Correlation Between Hemoglobin Levels and Transcranial Doppler Velocities: A Retrospective STOP 2 Analysis in Children With Sickle Cell Disease

Jennifer H. Voeks, PhD1; Sarah Gray, PhD2; Josh Lehrer-Graiwer, MD, MPhil, FACC2; Robert J. Adams, MD4
1Medical University of South Carolina, Charleston, SC, USA; 2Global Blood Therapeutics, South San Francisco, CA

BACKGROUND

Sickle cell disease (SCD) is an inherited disorder in which pathology is driven by sickle hemoglobin (HbS) polymerization and erythrocyte sickling, leading to chronic hemolytic anemia and episodic vaso-occlusive crises (VOC).1,2

Transcranial Doppler ultrasound (TCD) measurement of intracranial blood flow velocities can be used to identify children at an increased risk of developing overt stroke and silent cerebral infarcts, which may result in physical and neurocognitive deficits.3,4

Children with abnormal blood-flow velocities (≥200 cm/s) are at the highest risk of developing a stroke compared to those with conditional (170 to 199 cm/s) and normal (<170 cm/s) TCD velocities.5,6

Prophylactic transfusions can reduce the risk of strokes in children with SCD, and the Optimizing Primary Stroke Prevention in Sickle Cell Anemia (STOP 2) trial demonstrated that the discontinuation of transfusion may be safe in children with SCD who converted from high to low stroke risk.7

Background velocities can be used to identify children at an increased risk of developing overt stroke and silent cerebral infarcts, which may result in physical and neurocognitive deficits.3,4

METHODS

Study Design

The randomized, controlled STOP 2 trial assessed whether transfusions can be safely discontinued in children with SCD who converted from high to low stroke risk while receiving transfusions, as assessed by TCD velocities.7

Patients who reached TCD normalization after transfusions for 10 or more months were randomized 1:1 to continue or discontinue transfusions and had their TCD velocities and Hb levels monitored every 3 months (Figure 1).

RESULTS

Baseline Characteristics of Patients Included in the Longitudinal Analysis

Of the 79 patients randomized to continue or discontinue transfusions in STOP 2, 57 patients with time-matched Hb and TCD assessments were included in the baseline evaluation, and 47 patients with time-matched Hb and TCD assessments over time were included in the longitudinal analysis.

Baseline characteristics of the 47 patients included in the longitudinal analysis are shown by study arm in Table 1. The relationship between baseline Hb levels and baseline TCD velocities was examined.

Table 1. Baseline Characteristics of Patients Included in the Longitudinal Analysis

**Correlation Between Hemoglobin Levels and Transcranial Doppler Velocities:**

The primary objective of this retrospective analysis was to evaluate the relationship between changes in Hb level and changes in TCD flow velocity.

- STOP 2 randomized subjects with time-matched assessments of Hb level and TCD flow velocity were included in the analysis.
- The relationship between changes in Hb level and TCD velocity from baseline was assessed using a mixed-effects model for repeated measures (MMRM) analysis.
- To assess consistency of results, analysis using each patient’s average change from baseline in Hb and average change from baseline in TCD velocity was undertaken.
- The relationship between baseline Hb levels and baseline TCD velocities was also examined.

Similarly, the longitudinal relationship of change in Hb level and change in TCD velocity was negatively correlated (Figure 2; r = -0.59), and a Hb increase of 1 g/dL from baseline was associated with an 11.6 cm/s decrease in TCD velocity (95% CI: 8.7–18.2 cm/s; P < 0.0001).

- The effect of Hb change on TCD velocity remained statistically significant after adjusting for gender, baseline age, baseline Hb, baseline TCD, and time since baseline.

The effect of Hb change on TCD velocity remained statistically significant after adjusting for gender, baseline age, baseline Hb, baseline TCD, and time since baseline. Therefore, the effect of Hb change on TCD velocity was consistent and significant, even after adjusting for other factors.

CONCLUSIONS

- A retrospective analysis of STOP 2 data demonstrated that higher Hb levels were associated with decreased TCD velocities in children with SCD.
- An increase in Hb level likely conveys a reduction in stroke risk and highlights the need for alternative therapies that improve Hb level to potentially prevent strokes in this population.

ACKNOWLEDGEMENTS

- This study was supported by grants (U01 HL 052193 and U01 HL 052016) from the National Heart, Lung, and Blood Institute.
- We are indebted to the patients and their families for their contribution to this research.

REFERENCES


DISCLOSURES

- Nelson Jem, PhD (Healthcare Consultancy Group, with funding from Global Blood Therapeutics) provided editorial assistance in the preparation of this report.
- This retrospective study was sponsored by Global Blood Therapeutics.