris les indications cliniques et les résultats.

*Méthodes:* Cette étude descriptive prospective a été réalisée dans les villes de Libreville et Lambaréné du 1er janvier au 30 septembre 2016. Les enfants âgés de 1 mois à 15 ans, hospitalisés et transfusés ont été inclus dans l'étude.

Résultats: Nous avons inclus 287 enfants qui représentaient 17.1% de tous les enfants hospitalisés. Le rapport garçons/filles était de 0.95 et l'âge moyen était de 3.7 ans. Des concentrés de globules rouges (CGR) ont été administrés à 99.3% des patients anémiques. L'anémie définie par l'Organisation Mondiale de la Santé (OMS) (hémoglobine <7 g/dL) était la principale indication (95.1%), le taux moyen d'hémoglobine (Hb) avant transfusion étant de 5.1 g/dL  $\pm$  2.7 g/dL, et le gain d'hémoglobine après transfusion était de 2.9 g/dL  $\pm$  1.2 g/dL. Le paludisme était présent chez 79% des patients transfusés et 46.9% des enfants dépistés étaient homozygotes pour la drépanocytose. Aucun incident post-transfusionnel n'a été signalé, bien que le signalement ait pu être incomplet.

Conclusion: La transfusion sanguine est fréquente dans notre contexte; l'issue clinique est généralement favorable.

#### INTRODUCTION

Blood transfusions including packed red blood cells (PRBC) save thousands of lives every day in developing countries and are frequently administered to children with severe anaemia under 5 years of age. The major indications for transfusion include anaemia associated with malaria, sickle cell anaemia, and for patients living with HIV. The objective of this work was to determine indications and clinical outcomes of PRBC transfusions used in hospitalised anaemic children of Gabon, Africa.

## **METHODOLOGY**

#### Patients and methods

This prospective descriptive study was conducted from 1 January to 31 September 2016 in three hospitals in Gabon: Georges Rawiri Regional hospital in Lambaréné (CHR GR), Melen regional hospital centre (CHR M) and Army Training hospital Omar Bongo Ondimba of Libreville (HIAOBO).

#### Study population

Hospitalised children aged 1 month to 15 years who received a blood transfusion during the study period were included. Blood cell counts were performed before and 48 hours after the transfusion. Patients whose transfusion was administered before admission to one of the three hospitals were not included.

# Design of study

Socio-demographic and medical history were collected by the same investigator for each patient. Nutritional status was estimated by measuring the weight for each age group and comparing this to the published 2006 World Health Organization (WHO) Growth Charts.<sup>2</sup> Blood count was performed on a venous sample using an ethylenediaminetetraacetic acid (EDTA) tube by Sysmex© XP-300 less than one hour after collection. Each patient was tested before and at least 48 hours after the transfusion. Haemoglobin was interpreted according to WHO criteria for anaemia<sup>3</sup> including mild anaemia haemoglobin levels being between 10 and 11 g/dL for an age between 6 months and 5 years and between 10 and 12 g/dL for an age between 6 and 14 years, moderate anaemia having a haemoglobin between 7 and 10 g/dL and severe anaemia having a haemoglobin less than 7 g/dL. Also documented were the sickle cell status and blood type of each patient and the donor, blood volume transfused, duration of transfusion, adverse reactions if documented, diagnosis and clinical course. We also had to take into account clinical tolerance (dyspnoea/tachycardia) in the decision to transfuse, particularly in patients with sickle cell disease. The blood derivatives used at HIAOBO and CHRM originated from the National Blood Transfusion Centre, each of which had a storage and distribution unit. GR CHR had a unit of collection, processing and

distribution of labile blood products.

## Data collection and analysis

Data were collected on an anonymous and standardised collection card. The informed consent of a parent or caregiver of the patient was obtained after explaining the objectives of the study. Data were entered on the software Epi info7 version 8.3. Quantitative variables were expressed as averages or medians. The qualitative variables were expressed in percentages and analysed by the Chi-square test. The significance level was defined by p<0.05.

## **RESULTS**

# General characteristics of the population

During the study period, 1674 children were hospitalised in the three facilities and 17.1% (n=287) were transfused; 48.8% boys (n=140) and 51.2% girls (n=147) resulting in a sex ratio of 0.95. The mean age was  $3.7 \pm 3.2$  years with a median age of 27 months. The age group of 12 to 60 months constituted 59% of transfused patients.

