

Hyperhemolytic Syndrome Due to Hemoglobinopathy in Sub-Saharan Africa

Alphonsus O. Ogbuabor^{1*}, Peter U. Achukwu², Silas A. Ufelle^{1,2}, and Daniel C. Ogbuabor^{1,3}¹Department of Hematology and Blood Transfusion, Blood Bank Unit, Enugu State University of Science and Technology Teaching Hospital, Parklane, Enugu, Enugu State, Nigeria²Department of Medical Laboratory Sciences, Faculty of Health Sciences and Technology, College of Medicine, University of Nigeria^{1,3}Department of Health Administration and Management, Faculty of Health Sciences and Technology, University of Nigeria

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***Corresponding author:** Alphonsus Ogbuabor, Department of Hematology and Blood Transfusion, Blood Bank Unit, Enugu State University of Science and Technology Teaching Hospital, Parklane, Enugu, Enugu State, Nigeria, E-mail: ogbuaborao@yahoo.com

Abstract

Globally, hemoglobinopathies remains a common genetic disorder of blood with highest prevalence recorded in the developing countries particularly those of the sub-Saharan Africa. Although there is progress towards a permanent cure, life-long transfusion therapy remains a life-saving option for patients. While the safety of blood to patients are established in the developed countries, adverse reaction from blood transfusion are recurrent in developing countries with transfusion reactions rendering blood safety a major public health issue. While transfusion reactions could be a result of infectious or non-infectious agents the majority of blood transfusion reactions are nonetheless non-infectious with outcomes ranging from mild, adverse effects to death. We present an overview of hyperhemolytic syndrome for patients with hemoglobinopathies in Sub-Saharan Africa.

Keywords: Hemoglobinopathies; Hyperhemolysis Syndrome; Sub-Saharan Africa

Introduction

Hemoglobinopathies are genetic hemopathies caused by mutations in the α -globulin and/or β -globulin genes of the haemoglobin molecule which results in either quantitative and/or qualitative abnormality of the globulin molecule [1,2]. They range from asymptomatic to symptomatic conditions with the different symptomatic conditions such as α -and- β thalassemia, Sickle cell disease, HbE disease and HbC disease requiring a life-long blood transfusion therapy [3,4]. They have been reported to be more prevalent in the malaria endemic regions of the world such as the Mediterranean, Asia and sub-Saharan African due to natural selection [5]. This paper presents an overview on hyperhemolytic syndrome, hemovigilance and management for patients with hemoglobinopathies in the Sub-Saharan Africa.

Hyperhemolysis Syndrome is a Common Complication in Hemoglobinopathies

Life-long dependent blood transfusions are currently a major therapeutic option for patients with hemoglobinopathies in sub-Saharan Africa. Regardless of the associated adverse effects, pre-transfusion tests for blood and blood products in most countries in this region involves only ABO, Rhesus D grouping and cross-matching without Red Blood cell antibody screening [6,7]. A major complication of transfusion therapy in patients with hemoglobinopathies is an alloimmune response to Red Blood Cell antigens. This leads to the development of a life-threatening type of delayed transfusion reaction referred to as hyperhaemolytic syndrome [8,9]. Hyperhemolysis results in the destruction of transfused Red Blood Cells within 1-2 weeks post transfusion at extra vascular sites due to agglutination, opsonization and/or subsequent phagocytosis by macrophages [10]. Studies have reported an alloimmunization rates of 20-50% in patients with hemoglobinopathies [11]. Currently, the International Society

of Blood Transfusion (ISTB) recognizes about more than 300 blood group antigens that can be identified serologically which corresponds to more than 30 genetically different blood group systems. Antibodies against these antigens have equally been identified which can cause Red Blood Cell destruction along with the corresponding antigen [12].

Mechanism of Hyperhemolysis in Patients with Hemoglobinopathies

Although the pathophysiology has not been clearly defined, hyperhemolytic syndrome is suggested to be a result of much aetiology due to its consumptive effect. Among the proposed aetiologies are (i) acute generation of oxygen radicals due to oxidative stress (ii) immune complexes and complement activation priming autologous cells for phagocytosis (Bystander hemolysis) and (iii) suppression of erythropoiesis. These mechanisms has been proposed due to increased destruction of Red Blood Cells by activated macrophages, expression of phosphatidylserine and a secondary immune response induced by the production of atypical antibodies [13,14,15].

