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Research Article

Evaluation of Advanced Oxidation Protein Products in Sickle Cell Disease in Brazzaville

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Abstract

The main objective of this study was to evaluate advanced oxidation protein products (AOPPs) in sickle cell nephropathy. This was a case-control study of 70 patients. They were subdivided into 2 groups: The group of 30 patients with nephropathy called the case group and the control group consisting of 40 people, subdivided into 2 groups: the T1 group with 20 SS patients without nephropathy and the T2 group with 20 AA patients without nephropathy. There was a small increase in the AOPPs in the group of patients with nephropathy compared with the control group (P = 0.053). Renal biomarkers showed no statistically significant difference (P > 0.05). No correlation was found between AOPPs and renal clearance and between AOPPs and microalbuminuria (r = 0,07; r = 0,043 and P > 0,05). The small sample size of this study does not allow the necessary conclusions to be drawn regarding the effects of AOPPs in sickle cell disease in the Congolese population, especially as this is a preliminary study.

Keywords: Sickle Cell Disease; Nephropathy; Advanced Oxidation Protein Products (Aopp)

Introduction

Sickle cell disease is an autosomal recessive inherited disorder linked to the mutation of a gene coding for the beta-globin chain of glutamine in position 6 replaced by a valine [1]. In sickle cell disease, the auto-oxidation of hemoglobin produces an excess of free radicals that cause oxidative stress, leading to increased oxidation of biomolecules [2,3]. This production could be involved in the development of renal abnormalities in sickle cell patients. The progression of renal abnormalities is often accentuated by the accumulation of reactive oxygen species (ROS) free radicals leading to oxidative stress [4]. The prevalence of sickle cell nephropathy also increases with age and varies around 5-18% [5,6]. Several studies have shown the involvement of oxidation products of biomolecules in sickle cell renal defects, the most important of which are advanced oxidation protein products (AOPPs) [7].

Patients and Methods

This was a case-control study conducted between June and November 2021. The pre-analytical stage consisted of a simple random draw. The data were collected using a questionnaire on a form guaranteeing confidentiality. At the end of this draw, 70 patients aged 18 years or more were included. They were divided into two groups: the group of 30 patients with nephropathy and the group of controls consisting of 40 patients subdivided into two

groups: group T1 with 20 SS patients without nephropathy and group T2 with 20 AA patients without nephropathy carried out at the National Reference Center for Sickle Cell Disease "Madam Antoinette Sassou Nguesso" in Brazzaville. Venous sampling was performed at the elbow folds for all patients included in this study. Two dry tubes of 5ml were used for the determination of advanced oxidation protein products (AOPPs), creatinine, uremia, phosphoremia and calcemia. Urine was collected in sterile plolypropylene plastic bottles with a quantity of 5ml for the determination of Microalbumunuria. The collected blood was centrifuged at 3000 rpm for 5 minutes. Aliquots of 200-500 ul of serum were stored at +4o C and -80°C for future analysis. The serum concentration of AOPPs was determined by a quantitative test based on the principle of sandwich immunodetection (Elisa kit from China) and for the other biochemical parameters (creatinine, uremia, calcemia, phosphorus, microalbuminuria) the assays were carried out using an Architect C4000 automated system adapted to potentiometric and photometric methods. Urine samples collected within 8 hours of collection were processed by the same machine to determine microalbumunuria and renal clearance was calculated using the simplified MDRD formula.

R Studio software was used for data processing. One-way ANOVA tests were used to compare the means of the proportions of each group, and correlation tests were used to study the interdependent relationships between AOPPs-Microalbuminuria on the one hand and AOPPs-Renal Clearance on the other. The significance level was set at $P < 0.05$.

Results and Comments

Socio-demographic parameters

A total of 70 patients were included in this study. Table 1 summarizes the general characteristic of the study population. The sex ratio of sickle cell patients with nephropathy was 0.6. The mean age of the population was 30.16 ± 10.42 with two extremes ranging from 18 to 57 years, the mean ages in the group of sickle cell S cases, sickle cell S control and normal A control were 25.3 ± 8.74; 27.25 ± 8.49 and 40.35 ± 6.99 respectively; the difference found was statistically significant (p = 0.049); the most represented age group was 18-27 years, i.e. 35% of our study population.

