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Original article

Use of Transcranial Doppler for the Monitoring of Major Sickle Cell Syndromes in Senegal: A Preliminary Analysis

Utilisation du Doppler transcrânien pour la surveillance des syndromes drépanocytaires majeurs au Sénégal : une analyse préliminaire

I Diop*[1,4], ID Ly[2,4], MA Ndao[4], A Kane[2,4], S Dieye[4], AL Fall[2,4], I Diagne[3], O Ndiaye[2,4]

Résumé

La vasculopathie cérébrale expose les patients atteints de syndromes drépanocytaires majeurs (SDM) à un risque élevé d'accident vasculaire cérébral (AVC), pouvant entraîner la mort ou un handicap significatif. Le Doppler transcrânien (DTC) est une technique d'imagerie médicale non invasive qui mesure la vitesse du flux sanguin dans les vaisseaux cérébraux et détecte le risque de cette complication majeure de la drépanocytose. L'introduction d'un traitement transfusionnel approprié réduit le risque de morbidité et de mortalité chez les enfants. Au sein de l'Unité de Soins Ambulatoires pour Enfants et Adolescents Drépanocytaires (USAD) du Centre Hospitalier National d'Enfants Albert Royer (CHNEAR), la réalisation du DTC a été initiée en 2021. L'objectif de notre étude était de décrire les résultats obtenus lors du suivi des patients ayant bénéficié du DTC.

Il s'agissait d'une étude rétrospective, descriptive et analytique chez des patients suivis pour SDM à l'USAD ayant réalisé un Doppler transcrânien du 30 juin 2021 au 30 juin 2022.

Au cours de notre période d'étude, 4836 patients atteints de SDM ont été consultés, parmi eux, 51 ont bénéficié d'un DTC, soit un taux de réalisation de 1,16 %. Le ratio de sexe était de 1,78 et l'âge moyen était de 7,2 ans. Les enfants âgés de 6 à 10 ans étaient majoritaires (75,51 %). Concernant les résultats du DTC, 4 (7,85 %) étaient pathologiques, 8 (15,68 %) étaient limites et 39 (76,47 %) étaient normaux. Un lien statistiquement significatif a été établi entre les antécédents d'hospitalisation, le taux de réticulocytes (>150000 éléments/mm³) et la survenue de vitesses circulatoires anormales au DTC. Les patients présentant des DTC pathologiques ont été mis sous un sous-programme de transfusion mensuelle pendant 3 mois. L'hydroxyurée a été proposée en relais aux transfusions. Le suivi était trimestriel pour les résultats limites et annuel pour les résultats normaux. L'échographie Doppler transcrânienne permet de détecter précocement la vasculopathie cérébrale chez les enfants drépanocytaires, prévenant ainsi les AVC. Cette étude sénégalaise souligne l'importance d'un dépistage systématique pour améliorer la prise en

charge thérapeutique.

Mots-clés : échographie Doppler transcrânienne, vasculopathie cérébrale, drépanocytose, prévention des AVC.

Abstract

Cerebral vasculopathy exposes patients with a high risk of stroke in people with major sickle cell syndromes (MDS). This can lead to death or significant disability. Transcranial Doppler (DTC) is a non-invasive medical imaging technique that measures the speed of blood flow in the vessels of the brain and detects the risk of this major complication of sickle cell anemia. The introduction of appropriate transfusion therapy reduces the risk of morbidity and mortality in children. Within the Outpatient Care Unit for Children and Adolescents with Sickle Cell (USAD), of the Albert Royer National Children's Hospital Center (CHNEAR), the realization of DTC was initiated in 2021. The objective of our study was to describe the results obtained during the follow-up of patients in whom DTC was performed.

This was a retrospective, descriptive, and analytical study in patients followed for SDM at the USAD who underwent transcranial Doppler ultrasound from June 30, 2021 to June 30, 2022.

