Cellular Mechanisms for Iron Storage in B Thalassemia and Sickle Cell Disease and Correlation with Oxidative Injury

IRB# 2000-026
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Synopsis:

Sickle cell disease (SCD) is a hemoglobinopathy characterized by micro-vascular hypoxia-reperfusion, inflammation and leukocytosis. Studies in SCD have shown that leukocytosis is a strong predictor of stroke and disease severity. It is known that leukocytosis and inflammation contribute to increased leukocyte-endothelial adhesion and vasoocclusive events. Leukocytosis or increased leukocyte number is determined by the balance between proliferation and cell death programs (apoptosis). Both thalassemia and SCD patients often develop a secondary iron overload induced by transfusion. Iron overload is known to potentiate oxidative stress and tissue damage.

The purpose of the study was to explore the levels of proliferation and apoptosis in SCD as compared to thalassemia (a hemoglobinopathy that is vasculitis negative) and a control group. Additional emphasis was placed on determining if markers of iron overload and inflammation differ between thalassemia and SCD. Plasma lactate dehydrogenase (LDH), a marker of hemolysis, was also measured because hemolysis products have been shown to inhibit apoptosis.

Initial findings suggest that there is a greater increase in apoptotic markers and NTBI (non-transferrin bound iron) suggesting a higher level of oxidant stress in the white blood cells (WBC) of thalassemia compared to SCD. The higher level of apoptosis in thalassemia relative to SCD is consistent with the lower levels of neutrophils observed in thalassemia compared to SCD.

Conversely, an increase in WBCs, hemolysis and inflammatory markers found in SCD supports the hypothesis that inflammation is higher in SCD than thalassemia. The increase in intravascular hemolysis and inflammation in SCD may favor delayed cell death and enhanced cell proliferation in SCD, leading to increased circulating leukocytes. These changes may be related to hemolysis, increased levels of inflammatory cytokines, and lower amounts of NTBI in SCD. This leukocytosis increases the potential for vasoocclusive events that contribute to stroke, acute chest syndrome or renal tubule damage.

The study is closed to enrollment; all study procedures have been completed. Sample and data analysis continues.