Neonatal necrotising enterocolitis and perinatal exposure to co-amoxiclav

Two recent studies have reported an association between antenatal exposure to co-amoxiclav, either alone or in combination with erythromycin, and neonatal necrotising enterocolitis (NEC). Based on the analyses of secondary outcomes in these studies, the authors raised concerns about the use of co-amoxiclav antenatally and recommended further investigation of its use in the neonatal period.

We have completed a case-control study designed to test the hypothesis that perinatal exposure to co-amoxiclav is associated with an increased risk of NEC. During a 17 year period (1983–2000), 32 cases of NEC were diagnosed in preterm infants born to mothers inbooked at Liverpool Women’s Hospital. Of these, 17 were diagnosed at laparotomy, 12 had classical radiological features, and in three the diagnosis was made on clinical grounds alone. Two gestation matched controls were selected for each index case. Information on potentially relevant perinatal variables, including antenatal and postnatal exposure to co-amoxiclav, were collected from maternal and infant case notes.

Infants who developed NEC tended to be lighter at birth (median birth weight 853 (interquartile range [IQR] 717–1248) g) v 1037 (IQR 779–1613) g in controls, p = 0.065) and were more often delivered after absent or reversed flow identified on umbilical artery Doppler studies (p = 0.065) and were more often delivered after absent or reversed flow identified on umbilical artery Doppler studies (p = 0.065). Postnatally, Gram negative septicemia preceding NEC was significantly more common in cases than controls (p = 0.005). However, the frequency of perinatal exposure to co-amoxiclav was similar in both groups (table 1).

In summary, there is no evidence from this study of a link between perinatal exposure to co-amoxiclav and NEC. Our findings do not support the hypothesis that treatment with co-amoxiclav is causally associated with the development of NEC.

Table 1 Exposure of infants with necrotising enterocolitis (NEC) and controls to co-amoxiclav

<table>
<thead>
<tr>
<th>Exposure</th>
<th>NEC (n = 32)</th>
<th>Controls (n = 64)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal exposure</td>
<td>5</td>
<td>11</td>
<td>1.0</td>
</tr>
<tr>
<td>Postnatal treatment</td>
<td>19</td>
<td>30</td>
<td>0.25</td>
</tr>
<tr>
<td>Any perinatal exposure</td>
<td>20</td>
<td>34</td>
<td>0.38</td>
</tr>
</tbody>
</table>

*p2 or Fisher’s exact test

References

Birth weight of Chinese babies born in Italy

Fok et al note that the birth weight (BW) of the Chinese neonates they studied is lower than that of babies born in some western countries and state that a genuine genetic predisposition exists leading to the smaller size of Chinese infants.

In Tuscany, an Italian region with 3.4 million inhabitants, about 0.5% of the population are immigrants from the People’s Republic of China. Since the early 1990s, Chinese immigrants in Tuscany have formed a stable, endogamic, culturally defined, and economically well integrated community. They receive the same full free medical care as Italian citizens.

Using the registry of the Regional Cystic Fibrosis Neonatal Screening Programme, which covers 99.9% of the region’s neonates, we extracted the data for all the 4787 ethnic Chinese babies born in Tuscany from 1 January 1991 to 31 December 2002 to two ethnic Chinese parents. The forms that accompany the blood sample for the screening test are completed at birth by an obstetrician or nurse and contain the neonate’s sex, BW, and gestational age (GA). We calculated the mean BW of the Chinese babies for each sex and GA starting from the 35th week (missing data: 638 babies). To avoid errors in estimates, we excluded as unlikely for GA those BWs that were more than 1.5 interquartile ranges above the 75th or below the 25th centile for each GA and sex.

Compared with native Tuscan newborns, Chinese babies born in Tuscany have a higher mean BW at almost all GAs; only at the 40th, 41st, and 42nd weeks for boys and 42nd week for girls is the mean BW of the Chinese babies slightly lower, but not significantly so. Compared with those born in China, Chinese babies born in Tuscany have a higher mean BW at all GAs, except for the 42nd week (girls). The differences we found are in many cases statistically significant, despite the small size of our population.

Our data conflict with the hypothesis of Fok et al that Chinese newborns have a genetic predisposition to a smaller size than their white counterparts and suggest that, to explain the differences in BW they found, maternal and environmental factors should be taken into consideration.

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