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REVIEW

Clinical biomarkers in sickle cell disease

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Hypercoagulability

Abstract Sickle cell disease (SCD) is a hereditary blood disorder caused by a single gene. Various blood and urine biomarkers have been identified in SCD which are associated with laboratory and medical history. Biomarkers have been proven helpful in identifying different interconnected disease-causing mechanisms of SCD, including hypercoagulability, hemolysis, inflammation, oxidative stress, vasculopathy, reperfusion injury and reduced vasodilatory responses in endothelium, to name just a few. However, there exists a need to establish a panel of validated blood and urine biomarkers in SCD. This paper reviews the current contribution of biochemical markers associated with clinical manifestation and identification of sub-phenotypes in SCD.

Contents

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1. Introduction

Sickle cell disease (SCD) or sickle cell anemia (SCA) is an inherited disorder of hemoglobin (Hb) caused by substitution of a single nucleotide from thymine to adenine (GAG → GTG) in the β-chain of hemoglobin resulting in amino acid valine instead of glutamic acid (Rees et al., 2010). This point mutation is responsible for alteration in the properties of the hemoglobin tetramer, with a tendency to polymerize in the deoxygenated state (Ballas, 2002), altering normal, flexible biconcave shaped red blood cells (RBCs) into stiff, rigid, sickle cell. The rate of polymerization of Sickle cell hemoglobin (HbS) is directly related to fundamental pathophysiology of hemolytic anemia and vaso-occlusion (Samuel et al., 1990).

1.1. Biomarkers in SCD

The Biomarkers Definitions Working Group has defined a "biomarker" as a "characteristic that is objectively measured and evaluated as an indicator of normal biological or pathogenic processes, or pharmacological responses to a therapeutic intervention" (Biomarkers Definitions Working Group, 2001). There is high variability in terms of severity of SCD. Different major complications of SCD such as acute chest syndrome (Vichinsky et al., 2000), cerebrovascular disease (Ohene-Frempong et al., 1998), kidney failure (Scheinman, 2009) and early deaths (Platt et al., 1994) lead to variability in biomarkers.

Meaningful markers therefore have prime importance in the management of this disease. In this review, we will focus on the analysis of body fluids and tissues that have prime importance in the management of SCD. DNA markers (Steinberg and Adewoye, 2006) and imaging biomarkers will not be discussed in this review although they have been shown to be beneficial in the management of SCD (Adams et al., 1998).

1.2. Biomarkers used for HbS polymerization

Polymerization of the deoxygenated HbS is the leading phenomenon contributing to SCD related medical problems. The polymerization initiation rate is directly proportional to quantity of deoxygenated HbS within the RBC. Currently such biomarkers which can directly measure HbS polymerization