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Original Research Article

High blood viscosity is associated with high pulse wave velocity in African sickle cell trait carriers

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ABSTRACT

Background: Sickle cell trait (SCT) is the benign condition of sickle cell disease. Often asymptomatic, the SCT carriers have hemorheological disturbances such as blood hyper-viscosity compared to healthy subjects. These disturbances could lead to structural and functional changes in large vessels. The aim of the study was to evaluate the association between blood viscosity (ηb) and pulse wave velocity (PWV) in SCT carriers.
Methods: Thirteen SCT with high blood viscosity (SCT_hηb) aged 34±12 years (4 men) were compared to 13 SCT with low blood viscosity (SCT_lηb) aged 32±9 years (5 men) recruited from the National Blood Transfusion Center (CNTS) in Dakar (Senegal). Pulse wave velocity finger-toe (PWVft) was assessed using *pOpmètre® (Axelife SAS-France)*. Cardiovascular risk (CVR) was assessed according to the Framingham Laurier score.
Results: SCT_hηb had higher PWVft (m/s) than SCT_lηb respectively 8.98±1.98 and 7.11±1.18 (p = 0.004). CVR score (%) was higher in SCT_hηb than SCT_lηb, but this difference was not statistically significant (5.96±7.45 vs 2.09±2.15; p=0.31). Multivariate linear regression showed a positive correlation between PWVft and ηb and CVR score (r2=0.74, F=21.19, p<0.001).
Conclusions: Present results indicate that the SCT_hηb carriers have arteries stiffer than SCT_lηb and ηb and CVR could remain independent determinants of arterial stiffness in SCT carriers.

Keywords: Blood viscosity, Pulse wave velocity, Sickle cell trait

INTRODUCTION

Sickle cell is an inherited autosomal recessive disease. Abnormal hemoglobin S (HbS) comes from the replacement of glutamic acid with valine of the β chain of hemoglobin. It is the most common hemoglobinopathy, affecting over 270 million people worldwide and the major part is located in Sub-Saharan Africa.[1] In Senegal, the prevalence of Hemoglobin HbS is 8-10%.[2] There are mainly two great forms of sickle cell: sickle cell anemia (SCA) the homozygous form and sickle cell trait (SCT) the heterozygous form. The SCA in which the hemoglobin S level is very high is characterized by repeated vaso-occlusive crisis. Among the mechanisms involved in the physiopathology of circulatory disturbances described in the SCA population, include hemorheological abnormalities and oxidative stress phenomena.[3-5] Inflammatory factors such as IL-1β, IL-6

and TNFα have also been reported in subjects of SCA[6]. Although, SCT is generally considered as benign condition and SCT carriers (SCTc) are often asymptomatic, authors have shown that the SCT is characterized by high blood viscosity (ηb) associated with decreased red blood cell deformability compared to subjects with normal hemoglobin.[7,8] Moreover, recent studies have found in SCTc high level of oxidative stress markers and pro-inflammatory cytokines and hemorheological abnormalities which could disturb vascular function.[9-12]

Indeed, reactive oxygen species and pro-inflammatory cytokines are well described as inhibitory factor of synthesis of nitrogen monoxide (NO). Chronic exposure of endothelium to these free radicals could lead to structural modifications of conductance vessels, would give therefore stiffening of the arteries and would elevate the cardiovascular risk score.

Furthermore, *Bayramoglu and al* have recently showed that SCT had a non-significant high pulse wave velocity (PWV) compare to subjects with normal hemoglobin.[13] And according to our knowledge, few studies on vascular function in SCT population were performed. Based on these observations, we carried out this work to compare the PWV between SCT carriers with high ηb (SCT_hηb) and SCT carriers with low ηb (SCT_lηb) viscosity.

