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Research Article

Blood pressure variations in Subjects with different Haemoglobin Genotypes

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ABSTRACT

Previous studies on low blood pressure in patients with homozygous sickle cell disease (SCD) have sought various hypotheses on the mechanism of their low blood pressure. However, these studies have not compared the role of the single inheritance of the s-gene in the variations in blood pressures as well as relating the blood pressures in different haemoglobin (HB) genotypes to each other. Blood pressures in 20 steady and crisis states SCD patients respectively with 40 apparently healthy heterozygous HB AS and HB AA genotype (age and sex –matched). They were aged between 20 and 40 years. Results showed a significantly ($p<0.05$) lower blood pressure (systolic and diastolic) in SCD in stable (but not in crisis) state compared with the normal controls. The systolic blood pressures in control (HB AA) and SCD patients were 125.33 ± 2.25 versus 115.25 ± 2.9 (stable state); 125.33 ± 2.25 versus 124.83 ± 2.88 (crisis state, $p>0.05$), 82.33 ± 1.2 versus 72.25 ± 1.81 (stable state, $p<0.05$) and 82.33 ± 1.2 versus 99.5 ± 5.81 (crisis state, $p<0.05$). Also, HB AS subjects exhibited significantly higher diastolic pressure than HB AA and HB SS subjects during crisis. In conclusion, this study shows that systolic and diastolic blood pressures are lower in SCA patients in stable state (compared with control, HB AA subjects) but are relatively higher during crisis while diastolic blood pressure is significantly higher in HB AS than HB AA and HB SS subjects in crisis. Further work needs to be done to determine the mechanism for this variation.

INTRODUCTION

Blood pressure is simply defined as the force of blood pushing against the walls of the arteries as the heart pumps blood. If this pressure rises and stays high over time, it can damage the body through its effect on the bodily organs in many ways. Sickle cell anaemia (SCA) is due to a single point mutation that results in the substitution of valine for glutamic acid at the 6th position of the β-chain of the haemoglobin S (HB S) molecule (Hatch *et al*., 1989). Sickle cell anaemia is characterised by recurring acute vaso-occlusive episodes/crisis and chronic organ damage to multiple organs. Patients with sickle cell anaemia have considerably reduced tendency to be hypertensive than others with normal haemoglobins and the factors offering this protection remain obscure (Hatch et al., 1989; Ernst et al., 2000). Significantly lower systolic and diastolic blood pressure (BP) in patients have been reported in HB SS disease in comparison with values for non SCA patients (kurantsin-Mills et al., 1987; Rodgers et al., 1984; Jaja *et al*., 2008; Johnson and Giorgio, 1981). Many reasons have been suggested for these observations but none seems to have a general scientific acceptance. Lower BP has been intrinsically linked to low weights of the patients (Aderibigbe *et al*., 1999), while a direct vascular control mechanism has also been suggested - since SCA subjects exhibit decreased pressor response to angiotensin II but not to norepinephrine (Osarogiagbon *et al*., 2000). Also, Elevated right ventricular (RV) pressure has been well documented as a risk factor for death in adults with

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SCD (Ataga *et al*., 2006; Hagar *et al*., 2008) while Left Ventricular (LV) mass and LV diastolic dysfunction in SCD have been reported to be associated with asleep and waking oxygen saturation (Johnson *et al*., 2010). The growing body of literature suggests that SCA patients are subjected to increased oxidative stress, particularly during vaso-occlusive crisis and acute chest syndrome. Reperfusion of tissues after interruption of their vascular supply of blood causes free-radical generation that leads to tissue damage, a scenario referred to as "reperfusion injury" (Osarogiagbon *et al*., 2000) The occurrence of oxidant-mediated damage resulting from such ischaemia-reperfusion cycle has been demonstrated in several animal organ and tissue models (Southorn and Powis, 1988; Zimmerman and Granger, 1994). Because SS-RBCs generate excessive amounts of reactive oxygen metabolites due to the presence of unstable haemoglobin S and the spontaneous autoxidation of iron in haem the antagonistic effect on endothelium derived relaxation factor – Nitric oxide (EDRF-NO) will be pronounced and thus a contributory factor to abnormal vascular reactivity in SCD (Claster *et al*., 1984; Hebbel *et al*., 1988). Previous studies on low blood pressure in patients with homozygous sickle cell disease (SCD) have sought various hypotheses on the mechanism of their low blood pressure but have not compared the role of the single inheritance of the s-gene in the variations in blood pressures as well as relating the blood pressures in different haemoglobin genotypes to each other. We aimed at highlighting blood pressure variations in human subjects with different haemoglobin genotypes.

