Original Article

International Journal of Neurology and Neurosurgery
Volume 9 Number 2, July - December 2017
DOI: http://dx.doi.org/10.21088/ijnns.0975.0223.9217.7

Carotid Doppler in Children with Sickle Cell Anemia

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Abstract

The aim of the study was to perform Carotid Doppler in children aged 2-15 years with Sickle cell anemia. We also studied transcranial velocities in Internal carotid arteries & mean velocities in Common carotid, External carotid and Vertebral arteries. Correlation of increased velocity of blood flow with number of blood transfusions in past, HbF levels and Hydroxyurea therapy was also studied. *Materials and Method*: It was a hospital based cross-sectional study conducted in a Tertiary care hospital in Nagpur from 1st March 2016 to 28 February 2017. *Results*: Total 64 patients were enrolled. 51.6% ofpatients were in age group of 5-10 years. Transcranialvelocity in Internal carotid artery between 170-200cm/s was present in 37.5% of patients and 6.25% of patients had TCV of >200cm/s. There was no correlation of TCV with number of blood transfusions in past andHbF levels. Patients who were on Hydroxyurea therapy had reduced transcranial velocities as compared to those who were not on therapy.

Keywords: Transcranialvelocity; Sickle Cell Anemia; Hydroxyurea.

Introduction

Sickle cell anemia is a qualitative haemoglobinopathy that affects many systems in body [1]. The complications of sickle cell anemia are usually age dependent. One of the major complications of sickle cell disease is involvement of central nervous system in form of pyogenic meningitis (H.Influenzae& Pneumococcal), stroke, silent infarcts, posterior reversible leucoencephalopathyetc [3]. Stroke is one of the commonest complication of sickle cell disease after the age of 4 years and this can be prevented by doing periodical Doppler examination of carotid and middle cerebral artery and managing patients accordingly [2]. Hence this study was planned "Carotid doppler in children with sickle cell anemia"at our Institute.

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Received on 21.07.2017, **Accepted on** 17.08.2017

Aim & Objectives

The aim of the study was to perform Carotid Doppler in children aged 2-15yrs with sickle cell anemia.

1. To evaluate Transcranialvelocity(TCV)of theInternal carotid arteries (ICA) in patients with sickle cell anemia.
2. Correlation of increased velocity of blood flow in ICA with stroke.
3. Correlation of increased velocity of blood flow ICA with Hb F levels, number of bloods transfusions in past and patient onhydroxyurea therapy.
4. To study mean velocities in other arteriesCCA, ECA & VA.

Hypotheses: CNS complications in formof Stroke are more in children of older age andTCV velocities can be evaluated using Carotid approach and raised TVV indicate risk factor for stroke.

Study Design: Hospital based cross-sectional study

Study Setting: Paediatric wards of NKPSIMS & LMH, Nagpur.

Study Duration: 1st March 2016 to February 2017.

Inclusion Criteria: All children diagnosed as sickle cell anemia (SS pattern) by Hb Electrophoresis (HPLC method) in the age group of 2-15 years were included.

Exclusion Criteria

1. Childrendiagnosed with other hemoglobinopathies like Sickle Thal, HbC, Hb D etc.
2. Patients with h/o head injury, convulsions or h/o perinatal asphyxia were excluded.
3. Children < 2years and >15 years of age.

Selection of Cases: Childrenin age group2-15 years diagnosed as sickle cell anemia by Hb Electrophoresis (HPLC) SS pattern and who attended the opd or were admitted in Pediatric wards were selected.

Methodology: A detail history and clinical examination was done of the selected patients. Written consent was taken from parents and they were explained the procedure and its importance.

Vesselsstudied were: Internal carotid artery (ICA), External carotid artery (ECA), Common carotid artery (CCA) and Vertebral artery (VA). The USGmachine used wasEsoare USG with color Doppler, model MyLab 40, with a high frequency probe.

The ultrasonicapproachwas Carotid approach for evaluation of carotid arteries and sub- occipital approach for the vertebral artery.

Risk stratification of stroke by TCD was based on the time-averaged mean of the maximum velocity (TAMM) in the distal internal carotid artery and interpreted as follows [2]:

1. Inadequate image-when no readings could be obtained.
2. Unusual low velocity.
3. Normal velocity- Standard risk-all mean velocities <170 cm/sec.
4. Borderline velocity-Conditional -at least 1 mean velocity of 170 to 199 cm/sec.
5. High velocity- High risk-Abnormal at least 1 mean velocity of 200 cm/sec or higher [2].