METHODS

The present study was performed at the University Cheikh Anta Diop of Dakar (Senegal). The protocol was performed according to the statements of Helsinki and agreed by the ethics committee of the University (Ref: 017/2014 / REC / UCAD). Subjects were informed of the procedure and the purpose of the study. Twenty six (26) SCT carriers were recruited from the National Blood Transfusion Center (CNTS). Confirmation of hemoglobinopathy was done by electrophoresis of hemoglobin. None of the subjects carrying hemoglobin HbS was diabetic or suffering from known cardiovascular disease. Present subjects were subdivided in two groups according to the cut off mean value of ηb (5.80 $mPa.s^{-1}$) generally reported in subjects without hemoglobinopathy or cardiovascular risk.[14] Group 1: thirteen SCTc who had high ηb (ηb>6 $mPa.s^{-1}$, SCT_hηb) and Group 2: thirteen SCTc with low ηb (ηb<6 $mPa.s^{-1}$, SCT_lηb).

Measurements

Cardiovascular variables (systolic and diastolic blood pressures and heart rate) were evaluated at resting and fasting condition following the recommendations of the American Society of Cardiology.[15] Blood samples for measuring lipid profiles (LDL and HDL cholesterol, total cholesterol and triglycerides), for the measurement of hemorheological variables were taken at the first visit. The cardiovascular risk score (CVR) was assessed according to the Framingham Laurier score.[16]

Hemorheological variables

Blood viscosity (ηb) was assessed using a viscometer cone plane (Brookfield DV II + Pro, with CPE40 spindle; Middleboro, MA) at $225s^{-1}$ and at 37 ° C according to the recent Standards recommendations of technical of hemorheologic.[17] Haematocrit (Hct) was evaluated by the method of micro-centrifugation (Jouan-Hema-C, Saint Herblain, France) at a speed of 1500 g for 5 min at 25° C.

Assessment of arterial stiffness

Pulse wave velocity was measured as a good surrogate of Arterial stiffness. It was assessed using finger-toe pulse wave velocity (PWVft) with pOpmètre® (Axelife SAS, France) as recommended by *Alivon M and al*[18].

Statistical analyses

Data collected were analyzed using SPSS 16.0 software. The results of quantitative variables were represented as mean ± standard deviation. The comparison of quantitative variables between the two groups was calculated using nonparametric tests (Mann-Whitney U test). Linear regressions were used to identify correlations between the PWVft and other variables. The significance level was set at $p \leq 0.05$.

RESULTS

Anthropometric and cardiovascular data

No difference in age between the two groups was observed (Table 1). The analysis of the blood pressure showed that the cardiovascular profile of SCT_hηb was not significantly different to these of SCT_lηb, (Table 1). Also, the difference was not statistically significant between the CVR (%) of SCT_hηb and that of SCT_lηb respectively 5.96±7.45 and 2.09±2.15 (p=0.31) (Table 1).

Table 1: Anthropometric and cardio-vascular variables.

	SCT_hηb	SCT_lηb	P value
Age (years)	34±12	32±9	p=0.69
SBP (mmHg)	135.31±17.05	121.38±8.39	p=0.10
DBP (mmHg)	80.77±7.99	74.15±6.80	p=0.31
MAP (mmHg)	98.94±7.51	89.90±6.63	p=0.29
HR (bat/mn)	71±9	75±8	p=0.26
CVR (%)	5.96±7.45	2.09±2.15	p=0.31

Lipid and hemorheologic data

The results were reported in Table 2. There were no difference between the two groups for triglyceride, total and LDL cholesterol. But the SCT_hηb had lower HDL cholesterol compared to SCT_lηb, respectively 49.84±19.59, 62.00±13.56 (p=0.044). Blood viscosity (ηb) was significantly higher in the SCT_hηb than in the

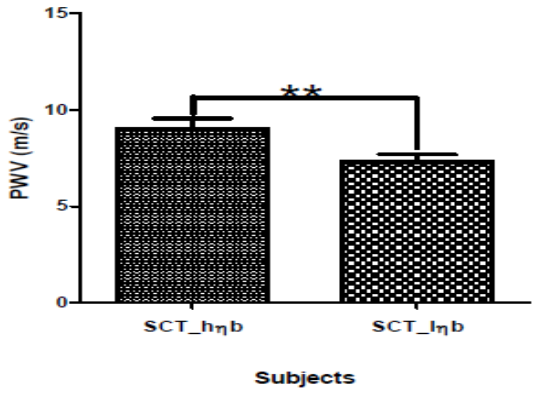
SCT_lηb (5.83±0.71≠4.91±0.55 $mPas^{-1}$; p=0.001). Regarding the Hct of SCT_hηb, it was significantly higher than those of SCT_lηb, respectively 41.10±3.09%; 39.74±6.63% (p=0.029).