SUBJECTS AND METHODS

Sickle cell patients attending University of Benin Teaching Hospital as well as some selected private hospitals in Benin metropolis(University of Benin Health centre, Citizen clinic and Amazing grace hospital, Benin city) were involved in the blood pressure (BP) measurements during their stable and crisis states as well as age and sex matched individuals belonging to Hb genotype AS and AA drawn from the University of Benin community. Verbal, informed consents were sought from willing patients before recruitment for the study. Blood pressure readings were taken from adult Sickle cell patients (Hb SS; n=20 in stable state, n=15 in crisis state) undergoing various crisis as well as the heterozygous (Hb AS; n=20) and Normal (Hb AA; n=20). Sample size was determined using the power analysis formula with prevalence estimated at 2% of the population($N=Pq/(E/\ 1.96)^2$, Where N=Sample size, E=Error margin, P =Prevalence, q= 1-P). Arterial blood pressure was measured on the right brachial artery in each subject using the auscultatory method. The first and fifth Korotkoff heart sounds represented the systolic blood pressure and diastolic blood pressure, respectively(Jaja et al., 2008).The mean values were calculated from a total of three readings in each case.

Statistical Analysis

Data were analysed with Microcal origin 5.0 statistical software. The Student t-test was used for data comparison. A P–value of less than 0.05 was considered significant.

RESULTS

Our results showed a significantly lower ($p<0.05$) blood pressure (systolic and diastolic) in SCA in stable (but not in crisis) state compared with the normal controls. On the other hand, Hb AS subjects exhibited significantly higher diastolic pressure than HB AA and Hb SS subjects in crisis

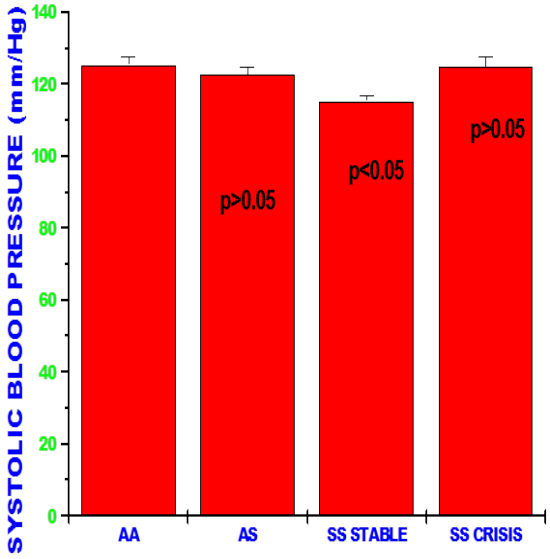

Fig 1:
There was a significant lower values in the systolic pressure of HB SS subjects at stable state compared with that of controls (HB AA subjects) and that of heterozygote HB AS ($P<0.05$ respectively).HB AA indicates control with normal haemoglobin genotype, HB AS are subjects with heterozygote single haemoglobin S-gene inheritance while HB SS are the subjects with homozygote Sickle cell anaemia (SCA) disease. SS stable indicates the SCA subjects in stable states(no crisis situation) while the SS crisis indicates the SCA subjects during vascular crisis.

