BLOOD AND URINARY KETOACIDS IN INDIAN CHILDHOOD CIRRHOSIS*

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The liver plays a key role in the metabolism of aminoacids and carbohydrates with ketoacids forming an important link connecting these two vital metabolic processes. Disturbed ketoacid metabolism has been described in various hepatic disorders including cirrhosis (Amatuzio et al. 1952, Seligson et al. 1952, Smith et al. 1953, Dawson et al. 1957), and their relation to hepatic coma and blood ammonia level through the Kreb's citric acid cycle has been speculated upon (Summerskill et al. 1957) although much remains to be explained (Sherlock 1963). Disturbances in amino-acid metabolism have already been described in cases of childhood cirrhosis (Chaudhuri et al. 1960, Ingle 1963, Mehta et al. 1964, Dhatt et al. 1967). So far no study regarding the disturbances in ketoacids in this disorder has appeared in the literature. The present work is the first attempt in that direction.

Material and Method

17 cases of Indian childhood cirrhosis were studied for their blood and urinary ketoacids. 16 cases were in an advanced stage and showed evidence of hepatocellular failure (6 in coma, 10 without coma). One case did not have any evidence of hepatocellular failure.

Five normal children in the same age group served as controls.

Morning samples of blood and urine were collected after an overnight fast and were analysed for α-ketoglutaric acid and pyruvic acid by the technique of unidimensional descending paper chromatography (Smith 1960), modified by Saini (1967).

Results

The observations are summarised in the table.

**Normal children**:

In the normal children fasting blood α-ketoglutaric acid values (mean 0.17 mg%, range 0.15-0.21 mg%) were lower than that of pyruvic acid (mean 0.45 mg%, range 0.43-0.50 mg%), while the reverse was the case in urine (α-ketoglutaric acid : mean 1.33 mg%, range 1.2-2.0 mg%, pyruvic acid : mean 0.84 mg%, range 0.70-1.03 mg%).

**Indian childhood cirrhosis**:

a) Case showing no evidence of hepatocellular failure: There was a considerable increase in urinary excretion of α-ketoglutaric acid (3.0

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Table 1. Blood and urinary α-ketoglutaric acid (α-KGA) and pyruvic acid (PA) values (mg/100 ml.)

<table>
<thead>
<tr>
<th>Normal</th>
<th>Indian childhood cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early (1 case)</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Urine α-KGA</td>
<td>1.33</td>
</tr>
<tr>
<td>Urine PA</td>
<td>0.84</td>
</tr>
<tr>
<td>Blood α-KGA</td>
<td>0.17</td>
</tr>
<tr>
<td>Blood PA</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*Estimated quantitatively in only two cases. (See text).

mg% while urinary excretion of pyruvic acid was only slightly affected (1.12 mg%). The blood levels of these acids remained within normal limits (α-ketoglutaric acid 0.15 mg% and pyruvic acid 0.48 mg%).

(b) Cases with hepatocellular failure but without coma: There was a slight fall in mean α-ketoglutaric acid level and in none of the cases the upper limit for normal was surpassed (mean 0.15 mg%, range 0.12–0.21 mg%) while blood pyruvic acid values rose (mean 0.69 mg%, range 0.56–0.96 mg%). In the urine also α-ketoglutaric acid excretion was within normal limits (mean 1.17 mg%, range 1.30–2.52 mg%) while there was a considerable rise in pyruvic acid excretion (mean 3.97 mg%, range 2.7–6.0 mg%).

(c) Cases with hepatocellular failure in coma: A further exaggeration of the tendency as seen in cases of hepatocellular failure without coma was observed. Mean blood α-ketoglutaric acid value was 0.15 mg% (range 0.12–0.18 mg%) while mean blood pyruvic acid was 0.76 mg% (range 0.61–1.32 mg%). In the urine mean α-ketoglutaric acid excretion was 1.72 mg% (range 3.6–5.8 mg%). In addition, in 4 cases out of 6 in hepatic coma there appeared in the urine three more ketoacids with rf values of 0.88, 0.85 and 0.76 in the solvent employed. One of them with rf 0.85 was partially overlapping the second band of pyruvic acid. That is why pyruvic acid could not be tested in all the cases of hepatic coma quantitatively. The concentration of these ketoacids as could be judged with the naked eye appeared to be quite small.

Discussion

Smith et al. (1953), Dawson et al. (1957) and Summerskill et al. (1957) found increased fasting blood α-ketoglutaric acid levels in hepatic diseases including cirrhosis but reported normal fasting blood pyruvic acid values before any evidence of neuropsychiatric disturbances appeared. Dawson et al. further reported that as the neuropsychiatric state deteriorated, both