SICKLE CELL DISEASE: CAN TRANSCRANIAL DOPPLER ULTRASOUND HELP PREVENT STROKE?

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ABSTRACT

Sickle cell disease (SCD) affects millions of people worldwide and there is no known cure. Management of SCD patients is complex and challenging. SCD is an inherited blood disorder that alters the shape and function of hemoglobin molecules. In turn, this causes red blood cells (RBC) to become misshapen, or "sickled". This shortens the lifespan of the RBC, which can lead to anemia. These sickle-shaped cells can occlude small blood vessels and arterioles, causing extreme pain and a host of complications such as organ failure, avascular necrosis, sepsis, and stroke. A keystone in reducing SCD patient mortality is the prevention of stroke. Elevated cerebral blood flow velocities in the Circle of Willis have been directly linked to stroke in SCD patients. An inexpensive ultrasound exam known as transcranial Doppler (TCD) has been used to evaluate cerebral blood flow in SCD patients. This systematic review of literature was conducted to examine the clinical effectiveness of using TCD results to guide interventions such as hydroxyurea administration for the prevention of stroke and to determine which criteria are most beneficial to SCD patients. Results show that TCD is an effective, safe, and non-invasive modality. Definitive blood flow velocity thresholds, protocols, and therapeutic/preventive interventions will be presented.

BACKGROUND

- SCD is a recessive, inherited blood disorder that affects the function of the hemoglobin molecule in red blood cells (RBC) and produces sickle-shaped RBCs.[5]
- In turn, these misshapen RBCs can occlude blood vessels and lead to a variety of complications such as organ damage, avascular necrosis, anemia, and infection.[5]
- SCD affects millions of people worldwide and there is no known cure.[5]
- A complication that is particularly concerning is stroke.[1]
- SCD patients are prone to elevated intracranial blood flow velocities due to their misshapen red blood cells. These elevated velocities can lead to stroke.[9]
- A non-invasive ultrasound study, TCD, can monitor these blood flow velocities. It is a safe, inexpensive, and accurate modality.[2]
- TCD evaluates vessels within the Circle of Willis that supply blood to the brain.[2]
- Velocities obtained from the TCD exam can be used to stratify the patient's risk for stroke.[1]
- This information can assist the healthcare provider when developing a treatment plan.[7]

METHODS

A discipline specific question was created, and a systematic review of literature was performed. The articles were chosen from PubMed and MEDLINE which were peer reviewed, reputable and written in English. To search for eligible studies the following Medical Subject Headings (MeSH) included: sickle cell disease, transcranial Doppler, stroke prevention in sickle cell patients, treatment of sickle cell, STOP criteria, Circle of Willis blood flow velocities, hydroxyurea and sickle cell blood transfusion. These articles were reviewed in order to gather information directly related to the use of transcranial Doppler as a screening method for reducing the incidence of stroke in sickle cell patients.

RESULTS

- According to the NHLBI,[6] the use of TCD screening, in conjunction with prophylactic blood transfusion, can significantly reduce the risk of stroke in patients with elevated flow velocities.
- Children with conditional (170-199 cm/sec) or abnormal (≥ 200 cm/sec) velocities be referred to a specialist who has experience in chronic transfusion therapy.[6]
- The NHLBI[6] considered this a "strong recommendation" based on "high quality evidence" from an analysis of two random controlled trials and fifty observational studies. More than 11,000 patients were enrolled in the observational studies.[6]
- According to Reeves et al,[8] "TCD screening is the only method to identify children with sickle cell anemia at the highest risk for stroke, and its importance has recently been underscored by NHLBI guidelines that strongly recommend children with sickle cell anemia receive annual TCD screening."
- Adams[1] described TCD as "well established as a predictor of future cerebrovascular symptoms in long-term prospective studies." TCD screening exams should begin at 2 years of age and continue until 16.[1]

TCD STROKE SCREENING CATEGORIES AND RECOMMENDATIONS[1]

CEREBRAL BLOOD FLOW VELOCITY	CATEGORY	RECOMMENDATION
< 170 CM/SEC	NORMAL	ANNUAL TCD SCREENING
170 TO 199 CM/SEC	CONDITIONAL	FOLLOW-UP TCD IN 3 MONTHS
≥ 200 CM/SEC	ABNORMAL	REPEAT EXAM IN TWO WEEKS/INITIATE BLOOD TRANSFUSION IF VELOCITIES REMAIN ELEVATED
≥ 220 CM/SEC	ELEVATED/VASCULOPATHY	IMMEDIATE TRANSFUSION

DISCUSSION

- The overall findings in the articles examined in this study confirm the utility of TCD in guiding stroke prevention efforts.
- It is a quick, non-invasive, sensitive, and relatively inexpensive modality that accurately measures cerebral blood flow velocities.
- These velocities can effectively stratify stroke risk in SCD patients. This enables healthcare providers to develop a treatment plan that can reduce the risk of stroke.
- This usually involves chronic blood transfusions. Without TCD evaluation, the possibility of placing patients on transfusion unnecessarily is increased. In turn, this could cause complications such as iron overload. The use of established protocols and velocity classifications have demonstrated significant efficacy.
- An important limitation of TCD that it is not effective for stroke screening in adult SCD patients.[6] This has meaningful clinical implications, as the risk for stroke does not decrease with age.[6]
- Future research should be conducted as to why TCD has not been effective for stroke screening in adult patients, and what can be done to change that.

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