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RESEARCH ARTICLE

A STUDY OF SERUM CALCIUM AND ENZYME CONCENTRATIONS IN PATIENTS WITH SICKLE CELL DISEASE

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ABSTRACT

Aim: Assesment of serum Calcium and enzyme concentrations in sickle cell disease in patients nearKing George Hospital in Visakhapatnam in Andhra Pradesh. The levels are in blood samples during stable state as well as during the crises state. The values are compared clinincal manifestations during in both conditions of Sickle cell patients.

Methods: 50 sickle cell patients were selected for study and blood samples for estimation of Serum calcium, uric acid, total bilirubin, lactate dehydrogenase, hydroxybutyrate dehydrogenase, and haemoglobin and also estimated in 28 of these patients during the Crises. 30 Normal persons were taken as control.

Results: Serum calcium tended to be lower in sickle cell patients than in healthy controls, while uric acid was higher. Crises did not make any difference to serum calcium but they increased the uric acid level significantly. All the other variables measured were significantly abnormal and more so during crises.

Conclusions: The variations in these cases compared to normal controls and also increase in their levels during Crises could be having Diagnostic value as well as for monitoring the disease in these patients (Nduka *et al.,* 1995).

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INTRODUCTION

The clinical manifestations of Sickle cell disease are well documented. Also the biochemical manifestations of SCD are recognized and the role they play in the clinic-pathological manifestations of this disease. Lower serum calcium and musculoskeletal changes with Radiological bone changes were noted. They were related with severity of the disease. Uric acid is proposed to have anti-sickling effect and this could related to hyperurecemia that occurs in SCD (Morgan *et al.,* 1984; Reynolds, 1983).There were also increase in Lactic dehydrogenase[5] and Bilirubin1[2]which are related to hemolytic episodes of SCD.

MATERIALS AND METHODS

50 patients were selected for the study. 28 of them are males and 22 of them are females (mean 18). 30 persons were also evaluated and taken as controls. The patients are from King George hospital, Visakhapatnam of Andhra Pradesh state (India). This disease is prevalent in a fisherman colony among several families near this hospital.

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This was thoroughly studied epidemiologically. The patients studied during crises were either in the emergency OP or as inpatients after admission. Venous blood was drawn from the patients of SCD during stable state as well as during crises state for some of the patients and also from controls. 80% of the crises states were of vaso-occlusive type. Hematological and biochemical studies were conducted on the obtained blood samples. Plasma was obtained by centrifugation of the samples for biochemical studies and used for the estimation of total bilirubin, calcium, uric acid, LDH, and the LDH1 oxobutyrate substrate analogue, α-hydroxybutyrate dehydrogenase (α-HBDH). Haemoglobin estimation was carried out with a Coulter counter S-plus IV model. Analyses of the biochemical variables were done with the Astra systems auto-analyser, except for the enzymes, which were analysed with the Dupont Dimension autoanalyser. Ciba "normal" and "abnormal" quality control sera were used for all the analyses. Coefficients of variation for the assays in our laboratory were 6-2% (bilirubin), 4-6% (calcium), 4-3% (uric acid), 6-3% (LDH and HBDH). Statistical analysis was done using Student's t test to obtain statistical significance of the differences between the mean for each variable in the sickle cell disease patients compared to the control (HbAA) subjects. P values <0 05 were

considered significant. Data are presented as mean (SD), and 95% confidence interval (CI), with significance of difference between means evaluated by unpaired CI testing.

RESULTS

Values of the various biochemical variables for the different subject groups investigated are presented in table 1. The statistical significance between the mean values for sickle cell disease patients and their matched controls (HbAA) are indicated in the table. The results show that the mean serum calcium level was lower, while the uric acid level was higher, in the sickle cell disease patients than in the control subjects. The results show that the mean serum calcium level was lower, while the uric acid level was higher, in the sickle cell disease patients than in the control subjects. The uric acid level was higher. Total bilirubin, LDH and oa-HBDH were significantly higher, while the Hb values were significantly lower, in the sickle cell disease patients than in the control Subjects.

Table. 1. Biochemical variables in the Sickle cell disease in age and sex matched controls. The variables are mean values(SD)

Biochemical variables	Group	SCD	Controls	Staistical significance
Calcium(mmols/L)	Males+Females	2.19(0.39)	2.4(0.029)	not significant
Uricacid(mg/dl)	Males	4.83(1.21)	4.23(0.94)	not significant
	Females	4.03(1.20)	3.5(0.94)	not significant
Total Bilirubin(mg/dl)	Males+Females	2.76(1.29)	0.5(0.05)	p<0.001
LDH(U/L)	Males+Females	350(49)	175(26)	p<0.001
α-HBDH (U/1)	Male + Females	227 (24)	119 (16)	p<0.001
Hb (g/dl)	Male + Females	9-26 (1-2)	14-83(1-51)	p<0.001
	Male	9-17 (1-7)	15-11(1-39)	p<0.001
	Female	9 10 (1-89)	13-71(1-42)	p<0.001

