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COMPARISON OF OXYGEN SATURATION IN SICKLE ANAEMIA PATIENTS IN STEADY STATE WITH THOSE IN VASO-OCCLUSIVE CRISIS.

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ABSTRACT

Background: Sickle cell anaemia (SCA) is an inherited condition in which the abnormal haemoglobin molecule under sickling under low oxygen saturation. This leads to widespread micro-vascular occlusion and tissue hypoxia, which may manifest as recurrent episodes of painful bone crisis. Hypoxemia is a common finding in patients with SCA; it is recognized as a marker for vaso-occlusive events, such as, acute chest syndrome, stroke and recurrent painful crisis.

Aims and Objectives: to compare the oxygen saturation of SCA patients in steady state with those in VOC, and to determine its relationship with some clinical parameters.

Materials and Methods: This is a prospective cross-sectional study involving 102 adults with SCA in steady state and 61 with vaso-occlusive crisis carried out between January to July 2017. The oxygen saturation was recorded using a finger pulse oximeter (Suaoki, Model FS20A).

Results: There was significant difference between the pulse rate (p=0.005) and systolic blood pressure (p=0.02) of the VOC group compared with the steady state group. The mean SpO_2 level for subjects was 94.4% (±4.04), and was significantly lower when compared with the mean SpO_2 level for the Controls of 95.7% (±3.8)(p=0.04). There was significant correlation between $SpO_2$and age only amongst the subjects group; otherwise there was no correlation between $SpO_2$and other measured clinical parameters in both subjects and control group.

Conclusion:
A high prevalence of hypoxemia was observed during vaso-occlusive crisis compared to the steady state. Routine monitoring of SpO_2 is recommended, as it will provide data on the consistency of patients SpO_2 measurements and allows for comparison during acute illness.

KEYWORDS

Hypoxemia, Pulse Oximetry, Sickle Cell Anaemia, Vaso-occlusive Crises

Introduction:
Sickle cell anaemia (SCA) is a genetic disorder that results from the substitution of glutamic acid by valine in the beta subunits of the haemoglobin molecule. Upon exposure to low oxygen tension, the abnormal haemoglobin becomes less soluble and aggregates into large polymers within the red cells which assume the sickle shape (1). This results in microvascular occlusion and tissue hypoxia, which is responsible for the wide clinical manifestation of this disorder. Hypoxia within the marrow tissue results in vaso-occlusion and ischemia leading to painful bone crisis, the hallmark of this condition (2). The haemoglobin-oxygen dissociation curve, which measures the affinity of oxygen to haemoglobin and its delivery to tissue is right-shifted in SCA, resulting in low oxygen saturation (SpO_2) observed in this condition, even at sea level and when gas exchange is normal (3,4). In the lungs, alveolar hypoxia results in entrapment and sickling of red cells within the pulmonary microvasculature resulting in a further cycle of arterial and tissue hypoxia (1,3). Low oxygen saturation or hypoxemia is a common finding in patient with SCA (5,6). It is recognized as a marker for vaso-occlusive events, such as acute chest syndrome (4), frequent episodes of painful crisis in children (7) and an increased likelihood of central nervous system events (strokes, transient ischemic attacks and seizures) (8). On the other hand, there were significant associations between a decreased pain rate and higher mean oxygen saturation (7). In this study, we sought to compare the oxygen saturation between SCA in steady state with those in vaso-occlusive crisis (VOC), and to determine the relationship between oxygen saturation and some clinical parameters.

Aims and Objectives: to compare the oxygen saturation of SCA patients in steady state with those in VOC, and to determine its relationship with some clinical parameters.

Materials and Methods:
Study area: the study was carried out at the Accident and emergency unit, day care ward and outpatient clinic of the Haematology and Blood transfusion unit of the University of Maiduguri teaching hospital, Borno state. Nigeria.

