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Hepatic function tests in children with sickle cell anaemia during vaso occlusive crisis

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SUMMARY

Thirty children with sickle cell anaemia had their serum alanine aminotransferase, alkaline phosphatase, total protein, albumin and bilirubin, assayed during vaso-occlusive crisis and at recovery.

Alanine aminotransferase, alkaline phosphatase and bilirubin levels were significantly higher during crisis than at recovery, ($p < 0,005$) especially in the young patient. However, the total protein and albumin levels were not significantly different in crisis and at recovery.

A transient hepatic functional derangement during vaso-occlusive crisis is a probable explanation for the reported changes.

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INTRODUCTION

There is evidence in the literature suggesting that biochemical and morphological hepatic changes occur in sickle cell anaemia patients.[1-7] It is however, uncertain whether or not these changes which occur during crisis are reversible. Earlier studies have demonstrated an impairment of liver functional integrity with a rise in serum transaminases, but the extent of the hepatic injury has not been documented.[4,5] This study was conducted to assess the hepatic functional derangement that occurs during vaso-occlusive crisis using biochemical techniques, to document the extent of derangement, and whether or not there was recovery.

MATERIALS AND METHODS

Sickle cell anaemia (SCA) patients whose haemoglobin electrophoresis is "SS" using the cellulose acetate paper were studied during vaso-occlusive crisis and at recovery. Serum levels of alanine aminotransaminase (ALT), alkaline phosphatase (ALP), total protein, albumin and bilirubin were measured during crisis and at recovery, each SCA patient being its own control. Vaso-occlusive crisis is defined, for the purpose of this study, as painful crisis in any of the bones and abdomen without any organic cause apart from sickle cell anaemia. Recovery is defined as four weeks after painful crisis by which time the patient is totally symptom free.

Observing the rules of asepsis, venous blood was taken from all the SCA patients during vaso-occlusive crisis and at recovery and the blood samples were processed within two hours of collection.

Analytical method: Serum alanine aminotransaminase activity was analysed by the calorimetric method using 2-4 dinitrophenyl hydrazine.[9] Aspartate aminotransferase activity was not assayed routinely in our laboratory.

Alkaline phosphatase was analysed by the colorimetric method using phenlyphosphate as substrate.[10] Bilirubin was analysed by the Malloy and Evelyn method using methanol as an accelerator.[11] Serum proteins were analysed by the BIURET method.[12]

Statistical analyses were done using appropriate methods (student's t-test and correlation coefficients).

RESULTS

Thirty patients with sickle cell anaemia, 16 males and 14 females were studied. The mean age was 8,95 years with a range of one to 18 years.

Table I shows the various enzyme levels both during the crises and recovery. The mean level of alanine aminotransferase (ALT) during crises (84,5 iu/l) was significantly higher than in the steady state (14 iu/l) ($p < 0,005$). During crisis, 23 (76 pc) of the 30 SCA patients had raised enzyme levels (>15 iu/l) and only five (16 pc) still had raised levels at recovery. The young SCA patients had a higher value than the older ones during crises.

Table I: Mean serum levels of alanine aminotran-sferase, alkaline phosphatase, total protein, albumin and bilirubin during crisis and at recovery.

Parameter	Crisis (n = 30)	Recovery (n = 30)	t	p
Alanine transaminase (Iu/l)	48,5 ± 12,32 (10–98)	14 ± 5,26 (4–32)	3,38	< 0,005
Alkaline phosphatase (Iu/l)	128,5 ± 26,8 (100–300)	98,4 ± 31,5 (72–180)	2,15	< 0,025
Total protein (Gm/l)	66,62 ± 9,75 (60–72)	68,2 ± 10,28 (62–76)	1,52	> 0,05
Albumin (Gm/l)	32,2 ± 4,55 (30–35)	34,0 ± 5,75 (30–40)	1,15	> 0,05
Total bilirubin (umol/l)	114,25 ± 23,5 (39–396)	47,5 ± 16,56 (18–88)	3,33	< 0,25
Conjugated bilirubin (umol/l)	87,8 ± 19,71 (20–221)	11,2 ± 5,52 (0–32)	3,45	< 0,001
Albumin/globulin ratio	0,935	0,935		

The figures in bracket represents the ranges of values.
Each parameter has 58 degrees of freedom.

