

SICKLE CHILDREN VS NORMAL CHILDREN: A TRANSCRANIAL AND EXTRACRANIAL DOPPLER STUDY

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ABSTRACT

A prospective hospital based study was carried out to evaluate the role of transcranial Doppler in sickle cell anemia for period of 2 yrs (July 2009- August 2011). A total of 100 children, 50 normal individuals in control group and 50 diagnosed sickle cell disease patients in sickle group were evaluated in the age group. Children were from Newborn to 15 years of age, of which 62% were males and 38% were females. Common Carotid Artery (CCA), External Carotid Artery (ECA), Internal Carotid Artery (ICA), Vertebral Artery, Middle Carotid Artery (MCA), Anterior Carotid Artery (ACA), Posterior Carotid Artery (PCA) was evaluated by Transcranial and Extracranial Doppler on both sides in sickle cell patient. The mean velocities in all the vessels were higher in sickle group patient as compared to normal group patients. Evaluation of Extracranial carotid vessels has not been done in previous published studies. Our study can act as benchmark in extracranial Doppler studies of sickle cell patients. We have not followed the patients of sickle cell disease till stroke, but we can say with certainty that increased values of velocity >200 cm/sec is an absolute indication for blood transfusion to prevent stroke, which was observed in 10% of sickle cell patient in our study where velocities reduced by 20-25 cm/sec after blood transfusion.

KEYWORDS: Extracranial, Intracranial, Doppler, Sickle cell, Anaemia, Transcranial.

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INTRODUCTION

Sickle cell anemia is a disease that is responsible for considerable amount of morbidity and mortality in children in Central India and Vidarbha and particularly in area near Wardha district [1]. It not only has an adverse effect on the growth [2] of the child but significantly affects quality of life [3]. Prompt intervention at regular intervals along with good nutrition, regular follow up and screening for impending complications can reduce the morbidity and

mortality associated with sickle cell anemia. One of the complication of sickle cell disease is stroke.

Strokes in these children usually result from narrowing or closure of arteries supplying blood flow to the brain. Transcranial and Carotid doppler can be used as one of the modality to predict the occurrence of stroke, which can be avoided by blood transfusion. It can help to predict the occurrence of stroke by detecting increased velocity.

Transcranial Doppler ultrasonography (TCD) is a diagnostic tool that can be used at bedside to assess the cerebral vasculature noninvasively. It is inexpensive, safe, and reliable. Therefore we decided to measure the velocity of the cerebral vessels by transcranial Doppler in sickle cell disease patients.

Aim and Objectives: To establish which vessel evaluation in Transcranial Doppler (TCD) and Extracranial doppler (ECD) is ideal in sickle cell disease among all the vessels.

MATERIALS AND METHODS

This was a prospective study carried out in the Department of radio-diagnosis. Acharya Vinoba Bhawe Rural Hospital, Sawangi (Meghe), Wardha from July 2009 to August 2011.

Selection of cases: 50 normal individuals as control group and 50 cases of pathologically confirmed sickle cell disease for transcranial and Carotid Doppler study assess the Doppler values.

Inclusion criteria: Newborn to 15yrs with no deficits on neurological examination and approval & informed consent of subject's caretaker.

Exclusion criteria: Patient with history of hydroxyurea therapy in sickle cell patient, major head injury requiring visit to an emergency department, seizure disorder requiring anticonvulsant therapy and history of prenatal and perinatal hypoxic ischaemic brain injury

Methodology: All the selected patients were evaluated with detailed clinical history, clinical examination.

The children were placed in supine position for extracranial doppler and sitting position for transcranial doppler. The examined surface was exposed and cleaned. Bed sheet was put to cover rest of the body. Patient was made comfortable by explaining the procedure in elder children and by giving sedation in younger children. Written consent was taken from the parent. Sonographic jelly was applied to achieve acoustic coupling and ultrasound transducer was placed

Examination: TCD is based on the use of a range-gated, pulsed-Doppler ultrasonic beam of 2 MHz frequency. The ultrasonic beam crosses the intact skull at points known as 'windows' and is reflected back from the moving erythrocytes in

its path. The difference between the transmitted signal and the received signal is called the Doppler shift, and can be expressed by the formula:

$$\text{Doppler frequency shift} = 2 \cdot V \cdot F_t \cdot \cos u / C$$

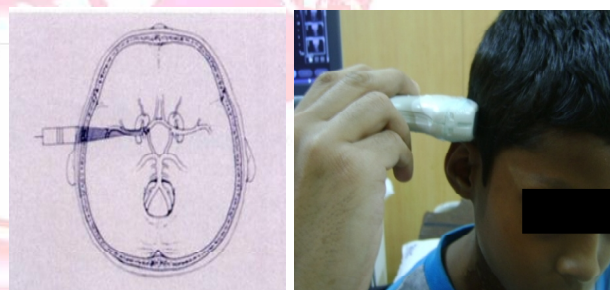
Where V is the velocity of the reflector (red cells), F_t is the transmitted frequency, C is the speed of sound in soft tissue, and $\cos u$ is the correction factor based on the angle of insonation (u).