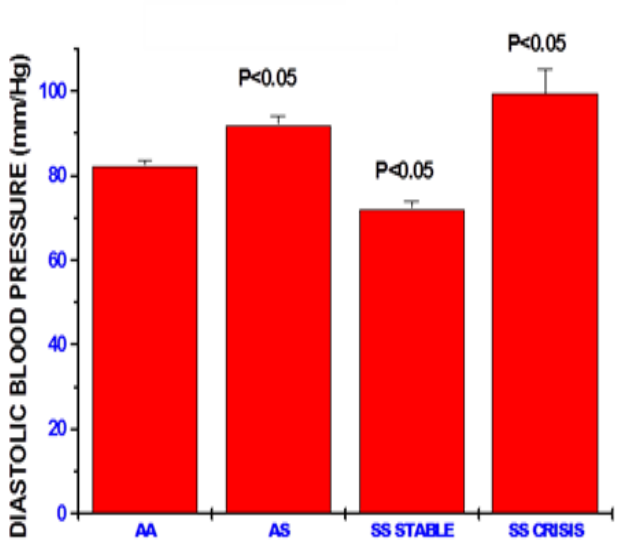

Fig 2:
Diastolic blood pressure Values for HB SS (stable state) showed significantly lower values compared with controls, HB AA and HB AS (P<0.05, respectively), while HB SS (in crisis) and HB AS showed significantly increased values compared with HB AA (P <0.05, respectively).

DISCUSSION

In this study, we have observed significantly lower systolic and diastolic blood pressures in sickle cell anaemia (SCA) patients compared with controls (P<0.05, respectively) which increases relatively during crisis. These observations are consistent with the previous reports of (Johnson and Giorgio, 1981; Hatch et al., 1989; Ernst et al., 2000). However, HB AS subjects exhibited significantly higher diastolic pressure than HB AA and SS in crisis. This observation is in line with that of Reid and Anah, (1985). They reported persistent increase in diastolic blood pressures in HB AS hypertensives than HB AA counterparts and suggested further that the patients are either resistant or are less responsive to conventional anti-hypertensive therapy. Although HB SS in stable state appears to have much lower systolic and diastolic blood pressures, the immediate cause for the higher diastolic values in heterozygote HB AS seems difficult to explain but appears to be intrinsically associated with such haemoglobin aberration. The higher values in SCA during crisis may be due to the reported vascular injury due to interactions between sickled red cells and endothelium which is known to up-regulate the release of diverse agents like inflammatory cytokines, oxidative compounds and nuclear factor-κB by distinct intracellular pathways that involve reactive oxygen species (ROS) as a common messenger (Radi et al., 1991; Polman and Harlan, 2000). The report of Johnson et al., (2010) seems to corroborate this observation too. It should be noted however, that these increases are relative to SCA status only, the systolic blood pressure values during both stable and crisis states were still lower than that of normal HB AA control subjects, relatively though, the pressures are higher during crisis.

Our observations of increased diastolic blood pressures in heterozygote HB AS and HB SS during crisis underscore the possible contributory role of the S-gene in cardiovascular functions. Patients with SCA have been associated with left ventricular diastolic dysfunction as an independent risk factor for mortality (Hankins et al., 2010), and several postulations have been made to explain this effect which include increase body iron burden due to repeated transfusions and continuous haemolysis, increased cardiac activity and possibly increased angiotensin production (Hankins *et al*., 2010). In Contrast, Osarogiagbon *et al*., (2000) reported that SCA patients have decreased pressor response to angiotensin II but not to nor-epinephrine while LV diastolic dysfunction was dissociated from iron overload in children with SCA (Hankins et al., 2010), therefore the most plausible explanation may reflect more on disease pathophysiology and severity especially in older patients and may predispose them to stroke and other cardiovascular complications and deaths.

This study has therefore, re-iterated that blood pressures are significantly lower in SCA than in non-sickle cell control subjects and for the first time, demonstrated that diastolic blood pressure values are significantly higher in HB AS subjects, and SS subjects during crisis than in HB AA control subjects. The role of heterozygote S-gene inheritance in diastolic blood pressure modulations could not be explained in this present study.

Studies on vascular interactions with erythrocytes from different HB genotypes and their components under different physiologic and pharmacologic manoeuvres may be necessary to give possible explanations to these observations.

