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Physicians' Opinion on the Practice of Exchange Blood Transfusion for Treatment of Stroke in Sickle Cell Anaemia

AJ Madu[1]*, B Nwogoh[2], K Korubo[3], H Okoye[1], C Efobi[4] and N Ugwu[5]

[1]Department of Haematology and Immunology, University of Nigeria Enugu Campus, Nigeria

[2]Department of Haematology, University of Benin, Nigeria

[3]Department of Haematology, University of Port Harcourt, Nigeria

[4]Department of Haematology and Immunology, Chukwuemeka Odumegwu Ojukwu University, Nigeria

[5]Department of Haematology, Teaching Hospital Abakaliki, Nigeria

***Corresponding author:** Anazoeze Jude Madu, Department of Haematology & Immunology, University of Nigeria, Enugu Campus, Nigeria, Tel: +2348037861784; Email: anazoeze.madu@unn.edu.ng

Research Article

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Abstract

Background: The current most effective preventive as well as therapeutic modality for stroke in sickle cell anaemia (SCA) is the use of exchange blood transfusion (EBT) in a chronic transfusion program. The challenges with this procedure abound in some settings without an organized transfusion service

Aim: To assesses the extent of stroke in SCA and to evaluate the opinion of haematologists across Nigeria on issues of acceptability, practice of EBT and challenges of this life-saving protocol.

Materials and Methods: A 12-item pre-validated and pretested questionnaire was used to obtain responses from doctors working in haematology units across the country who attended the annual general meeting of the Nigerian Society for Haematology and Blood transfusion held in October 2016.

Results: 53 out of the 76 doctors who were in attendance, working in 30 health facilities across the country responded. There were 64 cases of stroke in the last 1 year out of 14,788 registered patients, giving a prevalence of 0.46%. Trans-cranial Doppler ultrasonography (TCD) was available in 50% of the centres while 75.9% had computerized tomography (CT) scanning facilities. Majority of the doctors (75.9%) counselled their stroke patients on the need to be placed on a chronic transfusion program while only 15.9% of them got on a transfusion program. EBT was not done in 38.7% of the cases due to poor patient compliance while paucity of safe blood and funds was noted in 16.7% of the cases.78.4% of the doctors would commence EBT if safe blood was available and they had adequate staff and facilities, while 21.6% of the doctors would not.

Conclusion: More tertiary health centres had CT scanning facilities than TCD. The practice of EBT for management of stroke is still poor amongst Nigerian haematologists. Majority of haematologists suggested chronic transfusion program for their SCA stroke patients. The practice of EBT in most cases was hampered by lack of safe blood and poor financial state of the patients.

Keywords: Exchange blood transfusion; Sickle cell; Stroke

Abbreviations: SCA: Sickle Cell Anaemia; EBT: Exchange Blood Transfusion; TCD: Trans-Cranial Doppler Ultrasonography; CT: Computerized Tomography; MRI: Magnetic Resonance Imaging.

Introduction

Sickle cell anaemia (SCA) is an inherited genetic disorder of the beta globin chain with consequent chronic haemolysis and occurrence of vaso-occlusion due to activated leucocytes and deformed red cells. This occlusion also occurs in terminal vasa vasorum supply to the cerebral arterial vasculature (especially the middle cerebral artery) with consequent vascular endothelial necrosis. Healing occurs by fibrous tissue replacement leaving a weakened and dilated saccular aneurysm called "berry" aneurysms.

Rupture of these aneurysms causes haemorrhagic stroke, a distinct feature in some young SCA patients. Some authors have recorded a predominance of ischaemic stroke in children with sickle cell disease [1,2]. The prevalence of stroke in SCA has been estimated to be 12.4 per 1,000 patients by Madu, et al. [3] while higher rates of up to 25-40% had been observed in other populations [4] Stroke prediction by measurement of flow velocity in the middle cerebral artery has been used to identify individuals at risk who are usually commenced on a chronic transfusion program [1,5]. The risk of stroke in patients with velocities above 200m/s has been found to 44% while risk of recurrence after a first stroke is 66%.