Vessels to be studied are: 1. Middle cerebral artery, 2. Posterior cerebral artery, 3. Anterior cerebral artery, 4. Internal carotid artery, 5. External carotid artery, 6. Common carotid artery and 7. Vertebral artery.

Sl. No.: 1, 2 & 3 by TCD and 4,5,6 & 7 by ECD

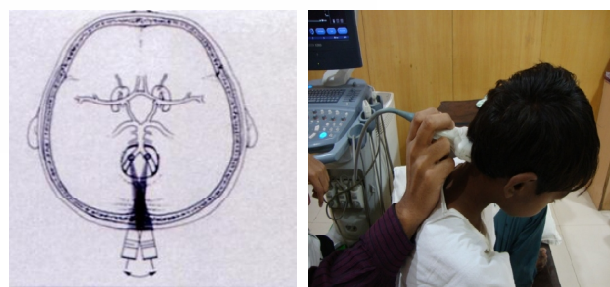
Main ultrasonic approaches for TCD

Fig. 1: Transtemporal approach – probe will be placed on the temporal aspect of the head, cephalad to the zygomatic arch. Posterior, anterior and middle cerebral arteries will be evaluated by this approach.



1. Transtemporal approach (figure 1) – probe will be placed on the temporal aspect of the head, cephalad to the zygomatic arch. Posterior, anterior and middle cerebral arteries will be evaluated by this approach.

Fig. 2: Suboccipital approach – probe will be placed between the posterior margin of the foramen magnum and palpable spinous process of first cervical vertebrae with beam aimed at bridge of the nose. This approach is essential for screening the vertebral arteries and posterior cerebral arteries.



2. Suboccipital approach (figure 2) – probe will be placed between the posterior margin of the

foramen magnum and palpable spinous process of first cervical vertebrae with beam aimed at bridge of the nose. This approach is essential for screening the vertebral arteries and posterior cerebral arteries.

Fig. 3: Carotid Approach – Carotid vessels will be evaluated by this approach.



Scanning protocols and follow-up:

The scan results should be divided into five categories depending on the time averaged maximal mean (TAMM) velocity recorded: 1. Inadequate image, 2. Unusual low velocity, 3. Normal velocity - 'low risk', 4. Borderline velocity - 'conditional' and 5. High velocity - 'high risk'.

CLASSIFICATION OF TCD IMAGING [5]: 1. NORMAL VELOCITY – 'STANDARD RISK' <170 CM/S, 2. BORDERLINE VELOCITY – 'CONDITIONAL' 170 TO 199 CM/S and 3. HIGH VELOCITY – 'HIGH RISK' >200 CM/S.

OBSERVATIONS AND RESULTS

Table 1: Age wise distribution of patients in all the groups.

Age Group(yrs)	Control Group	Sickle group	value-2x	p-value
< 5	17 (34%)	20 (40%)	0.51	0.77 NS,p>0.05
5-Oct	18 (36%)	15 (30%)		
>10	15 (30%)	15 (30%)		
Total	50 (100%)	50 (100%)		
Mean Age	6.67	6.89		
SD	4.47	4.36		

Table 2: Comparison of groups on the basis of Trans Cranial Doppler Results.

TransCranial Doppler Results (Mean Velocity)	Control Group	Sickle Group
Normal (<170 cm/sec)	46 (92%)	26 (52%)
Conditional (170-199 cm/sec)	0 (0%)	15 (30%)
High Risk (>200 cm/sec)	0 (0%)	4 (8%)
Inadequate	4 (8%)	5 (10%)
Total	50 (100%)	50 (100%)
value-2x		
p-value	P<0.0001 S	

Table 3: Correlation of no of patient in each vessel which belong to conditional and high risk group patients.

Vessels	Total number of patients	Right Side		Left Side	
		No of patient with conditional velocity	No. of patient with high risk velocity	No of patient with conditional velocity	No. of patient with high risk velocity
CCA	50	8	0	8	0
ICA	50	7	1	7	1
ECA	50	9	0	9	0
Vertebral	50	1	0	1	0
MCA	50	15	4	15	4
PCA	50	19	2	20	2
ACA	50	6	0	7	0

DISCUSSION

Hemoglobinopathies occur widely across the world and an increased numbers of annual affected births and high rates of mortality and morbidity are still observed in the majority of affected countries of the developing world. In view of this prevalence, different studies have been done on sickle cell disease.

It was in 1910 when Dr James Herrick observed, "peculiar elongated sickle shaped RBCs" in the blood of an African medical student [5]. Neel [5] and Beet [6] clarified the genetic basis of sickle cell anemia by demonstrating that heterozygosity for the sickle cell gene resulted in sickle cell trait without significant clinical symptoms, whereas homozygosity resulted in sickle cell anemia. Initially the single mutation theory was postulated. But it is now clear that the sickle cell mutation has occurred as several independent events.

As Vidharba is one of the sickle belt in india, we

have come across diagnosed cases of sickle cell anaemia. In these cases stroke is a dreaded complication. This study is aimed at reducing the incidence of stroke by TCD studies. We can warn the clinicians for impending stroke so that prompt treatment can be given to avoid stroke.