Variables	cas SS	tem SS	tem AA	Total	p value
	n(%)	n(%)	n(%)	n(%)	
Sex					0,090
F	19(40,43)	12(25,53)	16(34,04)	47(67,14)	
M	11(47,83)	8(34,78)	4(17,39)	23(32,86)	
Age					0,049
18-27	23(32,85)	0(0)	12(17,14)	35(50)	
28-37	3(4,28)	9(12,85)	4(5,71)	16(22,85)	
38-47	3(4,28)	8(11,42)	4(5,71)	15(21,42)	
48-57	1(1,42)	3(4,28)	0(0)	4(5,71)	

Table 1: Socio-demographic variables.

The biochemical parameters (See annex table 2)

The mean of biochemical parameters of renal exploration like Urea, Creatinine, Phosphorus, Calcium and Renal Clearance were normal. Slight variations in microalbuminuria in relation to their standard deviation were noted with a mean of 52.33 ± 47.75. We note that our results show no statistically significant difference for all the parameters considered ($P > 0.05$).

Variables	cas SS	tem SS	tem AA	P value
Creatinine levels (mg/l)	7,9 ± 4,19	6,5 ± 1,10	9,25 ± 2,02	0,600
Phosphore (mg/l)	42,76 ± 8,18	37,5 ± 8,0	33,65 ± 5,12	0,700
Urea (g/l)	0,10 ± 0,02	0,1 ± 0,002	0,10 ± 0,01	0,800
Calcium (g/l)	94 ± 9,54	95,6 ± 6,67	98 ± 7,9	0,800
Micro Al (mg/l)	52,33 ± 47,75			
Renal clearance (ml/mn)	140 ± 58,94	147 ± 58,94	147 ± 58,94	0,904

Table 2: Biological variables.

Comparison tests (See annex figure 01; 02; 03)

After evaluation of AOPPs in the three groups of our study by one-way ANOVA, we noted a small increase in AOPPs in the case group compared with the control groups with no significant difference P = 0.053 (Figure 1).

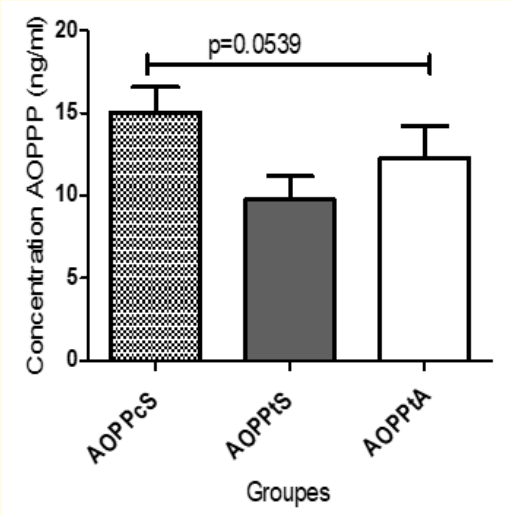

Figure 1: Evaluation of AOPPs in the three groups of our study by one-way ANOVA.

As well as the correlations of respective expression of AOPPs, renal clearance and microalbuminuria, which showed non-significant interdependent relationships (r = 0.07 r = 0.043 and P > 0.05) (See Appendix Figure 2 and 3).

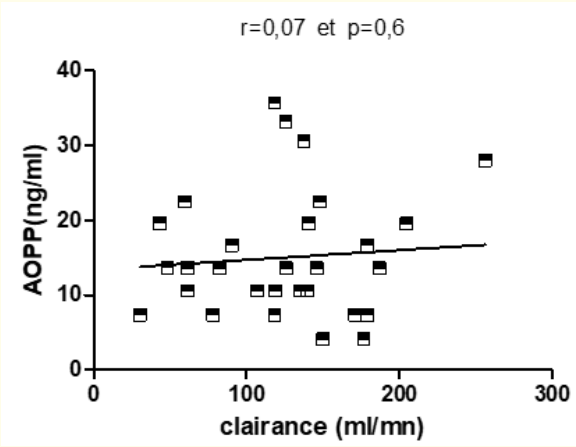

Figure 2: The correlation of respective expression of AOPPs and renal clearance.

