Cord γ glutamyl transpeptidase activity and neonatal jaundice

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Davidson, D. C., McIntosh, W. B., and Ford, J. A. (1976). Archives of Disease in Childhood, 51, 286. Cord γ glutamyl transpeptidase activity and neonatal jaundice. γ Glutamyl transpeptidase (GGT) activity was measured in normal neonates and in maternal serum post partum. Levels were above the normal adult range (351 U/l) in all neonates and a significant correlation was found between enzyme activity and bilirubin levels on day 7 (P<0.005). The mean bilirubin level on days 4 and 7 was higher in babies with cord values <90 IU/l.

In certain circumstances increased plasma GGT activity may serve as an index of enzyme induction. However, our results suggest that raised levels in the neonate may reflect hepatic microsomal damage with subsequent impairment of bilirubin conjugation. Further evaluative studies of cord GGT activity in neonates at risk, with a view to early prophylactic or therapeutic measures, are indicated.

Hepatic glucuronyl transferase, important in the conjugation of bilirubin, is located chiefly in the microsomal fraction and functional immaturity of this enzyme is implicated in the aetiology of physiological jaundice in neonates. As direct assessment of the enzyme is not possible, other indices which may reflect hepatic microsomal enzyme activity have been investigated. Hepatic glutamyl transpeptidase is such an index. It is predominantly microsomal in location, is readily measurable in small quantities of plasma, and high levels are present in the cord blood of normal neonates at term (Richterich and Cantz, 1972; Shore et al., 1975). This study was designed to establish the significance of this observation, particularly in relation to bilirubin values in the first week of life.

Subjects and methods

Twenty-nine mothers with spontaneous deliveries and their babies were studied after obtaining informed maternal consent. In each neonate the Apgar score at one minute was >7, and estimated gestational age >38 weeks. Direct Coombs antiglobulin test was negative in all babies and those with potentially ABO incompatible groups were excluded. Further details of the infants studied are shown in Table I.

<table>
<thead>
<tr>
<th>No.</th>
<th>Birthweight (kg)</th>
<th>Group A</th>
<th>Group B</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(2.55—3.82)</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>3.09</td>
<td></td>
<td>3.29</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>5 (42%)</td>
<td></td>
<td>1 (50%)</td>
</tr>
<tr>
<td>Oxytocin infusion</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Maternal venous blood was sampled immediately post partum and initial neonatal specimens were obtained from the umbilical vein. Further samples of venous blood were taken from dorsal hand veins of neonates on day 4 (29 specimens) and day 7 (23 specimens) of life. Early discharge of patients was responsible for the smaller number of specimens on day 7. All specimens were centrifuged promptly upon withdrawal and stored at −20°C until analysed within 24 hours.

γ Glutamyl transpeptidase (GGT) was measured at 37°C by the use of a commercial kit (Boehringer, Mannheim) which employs the kinetic photometric method of Szasz (1969), and bilirubin by a standard method (Lathe and Ruthven, 1958). The results were analysed by Student's 't' test and Kendall's rank correlation method.

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Results

The mean (±SEM) values of GGT activity were maternal 20·2±1·9 IU/l; cord 77·5±5·4 IU/l; day 4 60·2±6·8 IU/l; day 7 72·0±6·1 IU/l. Maternal levels were significantly lower than levels in the neonate during the first week (P<0·001).

For the purpose of this study, the neonates were divided into two groups. Group A comprised 19 infants (12 males, 7 females) with cord GGT activity of 90 IU/l and below in respect of cord and day 4 specimens. For reasons mentioned above, only 13 (7 males, 6 females) were sampled on day 7. Group B contained 10 infants (5 males, 5 females) with cord GGT levels in excess of 90 IU/l. All 10 infants were sampled on both day 4 and day 7. The GGT value of 90 IU/l was chosen in order to divide the neonates on the basis of previously published data on the normal range of the enzyme in cord blood (Richterich and Cantz, 1972).