Placing patients at risk for stroke on a chronic transfusion program prevents the reoccurrence of stroke and has reduced the prevalence of stroke significantly from 11% to about 1% [6]. Elective long term transfusions are superior to hydroxyurea therapy in the prevention of stroke and may be done by simple top up transfusions or exchange blood transfusion [7]. Transfusion either given as EBT or top up transfusions are not without its risks which include allo-immunization, iron overload and transfusion transmitted infections [8]. Although simple top up transfusions are easier to do, they have the disadvantage of causing hyperviscosity and iron overload, therefore patients on long term top up transfusions will require iron creation therapy at some point [9]. Exchange blood transfusion on the other hand is less associated with iron overload but since it requires more units of blood, may lead to allo-immunization faster. The aim of transfusion therapy is to reduce the percentage of HbS to less than 30% [10].

Chronic transfusions suppress the erythropoietic drive thereby suppressing the production of HbS. This is better achieved with EBT than with top up transfusions because EBT gives a better control of the HbS%, compared to top up transfusions [11]. EBT is therefore superior to both top-up transfusions and hydroxyurea therapy in the primary or secondary prevention of stroke in SCA [12-14]. Paucity of blood and blood components, high cost of transfusion as well as culture of non-acceptance of blood transfusion has greatly hampered the ability of most physicians to institute this treatment protocol. Screening and monitoring of patients requires an available and affordable trans-cranial Doppler ultrasound and means of assessing HbS levels, which may be lacking in most Nigerian tertiary health institutions.

This study seeks to explore the magnitude of the clinical problem that can be ascribed to stroke in sickle cell. We also strived to assess the acceptability of EBT, availability of facilities and blood components in the tertiary health institutions across Nigeria. The practice pattern amongst doctors in haematology units across the country with regards to EBT for stroke in SCA will also be evaluated.

Materials and Methods

This is a cross-sectional observational study conducted amongst different cadre of doctors working in

haematology units in various tertiary health institutions across Nigeria. The data instrument was a 12-item pre-validated self-administered questionnaire. Data was computed and analyzed using SPSS 20.0 (IBM- Chicago Illinois) and results were expressed as proportions, rates and ratios.

Results

There were 53 respondents out of a total of 77 doctors with a median of 6 years working experience in the care of people living with sickle cell were interviewed. These were doctors managing sickle cell patients in 30 health facilities in different parts of the country. Table 1 shows the categories of health institutions which was covered in this survey. Sixty four patients were observed to have been diagnosed with stroke in sickle cell in the past 12 months out of 14,788 patients registered in the various institutions across the country, giving a 0.43% stroke prevalence rate. The years of experience and number of registered patients as well as the number of patients who had stroke in the last one year are shown in Table 2.

No of Institutions represented	23
Nature of Facility	No of respondents
Federal Teaching Hospital	31 (57.4)
Federal Medical Centres	5 (9.3)
State Teaching Hospital	12 (22.2)
General Hospital	1 (1.9)
Private University Teaching Hospital	2 (3.7)
University Health Centre	1 (1.9)
Unspecified	2 (3.7)

Table 1: Types of health institution and number of respondents.

	Median	IQR	Range
Work years experience with SCD patients (Median)	6	4 – 9	Feb-20
Estimate of registered SCD patients	150	35 - 300	Oct-00
Estimate of SCD patients with stroke in last 1 year	1	0.0 – 2.0	0 – 8

Table 2: Years of experience, number of registered patients and one year stroke prevalence.

Facilities for screening using transcranial Doppler ultrasonography was reported to be available in 50% of the tertiary health institutions, while computerized tomography (CT) scanning and magnetic resonance imaging (MRI) was available in 75.9% and 37% of them, respectively. Some institutions had more than one of these facilities while 8% had none. Table 2 shows the category of the health institutions investigated as well as the number of registered patients and the frequency distribution of the stroke patients observed in the past one year. However [10] 19.2 % of the respondents had access to all 3 investigative modalities while [8] 15.4% had none. Manual exchange blood transfusion was the commonest modality of managing stroke in sickle cell as reported by 35 (66%) respondents, 9 (16.9%) respondents had access to automated red cell exchange facilities, while simple top up was used additionally by 13 (24.5%) respondents.