Neish et al [7], 2002 conducted the study in Children's Health Care of Atlanta at Scottish Rite, in which they enrolled 66 children with mean age of 9.3 yrs (range 3.8-19 yrs). Pawlak et al [8], 2009 conducted the study in Hospital of the University of Pennsylvania, U.S in which they enrolled 68 children with mean age of 7.1 ± 3.3 yrs (range, 2-14 yrs) which is almost similar to our study. Bernaudin et al [9], 2005 conducted the study in Centre Hospitalier Intercommunal, France in which they screened 291 children with mean age of 8.2 yrs (range of 2 months – 18 yrs). McCarville et al [10], 2004 conducted the study in St. Jude Children's Research Hospital, Memphis in which they screened 53 children with mean age of 10 yrs (range, 2-17 yrs)

From the above review of literature we can assess that average age of presentation was 8 years.

In Our study total number of patients was 100, 50 in control group and 50 in sickle group. In sickle group we included patient with age range of 1-15 yrs. Maximum 20(40%) patients belonged to the age group of <5 years and 15(30%) patients belong to 5-10 yrs and 15(30%) belong to >10 yrs with a mean age of 6.89 ± 4.36 yrs which is almost similar to above conducted studies.

We included age group 1-15 yrs because stroke have been reported in 11% of patients with sickle cell anemia by the age of 20 yrs.¹¹

National Heart, Lung, and Blood Institute (NHLBI) conducted the study "Stroke Prevention in Sickle Cell Anemia (STOP 1)" in July 1994 to reduce episodes of first time stroke by 75 percent in children with sickle cell anemia by the administration of prophylactic transfusion therapy. The clinical trial demonstrated a significant benefit of chronic red cell transfusion in reducing the risk of a first stroke by 90%, such that it was halted before its scheduled closure on the advice of the study's data and safety monitoring board. Based on these findings, the

National Heart, Lung, and Blood Institute issued a Clinical Alert recommending TCD screening of children with SCD (Sickle Cell Disease) and consideration of chronic transfusion to prevent stroke for those who are identified to be at high risk for stroke.

ROLE OF CAROTID DOPPLER IN COMMON CAROTID ARTERY, EXTERNAL CAROTID ARTERY AND VERTEBRAL ARTERY IN SICKLE CELL ANAEMIA: In our study we screened common carotid artery, external carotid artery and vertebral artery in 100 patient, 50 in control group and 50 in sickle group. The mean velocity of CCA (1-15 yrs age) in control group was 79.12 cm/sec and in sickle group on right and left side were 137.47 cm/sec and 139.16 cm/sec respectively.

The mean velocity of ECA (1-15 yrs age) in control group was 65.02 cm/sec and in sickle group on right and left side were 131.66 cm/sec and 131.99 cm/sec respectively.

The mean velocity of vertebral artery (1-15 yrs age) in control group was 35.47cm/sec and in sickle group on right and left side were 109.62 cm/sec and 110.90 cm/sec respectively.

In literature, role of carotid doppler of common carotid artery, external carotid artery and vertebral artery in sickle cell anemia has not been studied, so we have not got any references to correlate them with our study.

In our study we concluded that velocities in CCA, ECA, Vertebral arteries in sickle group were significantly ($p < 0.05$) increased compared to control group. The sensitivity in identifying and measuring these carotid vessels (98%) is more than intracranial vessels (90%), so the carotid vessels can be used as screening vessels in sickle cell patients when intracranial vessels are not identified or measured.

EFFECT OF TRANSFUSION IN SICKLE CELL ANAEMIA: Venketasubramanian N et al [12], 1994 in his study screened 10 patients (7 with strokes, 3 without) undergoing transfusion therapy using TCD. Vessels showed reduction of median blood flow velocities by 20-25 cm/sec after transfusion. Adams et al [11] 1998 in his study screened 130 children, and 63 were randomly assigned to receive transfusions. There was 92 percent difference in the risk of stroke

after transfusion. Kwiatkowski J et al [14] 2011 in his study screened 88 children who have started transfusions for abnormal TCD (>200 cm/sec). Out of 88 children, 46 (52%) converted to normal TCD after a mean of 4.3 months of transfusions. The median TCD velocity was lowered by 38 cm/sec within 3 months of initiating transfusions.

In our study, out of 50 sickle cell children, 5 children with higher velocities were given transfusion. The difference of mean velocity before transfusion and after transfusion was approx. 20-25 cm/sec on both sides. This shows that transfusion reduces the risk of stroke by reducing the velocities which was well correlated with the literature.

CONCLUSION

Our study can act as benchmark in extracranial Doppler studies of sickle cell patients. We have not followed the patients of sickle cell disease till stroke, but we can say with certainty that increased values of velocity >200 cm/sec is an absolute indication for blood transfusion to prevent stroke, which was observed in 10% of sickle cell patient in our study where velocities reduced by 20-25 cm/sec after blood transfusion.

Conflicts of Interests: None

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