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CONTRIBUTION OF A TYPE VASODILATOR GINKGO BILOBA IN REDUCING THE OCCURRENCE OF SICKLE CELL VASO-OCCLUSIVE CRISES IN THE HEMATOLOGY DEPARTMENT OF IGNACE DEEN UNIVERSITY HOSPITAL IN CONAKRY

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SUMMARY

Introduction: Sickle cell anemia is a hemoglobinopathy linked to a structural abnormality of the globin beta chain. **Objective:** evaluate the effectiveness of Ginkgo Biloba extract in reducing sickle cell vaso-occlusive crises. **Methods**: this was a descriptive and analytical observational cohort study involving two groups of sickle cell patients: Group 1 consisting of patients on Ginko Biloba derivatives with symptomatic treatment and Group 2 benefited only from symptomatic treatment. **Results:** We selected 80 patients and we found a statistically significant reduction (P = 0.03) in STA with an average of (0.15 ± 0.48) in patients in group 1 compared to those in group 2 (0.43±0.63), a statistically significant reduction (P=0.05) in abdominal pain crisis in patients in group 1 compared to those in group 2 as well as in priapism (P=0.03) compared to group 2. A statistically significant reduction (P = 0.05) in the number of hospitalizations in patients in group 1 compared to those in group 2. However, the reduction in osteoarticular pain crises was not significant (P = 0.38) with an average of (1.77 ± 1.73) in patients in group 1 compared to those in group 2 (2.2 ± 1.68). Regarding chronic ischemic complications, aseptic necrosis of the femoral head was less frequent (38.80%) in patients in group 1 compared to those in group 2 (56.25%). Microalbuminuria was less frequent (27.53%) in patients in group 1 compared to those in group 2 (37.50). **Conclusion :** With the difficulties of access to hydroxyurea in our context, Ginko Biloba Extracts can be used in our context, as alternatives in the basic treatment of sickle cell patients.

KEYWORDS: Ginkgo biloba, CVO, Sickle cell disease, CHU Ignace Deen Conakry.

INTRODUCTION

Vaso-occlusive crises (VOC) are the clinical manifestation of the polymerization of hemoglobin S, the deformation of red blood cells, their adhesion to the endothelium and the increase in blood viscosity, leading toaischemia andtheretissue necrosis in the affected area.[1]

The frequency of CVO varies depending on the age of sickle cell patients; it is estimated between three and ten per year in adults according to certain authors, two and five per year in children.[2]

Nowadays, the effectiveness of hydroxyurea has been demonstrated in reducing the occurrence of vaso-occlusive crises as well as certain major complications of sickle cell disease while having low toxicity. However, this molecule remains poorly accessible in sub-Saharan Africa and its cost remains high, estimated at $65 for a patient weighing 30 kg on average.[3]

Ginkgo biloba extract is a vasodilator frequently prescribed in certain sub-Saharan African countries to reduce the occurrence of CVO and certain major complications of sickle cell disease, however its effectiveness has not been regularly demonstrated.[2]

In 2008 in Mali in a study carried out on the evaluation of the quality of the management of sickle cell disease by health workers, 72.1% of health workers prescribed

vasodilators in the management of the sickle cell crisis. and 78.69% systematically prescribed vasodilators outside of sickle cell crisis. Among these vasodilators the most prescribed was Ginkgo biloba extract.[4]

The high frequency of prescription of vasodilators (Ginkgo biloba extract), the absence of previous studies showing the effectiveness of Ginkgo biloba extract in reducing vaso-occlusive crises, as well as the desire to explore avenues of access to care for patients leaving in our contexts where everything is the responsibility of the patient, motivated the completion of this work. The aim of this study was to evaluate the effectiveness of Ginkgo biloba extract in reducing the occurrence of sickle cell vaso-occlusive crises in the hematology department of the Ignace Deen National Hospital.

MATERIAL AND METHODS

It was a 9-months descriptive and analytical observational cohort study on two groups of patients with sickle cell disease:

- Group 1: represented sickle cell patients whose basic treatment had been Ginkgo Biloba extract for 6 months, folic acid and usual analgesics with a total treatment duration of one year.
- Group 2: represented sickle cell patients who were naive to Ginkgo Biloba extract and had only folic acid and usual analgesics as basic treatment.

