Flow Cytometry Study of splenic Functions in Children with β Thalassemia and Sickle Cell Anemia

Thesis

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By

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Ekram Ahmed.

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List of Abbreviations

ACS	Acute chest syndrome
ASSCs	Acute splenic sequestration crises
BM	Bone marrow
β-TM	β thalassemia major
DFO	deferoxamine
DFP	Deferiprone
DFX	Deferasirox
GIT	Gastrointestinal Tract
G6PD	Glucose 6 phosphate dehydrogenase
HJB	Howell Jolly Bodies
Hb	Hemoglobin
Ig	Immunoglobulin
IL	Interleukin
NK	Natural killer
OPSI	Over whelming post splenectomy infection
PSS	Post-splenectomy sepsis
RBC	Red blood cell
ROS	Reactive oxygen species
SCA	Sickle cell anemia
SCCLD	Sickle cell chronic lung disease
Sig	Significant
TM	Thalassemia major
VOCs	Vaso occlusive crises

Introduction **and Aim of the Work**

Introduction

Sickle cell disease refers to a group of conditions caused by hemoglobin S (HbS) which is formed by a single amino acid substitution, valine for glutamic acid in the sixth position from the N-terminal of the β -chain of the hemoglobin molecule. The heterozygous state (sickle β thalassemia) is a combination of both sickle cell anemia and β thalassemia (**Roy, 2009**).

Beta-thalassaemias are a group of hereditary human diseases caused by more than 200 mutations of the human β-globin gene, leading to low or absent production of adult β-globin and an excess of α-globin, causing ineffective erythropoiesis and low or absent production of HbA (adult haemoglobin) (**Patrinos et al., 2005**).

The spleen is the largest lymphoid organ in the human body. Its rich and diverse population of immune cells and its ingenious anatomy that enables optimal surveillance and phagocytosis of circulating blood elements play an important role in the defence against pathogens (**Bisharat et al., 2001).**

Many diseases are associated with a dysfunction spleen and the degree of splenic dysfunction varies between patients (**Willia and Corazza, 2007)**. For these patient suspected to have a spleen with diminished function, it is important to quantify their splenic function in order to assess the risk of developing overwhelming infection. Subsequently, preventive measurements can be taken and, in the case of infection, therapy can be started without delay (**De porto et al., 2010).**

The spleen is one of first organs damaged in sickle cell anemia. Consequences of this damage, increased risk of invasive pneumococcal infection and splenic sequestration, are difficult to predict for a given child **(Thompson et al., 2010).**

Aim of the Work

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Aim of the work is to quantify Howell-Jolly Bodies by flow cytometry in children and adolescents with sickle cell anemia, sickle β thalassemia and β thalassemia as a measure of splenic function.

Review of Literature

β-thalassemia

Definition:

β-thalassaemias are a group of hereditary human diseases caused by more than 200 mutations of the human β-globin gene, leading to low or absent production of adult β-globin and an excess of α-globin, causing ineffective erythropoiesis and low or absent production of HbA (adult haemoglobin) **(Patrinos et al., 2005).**

Pathophysiology:

The excess α-globin chains aggregate in red cell precursors forming inclusion bodies interferes with most stages of normal erythroid maturation, both intramedullary death of red cell precursors through arrest in the G1 phase of the cell cycle and accelerated intramedullary apoptosis of late erythroblasts (**Angelucci et al., 2002**). The red cells that survive to reach the peripheral circulation are prematurely destroyed in the spleen which becomes enlarged, eventually leading to hypersplenism **(Testa, 2004).**