

Transcranial Doppler Study Among Children with Sickle Cell Anaemia Vs Normal Children

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Abstract

Introduction: Role of transcranial Doppler in prevention of stroke in sickle cell children has been well appreciated. Studies are being done to develop the protocol in children. Since we don't find stroke very commonly in this part of the world, this study was done in order to see the prevalence of abnormal flow velocity in sickle children attending sickle cell clinic. The aims of this study were to measure mean flow velocity in different vessels in homozygous sickle cell patients using transcranial Doppler study, to compare the mean velocity in sickle children with age and sex matched controls and to correlate mean velocity with headache or stroke if any and also to correlate mean velocity with number of transfusions. **Materials and Methods:** The study was done in Paediatric wards. It was a prospective crosssectional comparative study. Twenty six children below 14yrs of age with homozygous sickle cell disease attending the Sickle cell clinic were selected as the cases. Forty cases of similar age and sex were recruited as normal control group. Transcranial Doppler was done in six different vessels in both the groups and mean flow velocity was measured. Mean flow velocity was correlated with symptoms and number of transfusions. Velocity was classified as normal (<170cm/sec), conditional (170-199cm/sec) or abnormal (>200cm/sec). Statistical analysis was done using SPSS 10 software. **Results:** In normal age and sex matched controls mean blood flow velocity was 50cm/sec where as in the cases of sickle cell disease was 180cm/sec. Maximum mean velocity was observed in middle and posterior cerebral artery. In two Sickle cell cases (8%) blood flow velocity was abnormal, these children had headache though received 5-10 transfusions/year. In only 4% sickle cell children flow velocity was normal and rest had conditional velocity. Among these children 39% received less than 5 and rest received 5-9 transfusions /yr and had no symptoms of stroke. **Conclusions:** Flow velocity measured by Transcranial Doppler is highest in middle cerebral artery and Posterior cerebral artery which appear to be the best arteries for this test in this region. Flow velocity was significantly high in children with sickle cell disease as compared to normal children. Prevalence of abnormal flow velocity in our children was 8% and children with abnormal mean flow velocity presented with headache.

Key words: Transcranial Doppler, Homozygous sickle cell, Stroke, Flow velocity.

Introduction

Wardha district is situated in Vidarbha region of central India and this area is popularly called sickle belt due to high prevalence of this condition. Acharya Vinoba Bhave Rural Hospital is running a sickle cell clinic where registration, free treatment and follow up of these patients is done regularly.

Prevalence of Stroke in children with sickle cell disease is described to be around 7 to 12%^{1,2,3}. Stroke Prevention Trial (STOP) I and II trials were done for its prevention and showed that regular transfusion, based on report of transcranial Doppler, can effectively prevent stroke^{4,5}.

Our patients rarely complained of headache and limb weakness. This study was done out of curiosity to see whether our patients differed from patients elsewhere? May be they are already receiving too many transfusions for other reasons which keeps the velocity

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low and hence prevents stroke. This study is an effort to compare flow velocity in different vessels of children with sickle cell disease and normal children.

The objectives of this study were 1) To measure mean flow velocity in different vessels in homozygous sickle cell patients using transcranial Doppler study. 2) To compare the mean velocity in sickle children with age and sex matched controls. 3) To correlate mean velocity with headache or stroke if any. 4) To correlate mean velocity with number of transfusions.

Materials and Methods

It was a prospective observational study. Children below 15yrs diagnosed as sickle cell anemia (by hemoglobin electrophoresis) and attending sickle cell clinic for 1 year were included in the present study. Age and sex matched normal children attending Paediatric OPD for minor illnesses were used as controls. Detail history including presenting symptoms, number of transfusions and examination features were noted. Transcranial Doppler study was done over internal, external and common carotids, middle and posterior cerebral and vertebral artery on right side using 500 MDMR3 ultrasound color Doppler machine with 2-3 MHZ probe. The velocity over the vessel was noted.

Doppler study was done after acute stage (crisis) was over. The velocities were noted and correlated with symptoms and number of transfusions. Other investigations were done as indicated.

As per STOP study^{1,2} velocities were classified as below.

Normal - < 170cm/sec

Conditional – 170-199c m/sec

High or abnormal- > 200cm/sec

Results

Doppler study was done in 26 sickle cell homozygous patients and 40 normal controls. Their age and sex wise distribution is given in Table 1.

Fever (60%), bone pain (60%) and pain in abdomen (39%) were most common complaints. Around 14% patients complained of pale skin and only 8% presented with headache. On examination most common finding was pallor (20%) and fever (18%). Systemically bones and joint problems and hepato-splenomegaly were most common finding (53% each). Only 2 (8%) children presented with headache, none had hemiparesis.

Around 39% children with sickle cell anaemia received less than 5 and rest received 5-10 transfusions per year. Children with headache (8%) received 5-10 transfusion/yr.

