plasma osmolalities suggested that hydration was adequate.

A rapid decrease in jaundice when breast feeding is stopped and a recurrence with the reintroduction of breast milk certainly suggests that at least one inhibitor is present in breast milk. Its nature, however remains unknown.

References


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Alpha-thalassaemic hydrops fetalis

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SUMMARY Concentrations of total protein, albumin, colloid osmotic pressure, and immunoglobulins G and M were measured in the umbilical venous plasma of 4 infants with α-thalassaemic hydrops fetalis. Total protein, albumin, and colloid osmotic pressure concentrations were low, and these are likely to be contributory factors in the formation of fetal oedema. Immunoglobulin G levels were low suggesting a reduction in placental transfer probably due to placental oedema.

Infants affected with the homozygous form of α-thalassaemia are invariably hydropic at birth. The mechanisms for the formation of this intrauterine oedema are still poorly understood and chronic anaemia, congestive cardiac failure, and hypoproteinaemia have all been suggested as factors; it is unlikely that any one of these alone is responsible.

Such infants suffer from severe anaemia due to the chronic haemolysis associated with the abnormal haemoglobin resulting from defective alpha chain synthesis. It is thought that this may lead to high output cardiac failure as well as causing anoxic damage to the capillary walls thereby increasing their permeability to plasma proteins. In other conditions however, equally low levels of haemoglobin do not cause hydrops nor is there any clear evidence that tissue oxygenation is disturbed in utero. Indeed a normal acid-base balance was reported in one newborn infant. A third possible factor, that of hypoproteinaemia, has not previously been studied in cases of α-thalassaemia, although it is known that both plasma proteins and colloid osmotic pressure may be reduced in hydrops fetalis associated with rhesus isoimmunisation.

We now report a study of plasma proteins in α-thalassaemic hydrops fetalis.

Materials and methods

Blood was collected from the umbilical vein of 4 infants with hydrops fetalis immediately after birth. In each case the diagnosis of α-thalassaemia was confirmed by haemoglobin electrophoresis. Clinical data were available for the 3 infants (Cases 1-3) born
in Chiang Mai. The fourth sample was provided by Dr Ganesan in Kuala Lumpur and no clinical details are available.

The plasma was separated and stored at −20°C except during the flight to England when it was carried on dry ice. Albumin was measured by a modification of the bromcresol green method. IgG and IgM levels were measured by radial immunodiffusion by the Fahey method using plates from the Boehringer Corporation Limited. Plasma colloid osmotic pressure was measured using a modification of Hansen’s pressure transducer osmometer.

Results

Clinical and laboratory data for the 3 infants and laboratory data for Case 4 are shown in the Table. All infants were grossly hydropic.

The Figure shows the total protein and colloid osmotic pressure levels in the α-thalassaemic infants compared with two groups of white infants—one normal and the other rhesus immunised with hydrops fetalis.

In each case total protein, albumin, and colloid osmotic pressure levels were well below the normal range, as was the cord IgG concentration (normal range 72–175 IU/ml); IgM concentrations in the cord blood were just above the normal range in 2 infants (0–24 IU/ml).

Discussion

Our findings confirm that both the total protein and albumin concentrations are low in α-thalassaemic infants and the very low colloid osmotic pressure associated with these low levels is likely to be, at least in part, responsible for the oedema formation. It is not clear why protein levels should be low in states of chronic intrauterine haemolysis.6 Protein synthesis may be reduced secondarily to a disturbance in the function of the abnormal liver whose architecture is grossly disturbed by extramedullary haemopoesis.

All 3 infants had large oedematous placentae and in each case the placental/fetal weight ratio was extremely high. It would not be surprising if this oedema affected materno-fetal transfer. The placental membrane is thickened by the oedema and the swollen villi may encroach into the intervillous space thereby reducing maternal blood flow.6 A reduction in available maternal amino-acids could restrict protein synthesis still further in the fetus. But if the placental oedema were the cause of the hypoproteinaemia there must obviously be another cause of the initial feto-placental oedema.

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Table Clinical data and umbilical cord plasma levels of protein and colloid osmotic pressure in 4 infants with α-thalassaemic hydrops fetalis

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Gestation (weeks)</th>
<th>Birthweight (g)</th>
<th>Placental weight (g)</th>
<th>Total protein (g/l)</th>
<th>Albumin (g/l)</th>
<th>Colloid osmotic pressure (cmH2O)</th>
<th>IgM (IU/ml)</th>
<th>IgG (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>32</td>
<td>1800</td>
<td>1200</td>
<td>33</td>
<td>17</td>
<td>13</td>
<td>42</td>
<td>55</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>33</td>
<td>2580</td>
<td>1160</td>
<td>29</td>
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<td>11</td>
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<tr>
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<td>F</td>
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<td>20</td>
<td>8</td>
<td>14</td>
<td>0</td>
<td>25</td>
</tr>
</tbody>
</table>

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Figure Total protein and colloid osmotic pressure levels in 3 infants with α-thalassaemic hydrops fetalis compared with normal levels for white newborn infants (the lines show the 95% confidence limits) and hydropic infants with rhesus isoimmunisation.
In other conditions associated with placental oedema—such as the fetofetal transfusion syndrome, and hydrops fetales due to rhesus isoimmunisation or congenital syphilis—low levels of the maternally synthesised immunoglobulin IgG have been found in the cord bloods of the infants. These findings suggest that placental transfer of IgG is also reduced.

We, like Chiang and Wei, found that the cord IgG levels were below the normal range for a white population (72–175 IU/ml). As studies have shown that mothers in tropical countries, and therefore their babies, tend to have higher levels of IgG, it is likely that the levels are even further outside the normal range for a Thai population. Unfortunately no data are available, but studies on unaffected infants and their mothers from Taiwan support this suggestion.

The whole complex pathophysiology of oedema in the fetus and newborn infant needs further study. Alpha-thalassaemic hydrops fetales is an example of the most extreme form of intraterine oedema and provides a unique model for investigation of the underlying mechanisms of oedema formation. Now that rhesus isoimmunisation can be prevented (or its effects altered in utero), there is no other condition in which hydrops fetales can be predicted and thus be accessible to study from early pregnancy.

We thank Dr S Silpisornkosol for allowing us to study patients under her care, Dr T Seesuwan for collecting the blood samples, and Dr David Baum for help and encouragement.

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References


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Factors influencing mortality and morbidity after clinically apparent intraventricular haemorrhage

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SUMMARY Twenty newborn infants with clinically apparent intraventricular haemorrhage were studied in order to determine the factors associated with mortality and morbidity. Ten survived, 4 without handicap and 2 with only moderate handicap. Maturity and not size of haemorrhage appeared to be the main factor affecting mortality and morbidity at 1 year. Coma longer than 24 hours after intraventricular haemorrhage distinguished survivors with handicap from those without and may be a useful prognostic sign.

Intraventricular haemorrhage (IVH) is a common event in preterm infants. In about half the cases it may be occult, detectable only by computerised tomography (CT) scans or ultrasound. When it is clinically evident, it is associated with a high mortality and, in the event of survival, with a high morbidity. Survival may be complicated by hydrocephalus too. Changes in methods of life support now lead to greater numbers of survivors of IVH, many of whom are surviving with handicap. We have examined our experience in order to determine which factors influence mortality and morbidity from IVH.

Methods

Babies born between 1 January 1977 and 1 January
Alpha-thalassaemic hydrops fetalis.

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