

Nocturnal Hypertension Associated with Stroke and Silent Cerebral Infarcts in Children with Sickle Cell Disease



Kaitlin Strumph DO, Michael Hafeman MD, Saritha Ranabothu MD, William Gomes MD, Steven Benitez MD, Frederick Kaskel MD, Deepa Manwani MD*, Joseph Mahgerefteh MD*



*authors contributed equally to this work

Background

- Sickle cell disease (SCD) is an inherited red blood cell disorder characterized by chronic anemia, hemolysis and intermittent vascular occlusion causing tissue ischemia and end organ damage
- Ischemic cerebral injury is a leading cause of morbidity and mortality
- Strokes occur in ~1.9% of children with SCD
- Silent cerebral infarcts (SCIs), defined as infarct-like lesions seen on Brain MRI that do not correspond to overt neurologic deficits, occur in up to 39% of children with SCD by age 18
- SCIs are associated with lower cognitive test scores, poor academic attainment, and a full-scale IQ decline of 5 points
- Hypertension (HTN) regarded as the single most important modifiable risk factor for ischemic cerebral injury in the general population
- Despite having relatively lower blood pressures compared to age matched norms, children with SCD have been noted to have a high prevalence of abnormalities on 24-hour ambulatory blood pressure monitoring (ABPM)

Primary Aim

- This study aimed to determine if there is an association between blood pressure abnormalities on ABPM with stroke and silent cerebral infarcts in children with SCD

Methods

Study Design

- Cross-sectional study examining the association between ABPM and end-organ outcomes in children with SCD
- November 2015 - October 2017
- All patients enrolled underwent 24-hr ABPM and had blood and urine samples drawn

Inclusion criteria for cerebrovascular outcomes

- HgbSS or HgbSB⁰
- Age 5-21
- MRI Brain documented within 1 year of the ABPM

ABPM Definitions

Systolic or Diastolic BP Load	The percentage of BP measurements that are above the 95th percentile for healthy children of the same age, height and sex.
Ambulatory HTN	24 hour systolic or diastolic load $\geq 25\%$ with mean BP $\geq 95^{\text{th}}$ percentile
Nocturnal HTN	During sleep, systolic or diastolic load $\geq 25\%$ with mean BP $\geq 95^{\text{th}}$ percentile for age, height and sex
Masked Hypertension	Normal clinic blood pressure despite having ambulatory and/or nocturnal hypertension

Results

Characteristics of Participants Based on Presence of SCI or Stroke

Total Subjects n = 42	No SCI or Stroke (n=28)	SCI or stroke (n=14)	p-value
Age, years, median (IQR)	12 (10, 16.5)	16 (12, 19)	0.17
Sex, male, n(%)	15 (54)	7 (50)	0.83
On chronic transfusions, n(%)	5 (18)	8 (57)	0.02
Hydroxyurea use, n(%)	21 (75)	7 (50)	0.17
Hgb, g/dL, median (IQR)	8.5 (7.6, 9.3)	9.8 (8.8, 10.2)	0.01

Characteristics of Participants Based on Presence of Nocturnal HTN

Total Subjects n = 36	No Nocturnal HTN n = 27	Nocturnal HTN n = 9	p-value
Age, yrs, median (IQR)	16 (11, 19)	12 (9, 13)	0.06
Sex, male (%)	15 (55%)	4 (44%)	0.71
On chronic transfusions, n(%)	6 (22%)	4 (44%)	0.23
Hydroxyurea use, n(%)	19 (70%)	4 (44%)	0.24
Hgb, g/dL, median (IQR)	8.9 (8.1, 9.8)	9 (7.8, 9.8)	0.95

Nocturnal/Masked HTN and Stroke/SCI

Total Subjects n = 42	No stroke or SCI n = 28	Stroke or SCI n = 14	p-value
--------------------------	----------------------------	-------------------------	---------

24 Hour Blood Pressures

Ambulatory HTN	2 (7%)	1 (7%)	1.00
----------------	--------	--------	------

Total Subjects [^] n = 36	No stroke or SCI n = 25	Stroke or SCI n = 25	p-value
---------------------------------------	----------------------------	-------------------------	---------

Overnight Blood Pressures

Nocturnal HTN	3 (12%)	6 (55%)	0.01
---------------	---------	---------	-------------

Overall Blood Pressure Assessment

Masked Hypertension	3 (12%)	6 (55%)	0.01
---------------------	---------	---------	-------------

[^]Overnight blood pressure data only available on 36 patients

Conclusions

- Relying on clinic blood pressures to screen for HTN appears to be insufficient in the pediatric SCD population
- Masked hypertension and isolated nocturnal hypertension in children with SCD are shown to be associated with stroke and silent cerebral infarcts
- Prospective studies are needed to confirm these findings and evaluate the contributory nature of 24-hour blood pressure abnormalities to ischemic cerebral injury in children with SCD

Strumph K, Hafeman M, Ranabothu S, et al. Nocturnal Hypertension Associated with Stroke and Silent Cerebral Infarcts in Children with Sickle Cell Disease. *Pediatr Blood Cancer* 2021 Jan;e28883 [Online ahead of print] PMID: 33405393

This research was supported by NIH/National Center for Advancing Translational Science (NCATS) Einstein-Montefiore CTSA Grant Number UL1TR001073