Does ABO incompatibility matter?

Sir,

Quinn et al show with the progression from ABO compatibility to ABO incompatibility and then to ABO incompatibility with a positive Coombs test that there is an increasing incidence of jaundice, but the jaundice decreases in severity (see table).1 About half of the ABO incompatible babies who had a positive Coombs test had a peak bilirubin concentration less than the lower limit of bilirubin in the jaundiced ABO compatible babies.

It is clear that jaundice, a positive Coombs test, and ABO blood group incompatibility are not sufficient criteria on which to base a diagnosis of ABO incompatible jaundice. The data are entirely compatible with the assumption that ABO incompatible jaundice is a figment of the paediatricians’ vivid imagination.

Reference

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We concur with Dr Williams’ interpretation of our data. There is little doubt that bias was introduced into the ascertainment of jaundice because of the paediatricians’ prior knowledge of the result of the elution and Coombs test. This would explain increased frequency of detection with lesser severity in elution and Coombs positive cases. We are not sure whether ABO incompatible jaundice is a figment of the paediatricians’ imagination or whether the elution and Coombs test are inappropriate for its detection. Brouwers et al recently published data suggesting that a combination of the antibody dependent cell mediated cytotoxicity assay and antigen density of A or B antigens on the red cells together provide a good screening test for ABO incompatibility.1 Unfortunately these investigations are not widely available.

Table Details of infants from Quinn et al1

<table>
<thead>
<tr>
<th>Group</th>
<th>ABO compatible (control group)</th>
<th>ABO incompatible</th>
<th>ABO incompatible with positive Coombs test</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=110)</td>
<td>(n=110)</td>
<td>(n=36)</td>
<td></td>
</tr>
<tr>
<td>No (%) with jaundice</td>
<td>18 (16)</td>
<td>29 (26)</td>
<td>14 (39)</td>
</tr>
<tr>
<td>Median peak serum bilirubin of jaundiced babies (μmol/l)</td>
<td>190</td>
<td>171</td>
<td>162</td>
</tr>
<tr>
<td>Range</td>
<td>159–295</td>
<td>111–282</td>
<td>111–236</td>
</tr>
</tbody>
</table>

Rectal nifedipine in acute severe hypertension in young children

Sir,

We read with interest the paper by Evans et al on sublingual nifedipine for the treatment of acute severe hypertension.1 They found that sublingual nifedipine rapidly lowers blood pressure in children with acute severe hypertension and we agree with them.

Evans et al did not experience hypertensive children under the age of 5 years.1 It is difficult to administer a liquid medicine sublingually to young infants. We, therefore, attempted rectal administration of nifedipine in hypertensive children including infants.

The volume inside a 10 mg capsule of nifedipine is 0.34 ml. Based on our dose range (0.2 to 0.5 mg/kg), we aspirated the extra contents from the capsule with a syringe. We made another hole in the capsule which we then administered rectally. We treated nine severely hypertensive children aged 10 months to 15 years,2 five of whom were under the age of 5. The hypertension was secondary to glomerulonephritis in three, renovascular hypertension in three, and other causes in three. We observed successful effects of rectal nifedipine in all cases, although Evans et al failed to control blood pressure in some patients.1 Its effect in lowering blood pressure appeared within 10 minutes after administration, and lasted more than three hours. Side effects were mild and infrequent; they included asymptomatic tachycardia and mild flushing.

Nifedipine is an excellent drug for the treatment of acute severe hypertension as reported.1 We are sure that rectal administration is reliable in young children.

References
2 Uchiyama M, Hayakawa H, Ogawa T, Hayashi M, Sakai K.
Sublingual nifedipine in acute severe hypertension

Sir,

We read with interest the recent article by Evans and associates in which sublingual nifedipine was shown to be safe and effective for the treatment of acute severe hypertension in children; this is consistent with previous studies. However, van Harten et al.2 and McAllister3 reported negligible sublingual absorption of nifedipine in adults, suggesting that significant nifedipine plasma concentrations are not achieved until the contents of the capsule reach the stomach and are then absorbed. They observed a higher peak nifedipine plasma concentration and a shorter time to reach peak concentrations when a patient bites the capsule to liberate its liquid contents, and then swallows, compared with when they squeeze the contents under the tongue.

Siegler and Brewer reported a mean of 57 minutes (range 15 to 90 minutes) for the time to achieve maximum decrease in blood pressure when nifedipine was administered orally to children while sublingual administration resulted in a mean time to maximum effect of 24 minutes (range 10 to 45 minutes).4 In this study, nifedipine was administered by the oral route in young patients for whom reliable sublingual administration could not be assured. Thus a possible explanation for the longer time to maximum effect observed in this study with the oral route may be due to pharmacokinetic differences between infants and children. It would be interesting to know the change in blood pressure observed at 15 minutes in the study by Evans and colleagues. This information could then be compared with the onset of action in adults who swallowed the contents of the capsules after biting them and to the onset in infants and children who swallowed the contents of the capsules.

In addition some patients do not tolerate the strong mint taste of the liquid contents of a nifedipine capsule; this can result in nausea and vomiting of the medication. Therefore, in these patients oral administration may be an appropriate alternative as time to peak nifedipine plasma concentrations after oral administration of the capsule in adults appears to occur within 30 minutes.3

The data presented by Evans and associates further supports the effectiveness of nifedipine for the purpose of rapidly lowering blood pressure; however, the sublingual route may not be the optimal route of administration in children who can swallow a capsule.

Drs Evans, Shaw, and Brocklebank comment:

In our study in those subjects where we recorded values for fall in blood pressure at 15, 30, and 60 minutes after the administration of sublingual nifedipine the maximum fall in blood pressure was seen at 30 minutes.

The mean fall in mean arterial pressure at 15 minutes was 22 mm Hg and at 30 minutes was 32 mm Hg (this excludes values on two non-responders). These results are consistent with the rapid onset of action reported by Siegler and Brewer. However, we fear they do not further our knowledge as to the route of absorption. It may well be that the oral route is preferable (particularly in infants) not because of better absorption but because it produces a slower fall in blood pressure.

Heparin and suspected Sanfillipo syndrome

Sir,

Initial screening of urine from a child with undiagnosed severe learning difficulties suggested a diagnosis of Sanfillipo syndrome. One dimensional electrophoretic separation of mucopolysaccharides1 from this child's urine showed a large band migrating in the heparan sulphate region (figure). The child had no other features of Sanfillipo syndrome and further urine samples from the same child were normal. Examination of other children, however, from the same school resulted in the fortuitous identification of Sanfillipo A in a previously undiagnosed child.

It seemed unlikely that the original specimen had been collected from the wrong child. It was suggested that the urine sample could have been inadvertently collected into a cytogenetics sample tube. Blood samples for cytogenetic analysis are collected into heparinised 25 ml universal tubes that are otherwise identical to the tubes used by chemical pathology laboratories for urine samples. Repeated analysis of normal urine samples collected into cytogenetics tubes confirmed that the abnormal band originally identified as heparan sulphate was, in fact, heparin.

References

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