Majority, 75.9% of the doctors would always counsel stroke patients on the need to commence EBT while 15.9% do not routinely counsel these patients on this need. However, only 34.9% of the respondents would always eventually commence EBT on these patients while 65.1% of them would either do this sometimes or not at all. The main reason why EBT was not done (38.7%) was due to poor patient compliance while lack of safe blood and funds for processing blood was the reason in 16.7 % of the cases.

If safe blood was made available, 66% of the doctors would place their stroke patients on a chronic transfusion program, however 34% of them would do this sometimes or not at all. A further 78.4% of them would perform EBT if they also had adequate staff and facilities to do this while 21.6% of the doctors still would not.

With regards to access to facilities for monitoring the outcome of EBT; 20 (37.7%) had HPLC, 27 (50.9%) did microscopy to estimate the percentage of permanently sickled red cells, while 36 (67.9%) respondents relied on overt clinical improvement, either alone or in combination with laboratory parameters. However, 15 (28.3%) respondents relied on clinical improvement alone. See Table 3 for the distribution of facilities and resources for carrying out EBT across health institutions in the country.

Diagnostic facilities available	
CT Scan	41 (75.9)
Transcranial Doppler	27 (50.0)
MRI	20 (37.0)
None	8 (14.8)
Stroke Management Modality	
Automated EBT	9 (16.7)
Top up transfusion	36 (66.7)
Cranial decongestion	13 (24.1)
Manual exchange	5 (9.3)
Referal	2 (3.7)
Others	4 (7.4)
Counselling of EBT/Chronic transfusion Programme	
Yes	37 (68.5)
No	8 (14.8)
sometimes	6 (11.1)
Application of Chronic Transfusion Program	
Yes	17 (31.5)
No	18 (33.3)
sometimes	15 (27.8)
No response	4 (3.7)
Reasons for lack of chronic transfusion plan	
Lack of safe blood	5 (9.3)
Lack of Funds	6 (11.1)
Lack of manpower	5 (9.3)
Poor patient's compliance	12 (22.2)
Not convinced of its efficacy	1 (1.9)
Others	4 (7.4)
If safe blood is available, would you recruit SCD patients with Stroke into a chronic transfusion programme?	
Yes	34 (63.0)
No	9 (16.7)
Not sure	8 (14.8)
If facilities and support staffs are available, would you recruit SCD patients with Stroke into a chronic transfusion programme?	
Yes	40 (74.1)
No	6 (11.1)
Not sure	5 (9.3)
Available facilities for monitoring effectiveness of EBT in Stroke SCD patients.	
HPLC	21 (38.9)
Percentage of sickled cells	23 (42.6)
Clinical improvement	37 (68.5)

Discussion

Sickle cell disease is the most common inherited disease in Africa and carries a high mortality of some of which is due to stroke. This study found that the prevalence of stroke in Nigeria is 0.43%. This is significantly lower than the prevalence rate observed in a study done in Port Harcourt, Nigeria [15] and also by Munube, et al. [16] in Uganda which stated the prevalence as 4.3% and 6.8% respectively. This observed difference may be due to the nature of this study which is questionnaire based. However, Munube retrospectively studied the prevalence in children admitted with sickle cell in emergency room and this might account for the higher prevalence values noted. It also may have been affected by the age of the study population, as stroke occurring in SCA is commoner in children who are managed more frequently by paediatricians than haematologists.

Screening for the risk of stroke in SCA patients is done using a transcranial Doppler. Nigeria is one of the countries most affected by SCA with a prevalence rate of 2%, unfortunately facilities for transcranial Doppler were only available in about 50% of the tertiary centres in the country. This directly impacts on the number of patients who can be identified as being at risk and therefore intervention with EBT cannot be achieved. Lack of a modality for screening of this debilitating complication increases the number of patients who eventually develop stroke, thereby increasing the morbidity and mortality from stroke. Computerized tomography, though available in several centres may not be affordable as a screening modality.

