PREDICTION OF THE ONSET OF PAIN THRESHOLD IN SICKLE CELL DISEASE

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ABSTRACT
Pain is a major characteristic feature of sickle cell disease (SCD) and acute pain crisis is the major cause of hospitalization and readmission of sickle cell patients. Previous studies found excellent correlation between the red blood cell (RBC) deformability index and dense cell density. Patients with high RBC deformability index experience more crises and crisis days than those with low RBC deformability. However, patients with a high percentage of dense cells had a relatively mild disease. These two indicators can be used as markers for pain onset in sickle cell patients. Regarding kinetic models, previous works have obtained the rate of reaction through homogeneous and/or heterogeneous nucleation mechanism, containing parameters that are not easily determined. In this study, the focus is on the development of a theoretical prediction of the onset of the pain threshold in sickle cell disease. We developed a new model to characterize the polymerization of Hb SS reaction leading to vaso-occlusion responsible for pain episodes. The new kinetic model utilizes the sigmoidal progress of the reaction in a two-step scheme that is devoid of detail mechanistic considerations, thus, yielding global rate expression for the polymerization reaction. In addition, a model for the hydrodynamics of blood flow was developed. Together, these two models provide equations for determining the rate constants for the residual reaction (k_1), the autocatalytic reaction (k_2), the delay time (t_D), and in particular, time required before the onset of SCD ($t_{1/2}$) through a MATLAB programing algorithm. The models presented here should facilitate the prediction of the onset of pain threshold thereby aiding the search for a threshold pain alert system.

Keyword: Sickle cell disease (SCD); Vaso-occlusion; Autocatalysis; Hydrodynamics of blood flow; Onset of pain threshold

1.0 INTRODUCTION

Pain is the critical manifestation of sickle cell disease (SCD) and acute pain crisis is the major cause of hospitalization of sickle cell patients. One of the major factors responsible for the painful episodes is vaso-occlusion (see Table 1) as vaso-occlusion is a pre-requisite for the development of acute sickle cell pain (Ballas, 2007). Tissue damage due to vaso-occlusion releases numerous inflammatory mediators that initiate the transmission of painful stimuli and the perception of pain. Sickle cell vaso-occlusion is the most important pathophysiologic event in SCD and explains most of its clinical manifestation (Embury et al., 1994; Serjeant et al., 2002; Boros et al., 1976; Powars et al., 1978). Tissue damage due to vaso-occlusion initiates a variety of complex biochemical, neurologic, and electrochemical sequence of events, collectively referred to as nociception, that culminate in the perception of acute pain, which, in turn, may become chronic in nature. Vaso-occlusion is also responsible for creating a state of chronic vascular