Study population: the participants consisted of one hundred and sixty three known sickle cell haemoglobinopathy patients confirmed by Hb electrophoresis using cellulose acetate at pH 8.6. The subjects were made up of sixty one patients presenting at the haematology day care ward or the Accident and emergency unit in vaso-occlusive crisis; defined as painful episodes having no other explanation than vaso-occlusion and requiring treatment prescribed by a health professional in a medical setting (2). The control population comprised of one hundred and two patients in steady state enrolled at the time of routine outpatient visits to the unit, and defined as clinically stable over the last 3 months without admission for painful crises or blood transfusion (2).

Study design: this was a prospective cross-sectional study conducted between the periods of January to June 2017. Data were obtained using a structured questionnaire containing information on biodata, medical history including respiratory signs and symptoms, blood pressure, heart rate and oxygen saturation of the patients.

Methods: The oxygen saturation was recorded using a finger pulse oximeter (Suaoki, Model FS20A). The appropriate sensor was placed on the right or left index finger and the measurement recorded after at least 2 minutes of stable SpO_2 determined in the presence of a regular pulsatile photoplethysmography signal apparent on the visual display of the oximeter. All measurements were made while the patient was breathing room air. Hypoxemia was defined as oxygen saturation less than 96%, because this would predict a PaO_2 less than 70 mm Hg based

on a normal oxyhaemoglobin curve (4).

Statistical analysis: The data was analyzed using the statistical package for social sciences version 20.0 (SPSS Chicago III USA.). Normality of data was tested using Kolmogorov-Smirnov test. Continuous variables were expressed using means (SD) and compared using Student's t-test. Pearson correlation was used to investigate the relationship between SpO_2 and other clinical parameters. SpO_2 was defined as the dependent variable; respiratory and pulse rates, systolic and diastolic blood pressure as independent variables. The independent variables were selected based on their clinical importance in causing cardio-respiratory symptoms. A p value of <0.05 was considered significant for all statistical analysis.

Results:

Demography and clinical characteristics of participants

The subjects were made up of 31(50.8%) males and 30(49.1%) females, while the controls were made up of 37(36.3%) males and 65(63.7%) females, with mean ages of 23.75(±6.28) and 22.94(±5.93) years for subjects and controls respectively (p=0.41). The mean pulse rates, respiratory rates, systolic and diastolic blood pressures of the participants are illustrated in Tables 1. There was significant difference between the pulse rate (p=0.005) and systolic blood pressure (0.02) of the VOC group compared with the steady state group.

Hypoxemia amongst the subjects and control

Hypoxemia was highest among the VOC group at 49.2% (30 patients) as against 30.4% (31 patients) observed in the control group(Table 1).The mean SpO_2 level for subjects was 94.4% (±4.04), and was significantly lower when compared with the mean SpO_2 level for the controls of 95.7% (±3.8)(p=0.04).

Correlation analysis:

The result of correlation analysis is shown in table 2. There was significant correlation between $SpO_2$and age only amongst the subjects group; otherwise there was no correlation between $SpO_2$and the other measured clinical parameters in both subjects and control group.

Discussion:

We found the prevalence of low oxygen saturation to be higher in patients with vaso-occlusive crisis. In, addition, the mean SpO_2 in this group was found to be significantly lower when compared with those of the control group (p= 0.04). Similar findings have been documented in other studies (2). Setty et al showed an inverse relation between low oxygen saturation and markers of inflammation, cellular activation molecules, such as, VCAM, P selectin, L selectin, leukotriene B. They inferred that release of cellular mediators during hypoxemia might play a role in the mechanism and frequency of vaso-occlusive crisis (9). The significance of oxygen desaturation and vaso-occlusive crisis is still unclear; it is thought that low oxygen saturation may promote vaso-occlusive complication through hypoxia-mediated pathway (9). Also, the exact mechanism by which oxygen treatment results in clinical improvement is not well known. Homi et al showed that inhalation of 100% oxygen in SCA patients with oxygen saturations below 90% consistently increased saturation to 99-100% (10), whereas, in another study, reduction in the number reversible sickled cells (involved in the pathophysiology of vaso-occlusion) by oxygen therapy did not result in reduction in the length of crisis (11). An in vitro study also failed to demonstrate any effect of hyperbaric oxygen on the morphology of sickled cells (12).