They were followed from September 1, 2022 to May 31, 2023 with an assessment of complications at inclusion and at the end of the study.

Study variables

Our variables were qualitative and quantitative divided into sociodemographic, clinical and paraclinical data.

Collection Procedure and Technique

Our data was collected according to this procedure:

- ✓ The investigation was carried out on the files of patients who came for consultation and those hospitalized for sickle cell disease while seeking the regular intake of a Ginkgo biloba extract.
- ✓ We then carried out monthly patient checks to ensure therapeutic compliance and determine the number of CVOs.
- ✓ At inclusion and at the end of the study, we performed a complete blood count, an ECG, a pelvic X-ray and a urine dipstick in all patients to look for ischemic complications.

Data analysis

Our data were analyzed using the EPI INFO software in version 7.4.0; the different epidemiological, clinical and paraclinical parameters were compared.

- The chi-square or Fisher exact test for comparing proportions or for estimating the association between two qualitative variables.

For any p-value less than or equal to 0.05 the statistical test was significant.

Ethical and Deontological consideration

The identity and confidentiality of patients were respected,written consent hassummerobtained for all participantsjust as the data collected and the results obtained were used only for scientific purposes.

RESULTS

We retained 80 patients divided into 2 groups.

A female predominance was noted in both patient groups with a M/F sex ratio of 0.8.

Concerning profession, pupils/students were the most represented in both groups followed by housewives.

The most common sickle cell form in both groups was the homozygous SS phenotype (92.5%).

Osteoarticular pain crises were the most frequent in the two groups of patients, the statistical analysis showed a non-significant decrease in the number of osteoarticular pain crises (P = 0.38) with an average of (1.37 ±1.27) in group 1 compared to group 2 (1.55± 1.10).

A statistically significant reduction in the number of Acute Chest Syndrome (P = 0.03) with an average of (0.15 ± 0.48) compared to group 2 (0.42 ± 0.47), in the number of priapism (P= 0.03) with an average of (0.02 ± 0.15) compared to group 2 (0.25± 0.63), the number of hospitalizations (P = 0.05) with an average of (0.90 ±1.01) compared to group 2 (1.30 ±0.67).

An abnormal pelvic x-ray was found in (32.50%) in group 1 versus (40.0%) in group 2. Among the complications, osteonecrosis of the femoral head was less frequent in group 1 (38. 80%) compared to group 2 (56.25%). A positivity of microalbuminuria in group 1 was lower (27.53%) than that in group 2 (37.50%).

	Group 1 N = 40	**Group 2 N=40**	**Value**
Sociodemographic characteristics			
Sex	Sex ratio (M/F) = 0.8	Sex ratio (M/F) = O.8	
Middle age Extremes 6 years and 46 years	23.16 years ± 8.87 years	22.15 years ± 8.75 years	
Types of sickle cell disease			
SSFA2	37 (92.50%)	37 (92.50%)	
symptomatic AS	1 (2.50%)	1 (2.50%)	

SC	1 (2.50%)	1 (2.50%)	
S/B0Thalassemia	1 (2.50%)	1 (2.50%)	
CVO numbersand acute complications			
Osteoarticular pain crisis	1.37± 1.27	1.57±1.10	0.38
STA	0.15± 0.48	0.42±0.47	0.03
Abdominal pain crisis	0.025 ± 0.15	0.25±0.65	0.06
Priapism	0.02 ± 0.15	0.25 ± 0.63	0.03
Number of hospitalizations during the six months.			
	0.90 ±1.01	1.30 ±0.67	0.05
Bone complications			
Osteonecrosis of the femoral head	5 (12.5%)	9 (22.5%)	
Osteomyelitis	1(2.5%)	-	
Coxarthrosis	7 (17.5%)	7 (17.5%)	
Kidney complications			
Microalbuminuria N	4 (10%)	7 (17.5%)	
Microalbuminuria 2N	6 (15%)	6 (15%)	
Microalbuminuria 3N	1 (2.5%)	2 (5%)	

DISCUSSION

Improving the quality of care for sickle cell patients in our country with the reduction of vaso-occlusive crises and chronic complications is an obligation. This is why we undertook a descriptive and analytical observational cohort study involving two groups of patients.

Difficulties and Limitations

The low socio-economic level of patients prevented certain examinations from being carried out (cardiac Doppler ultrasound, MRI).

We haveretained 80 patients for the groups.