Statistical Analysis: Done by Epi info Software and tests applied were Fischer exact and Chi square test.

Table 1: shows age groupwise and sex wise distribution of children of sickle cell anemia in our study.Most of the patients in our study group were more than 5 years of age. As CNS complications occur in age group of children > 5years of age hence in our study high risk group were more.

For statistical analysis we have categorised our data in 2 velocities- <200 cm/s&> 200cm/s, velocities between 170-200cm/s is conditional.

Table 1: Agewise distribution of patients

Age Group	Male	Female	Frequency	Percent
2-5	2	4	6	9.4
6—10	18	15	33	51.6
11—15	16	9	25	39.1
Total	36	28	64	100.0
		Mean ± S.D.		9.71±3.31

Table 2: Mean velocities in Internal Carotid arteries according to age groups

Age Groups	No. of children(n=64)	Velocity ICA		
		<170cm/s	170-200cm/s	>200cm/s
2-5 years	5	0	5(7.8%)	0
6-10 years	33	25 (61%)	6(9.3%)	2(3.1%)
11-15 years	26	14(21%)	10(38.4%)	2(7.6%)

Table 3.1 & 3.2: Shows the relation of velocity of blood flow in ICA with number of blood transfusions in past

No. Blood Transfusions	Velocity ICA	
	<200	>200
<10	49	1
>10	11	3
Fisher exact P =0.06		

No. Blood Transfusion	Velocity ICA	
	<170	>170
<10	37	16
>10	6	5
Chi square = 0.96, P=0.32		

Table 4.1 & 4.2: Shows relation of velocity of blood flow in ICAwithHb F levels

HBF	Velocity ICA	
	<200	>200
<20	37	4
>20	23	0
	Fisher exact p= 0.31	

HBF	Velocity ICA	
	<170	>170
<20	22	19
>20	21	2
	Chi square= 9.47, p=0.002	

Table 5.1 & 5.2: Shows relation of velocity of blood flow in ICAwith patient on Hydroxyurea therapy

Hydroxyurea	Velocity ICA	
	<200	>200
Yes	39	0
No	21	4
	Fisher exact p= 0.039	

Hydroxyurea	Velocity ICA	
	<170	>170
Yes	35	4
No	8	17
	Chi square= 23.04, p=0.000015	

Discussion

In our case study total 64 patients , 51.6% of patients were in age group between 5-10 years (Table 1). Neish et al, conducted a study in Children'sHealth Care of Atlanta at Scottish Rite, where they enrolled 66 children of mean age of 9.3 yrs (range 3.8-19 yrs) which was similar to our study [6]. Pawlak et al, 2009 conducted a studyin which they enrolled 68 childrenwith mean age of 7.1±3.3 yrs (range, 2- 14 yrs) at a Hospitalof University of Pennsylvania, U.S [7]. Study by Munube et al on prevalence of stroke in children admitted with sickle cell anemia , the mean age was 6.1years [8].

Of the total 64 patients in our study, 4 (6.25%) patients hadtranscranialvelocity in ICA 0f>200cm/s, 24 (37.5%) patients had velocity of 170-200cm/s (conditional velocity) while 36 (56.2%) patients had velocity below 170cm/s. (Table 2). In study done by Deane et al mean velocity in extracranialvelocity was 148cm/s [5]. In another study by Singhal et al , they compared mean velocities in CCA, ECA, ICA, VA in children with sickle cell disease and normal children and found higher mean velocities in sickle cell group [4].

Out of 64 patients, (50%) had received less than 10timesblood transfusion in past and 14% patient had >10 blood transfusion in their lifetime. On further analysis blood transfusion <10 times whose TCV velocity was >200cm/s was 1(1.5%), while those who needed blood transfusion > 10 times with TCV >200cm/s were 3 (4.6%) (Table 3.1). On applying Fischer exact test P value was 0.06 i.e. >0.05, so statistically not significant. Number ofblood transfusions in past is not significant with increase TCV (>200c/s) in our study. Studies likethe STOP trial and by Estcourt LJ et al studied relation of blood transfusion in preventing stroke and found normal velocities in children who received regular blood transfusions [2,9].

