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Cardiac Arrhythmias in Children with Sickle Cell Anaemia

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Summary

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Background : Sickle cell anaemia (SCA) is an important cause of morbidity and mortality in tropical Africa. Recurrent episodes of vaso-occlusive crisis often lead to organ ischaemia and/or infarction. Arrythmias are common and reliable manifestations of myocardial ischaemia and often follow infarction. The prevalence and pattern of cardiac arrhythmias among SCA patients has not been studied extensively, particularly in children.

Objective: To determine whether or not, patients with SCA are more prone than others to cardiac arrhythmias.

Patients and Methods: The standard 12-lead ECGs of 35 patients with SCA presenting during 40 episodes of vaso-occlusive crisis (Group A) were compared with those of 40 age- and sex-matched sicklers in the steady state (Group B) and with 40 age- and sex-matched patients with anaemia due to causes other than haemoglobinopathy (Group C).

Results: Cardiac arrhythmias were detected in four (10 percent) of the crisis episodes in Group A patients compared to three (7.5 percent) of patients in Group B and only one (2.5 percent) of the patients in Group C ($p>0.3$). In Groups A and B, the arrhythmias were all of atrial origin. The mean haematocrit level of Group A subjects with arrhythmias was significantly lower than those without ($p= 0.037$).

Conclusions: Although differences did not reach statistical significance, the results suggest that patients with SCA appear to be more prone to cardiac arrhythmias than others, whether or not they are in crisis. Further studies involving larger populations are indicated.

Introduction

SICKLE cell anaemia (SCA) remains an important cause of morbidity and mortality in tropical Africa.[1,2] The disease is associated with a chronic haemolytic anaemia and chronic tissue hypoxia, often with ischaemia, that is out of proportion to the degree of anaemia.[3,4] The four recognised types of crises often acutely worsen the hypoxia, and thus the organ or tissue ischaemia; this sometimes results in infarction. This is accomplished either by an acute worsening of the anaemic state, as in the hyperhaemolytic, aplastic and sequestration crises, or by microvascular occlusion through the aggregation of sickled red cells and microthrombus formation, as in the vaso-occlusive crisis.[5,6] Arrhythmias are common and reliable manifestations of myocardial ischaemia and often follow myocardial infarction.[7-12] ECG abnormalities are common in SCA patients[13] but the prevalence and pattern of cardiac arrhythmias among SCA patients in crisis or in the steady state have not been extensively studied. Maisel *et al*[14] found arrhythmias in 10 percent of standard surface ECGs of adult sicklers in crisis, but in 80 percent of their 24-hour ECGs. In a study focusing on children,[15] an incidence of 1.3 percent among steady state SCA patients was reported. In this report, we attempt to compare the frequency and types of cardiac rhythm abnormalities detected on the

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surface ECGs of children with SCA, during crisis and in the steady stat, with those of other anaemic children without SCA.

Patients and Methods

Children with SCA presenting during bone pain crisis at the Department of Paediatrics, University of Ilorin Teaching Hospital (UITH), Ilorin, were recruited into study group A. All those with clinical evidence of structural heart disease, renal impairment or diarrhoeal disease were excluded. So also were those known to be on cardio-active drugs. Thirty-five patients seen during 40 crisis episodes thus qualified for recruitment (five of the children were each seen during two different crisis episodes). The age, sex, height, weight, body surface area (BSA) and haematocrit of each subject was determined and recorded, as was a standard 12-lead surface electrocardiogram (ECG) with rhythm strip. Forty age- and sex-matched patients with SCA

Table I

Age, Sex distribution, Body Surface Area and Haematocrits of Study groups A, B and C

Parameter	*Group A*		*Group B*		*Group C*		*H**	*p-value*
	Range	*Mean±SD*	*Range*	*Mean±SD*	*Range*	*Mean±SD*		
Age (years)	3-17	10.2± 4.09	2-17	10.3 ± 4.31	2-15	8.5 ± 3.36	7.48	>0.1
BSA^{+} (m^2)	0.44-1.55	0.93±0.27	0.46±1.38	0.87±0.23	0.53-1.55	0.85±0.26	2.15	>0.5
Haematocrit (%)	13-34	23.32±4.61	17-30	22.7±4.05	6-29	22.58±5.6	2.08	>0.5
M:F **	1.67:1		1.35:1		1.86:1		0.52	>0.5

*H = Kruskal-Wallis one way analysis of variance test
**M: F = male : female ratio
$^{+}$BSA = Body Surface Area

Table II

Types of Rhythm abnormalities in Eight Subjects

Serial no.	*Group*	*Age (yrs)*	*Sex*	*Haematocrit*	*Rhythm abnormality*
1	A	12.5	m	22	premature atrial contraction
2	A	10.7	m	20	low right atrial rhythm
3	A	14.8	f	23	sinus pause, AER*
4	A	12.8	m	18	sinus pauses
5	B	4.2	m	29	sinus pause, AEB**, AER*
6	B	17.0	f	34	low right atrial rhythm
7	B	12.0	m	18	sinus pause, AEB**, AER*
8	C	5.0	m	9	PVC***

*AER = *atrial escape rhythm*
**AEB = *atrial escape beat*
***PVC = *premature ventricular contraction*

in the steady state attending the paediatric SCA clinic and who had been crisis and illness free for at least, four weeks prior to the date of the study, were recruited into the study Group B. Group C consisted of 40 anaemic patients (haematocrit less than 30 percent) whose haemoglobin electrophoresis pattern showed that they did not have sickle cell disease. Anaemia was of recent onset and followed an attack of malaria in the majority of group C subjects. Each subject had the similar data recorded as for group A subject.