During our study period, 4836 patients with SDM were seen in consultations, among them, 51 had benefited from DTC, i.e. a completion rate of 1.16%. The sex ratio was 1.78 and the average age was 7.2 years. Children aged 6-10 were in the majority (75.51%). Regarding DTC results, 4 (7.85%) were pathological, 8 (15.68%) were borderline, and 39 (76.47%) were normal. A statistically significant link was found between the history of hospitalization, the reticulocyte rate (>150000 elements/mm³) with the occurrence of abnormal circulatory velocities at DTP. Patients with pathological DTCs were put on a monthly transfusion subprogramme for 3 months. Hydroxyurea was offered as a relay to transfusions. Monitoring was quarterly for borderline results and annual for normal results. Transcranial Doppler ultrasound detects cerebral vasculopathy early in children with sickle cell disease, thus preventing stroke. This Senegalese study highlights the importance of systematic screening to improve therapeutic management.

Keywords: Transcranial Doppler ultrasound, cerebral vasculopathy, sickle cell disease.

Introduction

Sickle cell disease is the most common genetic disease in the world. It was recognized as a public health priority by international organizations between 2005 and 2008 [1]. Remarkable progress has been made in the management of the disease in the countries of the North, allowing a considerable improvement in the quality of life and life expectancy of patients. The situation is different in Africa, where patients encounter difficulties in accessing health facilities, consult especially at the stage of complications in facilities where specialists are absent or few in number and where the training of caregivers on sickle cell disease is insufficient [2]. Among the acute complications, severe vaso-occlusive accidents such as cerebrovascular accidents (CVAs) are the most dreadful. These strokes are responsible for heavy morbidity, high mortality and disability, due to motor, sensory-sensory, cognitive and psychological sequelae [3]. Indeed, sickle cell anemia is the 1st cause of stroke in children [4]. This risk in children with sickle cell disease is multiplied by 300, compared to children without sickle cell disease [5].

These strokes are the clinical expression of a cerebral vasculopathy that has been silent for a long time, which can be detected using DTP. It is a non-invasive medical imaging technique, used to identify patients at risk of stroke [6]. It was initiated by Adams in the 1990s in the USA [7]. Any recording of an abnormal acceleration of circulatory velocity, diffuse or localized, indicates the constitution of one or more arterial stenosis, constituted or pre-symptomatic [8].

Since the end of the 2000s, some teams in Sub-Saharan Africa have been implementing this screening as part of paediatric follow-up.

In Senegal, transcranial Doppler screening for cerebral vasculopathy is not yet systematic. There are no data on the velocimetric study of sickle cell patients. This is how we carried out this work, the general objective of which was to study cerebral circulatory velocities by DTC in children followed for SDM, and more specifically, to look for a relationship between DTC results and clinical and paraclinical data.

Methodology

We conducted a retrospective study (June 30, 2021 to June 30, 2022), descriptive and analytical. We conducted our study at the CHNEAR paediatric department in Dakar. We included all patients followed at the USAD for MDS and in whom a transcranial Doppler was performed during the study period, and whose records were available and usable.

We collected sociodemographic, clinical and paraclinical data, using a survey sheet.

The transcranial Doppler examination was done with a LOGIQ™ brand device by the same operator. A 2 Mhz probe was used. The examinations were performed in the temporal window (right, left) and in the occipital window using color Doppler and pulsed Doppler. The averages of the maximum velocities, obtained after a manual tracing of the envelope of a cycle, were recorded on the anterior, middle, posterior, carotid cerebral arteries and the basilar trunk.

We studied the following parameters:

- socio-demographic data: age, sex;
- clinical signs: history, examination signs;
- paraclinical examinations: haemoglobin levels, white blood cells, reticulocyte levels;
- DTC ultrasound results.

The report was written in the form of a table giving the speed of blood circulation in the nine (9) arteries studied.

The test result was classified into one of four categories: normal, borderline, pathological, or incomplete.

- Normal examination: all circulatory velocities are less than 170 centimetres per second.
- Limit examination: one of the speeds is between 170 centimeters per second and 199 centimeters per second.
- Pathological examination: at least one speed is greater than or equal to 200 centimetres per second
- Incomplete examination: If an artery is not visualized

The data was captured using Excel 2013 and analysed using Epi info 7.2 software. The significance threshold was a p-value of less than 0.05.

Results

During our study period, 4836 patients with major sickle cell syndrome were seen for consultations, among them, 51 had benefited from DTP. The mean age of patients was 7.2 years +/- 2.74 years and the median was 7.5 years, with extremes ranging from 3 years to 14.58 years.

- Sex

The male patients were 33/51, i.e. a sex ratio of 1.78.