Table 2: Lipid and hemorheologic variables.

	SCT_hηb	SCT_lηb	P value
Total_c (mg/dl)	163.62±42.08	176.92±32.93	p=0.24
Triglycerides (mg/dl)	51.23±24.97	47.46±16.01	p=1.00
LDL_c (mg/dl)	103.53±31.36	105.42±29.72	p=0.76
HDL_c (mg/dl)	49.84±19.59	62.00±13.56	p=0.044
Hct (%)	41.10±3.09	39.74±6.63	p=0.029
ηb ($mPa.s^{-1}$)	6.52±0.53	5.17±0.70	p<0.001

Pulse wave velocity

The SCT_hηb had a significantly higher PWVft than SCT_lηb, respectively 8.98±1.98 and 7.11±1.18 m/s (p = 0.004) (Figure 1).



PWV: Pulse Wave Velocity; SCT_hηb: Sickel Cell Trail with high blood viscosity; SCT_lηb: Sickel Cell Trail with low blood viscosity; **: p≤0.01.

Figure 1: Comparison of the pulse wave velocity between groups.

Table 3: Relation between PWVft and other variables.

PWVft with	Spearman R	P value
Age	0.40	p =0.046
ηb	0.61	p=0.001
CVR	0.55	p=0.004

Relation between PWVft and other variables

Positive association were observed between PWVft and some variables such as age (r=0.40; p=0.046); ηb (r=0.61; p=0.001) and CVR (r=0.55; p=0.004) (Table 3). However, only the ηb and the CVR were independent determinants of arterial stiffness (r2=0.74, F=21.19, p<0.001).

DISCUSSION

The results of present study show that SCT_hηb had higher PWVft than SCT_lηb. Although SCT_hηb had sub increase in blood pressures (SBP, DBP and MAP) and a score of CVR compare to SCT_lηb, this difference was not statistically significant. About the lipid profile, only the HDL cholesterol was significantly lower in SCT_hηb than in SCT_lηb. This is in accordance with the higher CVR in this group.

Our study is the first to compare the PWV of SCT subjects according to blood viscosity. Indeed, we found that SCT_hηb had stiffer arteries than SCT_lηb. Arterial stiffness is an important determinant of cardiovascular mortality.[19] Blood pressure remains the major contributing factor to arterial stiffness out of age. Indeed, in our SCT_hηb we noted a non-significant increase (due certainly to the number of subjects in the study) in systolic, diastolic and mean blood pressure which is observed usually with higher PWVft. Serum HDL cholesterol are protective against arterial stiffness.[20,21] In our study, the SCT_hηb had a low serum HDL, which would contribute more to high level of the PWVft in present SCT_hηb subjects.

SCT subjects are characterized by blood hyper viscosity compared with healthy subjects.[7] Hemorheological disturbances play an important role in atherosclerosis. Recently, it has been proved that blood viscosity can predict the occurrence of cardiovascular events.[22] Several authors have been interested in the association between blood viscosity and arterial stiffness. No association was found in healthy subjects, however, in patients who already have a cardiovascular risk factor, there were a positive correlation between arterial stiffness and blood viscosity.[23-24]

Present results could be renforced by the positive correlation between PWV and ηb. The CVR score of Framingham Laurier predict the occurrence of cardiovascular events in the next 10 years. It is clearly established that the CVR strongly influences the increase

in arterial stiffness.[25,26] In present study, there was a positive correlation between PWVft and CVR; this was confirmed in the literature for other populations than SCT.

CONCLUSION

It seems that SCT having high blood viscosity have stiffer arteries than those with lower blood viscosity. They are thus exposed to cardiovascular events hence the interest to promote preventive measures such as regular practice of moderate physical activity that would improve hemorheological disturbances encountered in this population. Varied multi-analysis controlled by age, have identified blood viscosity and CVR score as independent determinants of arterial stiffness in SCT subjects.

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