Clinical Manifestations of Hyperhemolysis Syndrome

Although could be asymptomatic in a few patients, most patients with hyperhemolysis syndrome presents with fever, chills, rigors, hives, flushing, itching, back pain, chest pain and unexplained discomfort occurring days to weeks following transfusion [16,17]. Many patients may develop jaundice while hemoglobinuria may be observed as red urine due to hemolysis that is primarily extravascular. In some cases, acute renal failure or disseminated intravascular coagulation may occur. Transfusion-associated graft-versus-host disease occurs rarely but mostly in immune compromised patients with symptoms of rash, fever and diarrhea. Patients could also present with purpura.

Laboratory Investigations for Hyperhemolysis Syndrome

Investigative approach to a suspected case of hyperhemolytic syndrome involves a differential diagnostic tests to rule out other forms of delayed hemolytic transfusion reactions. This gives an insight into a definitive diagnosis for confirmation of the syndrome. The routine differential laboratory investigations includes (i) Direct Anti-human globulin Test (ii) Antibody screening Tests (iii) Complete Blood Count (iv) Blood culture (v) Hemolysin Test (vi) Renal Function Test (vii) Coagulation Test (viii) Urinalysis (ix) HLA typing of recipient and donor (x) Skin Biopsy [18].

Transfusion associated graft-versus-host-disease may be identified by skin biopsy of the affected area which is confirmed with platelet antibody screening. The D-dimer, Prothrombin time test and Activated Partial Thromboplastin Time may be elevated particularly with Disseminated Intravascular Coagulation. An elevated lactate dehydrogenase concentrations, elevated bilirubin concentration,

low serum haptoglobin and presence of free hemoglobin in urine supports the diagnosis of hemolysis. A reduced post-transfusion hemoglobin below the pre-transfusion concentrations, markedly elevated lactate dehydrogenase, indirect hyperbilirubinemia and hemoglobinuria in the presence of reticulocytopenia in contrast to other types of hemolytic reactions characterized by reticulocytosis is confirmatory for hyperhemolytic syndrome [14,19].

Management of Hyperhemolytic Syndrome

Depending on the severity of reaction, the first line treatment involves some supportive care to address the patient's cardiac, respiratory and renal functions as well as providing symptomatic therapy [20]. Further management strategies depend on the degree of anemia and severity of hemolysis. In the case of mild hemolysis, additional transfusion is avoided with oral prednisolone (1-2mg/kg/day) given. In an event of rapid severe hemolysis, additional transfusion is given with intravenous immunoglobulin steroid-based therapy since the additional transfusion may precipitate further hemolysis. Intravenous immunoglobulin in a low-dose regime of 0.4g/kg/day for 5days with intravenous methylprednisolone 0.5g/day (adults) and 4mg/kg (pediatric) for 2 days is recommended [18].

The Situation in Sub-Saharan Africa

It is currently a few countries that operate a functional hemovigilance system in the region despite the WHO guidelines on the safety of blood and blood products to patients. The WHO guideline defined hemovigilance as the fulcrum of its quality management system. It therefore recommended that each country establish an effective national, regional and local hemovigilance system. A functional hemovigilance system involves proper monitoring of the whole chain of events of blood transfusion to patients, documenting any undesirable effects and introducing measures to addressing them as well as preventing future recurrence.

Conclusion

Hyperhemolytic syndrome is a well-documented complication in patients with haemoglobinopathies. It is the main cause of morbidity and mortality in patients with hemoglobinopathies in the sub-Saharan Africa. Hemovigilance are indispensable in sub-Saharan Africa due to the current high prevalence of hemoglobinopathies. There is an urgent need to review its policy guidelines and implementation for this region.

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*Corresponding author: Alphonsus Ogbonna Ogbuabor, Department of Hematology and Blood Transfusion, Blood Bank Unit, Enugu State University of Science and Technology Teaching Hospital, Parklane, Enugu, Enugu State, Nigeria, E-mail: ogbuaborao@yahoo.com

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