Genital mycoplasmas in preterm infants: prevalence and clinical significance

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Abstract. The genital mycoplasmas: Ureaplasma urealyticum and Mycoplasma hominis have recently assumed an increasing importance as neonatal pathogens. The aim of the present survey was to determine the prevalence of infections with these organisms in preterm infants in two neonatal intensive care units in Israel. Among 99 preterm infants, 24 (24%) harboured mycoplasmas in their throats shortly after birth. U. urealyticum was the most common organism. M. hominis was isolated only from 3 infants. Six out of 27 (22%) mechanically ventilated infants secreted U. urealyticum in their lower airways. The rate of colonization was inversely correlated with gestational age; 80% of infants younger than 28 weeks gestation were found to be colonized as opposed to 17.9% at 28-36 weeks of gestation. No mycoplasmas were isolated in blood cultures drawn from 146 infants and CSF cultures obtained from 47 preterm infants. Neontal mortality, respiratory complications and intraventricular haemorrhage grade 3-4 were significantly increased in colonized infants. However, above gestational age of 27 weeks, colonization with mycoplasmas was not associated with a worse prognosis. We conclude that colonization with U. urealyticum is common in Israeli preterm infants, correlates inversely with gestational age and has no detrimental effect on neonatal morbidity and mortality of infants older than 27 wks of gestation.

Key words: Genital mycoplasmas – U. urealyticum – M. hominis – Premature infants

Introduction

The genital mycoplasmas, Ureaplasma urealyticum and Mycoplasma hominis are commonly found in human female genital tracts [14], amniotic fluid and placenta [1, 7]. Cassel et al. [5] have recently shown that U. urealyticum was the most common organism isolated from the lower airways of preterm infants. Its presence has been associated with a higher incidence of chronic lung disease and increased mortality of extremely low birth weight infants [5, 18]. In some of these infants mycoplasmas were also cultured from blood or CSF [17].

If these observations are confirmed, the addition of antimycoplasma agents (such as erythromycin) should be considered as a part of the routine antibiotic regimen used in neonatal units. It is prudent therefore, to extend these studies to more neonatal centres. The goal of the present survey was to determine the prevalence and clinical significance of colonization and infection with genital mycoplasmas in preterm infants in Israel.

Materials and methods

Population and study design

Preterm infants hospitalized in the neonatal intensive care units of two hospitals during an 8-month period, were included in the study.

Blood and throat cultures were collected during the first hours of life as a part of our admission protocol. Tracheal aspirates from the mechanically ventilated infants were obtained during the 2nd or 3rd day of life. CSF was collected from infants undergoing lumbar puncture for suspected sepsis/meningitis during the 1st week of life. Placentas of preterm infants which were sent to the microbiology laboratory for bacterial isolation, were also cultured for genital mycoplasmas.

Maternal fever was defined as a temperature greater than 38°C during delivery. Asphyxia was determined by a 5 min Apgar score of <6 or cord blood pH <7.2. Hyaline membrane disease was defined as oxygen requirement within hours of birth with chest X-ray film demonstrating ground-glass appearance. Brain sonography was performed routinely. Intraventricular haemorrhage grade 3 was defined as bleeding in one or both ventricles with some degree of ventricular dilatation. If the bleed extended to the parenchyma it was classified as grade 4.

Culture specimens

Throat cultures were taken by a swab with transport medium (Transwab, Medical Wire and Equipment Co. Potley, England).
Tracheal aspirates were obtained through suction from the endotracheal tubes into a sterile container. Blood (0.5–1 ml) and CSF (0.1 ml) were collected aseptically and inoculated directly onto a sterile test tube containing 2 ml of special mycoplasma broth (A-7 and arginine) [2, 12, 13]. Placenta were transferred in a sterile container. All specimens were transferred immediately to the mycoplasma laboratory.

Special A-7 and arginine broth and agar were used for isolation of genital mycoplasmas as described [2, 11-13]. All specimens were also cultured routinely for bacterial pathogens by standard methods.

Statistics

All intergroup variables were analysed by Fisher's exact probability test. Gestational age and birth weight were compared by two-tailed t-test. The level of significance was set at 0.05.

