Posterior Circulation Evaluation in Patients with Sickle Cell Anemia

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Background: The role of transcranial Doppler (TCD) ultrasonography in identifying children with sickle cell anemia (SCA) at risk for stroke is well known; however, the major studies that evaluated TCD velocities in children with SCA did not report posterior circulation evaluation data. The objective of our study was to describe the pattern of blood flow velocities in the posterior circulation of patients with SCA and to examine their relationship with findings on magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA). *Methods:* All adult patients with SCA followed in the outpatient clinic of our hospital were evaluated with TCD and MRI/MRA. The highest velocities of the middle cerebral arteries or internal carotid arteries were taken as the time-averaged maximum mean (TAMM) velocity for each patient and the maximum mean flow velocities in the posterior circulation (TAMMpost) were recorded. *Results:* Fifty-six patients with SCA and 56 healthy nonanemic volunteers were evaluated. The mean TAMMpost in the basilar, vertebral, and posterior cerebral arteries (PCAs) were significantly higher among cases than controls ($P < .01$). In patients with SCA, the TAMMpost in all posterior circulation arteries had a positive correlation with TAMM. Only 1 patient with stenosis in the posterior circulation (right PCA) was identified. *Conclusion:* We found a low frequency of stenosis but high blood flow velocities in the posterior circulation in patients with SCA. The role of increased TCD velocities in the posterior circulation upon stroke risk in patients with SCA should be further examined. **Key Words:** Sickle cell anemia—transcranial Doppler—posterior circulation—magnetic resonance imaging—stroke—intracranial stenoses.

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Introduction

The role of transcranial Doppler (TCD) ultrasonography in identifying children with sickle cell anemia (SCA) at risk for stroke is well known and is one of the major advances in the management of the disease.[1,2] Typically, for children with middle cerebral artery (MCA) TCD mean blood flow velocities of 200 cm/second or higher, the risk of stroke is about 10% per year over 30 months. Chronic blood transfusion, the recognized modality of management of such children, reduces this risk in about 90%.[3]

SCA predisposes to stroke in the anterior circulation, mostly related to a vasculopathy of the internal carotid artery (ICA) and its branches.[4] It is postulated that high blood velocities in such arteries might be the trigger for endothelial and proliferative changes. This hypothesis seems to be supported by the finding that high blood flow velocities detected by TCD is a strong risk factor for stroke even in patients without intracranial stenoses.[4,5] The major trials that evaluated TCD velocities in children with SCA did not report posterior circulation evaluation data.[6,7] Therefore, the pattern of TCD velocities in the posterior circulation and its relationship to the anterior circulation blood flow velocities in patients with SCA have not been fully explored. The objective of our study was to evaluate blood flow velocities in the posterior circulation of patients with SCA using TCD and to examine their relationship with velocities in the anterior circulation and findings on magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA).

Methods

We evaluated all patients with hemoglobin SS (HbSS) disease who were older than 16 years old and followed in the outpatient clinic of the Department of Hematology of the Federal University of Sao Paulo, Brazil, in 2004. Patients on chronic blood transfusion were excluded. Controls were age-matched healthy nonanemic volunteers. The TCD characteristics of the anterior circulation and neuroimaging findings of this population were previously published alone and in combination with other service data.[8,9] The protocol received institutional review board approval. Written informed consent was obtained from all patients.

TCD Ultrasonography

TCD ultrasonography was performed with a 2-MHz Pulsed Doppler Ultrasonograph (TC2000; Nicolet/EME, Madison, WI) during outpatient visits according to Stroke Prevention Trial in Sickle Cell Anemia (STOP) protocol, also including complete posterior circulation evaluation. Transcranial color imaging was not used in this study. If the patient had received a blood transfusion in the last 30 days or had fever, pain, or another acute illness, TCD was deferred. The highest mean flow velocities were recorded bilaterally in the ICAs, middle cerebral arteries (MCAs), and anterior cerebral arteries. The highest velocities of the MCAs or ICAs were taken as the time-averaged maximum mean (TAMM) velocity for each patient. The maximum mean flow velocities in the posterior circulation (TAMMpost) in the basilar, vertebral, and posterior cerebral arteries (PCAs) were recorded. The basilar and vertebral arteries were studied using a suboccipital approach, whereas the PCAs were evaluated through the transtemporal window. A complete blood count was collected on the day of the TCD examination.

MRI

Brain MRI was performed on a 1.5-T device (Sonata Maestro Class; Siemens Medical Systems, Malvern, PA). Full details of the neuroimaging protocol are described elsewhere.[9] MRI images were evaluated by 2 neuroradiologists unaware of the TCD results. The magnetic resonance images were evaluated by 2 independent neuroradiologists. Discordant readings were resolved by consensus and evaluation of the images at a workstation with new reconstructions was performed. Lesions were defined to include lacunar infarction, encephalomalacia, leukoencephalopathy, and atrophy according to the classification previously published by Steen et al.[10] MRA (3D time of flight) was evaluated for stenosis or apparent occlusion of any vessel.[10] Stenosis was defined as an obvious narrowing or focal signal dropout in a major artery (MCA, anterior cerebral artery, PCA, ICA, and basilar artery).

Statistical Analysis

Descriptive statistics were used to report patients' characteristics. The mean TAMMpost in patients and controls were compared with the independent sample *t*-test. The correlation between TAMMpost and TAMM was evaluated using Pearson correlation, which was also used to examine the association between TAMMpost with age, hemoglobin level, fetal hemoglobin level, hematocrit, leukocyte, platelet, and reticulocyte counts. Results were considered significant when the *P* value is less than .05. Statistical analysis was performed with SPSS 15.0 (SPSS Inc., Chicago, IL).

Results

Fifty-six patients with SCA and 56 age- and gender-matched healthy nonanemic volunteers were evaluated (Table 1). Five patients (8.9%) had a stroke in the past, 2 patients (3.6%) had a history of transient ischemic attack, and 10 patients had a previous diagnosis of acute chest syndrome (none of the patients had pulmonary hypertension).

TAMMpost in the basilar and vertebral arteries and in the PCA were significantly higher among cases than controls ($P < .01$) (Table 1). In patients with SCA, the