#### Medical history

Haemoglobin electrophoresis for sickle cell disease was not performed in 67.9% of children (n=195). Nonetheless, 44.6% (n=41) of children screened before transfusion carried Haemoglobin SS. Four children were infected with the Human Immunodeficiency Virus (HIV), the remainder were HIV negative. This was the first PRBC transfusion for 73.4% of children (n=196) and 78% of sickle cell patients had already been transfused. Underweight status (WHO monogram) was found in 20.9% (n=60) of patients and of this subgroup 21% had a weight for an age lower than 2 standard deviations from the acceptable WHO minimum weight.

# Biological characteristics of anaemia before transfusion

Severe anaemia according to the WHO classification was found in 94.1% (n=270) of transfused patients. The average admission haemoglobin level was 5.1 g/dL  $\pm$  2.7 with extremes of 1.4 g/dL and 9.7 g/dL. Haemoglobin levels below 5 g/dL were found in 44.2% (n=127) patients. Mean cell volume was 77.6 fL  $\pm$  11.8, mean corpuscular haemoglobin content was 24.6 pg  $\pm$  0.2, and 62% of the patients (n=178) had hypochromic microcytic anaemia.

## Temporal pattern of transfusion

Fifty-eight percent of PRBC transfusions occurred during the months of April, May and June (n=167). All transfusions were performed less than 24 hours after prescription. PRBC was administered to 99.3% (n=285) of the population. Platelet concentrate and fresh frozen plasma were each used in one patient. The volume of PRBC transfusion was calculated by the formula 20 ml x body weight in kg in 82% (n=237) of the patients, by the

formula (haemoglobin level targeted–measured haemoglobin) x 3 x weight in kg in 12% (n=35) of the patients, and otherwise for 6% (n=15) of the patients. The transfused product was ABO matched for 96.6% (n=280) of children and iso-rhesus for all. The average duration of the transfusion was 3 hours. The mean haemoglobin level after transfusion was 9.3 g/dL  $\pm$  2.3. The average gain in haemoglobin was 2.9 g/dL  $\pm$  1.2 between pre- and post-transfusion haemoglobin levels.

### Diagnoses

Malaria was present in 77% (n=221) of transfused children, anaemic sickle cell crisis in 9%, pneumonia in 6%, and other diseases including HIV, acute diarrhoea, meningitis bacteria and ear, nose and throat (ENT) infections accounted for 7% of patients. Anaemia less than 5 g/dL haemoglobin was more common in sickle cell patients, children aged 12 to 60 months, and those who were underweight (p<0.05).

A second transfusion was necessary despite a correct blood transfusion volume for 11.1% (n=32) of patients and a third for one patient. The diagnoses of these patients included malaria (n=16), sickle cell disease (n=7), haemorrhagic syndrome (n=4), bacterial infection (n=3), and AIDS (n=2). The average duration of hospitalisation was 4.7 days with extremes of 1 to 31 days. The clinical course was favourable for 98.3% (n=282) of patients and was unfavourable for 5 patients (1.8%), of whom 3 (1%) were transferred to a higher-level structure and 2 died due to disease process (0.7%). Severe malaria in its anaemic form was the diagnosis in each of these cases. No post-transfusion adverse reaction has been reported but documentation accuracy is unknown.

## **DISCUSSION**

Despite important natural resources, and a high per capita income, the Gabonese population is defined by the World Bank as an upper-middle-income country. This disparity in the distribution of wealth is characterised by a poorly organised health system, with a low rate of access to basic health care, and low coverage of malaria prevention, the main cause of anaemia. The prevalence of severe anaemia in paediatric populations is estimated at 2%. A survey on the management of severe anaemias was necessary. 4,5

# General characteristics of the population

Most children came from CHR M, which is a government funded public hospital in the most populous region of Libreville. The prevalence of PRBC transfusion among general paediatric services in developing countries varies among previous studies. Diouf demonstrated a transfusion rate was 11.8% for Senegal while Thomas demonstrated a 5% rate in Kenya. 6,7 The lack of predominance of one sex has been demonstrated previously. 8,9 In

other developing countries, 65% of blood transfusions are given to children under 5 years of age. <sup>10</sup> The prevalence of anaemia among preschool children was estimated globally to be 47.4% between 1993 and 2005 and 67.6% in Africa. <sup>11</sup> In Gabon, the anaemia rate is estimated to be 60% with 2% having severe anaemia. <sup>12</sup> Children under five are the population most affected by anaemia in our region due to the high prevalence of malaria and iron deficiency. <sup>9,6,13</sup>