Exchange blood transfusion is the recommended therapy in stroke prevention [7]. It may be performed manually or by red cell apheresis with the use of an apheresis machine. Manual exchange is easier, does not require much training and can be performed at the patient's bedside. Manual exchange are not as effective as automated exchange in reducing the HbS percentage but can still achieve this if the procedure is performed regularly, [17] though with a higher risk of iron overload than automated exchange. Automated EBT is a faster and neater procedure which takes approximately 2 hours but requires sophisticated machines and trained health personnel. As a developing nation, only a few centres in Nigeria currently have the facility for automated red cell exchange. This procedure (manual or automated) is used of importance in both the treatment and prevention of stroke in sickle cell. Unfortunately, our study shows that only about a third of the haematologists will definitely commence exchange blood transfusion on patients "at risk" or those who have already developed stroke. This is similar to the findings of the study by Diaku-Akinwunmi, et al. [18] also done across several Nigerian health facilities [18]. This shows a poor acceptance of the practice of EBT in our environment which is most likely due to challenges in availability of safe blood for transfusion in this environment as observed by Ahmed and his colleagues in a study conducted in Northern Nigeria [19] and also the financial burden on the patients and their relatives. The practice of EBT as observed in this study is contrary to what is obtainable in other climes as observed by Ohene-Frempong [20].

Although EBT significantly reduces the incidence of stroke in SCA patients, our study showed that 21.6% of the respondents will still not perform EBT even if safe blood was readily available. The reason as to why they would withhold EBT from their patients was not stated, but it may be related to the cumbersome nature of performing a manual EBT since facilities for automated EBT was only available to about 16.9% of the haematologists. It is noteworthy that similar patterns have been observed with regards to physicians' attitude to chronic transfusion in sickle cell patients [21]. Also of note is that some physicians may be of the opinion that oral hydroxyurea may be as effective as EBT in the prevention of stroke in SCA; a rather contentious but yet to be widely accepted opinion.

We found out that manual exchange blood transfusion was the commonest modality for managing stroke in sickle cell disease amongst the respondents followed by simple top up transfusion and automated red cell exchange facilities in that order. This was also observed by Lindsey T, et al. [22] who noted that manual exchange blood transfusion is what is available in most hematology programs. This is probably due to cost of machinery required for automated exchange. The risk of iron overload from simple transfusions may favor manual EBT performed by the respondents as suggested by Savage WJ and colleagues [23].

Just as observed by Makani, et al. [24] this study shows the poor distribution of facilities required for screening of patients at risk for stroke [24]. Majority (78.4%) of the respondents were willing to do EBT for their stroke or at risk patients if necessary facilities and personnel were available. There is urgent need for provision of basic facilities for early detection and management of stroke to all government owned hospitals in Nigeria, especially in

states with higher burden of sickle cell disease so as to reduce mortality and morbidity associated with it. The efficacy of a chronic transfusion program has to be assessed using quantitative methods to determine the percentage of HbS to ensure that it is <30%. Unfortunately, HPLC facilities are still lacking in a lot of centres as only 37.7% of haematologists had access to this facility. The majority of respondents had to rely on clinical parameters and changes in the blood film for patient monitoring.

Conclusion and Recommendations

This study found that the practice of exchange blood transfusion for management of stroke in sickle cell disease patients in Nigeria is still poor and is mostly due to non-availability of safe blood and poor patient compliance as well as lack of adequate facilities and personnel. Moreover, haematologists were more willing to perform an automated rather than manual EBT. Haematologists should also be ready to carry out manual EBT in stroke or at risk SCA patients since that is the readily available method of EBT in most centres in Nigeria.

There is need for more effective counselling of patients on importance of exchange transfusion in prevention and management of stroke in sickle cell disease patients, provision of safe blood for transfusion and adequate facilities for screening and follow up of stroke patients. The burden of sickle cell anaemia in Nigeria warrants the provision of facilities required in the holistic management of the disease.

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