All ECGs were recorded using a portable electronic ECG machine (*Model 9953, Seward, UK*). Recordings were obtained in a quiet room, with the caregiver present, to allay fear and anxiety as much as possible, especially in young children. Cardiac rhythm was determined from the surface ECG using standard criteria.[16] The frequency and types of rhythm abnormalities in each group were determined and compared with those found in the other groups.

Results

The three study groups were similar with respect to their ages and sex distribution, mean BSA and overall mean haematocrit (Table I). Among group C subjects, anaemia was associated with malaria in 24 patients (60 percent), typhoid fever in six (15 percent), other bacterial infections in four (10 percent), and burns and acute myeloblastic leukaemia in one patient (2.5 percent) each. No immediately apparent cause was found in four (10 percent) of the subjects. The haemoglobin electrophoretic pattern was AA in 30 subjects (75 percent), AS in seven (17.5 percent) and AC in three (7.5 percent).

Rhythm abnormalities

Four (10 percent) of the 40 ECGs recorded in SCA (study group A) subjects in crisis exhibited rhythm abnormalities. These were all atrial arrhythmias consisting of one premature atrial contraction (PAC), one low right atrial rhythm (LRA) and two cases of sinus pauses, one with an atrial escape rhythm (SP+AER), and the other without any escape beats or escape rhythm (Table II). The ECG of a 14-year old girl who had a sinus pause of 1.16 seconds followed by an atrial escape rhythm, is shown in Figure 1. The rhythm strip shows an initial sinus rhytm with a PR-interval of 0.2 seconds. After 4 sinus beats there is a pause of 1.16 seconds, followed by an atrial ectopic rhythm which has a shorter PR-interval (016 seconds) and P-waves that are different in morphology from the sinus P-waves. Arrhythmias (all atrial) were also detected in three (7.5 percent) of the 40 sicklers in the steady state (Group B). They comprised sinus pauses with atrial escape beats (SP+AEB) in two subjects (one of whom also had SP+AER) and a LRA in the third subject (Table II). Notably, one of these subjects was not anaemic. In Group C, only one subject had a rhythm abnormality. This was a premature ventricular contraction (PVC) in a five-year old boy who developed acute severe anaemia (haematocrit nine percent) due to malaria infection and died before blood could be administered. Comparing the three groups, the differences in the frequency of arrhythmias were not significant ($p>0.3$).

Haematocrit and arrhythmia

Group A subjects with arrhythmia had a significantly lower mean haematocrit (20.75±2.22) than those who had none ($t = 2.09$, $p=0.037$). In contrast, group B

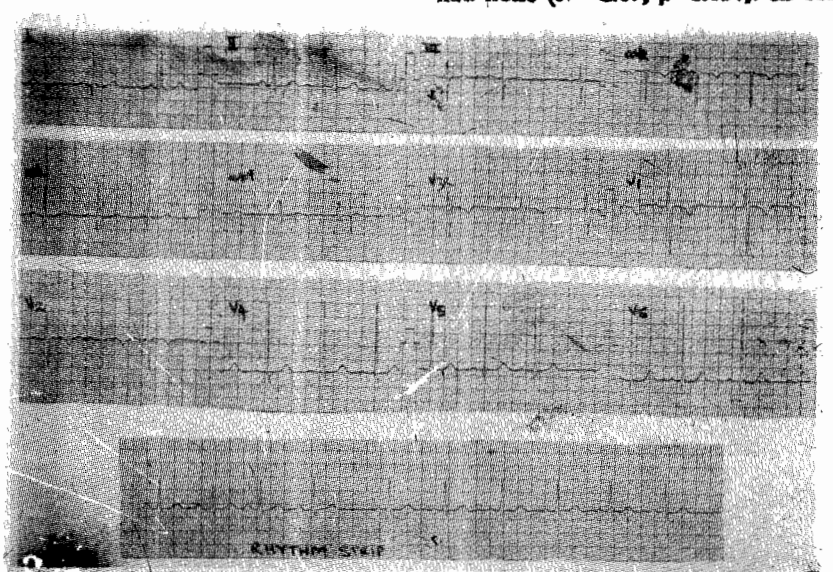

Figure 1: ECG of a 14 year old girl with sickle cell anaemia in vaso-occlusive crisis.