REFERENCES

Aderibigbe A, Omotoso AB, Awobusuyi JO, AkandeTM(1999). Arterial blood pressure in adult Nigeriansickle cell anaemia patients.*West Afr J Med* **18(2):**114-8.

Ataga KI, Moore CG, Jones S, et al., (2006). Pulmonary hypertension in patients with sickle cell disease: a longitudinal study. *Br J Haematol* **134(1):**109-115

Claster S, Chiu DT, Quintanilha A, Lubin B (1984). Neutrophils mediate lipid peroxidation in human red cells.

Blood **64(5):**1079-84

Ernst AA, Weiss SJ, Johnson WD, Takakuma KM (2000). Blood pressure in acute vaso-occlusive crises of sickle cell disease. *South Med J* **93(6):**590-2

Hagar RW, Michlitsch JG, Gardner J, Vichinsky EP, Morris CR (2008). Clinical differences between children and adults with pulmonary hypertension and sickle cell disease.*Br J Haematol.* **140(1):**104-112

Hankins JS, McCarville MB, Hillenbrand CM, Loeffler RB, Ware RE, Song R, Smeltzer MP, Joshi V. (2010). Ventricular Diastolic Dysfunction in Sickle Cell Anemia Is Common But Not Associated With Myocardial Iron Deposition. *Pediatr Blood Cancer***55(3):** 495–500

Hatch FE, Crowe LR, Miles DE, Young JP, Portner ME (1989). Altered vascular reactivity in sickle hemoglobinopathy. A possible protective factor from hypertension.*Am J Hypertens* **2(1):**2-8.

Hebbel RP, Morgan W.T, Eston J.W, Hedlund B.E. (1988). Accelerated autoxidation and heme loss due to `instability of sickle hemoglobin.*Proc. Natl Acad Sci USA* **85**: 237-41

Jaja SI, Kehinde MO, Ogungbemi SI (2008). Cardiac and autonomic responses to change in posture or vitamin C supplementation in Sickle cell anemia subjects. *Pathophysiology* **15:** 25-30

Johnson CS, Giorgio AJ (1981). Arterial blood pressure in adults with sickle cell disease. *Arch Intern Med* **141(7):**891-93

Johnson MC, Kirkham FJ, Redline S et al., (2010). Left ventricular hypertrophy and diastolic dysfunction `in children with sickle cell disease are related to asleep and waking oxygen desaturation. *Blood* **116 (1):** 16-21

Kurantsin-Mills J. Jacobs HM, Klugg PP, LessinLS (1987). Flow dynamics of human sickle erythrocytes in the mesenteric microcirculation of the exchange transfused rat. *MicrocircRes* **34(2):**152-167

Osarogiagbon UR, Choong S, Belcher JD, Vercellotti GM, Paller MS, Hebbel RP. (2000).Reperfusion injury pathophysiology in sickle transgenic mice. *Blood* **96(1):**314-20.

Pohlman TH, Harlan JM. (2000). Adaptive reponses of the endothelium to stress. *J surg Res* **89(1):**85-119

Radi R, Beckman JS, Bush KM, Freeman BA(1991). Peroxynitrite-induced membrane lipid peroxidation: the cytotoxic potential of superoxide and nitric oxide. *Arch BiochemBiophys* **288(2**):481-7

Reid HL, Anah CO (1985). Haemorheological parameters in hypertensive Nigerians with and without sickle cell trait.*Angiology* **36(6**):379-86

Rodgers GP, Schechuter AN, Noguchi CT, Klein HG, Nienbuis AW, Bonner RF. (1984). Periodic microcirculatory flow in patients with sickle cell disease.*N Engl J med* **311:**1534-8

Southorn PA, Powis G (1988). Free radicals in medicine. II. Involvement in human disease. *Science* **278(5339**):876-8

Zimmerman BJ, Granger DN (1994). Mechanisms of reperfusion injury. *Am J Med Sci*. **307(4):**284-92.