Results

One hundred and forty-six infants had blood cultures obtained during the first hours of life. In 47 a CSF culture was also performed. None of the samples grew any genital mycoplasma. Throat cultures were performed in 99 infants and mycoplasmas were isolated in 24 (24.2%). Of 27 infants with tracheal aspirates, 6 grew *U. urealyticum* (22.2%). Of 21 placentas sent for bacteriology, 9 were positive for mycoplasmas (42%). *M. hominis* was isolated from three throat and placenta cultures, in one case together with *U. urealyticum*. All the remaining cultures grew *U. urealyticum*. In all but one, the genital mycoplasmas were isolated in pure cultures. There were four cases of early bacterial sepsis diagnosed during the 1st day of life: two were caused by *Escherichia coli*, and by *Listeria monocytogenes* and one by *Enterococcus*.

The prevalence of vaginal delivery, premature rupture of membranes for longer than 24 h and maternal fever during labour were increased in infants with positive throat cultures. It is noteworthy that two colonized infants were born by caesarean section without rupture of membranes (Table 1).

Infants carrying *U. urealyticum* were of significantly less gestational age and birth weight than those with negative throat cultures (Table 1). The number of colonized infants and the prevalence of colonization in different gestational age groups are illustrated in Fig. 1. Of the infants younger that 28 weeks of gestation, 80% were colonized with *U. urealyticum*. The difference in colonization rate between this age group and the more mature infants was statistically significant (*P*<0.001, Fisher's exact test).

There were no statistically significant differences between colonized and uncolonized infants in other neonatal characteristics such as intra-uterine growth retardation, asphyxia, hyaline membrane disease and number of infants requiring mechanical ventilation. The neonatal outcome, however, was worse in the colonized group. There were more deaths, intraventricular haemorrhages and chronic lung disease (defined as oxygen requirement longer than 30 days) (Table 1).

The very high colonization rate in the very preterm (and therefore high risk) infants precluded analysis of the differential influence of gestational age and colonization with *U. urealyticum* on neonatal morbidity and mortality. However, comparison of the neonatal characteristics and outcome of infants of gestational age equal or above 28 weeks has not detected any negative influence of colonization with genital mycoplasmas.

Table 1. Genital mycoplasmas – throat cultures: maternal and neonatal characteristics

<table>
<thead>
<tr>
<th>Throat cultures</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive n=24</td>
<td>Negative n=75</td>
</tr>
<tr>
<td>Maternal characteristics</td>
<td></td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>19 (79%)</td>
</tr>
<tr>
<td>Premature rupture of membranes &gt;24 h</td>
<td>9 (37%)</td>
</tr>
<tr>
<td>Maternal fever</td>
<td>6 (25%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neonatal characteristics</th>
<th>Gestational age (weeks)</th>
<th>Birth weight (g)</th>
<th>Small-for-date</th>
<th>Asphyxia</th>
<th>Hyaline membrane disease</th>
<th>Mechanical ventilation</th>
<th>Deatha</th>
<th>Intraventricular haemorrhage grades 3-4</th>
<th>Oxygen &gt;30 da</th>
<th>At least one of above</th>
</tr>
</thead>
<tbody>
<tr>
<td>30.2 ± 0.7</td>
<td>1490 ± 111</td>
<td>1 (4%)</td>
<td>5 (20%)</td>
<td>7 (29%)</td>
<td>9 (38%)</td>
<td></td>
<td>3 (13%)</td>
<td>3 (13%)</td>
<td>4 (19%)</td>
<td>6 (25%)</td>
</tr>
<tr>
<td>32.7 ± 0.3</td>
<td>1808 ± 61</td>
<td>4 (5%)</td>
<td>15 (20%)</td>
<td>22 (29%)</td>
<td>19 (26%)</td>
<td></td>
<td>4 (5%)</td>
<td>0</td>
<td>3 (4%)</td>
<td>7 (9%)</td>
</tr>
</tbody>
</table>

NS, Not significant (*P* >0.05)

Excluding two deaths from major cardiovascular anomalies

Denominators include only patients who survived >30 d

Fig. 1. Genital mycoplasmas in throat cultures grouped by gestational age. The percentages over each bar represent the rate of colonization with mycoplasmas at the specific gestational age. Unfilled area – number of infants with negative cultures; filled areas – number of infants with positive cultures.