- Clinical signs

On physical examination, the most frequently observed signs were pallor of the mucous membranes and jaundice. Other signs found were splenomegaly and neurological deficits. (Table II)

- Paraclinical signs

The main blood count parameters of patients are shown in Table III.

Circulatory velocities were normal in 39/51 patients and abnormal in 12/51 patients, including 8 patients with limit velocities and 4 patients with pathological velocities. (Table IV)

- Pickup

Quarterly monitoring was performed in patients with borderline EDTC results.

An annual check-up was offered to children with normal circulatory velocities, EDTC.

Patients with pathological circulatory velocities at EDTC were put on a monthly transfusion subroutine. Hydroxyurea was offered as a relay to the transfusion program, in patients with pathological circulatory velocities. (Table V)

Table I: Distribution of patients by age group

Age range	Number (N)	Percentage (%)
3-6 years	8	15,68
6-10 years	39	76,47
More than 10 years	4	7,85
Total	51	100

Table II: Main clinical signs observed in patients.

Clinical signs	Frequency (N)	Percentage (%)
Pallor of mucous membranes	16	53,34
Jaundice	10	33,34
Splenomegaly	2	6,66
Motor deficit	1	3,33
Language disorder	1	3,33
Total	30	100

Table III: Main parameters of the patient's blood count

Blood count parameters	Average	Deviation	Median	Extreme
White blood cells (/mm3)	15.540	6.095	14.635	4300-35.090
Platelets (/mm3)	446.458	140.774	442.000	130.000-487.000
Hb (g/dl)	8,17	1,10	7,9	6,5-11
Reticulocyte count (/mm3)	299.221	100.931	284.300	148.928-460.000

Table IV : Patients' EDTC results.

Results	Frequency (N)	Percentage (%)
Speed limits	8	15,68
Normal speeds	39	76,47
Pathological Velocities	4	7,85
Total	51	100

Table V: Patient Management by EDTC Outcome

Type of care	Frequency (N)	Percentage (%)
3-month check-up	8	15,68
12-month check-up	39	76,47
Hydroxyurea + Transfusion Program	4	7,85
Total	51	100

Table VI: Factors Associated with Abnormal Circulatory Velocities

Comparison with the variables studied		Abnormal circulatory velocities	Chi2	P
Clinical aspects				
Fixed-term contract anemia	Yes	3 (33,33)	1,11	0,29
	No	3 (15,79)		
Fixed-term contract pain	Yes	1 (11,11)	0,83	0,40
	No	5 (26,32)		
CDD Infection	Yes	1 (12,5)	0,53	0,47
	No	5 (25)		
ATCD transfusion	Yes	8 (32)	0,81	0,36
	No	4 (20)		
ATCD CVO	Yes	12 (30,77)	2,51	0,11
	No	0 (0)		
ATCD hospitalization	Yes	11 (35,48)	3,96	0,05
	No	1 (7,14)		
		4 (22,22)		
Paraclinical aspects				
Type of sickle cell disease	SS	12 (25)	0,33	0,57
	SC	0 (0)		
Low base Hb	7	6 (35,3)	0,38	0,83
	8	5 (41,7)		
	9	1 (25)		
Leukocytes	>10000 elements/mm3	10 (27,78)	0,24	0,62
Reticulocytes	>150000	01 (10)	4,95	0,026
	<150000	1(100)		

Discussion

We recorded 51 transcranial Doppler ultrasound (DTAC) results, the number of patients recorded during our study was significantly lower than that of the series in the studies carried out in Mali, Côte d'Ivoire and the Arabian Peninsula with 572, 200 and 415 patients respectively [10,11,15]. Indeed, the small size of our sample can be explained, on the one hand, by the fact that it is a new activity initiated within the framework of the USAD project, and on the other hand, by the lack of human resources trained in the realization of DTC within the hospital. The average age in our patients was 7.2 years ± 2.7 years with extremes of 3 to 15 years. The age group of 6 - 10 years old was the most represented. This frequency of the first decade was found in some African studies [10, 11]. In our study population, male patients were the most represented with 32/51 patients, or 64%.