Uno female predominancewas notedin both patient groups with a M/F sex ratio of 0.8. Our data are similar to those found by Traoré M in Mali in 2021 who reported a female predominance with a sex ratio of 0.8.[5] Unlike the study carried out by Sidibé M. in Guinea in 2022 which reported a predominance of the male sex with 50.4%. These results confirm the literature data which states that it is an autosomal genetic disorder not linked to sex.

The most common sickle cell form in both groups was the homozygous SS phenotype (92.5%). Our study converges with that found by Roger D et al in Benin in 2018 who found that the homozygous SS phenotype dominated with (71.1%).[6] This high frequency in Guinea of the homozygous SS phenotype could be explained by the high frequency of consanguineous marriage among Guineans.

Regarding the nature of the vaso-occlusive crises, painful osteoarticular crises were the most frequent in both groups of patients, the statistical analysis showed a non-significant decrease in the number of painful osteoarticular crises (P = 0.38) with an average of (1.37 ± 1.27) in group 1 compared to group 2 (1.55 ± 1.10). This reduction, although not statistically significant, could be explained by the vasodilatory action of ginkgo biloba extract on small vessels (bone and joint arterioles) but also by its inhibitory activity on the effects of certain inflammatory mediators. (histamine, bradykinin, etc.) which are involved in the pathophysiology of vaso-occlusive crises.[7]

However, in our observation we noted a statistically significant reduction in the number of Acute Chest Syndrome (P= 0.03) with an average of (0.15 ± 0.48) compared to group 2 (0.42 ± 0. 47). These results could be explained on the one hand by the vasodilation induced by ginkgo biloba facilitating the circulation of sickle cells and on the other hand by the inhibitory action of ginkgo biloba on PAF and on certain mediators of inflammation thus reducing the inflammation but also platelet and erythrocyte adhesion to the vascular wall which are responsible for bone (ribs) and pulmonary infarction.

Indeed, thoracic syndrome results from several mechanisms
Pulmonary infarction in situ linked to increased adhesion of erythrocytes to the endothelium responsible for a prothrombotic state, inflammation and dysregulation of vascular tone with vasoconstriction.[8]

In our series we noted a statistically significant reduction in the number of priapisms (P = 0.03) with an average of (0.02 ± 0.15) compared to group 2 (0.25 ± 0.63). This result could be explained on the one hand by the activities of ginkgo biloba extract on microcirculatory rheology and the vasomotion of the vessels, and on the other hand by the anti-edematous action of the molecule. Indeed, venous congestion or sleep vagotonia would lead to a circulatory slowdown, with a drop in PO2, a sickling factor, itself aggravating stasis and promoting thrombosis of the corpora cavernosa following their obstruction by sickle cells, leading to blood stasis. , hypoxia and acidosis.[9]

We noted a statically significant reduction in the number of hospitalizations (P = 0.05) with an average of (0.90 ±1.01) compared to group 2 (1.30 ±0.67). This result could be explained by the fact that patients in group 1 had less CVO, which is the most frequent reason for hospitalization in sickle cell patients compared to group 2.

In our cohort, an abnormal pelvic x-ray was found in (32.50%) in group 1 versus (40.0%) in group 2. Among the complications, osteonecrosis of the femoral head was less frequent in group 1 (38.80%) compared to group 2 (56.25%). This result could be explained on the one hand by the vasodilator effect of ginkgo biloba on the small vessels which vascularize the femur and on the other hand by its PAF inhibitory action. Indeed, small vessels are quickly obstructed in the event of cellular adhesion to the vascular endothelium and hemolysis resulting in ischemia, hypoxia and necrosis.[1]

Microalbuminuria positivity in group 1 was lower (27.53%) than that in group 2 (37.50%). Indeed, recurrent vaso-occlusive crises lead to a progressive deterioration of renal perfusion and a loss of nephrotic mass, which results in the appearance in the first decade of life of renal impairment, the prevalence of which is estimated at 25%. in children and adolescents and reaches 40% in adults.[10] Thus the reduction in renal vaso-occlusion by ginkgo biloba could explain this result.

CONCLUSION

With the difficulties of access to hydroxyurea in our context, Ginko Biloba Extracts can be used in our context, as alternatives in the basic treatment of sickle cell patients. A multicenter evaluation would allow a broader reading.

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