Among sicklers only 2 children (8%) had flow velocity which was abnormal (> than 200m/sec) and they were the same children who presented with headache. Majority (88%) of sickle children had conditional values. Among normal children all had mean velocity below 170 cm/sec (Table 2).

Highest mean velocity was found in middle cerebral artery (155 cm/sec) followed by post cerebral artery (149 cm/sec) and common carotid artery (131.8cm/sec). Minimal velocity was 88 cm/sec in vertebral artery. This artery also showed widest variation which might reduce its reliability.

Table 1: Age and sex wise distribution of subjects

Age	Sickle Patients			Normal Patients		
	Male	Female	Total	Male	Female	Total
<5yrs	10	2	12	2	10	12
5-10 yrs	7	-	7	5	8	13
>10 yrs	2	5	7	12	3	15
Total	19	7	26	19	21	40

Table 2: Subjects at a glance

Mean velocity(cm/sec)	Sickle Patients		Normal Patients	
	Number	Percentage	Number	Percentage
Normal (<170)	1	4%	40	100%
Conditional(170-199)	23	88%		
High risk (>200)	2	8%		

Table 3: Velocity in different vessels at a glance

Arteries	Sickle Patients (N=26)		
	Above 170	Mean	Range
Middle cerebral artery	15	155.5	140-220
Posterior cerebral artery	12	149	130-190
Common carotid artery	4	131.8	100-175
Internal carotid artery	-	131	90-150
External carotid artery	-	115.6	100-145
Vertebral artery	-	88	80-160

Discussion

The prevalence of stroke described in sickle cell children¹ is around 10-12 %.In the present study only 8% children presented with headache without any neurodeficit.Some authors have found silent infarcts on neuroimaging⁶. We might have missed silent infarcts as we could not do neuroimaging due to financial constraint.

The vessels used for doppler in STOP trial⁵ were distal internal carotid and proximal middle cerebral arteries, We used all the vessels namely external carotid, internal carotid, common carotid, middle and posterior cerebral artery and vertebral artery. We wanted to see which artery gives highest velocity in our set up which in turn informs the site of stroke. Highest mean velocity found was in middle and posterior cerebral artery followed by common and internal carotids. Gordman and colleague used submandibular Transcranial Doppler and could pick up cases missed using internal carotid⁷.

In normal children mean velocity was in normal range (< 170cm/sec) where as in sickle children only 1 had normal velocity. Among sicklers 8% had abnormal and rest had conditional values. This shows our children are at risk of stroke but may be the velocities are just below abnormal values as 39% receive transfusion at least once in 2 months. Regular transfusions prevent first stroke as shown in STOP trial³. This fact does not explain Two children in our study with headache and higher velocities (>200m/sec) who were receiving 5-10 transfusions per year.

MR Angiography (MRA) has been correlated with Transcranial Doppler⁵ and MRA was found abnormal if TCD was abnormal. On transfusion, abnormalities normalize only if velocity normalizes. This emphasizes that noninvasive and cheaper transcranial Doppler is a good screening method to detect stroke. This finding might also suggest need to start transfusion therapy before vasculopathy sets in.

Result of STOP trial II clearly showed increase in stroke after stopping chronic transfusion therapy⁸

Heather et al.⁹ showed decreasing trend in stroke since children were on chronic transfusion therapy. Pegelow Macklin and Moser studied MRI in 266 sickle children and found infarcts(including silent ones) in 21% children and reported recurrence more common in children with silent infarcts¹⁰. Majumdar et al compared 6 different strategies of chronic transfusion and found screening with doppler upto the age of 6 and transfusion therapy up to age of 18 was the best strategy. Regular chelation therapy improved outcome¹¹. Scothorn and Price studied 137 children who were on chronic transfusion therapy for 5 yrs and found recurrent stroke is more common if first stroke was not with any other medical event like other types of crises¹².

Left and right velocity differences may be useful in identifying unilateral narrowing. Reference values in sickle cell children have been given by Krejza J et.al.¹³. In this study we could do TCD only on right side hence comparison was not possible.

Some authors also found other uses of abnormal TCD values^{6,14}. Kral et al found children with abnormal TCD values performed more poorly than children with conditional TCD values on measures of verbal intelligence and executive function^{14,15}. Infarctions may remain silent as far as neurodeficit is concerned but may give rise to poor intelligence as sequel^{15,16}. This aspect also needs further evaluation as it may be worthwhile to give chronic transfusion for better performance of children. Yerys and White showed better performance of children with memory strategy education as compared to only tutorials¹⁷. This study also emphasizes importance of screening for infarcts.

Overall this study shows that our children also are at risk of stroke as in other studies and TCD can be a screening method and should be used in sickle cell clinic regularly.

Conclusions

Flow velocity measured by Transcranial Doppler is highest in middle cerebral artery and Posterior cerebral artery which appear to be the best arteries for this test in

this region. It is significantly high in children with sickle cell disease as compared to normal children. Prevalence of abnormal flow velocity in our children is 8%. Children with abnormal mean flow velocity presented with headache.

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