Table III

Mean Haematocrit Values in Subjects with and without Arrhythmia

Group	Mean Haematocrit (percent)				
	All	*Subjects with Arrhythmia*	*Subjects without Arrhythmia*		
A	23.3±4.6	20.75±2.22 (n= 4)	23.64±4.74 (n=36)	2.09	0.037
B	22.7±4.1	28.33±6.03 (n=3)	22.24±3.59 (n=37)	-1.73	0.11
C	22.6±5.6	9 (n=1)	22.92±5.21 (n=39)	-	-

subjects with arrhythmia tended to have a higher haematocrit than those without; this was however, not significant (t = -1.73, p = 0.11; Table III). Among all the SCA subjects exhibiting an abnormal rhythm, those in crisis had a lower mean haematocrit than those in the steady state (group B). The difference was also not significant (p=0.09; Table III).

Discussion

Our results have demonstrated no significant difference in the frequency and types of cardiac arrhythmias exhibited by sicklers in crisis and those in the steady state. Both groups had atrial arrhythmias with a frequency of 7.5-10 percent. This is in contrast to the anaemic non-sicklers among whom no atrial arrhythmia was found. Rather, a PVC was detected in one subject shortly before he died from the effects of severe anaemia. It is possible that the terminal event could have been a fatal ventricular arrhythmia, but this was not demonstrated since no continuous monitoring was obtained. These findings suggest that for some reason, patients with SCA are more prone to atrial arrhythmias than children that are anemic from other causes. Since SCA is usually associated, from about the fourth month of age, with anaemia that largely persists throughout life, the higher frequency of atrial arrhythmias in these patients might be attributable to the effects of chronic anaemia. The fact that most of the sicklers with arrhythmia were above 10 years of age is in consonance with this.

The steady state sicklers with arrhythmia had relatively high haematocrits compared with their counterparts in crisis, This, and the fact that both groups of sicklers exhibited similarities in the frequency and types of arrhythmia they had, suggest that factors other than anaemia alone, may be involved in the aetiology of these atrial arrhythmias. In SCA, chronic anaemia results from chronic haemolysis of sickled red cells. These sickled cells, being rigid, often occlude small blood vessels. They also tend to clump together, further contributing to microvascular occlusion, and also resulting in an increase in blood viscosity.[6] These, coupled with the arterial hypoxaemia that results from the pulmonary complications of the disease, have been identified as the factors responsible for the marked tissue hypoxia in this disease, that is out of proportion to the degree of anaemia.[3,4] It is likely that this tissue hypoxia plays a role in the pathogenesis of the atrial arrhythmias. It has been suggested that the abnormalities of repolarisation frequently observed on the ECGs of SCA patients may reflect ischaemic myocardial injury from chronic hypoxia or microvascular occlusion.[17] It is quite possible that the atrial arrhythmias observed in the present series, may have a similar origin, resulting in malfunctioning of the sinus node and/or atrial myocardium.

Previous workers[14,15,18,19] have observed rhythm abnormalities on the surface ECGs of SCA patients. Klinefelter[18] noted the presence of ventricular extrasystoles or PVC, which were however, not observed among the SCA subjects in the present study. The fact that his subjects were slightly older (8 - 27 years) than ours (3-17 years) may account for the difference. Sample size appears to be an unlikely explanation since the total number of our sicklers was much higher than Klinefelter's.[12] No continuous ECG monitoring was carried out in our study, but Maisel *et al*[4] found ventricular arrhythmias in 30 percent of the adult sicklers that were monitored during crisis. It is possible that ventricular arrhythmias may develop in SCA patients with increasing age. Only one sickler had an abnormal rhythm out of 78 children with SCA in the steady state studied in Ibadan,[15] a much lower frequency than the 7.5 percent obtained in a similar group of patients in this study. The arrhythmia

frequency of 10 percent on the surface ECG which was reported by Maisel *et al*[14] for adult sicklers in crisis is similar to what we have observed among the children in the present study.

The rhythm abnormalities identified in our SCA subjects were all of a benign nature and are similar to what have been observed on 24-hour ECG recordings in normal subjects.[20-21] Such findings would be considered abnormal if detected on the standard surface ECG and we consider them to be so in our subjects, especially as no such arrhythmias were found among our anaemic children with no haemoglobinopathy. It is very likely then, that with 24-hour monitoring, the frequency and severity of the arrhythmias detected in the subjects of the present study would have been much higher, as was the experience of Maisel *et al*.[14]

This study has thus shown that atrial arrhythmias on the standard ECG are equally frequent among SCA patients in crisis and those in the steady state, and that the frequency appears to be higher among SCA patients than anaemic patients who do not have SCA. We suggest that the atrial arrhythmias are probably attributable to the chronic tissue hypoxia that is a feature of SCA. Further studies involving serial surface ECGs and/or 24-hour recordings are required, to further investigate these findings.

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