HbFlevels <20 there were 41(64%) patients, while HbF>20 were 23 (35.9%) patients (Table 4.1). In our study group with HbF levels >20 we did not find any patient of HbF levels >20 whose TCV was >200 cm/s while 4(6.2%) patients had HbF levels <20with TCV>200cm/s. We have applied Fischer exact test for statistical significance and p value was 0.31. Hence amount of Hb Fpresent in a case of SCA does not influence increase in TCV in our study. In studies by Nancy et al & Kratovil et al have suggested the protective role of Hb F from complication [10,11].

Third factor that was correlatedwas whether the patient was on Hydroxyurea therapy. (Table 5.1) 39 (60.9%) patients out of 64 were on hydroxyurea while

25 (39%) patients were not taking hydroxyurea. Statistically after applying Fischer Exact test between these two group pvalue was 0.034 i.e. less than 0.05 which is statistically significant. As HbF has protective effect against prevention of complicationshence hydroxyurea by increasing HbFlevels reduces complications, number of hospitalizations and hence the morbidity. [10,11,12,13].

As incidence of stroke increases with TCV >200cm/s but patients with velocity 170-199 cm/s alsohave high chances of progressive increasein velocity and sooner they will have velocity >200 cm/s. So this velocity of 170-199 cm/sec comesunder the category of borderline velocity-conditional, hence we have also done statistical analysis of patients with TCV <170cm/sec and > 170cm/sec.In our study of 64 patients, 43 (67.1%) patients had TCV < 170cm/s while 21 (32.8%) patients had >170cm/s. We have analysed these data and tried to find statistical correlation between no. of blood transfusions, HbF and patienton Hydroxyurea.

Soinour study 16 (25%) patients had received >10 times blood transfusion in past whose TCV was >170cm/s while 5 (7.8%) patients received >10 times blood transfusions and TCV in these patients was>170cm/s. By applying Chi square test p value was 0.32 which was not significant . There was no relation of increase in TCV and number of blood transfusions patient had received (Table 3.2).

In our study with TCV <170cm/s, 22 (34.4%) patients had HbF levels <20 while remaining 21 (32.8%) patients had HbF>20while in another group of TCV >170cm/s HbF level was less than 20 in19(29.6%) patients and 2 (3.1%) patients had TCS > 170cm/s (Table 4.2). By applying Chi square P value was 0.002 which was less than 0.05 hence it is statistically significant i.e. there is correlation between amount of HbF present and increase in TCD velocity. Hence increase in HbF levels protects against increasein TCV .

39 (60.9%) patients were on Hydroxyurea therapy whereas 23 (35.9%) patients were not onHydroxyurea. The TCV of patients who were on Hydroxyurea was less than 170 cm/sec in 35 (54.6%) patients while in 41 (64%) it was >170cm/s. (Table 5.2). Study by Ghafuri DL et al, they found that hydroxyurea therapystarted for disease severity prevention decreases the prevalence of abnormal TCD velocities [14]. The SACRED trial states that hydroxyurea lowers the TCD velocities and prevents conversion from conditional (170-199cm/s) to abnormal (greater than or equal to 200cm/s) velocities [13].

In 25 (39%) patients who were not on Hydroxyurea 8 (12.5%) patients had TCV< 170cm/s while 17(26.5%) patients had TCV >170cm/s. By applying Chi square test p value was 0.00015 which was less than 0.05 and hence statistically significant. Hence Hydroxyurea has a protective value against increase in TCV (Table 5.2). Similar results were there in study by Jane et al in which they inferred that hydroxyurea reduces TCD velocities in children with SCA and conditional velocities [12].

The mean velocities in CCA(R) was 110cm/s, CCA(L) 109cm/s, ECA (R) 102 cm/s, ECA(L) 104cm/s,VA (R) 86cm/s, VA (L) 86.7cm/s. Velocities in extracranial arteries have been studied by Deane & Singhal et al in which they found increased velocities in these vessels in children of sickle cell anemia and hence they can be used as screening vessels . In the carotid vessels the sensitivity in identifying and measuring these vessels is more than intracranial vessels and hence carotid vessels can be used as screening vessels in patients with sickle cell anemia [4,5].

Conclusion

Inpatients of Sickle cell anemia stroke is one of the major complication. Doppler screening for tran-scranial velocities can help detect patients at risk of stroke. Number of blood transfusions in past has no relation with stroke.

Raised HbF levels and Hydroxyurea therapy is protective .

Carotid vessels can be used as screening vessels in patients with sickle cell anemia.

Conflict of Interests: None

Limitations of study

Limited sample size.

Area based research.

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