No significant difference was shown in mean bilirubin levels between the groups at birth or, on day 4, while bilirubin was significantly higher in group B by day 7 (P<0·05) (Table II). Further-

TABLE II
Mean bilirubin levels at birth, on day 4 and day 7 (±SEM) and significance of differences between the groups

<table>
<thead>
<tr>
<th></th>
<th>Group A (cord GGT level ≤ 90 IU/l)</th>
<th>Group B (cord GGT &gt; 90 IU/l)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cord</td>
<td>2·4±0·27</td>
<td>2·4±0·23</td>
<td>NS*</td>
</tr>
<tr>
<td>Day 4</td>
<td>5·1±0·6</td>
<td>5·6±1·49</td>
<td>NS*</td>
</tr>
<tr>
<td>Day 7</td>
<td>2·8±0·406</td>
<td>7·2±1·31</td>
<td>&lt;0·05</td>
</tr>
</tbody>
</table>

*NS, not significant

more as shown in the Fig., there was a significant correlation between the individual bilirubin and cord GGT levels (P<0·005) on day 7. No such correlation was found between GGT levels at birth and cord or day 4 bilirubin levels. There was no significant relation between individual maternal GGT activity and that found in cord, day 4, or day 7 specimens from her baby.

Oxytocin infusion during labour did not seem to influence GGT activity in mothers or babies. We were unable to detect any difference in bilirubin levels between the groups brought about by oxytocin (χ² test, P not significant).

Discussion

Our finding of raised GGT in neonates in the first week of life confirms the observations of other workers (Richterich and Cantz, 1972; Shore et al., 1975). The source and significance of the increased enzyme activity in term neonates has hitherto been uncertain. Since we were unable to show a correlation between individual maternal and cord, day 4 or 7 GGT levels, it seems unlikely that antenatal placental transfer of the enzyme from the mother to the fetus is a significant source of the enzyme activity. Recently Shore et al., (1975) have shown that significant amounts of GGT are found in the placenta, and as these authors suggest it would be necessary to postulate preferential release of placental GGT into the neonatal circulation to explain the disparity between cord and maternal enzyme levels. It is possible that cord GGT arises from tissue other than hepatic or placental and further isoenzyme studies would be useful to establish the origin.

Raised GGT levels have been found in patients taking anticonvulsant drugs and have been thought to reflect hepatic microsomal enzyme induction (Rosalki, Tarlow, and Rau, 1971; Davidson, McIntosh, and Ford, 1974). In such patients, and in neonates born to mothers who have been given barbiturates, bilirubin levels are reduced (Trolle, 1968). This suggests that enzyme induction producing raised plasma GGT levels correspondingly increases the activity of the enzyme systems involved in the conjugation of bilirubin. In this study, however, GGT levels correlated directly with bilirubin levels, making it unlikely that the increased plasma activity observed in group B subjects resulted from microsomal enzyme induction. It is well recognized that increased plasma GGT activity is found in a wide variety of liver disorders (Szczeklik, Orłowski, and Szewczuk, 1961; Szewczuk 1966) and is thought to indicate
hepatocellular damage with release of the enzyme into the circulation (Rosalki, 1973). From our study it seems more likely that the increased cord GGT activity is attributable to minor insults to the microsomal systems acquired during labour or antenatally. Such damage, while not sufficient to produce hepatocellular damage and alter conventional liver function tests, may nevertheless be sufficient to cause microsomal dysfunction as reflected by raised plasma GGT and impairment of bilirubin conjugation. Both the higher bilirubin levels of group B subjects and the correlation between GGT and bilirubin levels on day 7 suggest this impairment of normal bilirubin conjugation. The finding of raised cord GGT activity therefore may serve as an early index of impending hyperbilirubinaemia allowing the early institution of prophylactic or therapeutic measures. Further evaluative studies of GGT levels in neonates at risk are clearly required.

**REFERENCES**


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