LDH = lactic dehydrogenase; α-HBDH = α-hydroxybutyrate dehydrogenase

Table 2. Level of some biochemical variables of sickle cell disease patients when in crises and steady states. Values are means (SD)

Biochemical variables	in Crisis State	In Steady State	Staistical
Uricacid(mg/dl)	5.10 (0.91)	4.41 (0.90)	p<0.05
Total bilirubin(mg/dl)	4.01 (1.10)	2.03 (0.72)	p<0.001
LDH(U/L)	522 (54)	290 (22)	p<o.001
α –HBDH (U/L)	288 (24)	204 (19)	p<0.001
Hb(g/dl)	7.55(1.02)	9.53(1.33)	p<0.01
Ca(mmol/L	2.22(0.04)	2.22(0.04)	NS

Uric acid, total bilirubin, LDH, and oc-HBDH levels were higher, while the Hb level was lower, during crisis than during steady state.

DISCUSSION

There is evidence now to show that calcium homeostasis is affected in sickle cell disease (Muhammed *et al.,* 1993; Al-Dabbagh *et al.,* 1989). A tendency towards hypocalcaemia in these patients has been found in this study, as in others (Nduka, 1987; Muhammed *et al.,* 1993; Al-Dabbagh *et al.,* 1989). The fact that patients with sickle cell disease are not universally hypocalcaemic may be explained by the complex nature of calcium homeostasis and the possible role of vitamins and hormones, as suggested recently (Muhammed *et al.,* 1993). the absence of variation in the calcium levels between crisis and steady state periods of sickle cell disease strongly suggest that the commonest presenting feature of the disease-the bone manifestations (Nduka, 1987; Al-Dabbagh *et al.,* 1989) is an inherent aspect of the disease and does not depend on the geographical location of the patients. From this study, we have shown that serum uric acid values in sickle cell patients tend towards the upper range of normal, but with only about 3% reaching the hyperuricaemic level. This tendency is similar to previous reports on Saudi Arabian sickle cell patients4 and other populations (Nduka, 1987; Morgan *et al.,* 1984; Gold *et al.,* 1968; Adeyokunnu, 1984). 80% of the crises in our population were of the painful vaso-occlusive type which also inflicts bone pain on the patients.

The fact that the uric acid elevation reverted to normal upon recovery from crisis lends credence to the suggestion of an antisickling role for uric acid (Ekeke, 1987). It can be infered from these findings that uric acid metabolism is compromised in sickle cell disease, albeit to a varying degree depending on ameliorating factors (Acquaye *et al.,* 1985). The severity clinical manifestations of sickle cell disease, depending on sex, age, and type of population, also vary (El-Hazmi *et al.,* 1989; Neely *et al.,* 1969; Morgan *et al.,* 1984; Gold *et al.,* 1968; Adeyokunnu, 1984). Increased levels of bilirubin is due to a higher than normal rate of breakdown of red blood cells in sickle cell disease patients. Also, sickle cell disease related infarcts, occurring in a variety of organs including the liver, have been reported (Acquaye *et al.,* 1985). Microinfarcts in the liver could exacerbate the rise in serum bilirubin and would account for the much higher level in crisis. Similarly, the low level of haemoglobin, which is further reduced in crises as observed in this study, is attributed to the continuous haemolysis in sickle cell disease. ours shows that both serum bilirubin and haemoglobin levels are affected during painful vaso-occlusive crisis.

The elevation of LDH levels are attributed to continuous haemolytic events and release from infarcted bone marrow. Infarcted muscles which release creatinine kinase (Hunt *et al.,* 1989) may also release the muscle LDH isoenzyme. Rise in LDH levels and decrease in Hemoglobin leves do not correlate as they occur independently. The mean α-HBDH level is higher in sickle cell disease patients than in control subjects. However, only 56% of the patients actually had levels higher than normal, though during crisis, this increased to 80%. The source of this raised enzyme in sickle cell disease may be necrotic bone marrow and in vivo haemolysis. However, because of the relative specificity of HBDH assays to cardiac events, it is probable that the major source could be infarcted cardiac muscle. This is supported by the frequent observation of "large heart" in children who die during sickle cell crises (Nduka, 1987).

Conclusions

It is thought that hypoxic damage to cells, and the tissue ischaemia which occurs in sickle cell disease crises, is implicated in these enzyme elevation. Thus the measurement of this predominantly heart specific enzyme could be used as a marker for monitoring severity and progression of crises. Assays of some of these variables show definitive differences between steady state and crisis state in this and other populations. Because of the relative ease with which these indices can be measured, they can be adapted for use both as biochemical markers for sickle cell disease crises and as tools to monitor the severity and progression of crises.

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