LETTERS TO THE EDITOR

A variant TATA box in the bilirubin UDP-glucuronosyltransferase 1 gene promoter does not contribute to neonatal jaundice in the Japanese population

EDITOR—A variant TATA box (A/TATA), designated as TA-7) in the promoter region of the bilirubin UDP-glucuronosyltransferase 1 (UGT1) gene has been reported to accelerate the increase in bilirubin concentration during the first two days of life. However, the relation between TA-7 and peak bilirubin concentration in the neonatal period has not been clarified, and it is also unclear as to whether TA-7 influences bilirubin metabolism in infants of different ethnic groups.

To investigate whether TA-7 is one of the risk factors for neonatal jaundice in the Japanese population, we performed genotyping analysis of the UGT1 gene in 74 Japanese newborn infants, and measured bilirubin concentrations at 4–5 days of age in healthy infants (n=55) and peak bilirubin concentrations in infants with jaundice requiring treatment, phototherapy, or exchange transfusion (n=19).

Informed consent was obtained from parents, and infants were enrolled at birth. All infants were born at 37–42 weeks of gestation and weighed more than 2500 g. They showed no blood incompatibility, had a negative direct Coombs test; they had no clinically significant antenatal and intrapartum complications, and none of the infants had any other pathological conditions except for jaundice. In healthy infants serum bilirubin concentrations were measured at 4–5 days after birth. In infants with jaundice requiring treatment, peak bilirubin concentrations were used in the analysis.

The TATA box region of the UGT1 promoter was amplified with the polymerase chain reaction (PCR) using the primers UGT1-A5 (5’-TAATCTGGTGATATCGATTGGTTTTGTG-3’) and UGT1-B9 (5’-ACA-GCCATGCGCCTTTGGT-3’). UGT1-A9 was labelled with a fluorescent dye, 6-carboxy-X-rhodamine. An aliquot of each PCR product was electrophoresed on a genetic analyser (ABI PRISM 310; Perkin-Elmer Applied Biosystems, Foster City, CA, USA) and then analysed using the GeneScan analysis software package (Perkin-Elmer Applied Biosystem). The electrophogram clearly separated the peaks for different TATA box alleles. The TATA box allele frequency is very rare in the Japanese population, as TA-7 allele frequency is 0.07, significantly lower than the value of 0.4 found in the North American and Eastern Scottish populations (p < 0.001, χ² analysis with one degree of freedom).

Ethnic differences in the incidence of neonatal jaundice have been reported. Neonatal jaundice occurs more often in East Asian infants than in Caucasian infants. Even if the presence of TA-7 could affect the metabolism of bilirubin in the neonatal period, it does not explain the high incidence of neonatal jaundice in Japanese infants, because the TA-7 allele frequency is very rare in the Japanese population. In the 74 infants in this study, we detected only one who was homozygous for TA-7, which happened to be a baby who was in the healthy control group. In the 19 infants with jaundice requiring treatment, we found a TA-7 allele in only one heterozygous case.

In conclusion, our findings indicate that the variant TATA box in the promoter region of the UGT1 gene does not contribute to the high incidence of neonatal jaundice in the Japanese population.

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Randomised controlled trial of cisapride in preterm neonates for gastric emptying time

EDITOR—We read with interest the study on the randomised controlled trial of cisapride in preterm neonates reported by by McClure et al. We have recently completed a randomised, double blind, placebo controlled study to evaluate the effect of cisapride on feed tolerance and gastric emptying of preterm neonates. (P S Reddy, A K Deorari, C S Bal, V K Paul, M Singh. Abstract 1705 presented to the Society of Pediatrics Research meeting, 1-4 May 1999, San Francisco, USA). After obtaining informed parental consent a total of 44 preterm neonates stratified by gestation into 29–32 weeks and 33–34 weeks, and randomly allocated to receive either cisapride or placebo at a dose of 0.2 mg/kg every 8 hours. The babies were enrolled once they were stable and receiving oral feeds amounting to 25 per cent of their fluid requirements.

The feeds were administered in a stepwise manner, around 20 ml/kg/day. Gastric emptying time was measured on days 6 to 8 after enrolment using a dynamic technetium scan using 100 µCi of radioactivity. This results in only 0.2 mSv of whole body absorbed dose. To offset the effect of type of feeding on gastric emptying, the two feeds before the nuclear study were of uniformly exposed breast milk. Gastric emptying time (mean (SD) and median) in the cisapride group (58.1 (32.2 mins) 48.8 mins) was not significantly different from that of the control group (53.8 (34.6 mins) 43.4 mins). Clinically significant gastro-oesophageal reflux was seen in 50% of babies in each group. Cisapride had no effect on either the number of episodes of feed intolerance or the length of feed intolerance. Weight gain and the day on which the total enteral feeding began were also comparable in the two groups.

