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[T]AA, designated as TA-7) in the promoter region of the bilirubin UDP-glucuronosyltransferase 1 (BUGT1) gene has been reported to accelerate bilirubin metabolism 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 BUGT1 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 no other congenital or family pathologies 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 BUGT1 promoter was amplified with the polymerase chain reaction (PCR) using the primers BUGT1-A (5'-TAACTTTGIGTGTGAT-GTGTTTTG-3') and BUGT1-B (5'-ACA-GCCATGGCCGCTTTGCT-3').

*Table 1. Clinical data and DNA polymorphism of all infants*

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<thead>
<tr>
<th>Table 1</th>
<th>Clinical data and DNA polymorphism of all infants</th>
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</thead>
<tbody>
<tr>
<td><strong>Healthy infants</strong></td>
<td><strong>Infants with jaundice</strong></td>
</tr>
<tr>
<td>Number of subjects</td>
<td>47</td>
</tr>
<tr>
<td>Male/female</td>
<td>22/25</td>
</tr>
<tr>
<td>Birthweight (g) (mean [SD])</td>
<td>3079 (350)</td>
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<tr>
<td>Gestational weight (mean [SD])</td>
<td>39.8 (1.1)</td>
</tr>
<tr>
<td>Breast-fed formula</td>
<td>25/22</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)*</td>
<td>10.0 (2.7)</td>
</tr>
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</table>

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

We also analysed 19 infants with jaundice requiring treatment; 18 normal homozygotes and one heterozygote. Thus the TA-7 allele was found in only one of 19 cases. The peak serum bilirubin concentrations in the 18 normal homozygotes were 18.8 (2.29) mg/dl and that in the heterozygote was 15.7 mg/dl. TA-7 allele frequency was calculated to be 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). The genotype distribution in the 74 Japanese infants was significantly different from that found in the North American and Eastern Scottish populations (p < 0.001, χ² analysis with two degrees 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 the 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 BUGT1 does not contribute to the high incidence of neonatal jaundice in the Japanese population.

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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 new-born female 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 through regular antenatal ultrasound scans. A karyotype revealed a microdeletion of chromosome 21. No other malformation had been verified. Caesarean section was performed because of intraterine growth retardation and breech presentation. At birth the boy weighed 2300 g, had multiple contractures of the limbs, bilateral coloboma of the iris, severe mandibular hypoplasia with a small oral orifice and a massive glossoptosis, and a systolic 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 failed twice. 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 a bag and mask ventilation was attempted 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 of 1:2, flow rate of 12 l/min, capillary blood gas analysis showed pH 7.30, PCO2 87, PO2 65, 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. Cranio-cranial echocardiography confirmed the absence of the corpus callosum. In view of the poor prognosis the parents requested the withdrawal of intensive care, and at necropsy the diagnoses were confirmed, with the addition of a micro larynx and a large pharyngo-oesophageal cleft. No signs of damage to the hypopharynx were found. The use of the laryngeal mask in our patient gained us time to establish a definite airway either through bronchosopic intubation or tracheotomy. The usefulness of the laryngeal mask during anaesthesia in such cases has been well documented, but we believe that the mask could also be a valuable tool for neonatologists who unexpectedly face a difficult airway.

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Multicentre trial of high frequency ventilation

EDITOR,—Cools and Offringa’s recent meta-analysis of elective high frequency ventilation (HFV) in preterm infants3 confirms that HFV reduces the risk of chronic lung disease (CLD) at 26 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 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 largest statistical power. 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. Long term neurodevelopmental and pulmonary outcomes will be evaluated up to 2 years of corrected gestational age; only two previously published studies4,5 have done this. Kessler 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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Antenatally diagnosed renal pelvis dilatation

EDITOR,—I read with interest the study by Jas- won et al on outcome in antenatally diagnosed renal pelvis dilatation.1

The cohort was recruited antenatally from pregnancies where renal pelvis dilatation had been diagnosed mostly on the 20 week ultrasound scan. VUR was described as “the most common clinically significant pathology” (23 out of 104 cases). Presumably all of the babies were asymptomatic. How can the authors be sure that this VUR was either clinically significant or indeed pathological?

Figure 2 shows that nine out of 23 babies had grade III or IV VUR despite a normal postnatal renal ultrasound scan. Is anything known of the natural history of these nine babies? The reference to the prevalent prevalence of VUR in infants is a “literature review” (method not stated by the author) of 14 papers published between 1916 and 1967—that is, predating the era of antenatal ultrasonography.

One baby went on to have hydroleplasty at 18 months of age, because of deteriorating renal function, due to PUJ obstruction, not VUR (table 1). This low rate of surgical intervention (one baby out of 139 pregnancies over 18 months) reinforces the notion that these findings are largely benign.3

The longer term follow up, or outcome, of the other 103 babies is not stated—for example, the most common clinically significant pathological outcomes.

The conclusion states that babies with ante- natal pelvis measurements of 5 mm or greater should be investigated, as they may have VUR. However, I am unclear as to what long term outcome measures will be improved by these sometimes invasive investigations.

Table 1 also contains data on 25 babies, but the text refers to persisting renal pelvis dilatation in 47 babies.

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