We did not find a statistically significant association between sex and the existence of abnormal circulatory velocities. Our results were similar to those of Niamkey et al, Côte d'Ivoire [11]. The clinical signs found in the study population were generally signs of hemolysis, namely mucosal pallor, jaundice and splenomegaly. Patients with abnormal circulatory velocities showed overall evidence of anemia, which supports the inverse relationship between hemolytic phenotypes and elevated circulatory velocities [10,18].

Indeed, the lower the baseline hemoglobin level, the greater the risk of increased circulatory speeds. These children had a history of hospitalization, blood transfusion, and other comorbidities. Moreover, a statistically significant relationship was observed between the history of hospitalization and a pathological EDTC result (p=0.05). In reality, hospitalizations are indicated in the event of complications of sickle cell anemia. They are the expression of a relatively symptomatic form of sickle cell anemia.

Biologically, the average hemoglobin level in our population was 8.17 g/dl ± 1.10 with extremes of 6.5 to 11 g/dl. We did not find a statistically significant relationship between patients' haemoglobin levels and alterations in cerebral artery circulation velocities. Our results were comparable to those of Niamkey et al, in Côte d'Ivoire [11]. However, other studies in Mali and Kenya had found an inversely positive relationship between patients' hemoglobin levels and circulatory velocity abnormalities [10, 12]. The mean white blood cell count in our study population was 15540 elements/mm3 ± 6095, with extremes of 4300 to 35090 elements/mm3. Indeed, the number of white blood cells is classically increased in carriers of SS and Sβ° sickle cell anemia, achieving leukocytosis, even in the absence of bacterial infection [13].

The existence of a significant relationship between increased leukocyte counts and cases of pathological or borderline EDTC raises questions about the role of these abnormalities in the pathogenesis of cerebral vasculopathy. Nevertheless, we did not find a significant link between the existence of hyperleukocytosis greater than 10,000 elements/mm3 and the occurrence of abnormal circulatory velocities. In Nigeria, Lagunju et al., reported in 2012 a statistically significant relationship between white blood cell count and abnormal circulatory velocities [14]. The mean number of reticulocytes in our population was 299221 elements/mm3 ± 100931, with extremes of 148928 to 460000 elements/mm3. A statistically significant relationship was observed (p = 0.026), as in the work of Adekile et al in the Arabian Peninsula, and in Nigeria [14, 15]. Indeed, reticulocytes are markers of bone marrow regeneration, in response to hemolysis phenomena. Bone marrow activity and hemolysis phenomena can cause endothelial activation and subsequent damage, as reported by Sommet et al, [16]. These abnormalities are thus likely to contribute to a rheological alteration in the cerebral circulation, responsible for vaso-occlusion, the starting point of cerebral vasculopathy. Therapeutically, quarterly monitoring was performed in patients with borderline EDTC results, i.e. 15.68% (8). An annual check-up was offered to those with normal circulatory speeds, i.e. 76.47% (39). Patients with pathological circulatory velocities were put on a monthly transfusion subroutine, i.e. 7.85% (4). Hydroxyurea was offered as a relay to the transfusion program, in patients with pathological circulatory velocities. The same types of care were reported in other African countries, including Mali, Nigeria, Niger and Côte d'Ivoire [10, 11, 14, 17].

Looking to the future, we recommend that EDTCs continue to be carried out to include a greater number of patients in order to have more perspective in the follow-up. Thus, the long-term evolution of patients with borderline or pathological EDTC results will make it possible to assess the prognosis and make recommendations according to the local context.

Conclusion

Transcranial Doppler ultrasound is an important examination in the early detection of cerebral vasculopathy in children with major sickle cell syndromes. It is an effective means of primary prevention of the risk of strokes, a major cause of disability, with the risk of recurrence. It is also a tool to help with therapeutic decision-making, in the event of a pathological result.

This preliminary study detected cerebral vasculopathy in patients followed for SDM at USAD, Senegal. These results underline the need to integrate this examination into the follow-up of children for systematic screening for cerebral vasculopathy and stroke prevention.

***Correspondence**

Ibrahima DIOP

ibkeb86@gmail.com

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1 : Private Institute for Medical Training and Research (IPFORMED)
2 : Cheikh Anta Diop University (UCAD)
3 : Faculty of Health Sciences, Gaston Berger University, Saint Louis
4 : Albert Royer National Children's Hospital, Dakar, Senegal

Conflict of interest : None

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