Oxygen delivery index in homozygous sickle cell disease: steady and crisis states

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ABSTRACT

One of the common complications of sickle cell disease is the vaso-occlusive crisis or sickle cell crisis which could result in impaired oxygen delivery to the tissues. This study investigates the oxygen delivery index (ODI) in 38 patients with homozygous sickle cell anaemia. Thirty-three patients were in the steady state and five were experiencing crisis at the time of recruitment. Whole blood viscosity was measured with a Wells Brookfield viscometer at a shear rate of 230 sec^{-1} and haematocrit was measured with an AC Tron Coulter Counter. The ODI, which is an indirect measure of the capacity of blood to deliver oxygen to tissues, was calculated as the ratio of haematocrit to whole blood viscosity values. There was no statistically significant difference in the ODI between the steady and crisis states, suggesting that tissue oxygenation is not the only factor involved in the sickle cell crisis.

KEY WORDS: Blood viscosity.
Hematocrit.
Hemoglobin SC disease.
Oxygen delivery index.

Introduction

The vaso-occlusive crisis or sickle cell crisis is a common painful complication of sickle cell disease. The pain may be localised in the bone or abdominal area. The bone pain is due to avascular necrosis of the bone marrow resulting from occlusion of the microvascular beds by sickle cells. The abdominal pain is thought to be due to bowel dysfunction secondary to an autonomic neuropathy.[1] Other complications of sickle cell disease include leg ulcers, stroke, spontaneous abortions and renal insufficiency.[2]

Skin cooling is considered the most common precipitating factor for crisis in Jamaican patients with sickle cell disease,[3] and this has been reported to cause a decrease in blood flow in homozygous sickle cell disease.[4] This reduction in blood flow could predispose to some form of hypoxia. Some other precipitating factors for crisis include dehydration, infection, exercise and psychological stress.[3]

One of the hallmarks of homozygous sickle cell disease is the reduction in haematocrit level,[1] which could affect tissue oxygenation and predispose the patient to hypoxia. It has been reported that hypoxia is involved in the pathophysiology of vaso-occlusive crisis.[3] In the microcirculatory beds, haematocrit reduction is secondary to haemoglobin S (HbS) polymerisation, another major contributor to vaso-occlusive events. However, this lowered haematocrit markedly reduces resistance in the macrocirculation, reflecting the remarkable heterogeneity of sickle cell disease.[5]

This study examines the oxygen delivery index (ODI) in sickle cell patients in steady and crisis states as an indirect means of determining the possible role of tissue oxygenation in sickle cell crisis.

Materials and methods

Clinical protocol

Approval for the study was given by the UHWI/UWI/FMS Ethics Committee. Volunteers gave informed consent and completed an interviewer-administered questionnaire. Thirty-eight participants homozygous for HbS were recruited from the Sickle Cell Unit, Tropical Medicine Research Institute, University of the West Indies, Mona Campus, Kingston. Five were in crisis at the time of recruitment.

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Sample collection

Venous blood (5 mL) was drawn from an antecubital vein into Vacutainer tubes (BD) containing potassium EDTA (1.5 mg/mL) anticoagulant and stored at room temperature (25°C) until measurements were undertaken.

Tests

Whole blood viscosity was measured with the Wells Brookfield viscometer at a shear rate of 230 sec^{-1}. Measurements were performed at native haematocrit and at a temperature maintained at 37°C. The haematocrit was measured using an AC Tron Coulter Counter. All tests were performed within three hours of venepuncture. The ODI was calculated as the ratio of haematocrit to whole blood viscosity.[5,6]

Statistical analysis

Statistical analysis was performed using SPSS version 12. Data were expressed as mean±standard deviation (SD) and analysed by the Student's *t*-test. The level of statistical significance was taken at the 95% confidence interval. $P<0.05$ was considered statistically significant.

Results

Mean haematocrit values were 21.66±5.42 and 23.30±5.51 in the steady and crisis states, respectively. There was a slight, non-statistically significant reduction in the whole blood viscosity in the steady state (1.76±0.61) compared with the crisis state (2.01±0.48). The ODI was marginally higher in the steady state compared with the crisis state, but this did not reach statistical significance. Table 1 shows the haematocrit, viscosity at 230 sec^{-1} and ODI in sickle cell patients in the steady and crisis states.

There was no significant difference in all the variables between the steady and crisis states.

Table 1. Haematocrit, whole blood viscosity and ODI values (mean±SD) in sickle cell patients in steady and crisis states.

	Steady state (*n*=33)	Crisis state (*n*=5)	Normal (AA) (*n*=34)
Haematocrit (%)	21.66±5.42	23.30±4.51*	41.38±4.86†
Viscosity (cP)	1.76±0.61	2.01±0.48	2.97±0.95
ODI	14.83±7.99	12.50±5.47	16.07±8.53

*Significant difference between AA and crisis state.
†Significant difference between AA and steady state.

Discussion

The results of the present study did not show any statistically significant difference between the ODI in steady and crisis states. This could be due to the fact that there are other precipitating factors for sickle cell crisis apart from tissue oxygenation. The Poiseuille equation, which shows an inverse relationship between viscosity and capillary flow, may show marked differences between *in vivo* and *in vitro* studies. It has been reported that this may be a consequence of important haemorheological mechanisms such as the Fahraeus-Lindquist effect.[7–9] Moreover, marginal variations may exist between the recorded values and actual microcirculatory oxygen delivery, as all viscosity studies, including the present study, have used samples taken from venous blood and then extrapolation made regarding delivery to tissues.

Precipitating factors in the genesis of sickle cell crisis include dehydration, infection, exercise and psychological stress.[3] The vasodilatory and anti-inflammatory actions of nitric oxide (NO) may also play a role in sickle crisis.[9–11] The present study did not investigate the precipitating factors for the crisis in the study population. However, the marginal reduction in ODI in the crisis state may suggest some form of impaired tissue oxygenation.

The marginal increase in blood viscosity in the crisis state in the present study is consistent with the reports of previous studies,[12–14] which found an increase in blood viscosity in sickle cell crisis due mainly to an elevated fibrinogen concentration.

In the management of vaso-occlusive crisis, oxygen therapy was found to be effective only in patients with hypoxemia and not in those with normal oxygen tension.[15] In another study,[16] the transfusion of human haemoglobin solution resulted in an increased haemoglobin concentration and increased oxygen delivery and pain relief in a sickle cell patient in crisis. This study highlights the role of improved oxygen delivery in pain relief during sickle cell crisis.

In conclusion, in the present study, the ODI was shown to be essentially the same in patients in steady and crisis states. This suggests that tissue oxygenation was not the principal precipitating factor in initiating the sickle cell crisis in the patient cohort studied. □

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