Our observations support the findings of McClure et al, that cisapride does not improve gastric emptying in preterm neonates and that its use for establishing enteral feeds is not warranted.

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Table 1. Clinical data and DNA polymorphism of all infants

<table>
<thead>
<tr>
<th>Healthy infants</th>
<th>Infants with jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TA-6/TA-6</strong></td>
<td><strong>TA-7/TA-7</strong></td>
</tr>
<tr>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td>22/23</td>
<td>2/2</td>
</tr>
<tr>
<td>3079 (350)</td>
<td>3001 (184)</td>
</tr>
<tr>
<td>39.8 (1.1)</td>
<td>39.6 (1.4)</td>
</tr>
<tr>
<td>25/22</td>
<td>3/2</td>
</tr>
<tr>
<td>10.0 (2.7)</td>
<td>9.2 (1.5)</td>
</tr>
</tbody>
</table>

* Bilirubin concentrations at 4–5 days old in healthy infants and the peak bilirubin in infants with jaundice.

Use of laryngeal masks in the resuscitation of a neonate with difficult airway

EDITOR,—Neonates with mandibulo-facial anomalies and respiratory distress present a challenge for neonatologists. We report a newborn boy with severe micrognathia who failed to breathe adequately immediately after birth. Tracheal intubation was unsuccessful, but he was ventilated for several hours using a laryngeal mask.

Case report

The boy was born to a 29 year old primigravida after 39 weeks of gestation. During the pregnancy, absence of the corpus callosum had been noted at 33 weeks of gestation using ultrasound. The birth weight was 2300 g, and multiple contractures of the limbs, bilateral coloboma of the iris, severe mandibular hypoplasia with a small oral orifice and a massive glossoptosis, and a syphilitic heart murmur. He made feeble attempts to cry, but remained cyanotic and bradycardic despite the jaw thrust manoeuvre and bagging. Oro-tracheal intubation with a 3 mm and a 2 mm tracheal tube twice failed. A lubricated number 1 laryngeal mask was easily put into the right position while holding the tongue with a Magill forceps. After sedation with fentanyl and midazolam, he tolerated intermittent mechanical ventilation well for three hours while investigations were carried out. At ventilator settings of PI 25 cm H2O, PEEP 4 cm H2O, RR 60 per minute, FIO2 0.4, I:E ratio 1:2, flow rate of 12 l/min, capillary blood gas analysis revealed pH 7.2, PCO2 46 mmHg, and base excess -5 mmol/l. Blood pressure and heart rate were within the normal range.

Echocardiography revealed a severely hypoplastic distal aortic arch with a wide open ductus arteriosus, and cranial echocardiography confirmed the absence of the corpus callosum. In view of the poor prognosis the parents requested the withdrawal of intensive care, and after consensual the diagnoses were confirmed, with the addition of a micro larynx and severe malformations of the iris, severe mandibular hypoplasia and breech presentation. A microdeletion of chromosome 21. No other anomalies and respiratory distress present a challenge for neonatologists. We report a newborn boy with severe micrognathia who failed to breathe adequately immediately after birth. Tracheal intubation was unsuccessful, but he was ventilated for several hours using a laryngeal mask.

Multicentre trial of high frequency ventilation

EDITOR,—Cools and Offringa’s recent meta-analysis of elective high frequency ventilation (HFV) in neonates with respiratory distress syndrome1 concludes that HFV reduces the risk of chronic lung disease (CLD) at 36 weeks of postconceptual age, but may be associated with an increased risk of severe intraventricular bleeding. Several areas of uncertainty remain, however, and they suggest that new clinical trials should be done in very preterm infants to evaluate the usefulness of elective HFV, using a high lung volume strategy, started as soon as possible after birth. We are currently running exactly such a trial in the UK—the United Kingdom Oscillation Study (UKOS).

This is a multicentre trial comparing high frequency oscillatory ventilation (HFOV) with conventional ventilation in preterm infants < 29 weeks of gestation. Previous trials have included more mature babies, but we have restricted recruitment to those babies with the highest incidence of chronic lung disease and of neurological complications. We expect to recruit 1200 babies over two years, making this the largest study of its kind so far, with the following four primary aims. To avoid selection bias, treatment allocation is by a central telephone randomisation service. Infants are given their allocated mode of ventilation within one hour of birth (up to 15 hours in previous studies) to assess the effect of early intervention with HFOV, which has been shown to be most beneficial in animal studies.2 Long term neurodevelopmental and pulmonary outcome will be evaluated up to 2 years of corrected gestational age; only two previously published studies3,4 have done this. Kesler and Dunn in North America (personal communication) also have an ongoing study of a similar nature, and we hope that the results of these trials will provide the evidence for future ventilation policy for very preterm infants.

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