Table II: The test values during crisis according to age groups.

Parameters	1–6 years (n = 9)	7–12 years (n = 14)	13–18yrs(n = 7)	"r"
Alanine Aminostransferase (Iu/l)	54,24 ± 14,601	43,67 ± 10,612	40,50 ± 8,80	0,898
Alkaline Phosphatase (Iu/l)	138,25 ± 23,936	127,2 ± 20,089	118 ± 24,77	0,890
Total Protein (Gm/l)	64,6 ± 10,704	66,56 ± 12,45	68,39 ± 7,95	0,951
Albumin (Gm/l)	32,4 ± 4,80	31,8 ± 4,706	27,67 ± 2,388	0,903
Total Bilirubin (umol/l)	117,0 ± 31,126	113,167 ± 25,62	117,833 ± 22,8	0,928
Conj. Bilirubin (umol/l)	97,2 ± 18,8	80,667 ± 11,511	81,146 ± 18,448	0,886

Correlation coefficient is "r".

Also, the mean alkaline phosphatase level (128 ± 12,32) was significantly higher during crisis as compared to the mean level (98,4 ± 31,5) at recovery ($p < 0,05$). Again the levels were higher in younger SCA patients where compared to the older ones.

The difference between levels of total protein and albumin in both crisis and recovery were not significantly different ($p > 0,05$). There was however, a slight rise in the level of each which may be clinically important. Albumin/globulin ratio was less than one (0,935 and 0,995) in crisis and recovery phases respectively (Table I).

The mean total serum bilirubin during crisis (114,25 ± 23,5 umol/l) was significantly higher than at recovery (47,5 ± 16,75 umol/l): ($p < 0,025$) and the hyperbilirubiaemia was predominantly conjugated.

Table II shows the effects of age on the various enzyme levels. The younger the patient the higher the level of alanine aminotransferase and alkaline phosphatase levels. The correlation coefficient for each (0,898, 0,890) was quite significant. The same trend was noted for serum albumin levels. However, for total protein, the reverse was the case. The correlation coefficient of 0,951 was noted for total protein level. The younger the patient the lower the total protein.

DISCUSSION

The mechanism of hepatic injury in sickle cell disease is uncertain. There is a transient hepatic functional derangement during crisis.[4,5] Barret-Connor emphasised the potential role of viral hepatitis observed in the group SCA patients she studied.[13]

In the group of children studied by us, alanine amino-transferase levels were higher during crisis, and these returned to normal at recovery. This finding is in agreement with earlier reports.[3-5] That the levels of the aminotransferase returned to normal at recovery suggest a transient hepatocytic injury during crisis. Hepatic necrosis in the region of the central vein has been described in adults with SCA at autopsies.[2,6,7] While the extensive work of Bauer, *et al*[15] supports hepatocelluar injury, findings of Omata *et al*[16] showed only acute or subacute infection but failed to show any evidence of hepatic necrosis.

The serum alanine aminotransferase was higher in the younger age group than in the older children with SCA which may suggest a more severe hepatocyte injury in the younger children with SCA. The reason for this phenomenon is not clear.

The alkaline phospatase levels were higher during crisis and more so in the younger age group. This finding is similar to that of Kaine and Udeoso[4] and may be due to a transient intrahepatic cholestatis suggesting hepatocyte swelling.[4,6,7] Cholelithiasis which may contribute to hepatobiliary obstruction was recorded in only 4,2 pc of Nigerian SCA children studied.[14] Since osseous activity in this age group is high, an assay of the isoenzymes of alkaline phosphatase would have thrown more light on the source of these raised enzyme levels during crisis. This question is being addressed in a separate study in our centre.

Serum protein levels did not show any significant difference during crisis and at recovery. This report is similar to the findings of Isichei[3] and Kaine and Udeozo.[4] The relative similarity in the values during crisis and at recovery is probably related to the long half-life of the protein which will not change much during the short period of acute SCA crisis.

In conclusion, this study suggests a transient but reversible hepatic functional derangement during thrombotic crisis, which may be due to some degree of hepatocellular injury with intrahepatic, cholestatitis. However, considering the chronic nature of the disease, the long term consequence of this probably repeated derangement on hepatic function remains to be ascertained.

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