In the index study, the overall prevalence of hypoxemia was 37.4%. This is almost thrice the value reported in a similar study carried out in this region in children with SCA (2). This may not be unexpected as our study consisted of adult population. Our result showed significant relation between SpO_2 and age in the vaso-occlusive group. Previous reports in children have shown age as a risk factor for hypoxemia (4,5). In one of such report, the mean $SpO_2$was 94% for age greater than five years and 97.2% for age less than five years (4). This finding suggests that pulmonary dysfunction may begin at an early age. Another investigator showed that the degree of steady-state desaturation increased with age, and much of the age-related decline in SpO_2occurs in the first 5 years of life. They attributed this finding to the normal developmental decline in Foetal Hb (Hb F) concentration; Hb F has higher oxygen affinity than Hb S, and it declines to a steady-state level over a period of 2–5 years (13). Hypoxemia in SCA has also been attributed to subclinical or chronic cardiopulmonary disease following repeated episodes of acute chest syndrome (13). Decrease bioavailability of nitric oxide (NO) from chronic haemolysis results in pulmonary vasculopathy leading to ventilation-perfusion mismatch and limited oxygen uptake (1). In the current study, we found significant difference in the pulse rates and systolic blood pressures between the VOC group compared with the control group, however, there was no relationship between SpO_2 and these variables. These finding may be due in part to release of catecholamine, as a stressor response to painful crisis, rather than the presence of a chronic cardiopulmonary disease. Other possible explanation for hypoxemia in SCA include anaemia, raised level of 2,3 DPG and the type of haemoglobinopathy (HbSS is associated with severe disease), all of which results in a right-shift of the oxygen dissociation curve(4,5,14). This is considered adaptive in anaemia, as it allow for offloading of large volume of oxygen to tissue at relatively high partial pressure of oxygen (3). The high diffusion pressure facilitates transfer of oxygen into poorly vascularized tissue and reduces the need for increase cardiac output.

Conclusion:

We observed lower oxygen saturation in patients with vaso-occlusive crisis, however, our finding is limited because we did not obtain serial measurement of SpO_2 both during steady state and vaso-occlusive episodes for each individual. We therefore recommend monitoring of SpO_2 as part of routine evaluation in patients with SCA. This practice will provide data on the consistency of patients SpO_2 measurements and allows for comparison between values obtained when the patient **is** clinically well and those measured in the setting of acute illness. A drop from their baseline SpO_2 may indicate an evolving acute chest syndrome or worsening chronic lung disease and allow for prompt and appropriate intervention.

Table 1: The mean demographic and clinical parameters of the Controls and Subjects

Parameters	Steady state (N=102)	VOC (N=50)	P value
Age	22.94 ± 5.93	23.75 ± 6.28	0.41
Respiratory rate	20.9 ± 2.44	21.8 ± 3.28	0.07
Pulse rate	89.17 ± 11.91	95.7 ± 15.2	0.005
SBP	112.8 ± 13.3	107.6 ± 14.3	0.02
DBP	63.9 ± 10.2	60.4 ± 11.33	0.05
SpO_2	95.7 ± 3.8	94.4 ± 4.04	0.04
% with SpO_2 < 96%	30.4%	49.2%	-
% with SpO_2 > 96%	69.6%	51.8%	-

*Significant value using student t test. SBP: systolic blood pressure, DBP: diastolic blood pressure, VOC: vaso-occlusive crisis

Table 2: Correlation between SpO2 and clinical parameters amongst controls and subjects

	Steady state Pearson R	P value	VOC Pearson R	P value
age	0.003	0.97	-0.338	0.016*
SBP	-0.001	0.99	0.116	0.427
DBP	-0.117	0.268	0.091	0.533
Pulse	0.24	0.820	-0.024	0.869
Respiratory rate	-0.069	0.515	-0.055	0.707

*Significant value

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