DECREASED HEART RATE VARIABILITY IS ASSOCIATED WITH INCREASED TRANSCRANIAL DOPPLER VELOCITIES IN CHILDREN WITH SICKLE CELL DISEASE

Objective: To explore the relationship between 24-hour blood pressure (BP) variability, heart rate (HR) variability, and transcranial Doppler velocity (TCDV) in a cohort of pediatric sickle cell disease (SCD) patients.

Design, Setting, and Participants: This is a retrospective study of 11 children aged 8–18 years with SCD who previously underwent 24-hour ambulatory BP monitoring and TCDV measurements.

Interventions: Medical records were reviewed for TCDV and 24-hour ABP data. TCDV in the right and left middle cerebral artery were examined, and the highest velocity was recorded. HR and BP standard deviations were used as markers of variability. The relationships between daytime, nighttime, and 24-hour blood pressures and heart rate variability were determined.

Results: Mean age, body mass index and hemoglobin levels were 11.2 ± 3.0 years, 18.7 ± 3.4 kg/m², and 9.1 ± 1.7 g/dL, respectively. Median transcranial Doppler velocity was 136 cm/s (125–142). Decreased day, night, and 24-hour heart rate variability were significantly associated with increased transcranial Doppler velocity (R = −.69, P = .02; R = −.82 P = .002; R = −.66, P = .03, respectively). BP variability did not correlate with TCDV. Night-time BP indexes were higher than daytime.

Conclusions: In this small cohort, decreased heart rate variability assessed by the standard deviation of HR was associated with increased transcranial Doppler velocities in children with SCD. No correlation between measurements of BP variability and TCDV was found. Our study provides new information on heart rate and blood pressure variability and TCDV, a surrogate marker of stroke risk in sickle cell disease. Larger multicenter studies are needed to confirm our findings. (Ethn Dis. 2014;24[4]:451–455)

Key Words: Sickle Cell Anemia, Transcranial Doppler Ultrasoundography, Ambulatory Blood Pressure Monitoring, Blood Pressure Variability, Pediatric

INTRODUCTION

Sickle cell disease (SCD) is associated with multiple comorbidities and remains one of the world’s most common hereditary disorders. Individuals with SCD suffer repeated vaso-occlusive events characterized by ischemia-reperfusion injury and inflammation. These chronic vascular insults lead to numerous target-organ complications such as avascular necrosis of bones, retinal infarction, stroke, acute chest syndrome, pulmonary hypertension, and skin ulceration. A seminal feature that sets sickle cell disease apart from other chronic hemolytic syndromes and that predicts disease severity is a chronic, intense inflammatory state. Sickle cell disease is a chronic inflammatory condition with an ongoing insult to the vascular tree and increased prevalence of microalbuminuria, oxidative stress and iron overload, abnormal nitric oxide, hypoxia and reoxygenation injury, inflammatory cytokines, leukocytosis and increased inflammatory markers such as CRPs.

Stroke is a devastating SCD morbidity and affects as many as 11% of children who inherit sickle hemoglobin from both parents (HbSS). The pathophysiology of stroke is multifactorial with vasculopathy due to ongoing inflammation and a state of nitric oxide (NO) resistance recently taking a central role. Wood et al. described sickle cell disease as a steady state of increased plasma cell-free hemoglobin and overproduction of reactive oxygen species (ROS) that scavenge endothelium-derived NO and metabolize its precursor arginine, impairing NO homeostasis. Human physiological and transgenic animal studies provide experimental evidence of cardiovascular and pulmonary resistance to NO and reduced NO bioavailability that is associated with vasoconstriction, decreased blood flow, platelet activation, increased endothelin-1 expression, and end-organ injury.

Transcranial Doppler (TCD) ultrasonography is a cost-effective, noninvasive tool used to identify vessel narrowing or occlusion within the large cerebral vessels to assess risk of stroke in children with SCD. Measured velocities greater than 200 cm/s in the large cerebral vessels are considered abnormal and associated with a higher risk of stroke. Healthy children have an average transcranial Doppler velocity (TCDV) of 79 ± 13 cm/s, while SCD children without overt stroke average 133 ± 19 cm/s in the middle cerebral artery (MCA).

24-hour ambulatory blood pressure monitoring (ABPM) provides superior assessment of blood pressure (BP) measurements and patterns as well as heart rate (HR). Studies have shown ABPM to better predict cardiovascular mortality than clinic blood pressure measurements; ABPM is valuable in determining BP and HR variability using the standard deviation of 24-hour ABP and HR readings. Blood pressure varies considerably throughout daytime hours and to a lesser extent during the night to accommodate differing ambulatory and environmental changes in normal persons.

Heart rate variability occurs in response to specific physical demands. Sympathetic and parasympathetic autonomic nervous system influences dynam-