## **Pathologies**

Sickle cell disease and underweight status are risk factors for transfusion for severe anaemia. Over a quarter of our population had already been transfused and this can be explained by a high rate of sickle cell disease. The prevalence of sickle cell disease in Gabon has been estimated at 1.8%. <sup>14</sup> Our population of sickle cell patients was probably underestimated due to the lack of predictable screening in all transfused children. Other authors have found a transfusion rate for heterozygous sickle cell of 5% and 10% in the Democratic Republic of Congo and Kenya respectively. <sup>7,9</sup> Undernutrition affected 8% of the paediatric hospital population transfused for Thomas <sup>7</sup> in Kenya which may explain the high transfusion rate.

#### Characteristics of anaemia

The average haemoglobin level found in our study was similar to that found in Kinshasa (5.6 g/dL). Haemoglobin lower than 5 g/dL was more frequently found in the sickle cell study population and Koko *et. al* showed that it is the leading cause of death in sickle cell children in Gabon. 15

# Temporal pattern of transfusion

The peak rate of transfusion corresponds to the rainy season during peak malaria transmission. Nguefack<sup>16</sup> demonstrated a higher rate of severe anaemia in children under 15 years during the same period. All transfusions were described as emergent due to clinical condition. No standard protocol for transfusion has been prescribed in these areas despite the high rate of sickle cell disease for which transfusions exchanges could be indicated. 17,18 PRBC were the most frequently transfused blood product. In France during 2016, 80% of the transfusions were with PRBC, 9.8% platelet concentrates and 10.1% of therapeutic plasma ANSM (French Agency for safety of medication and safety of drugs).<sup>19</sup> Whole blood is no longer distributed in our country although some facilities on the continent still use it. It is less effective in correcting anaemia, exposes to volume overload<sup>6,9,13</sup> and represents one of the risk factors associated with the mortality of transfused children.<sup>7,20</sup> The blood volume to be transfused contributes to the effectiveness of the transfusion by targeting a post transfusion haemoglobin level. In sickle cell disease, the recommended target is 1 to 2 g/dL above baseline haemoglobin. 18 A target haemoglobin level also makes it possible to avoid a volume overload to which the undernourished

patients are particularly sensitive. Ensuring blood type compatibility limits the immunological risks in particular in the multi-transfused patients or at risk of multiple transfusions. Adverse effects of the recipient have been poorly described in our work. Non-haemolytic febrile reactions were not distinguished from febrile peaks due to the underlying pathology. The frequency of adverse events of the recipient varies in the literature including 4.8% in Mali, 21 8% in Senegal<sup>6</sup> and 2.6% for ANSM in 2016. The most common reactions are fever, chills, and skin reactions.

Malaria was the main indication for transfusion in our study. Children with malaria in the studies in the Democratic Republic of Congo and Kenya resulted in 87 and 73% of transfusions reported respectively. 7,9 Severe anaemia is associated with the most common form of severe childhood malaria in Gabon accounting for 67% of cases and children under 2 years of age account for 68% of affected patients.<sup>22</sup> The haemoglobin level is inversely proportional to the parasite load.<sup>23</sup> Thus, an effective fight against malaria helps significantly reduce the number of blood transfusions in children by reducing the number of severe anaemia. 20 The clinical course was favourable for the vast majority of our patients. Of the patients transfused again during the same hospitalisation, 50% had severe

malaria and were treated with artesunate. Also, the occurrence of an autoimmune anaemia secondary to taking artesunate may result in persistent anaemia as demonstrated by Campubri et. al.24 Mayuku found a mortality rate of 1.6% in Kinshasa<sup>9</sup> which was close to ours. Higher mortality in studies by Thomas et. al. and Chelo were found with both demonstrating a 5% mortality death after transfusion. 7,13 The risk factors associated with this mortality were the presence of respiratory distress, undernutrition, malaria, bacterial meningitis, a transfusion delay greater than 24 hours, and the use of whole blood. 7,9,20

#### Conclusion

Blood transfusion during our study is a frequent and important event prescribed in the emergency context. Severe anaemia is the most common indication for transfusion and PRBC was the blood component most often administered. Malaria and sickle cell disease were the most common precipitating conditions. Malaria prevention, screening and regular monitoring of sickle cell children should reduce the number of blood transfusions. The clinical course of transfused children was favourable however, but the reporting of adverse effects needs to be improved through mandatory documentation.

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