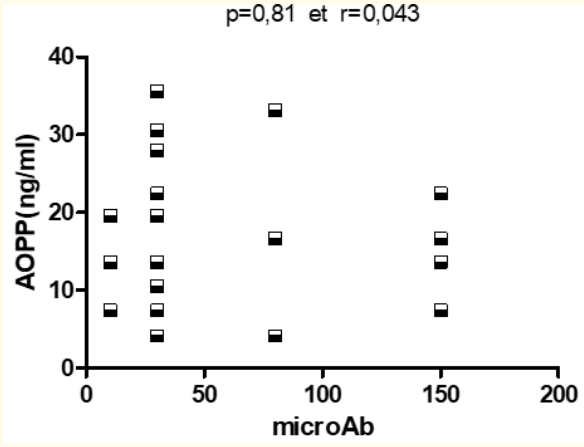

Figure 3: Represents the respective expression correlation of AOPPs and renal microalbumin.

Discussion

The objective of this work was to evaluate the activity of AOPPs in sickle cell nephropathy.

Thus the mean age of our study population found is 30.16 ± 10.42 years, seems to be close to those reported in Mali by Fongoro., *et al*. [8] who had a mean age of 30.1 years. On the other hand, in Nigeria Adbu., *et al.* in 2011 found a mean age of 23 years slightly lower than our study [9]. These discrepancies and concordances of the mean ages of our study with those cited by the authors seem to be related to the size of our sample.

A statistically significant difference in age means was found in the three groups of our study population with a p-value = 0.049. The mean ages in the group of sickle cell cases S and normal controls A were 25.3 ± 8.74 and 40.35 ± 6.99, respectively; this difference can be explained by the fact that in sickle cell subjects renal complications occur rapidly because of the chronicity of the disease.

The renal biochemical parameters considered in our study showed no statistically significant difference P > 0.05. This non-significance can be explained by the fact that some biochemical parameters such as phosphorus and calcium hardly vary during nephropathy. On the other hand, uremic parameters and renal clearance can be explained by the fact that the nephropathies listed are moderate but also the size of our sample does not reflect a good statistical power.

Our study showed a small increase in AOPPs in the case group compared to the control groups with statistically insignificant results (p = 0.053).

Also the variation of AOPPs in the two control groups is not considerable so our results agree with those reported by Bargnoux., *et al.* in 2009 [10]; who noted a strong elevation of ROS in the case of CKD, but noted a major involvement of AOPPs in the context of CKD and can be considered as amplifiers of the inflammation syndrome.

The non-significance of our results is explained by the fact that we did not identify cases of chronic renal failure (CRF) during the recruitment of our patients, although our cases presented a nephropathy, but the accumulation of AOPPs is more effective than in the context of CRF.

And the non-variability of AOPPs concentration in the two control groups shows that the elevation of the latter in the SS group confirms our hypothesis that AOPPs concentration are elevated in the context of sickle cell nephropathy.

However, we did not note a correlation between microalbumin concentrations and AOPPs (p = 0.8 and r = 0.043) on the one hand.

On the other hand between renal clearance and AOPPs (p = 0.6 and r = 0.07).

Although albumin is one of the uremic derivatives, it is much more involved in diabetic nephropathy and some vascular diseases as demonstrated by the studies of Vincent Bourquin and Marc Diovannini in 2007 [11]. The same study revealed that microalbumin is low in some cases of CKD.

However, the lack of correlation between renal clearance and the concentration of AOPPs can be explained by the size of our sample, which was small, and because among the nephropathies recruited we did not observe any variation in clearance compared to the control group. Indeed in 2016 by Capeillere-Blandin C., *et al.* reported that the concentration of AOPPs at different stages of advancement of CKD, increases successively with a decrease in glomerular filtration capacity (from 18 to 21% in patients with advanced stage of the disease Ccr = 20 to 40ml/min and more than 70% in patients in terminal phase Ccr<20 ml/min compared to patients of initial stage of CKD Ccr = 41-80 ml/min) [12].

However, we will try to add in our study other markers of oxidative stress with the new data of literature in the context of sickle cell disease, especially those correlated with AOPPs and increased the relevance of our study.

Limitations of the Study

In this study we encountered as a limitation, the sample size which was small. However, we wanted to carry out a preliminary study in order to have an idea and to find ways to circumvent the difficulties encountered.

Conclusion

This study, which aimed to assess AOPPs in sickle cell nephropathy, reported that AOPPs were slightly increased in the case group compared with controls, testifying to the involvement of oxidative stress in sickle cell nephropathy. This preliminary work on the assessment of oxidative stress in sickle cell nephropathy therefore requires further investigation to demonstrate the impact of AOPPs in Congolese sickle cell patents.

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