Total Lipids, Cholesterol, Phospholipids and Inorganic Phosphorus in the Amniotic Fluid of Premature Infants

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SUMMARY

Total lipids, total cholesterol, phospholipids and inorganic phosphorus were determined in the amniotic fluid of 36 normal and 12 premature neonates. Total lipids, phospholipids and cholesterol were significantly decreased in the premature patients and the extent of decrease was more pronounced in patients who developed respiratory distress syndrome. On the other hand, inorganic phosphorus content of the amniotic fluid was within the normal range.

Interest in the composition of human amniotic fluid remained at a fairly low level from 1930 to 1945. Since then, the number of publications on this subject has increased remarkably. In 1955 Hanon et al. reviewed the literature on the composition of amniotic fluid. More recently components of amniotic fluid were reported which related directly to fetal condition and maturity.

Lipids are present in liquor amnii in steady concentrations throughout normal pregnancy, phospholipids being the only ones that increase in concentration as term approaches. Amniotic fluid contains about 60 mg/100 ml total lipid. Lipid analysis revealed the presence of phospholipids, free cholesterol, cholesterol ester, monoglycerides, diglycerides and triglycerides. Low total lipid and phospholipid concentrations have been demonstrated in liquor amnii from premature infants suffering from respiratory distress syndrome (RDS) and in cases of anencephaly.

Recently, some investigators have reported that amniotic fluid phospholipids increase in the third trimester of pregnancy. A relationship between amniotic fluid triglyceride levels and fetal maturity has been found. Pomerance et al. reported that cholesterol constitutes 25% to 33% of total lipids. They also reported an increase in amniotic fluid free cholesterol and unesterified fatty acids in cases of prolonged intra-uterine fetal death.

Biezenski et al. determined the amounts and the percentage composition of the various lipid classes in the amniotic fluid to obtain a lipid profile at different stages of gestation. Amniotic fluid phospholipids and lecithin/sphingomyelin ratios have been used as an index of fetal lung maturity for prediction of respiratory distress syndrome, as shown by Nelson and others.

Since changes in concentrations of amniotic fluid constituents may help in the prediction of fetal condition and maturity, we thought it worthwhile to search for any correlation between liquor amnii total lipids, phospholipids and cholesterol and neonatal outcome in both normal and abnormal pregnancies.

PATIENTS AND METHODS

The study subjects comprised 12 premature infants (including 2 pairs of twins) of high-risk pregnant women selected from the inpatients of the Obstetric and Gynecology Department of Manial Hospital, Cairo University. A group of 38 full-term neonates (including 2 pairs of twins) of 36 normal pregnant women served as controls. The control babies were divided into 2 subgroups: 29 normally delivered mature full-term infants and 9 normally delivered small-for-term infants.

Clinical Appraisal

Complete medical histories of the pregnant women were taken and they were subjected to strict general and obstetrical examinations. The neonates were also subjected to complete clinical examination. Particular attention was given to the colour of the skin, the presence of asphyxia at birth, the respiratory and cardiovascular systems, Apgar scoring, assessment of the gestational age, the presence of congenital malformation, the presence of birth trauma, the weight and length of the baby and the presence of dysmaturity (Table I).

All babies were observed for at least 24 hours. Those who were ill were followed up until complete recovery or death.

Methods

Samples of amniotic fluid were taken by transvaginal amniocentesis during the first stage of labour or by transabdominal amniocentesis immediately before the performance of lower-segment Caesarean section. The samples were centrifuged, passed through filter paper with 0.22 μm pores and kept frozen at −20°C until analysed.

Amniotic fluid total lipids were determined by the method of Bligh and Dyer and total cholesterol by the method of Sackett. The inorganic phosphorus and phospholipid phosphorus, after being digested according to the method of Youngburg and Youngburg, were determined by the p-phenylenediamine method adopted by Parekh and Jung.
The data obtained for both subgroups are given in Table II.

The mean values for total lipids, total cholesterol, lipid phosphorus and phospholipids in the amniotic fluid of the mature full-term subgroup were higher than those obtained for the small-for-term control subgroup. The only significant difference between the mean values obtained for the two control subgroups was the concentration of total cholesterol. The level of liquor amnii inorganic phosphorus was slightly higher in the small-for-term control group than in the mature group.

In the 12 premature infants born to high-risk mothers the total lipid phosphorus, phospholipids and total cholesterol were very significantly decreased when compared with those of the 2 control subgroups. The inorganic phosphorus, however, did not differ significantly from that of the control group (Table II).

**DISCUSSION**

The mean value of 56.7 mg total lipids per 100 ml amniotic fluid in our control group was similar to that reported by Nelson. The values for amniotic fluid phospholipids of our control group were somewhat higher than those reported by Biezenski et al. and Gusdon and Waite. On the other hand, they were somewhat lower than those found by Gluck et al. and by Nelson.

In our control group the gestational age varied between 38 and 42 weeks. The gestational age of the patients in the series of Biezenski et al. ranged from 24 weeks to term, while those of Gusdon and Waite ranged from 18 weeks to term.

In our control group the total cholesterol represented roughly 25% - 33% of total lipids. Similar findings were reported by Biezenski et al. and by Pomerance et al. Yet, the individual data as well as the mean value for total cholesterol in our series were still higher.

Our values for liquor inorganic phosphorus were slightly lower than those obtained by Cantarow et al. and Bonsnes, but higher than those of Meritt and Bauer. The premature infants in this study were chosen at random, and RDS occurred in 6 out of 12 premature infants. The total lipids of amniotic fluid were lower in premature than in full-term infants. The mean value for lipids of the small-for-term control infants was 53.6 mg/100 ml, versus 13.6 mg/100 ml for all premature infants. The total lipids in premature infants who developed RDS was 9.98 mg/100 ml. The mean total lipid concentration in premature stillborn babies was also lower than the mean of 26.7 mg/100 ml in premature live infants who did not develop RDS.

Lipid phosphorus and phospholipid concentrations were significantly lower in premature infants than in normal controls and the decrease was more pronounced in infants who developed RDS. This lowering of phospholipids as well as the smaller contribution of tracheal fluid, which is known to be rich in lipids, to the amniotic fluid volume, may have accounted in part for the decreased total lipids.

In liquor amnii from premature infants with RDS, Nelson found low total lipids and phospholipids and a
decreased percentage of lecithin. Recently Gusdon and Waite,7 and Nelson1 have reported the relationship between amniotic fluid phospholipids and lecithin concentrations and RDS. They reported that amniotic fluid phospholipids increase in the third trimester of pregnancy and that lecithin levels above this value were associated with normal respiratory function even in premature infants. In contrast, predelivery amniotic fluid lecithin concentrations below 3.5 mg/100 ml were associated with the development of RDS.

In fact, all infants who developed RDS in the present series, except one, were below 36 weeks' gestation. Among living infants the incidence of RDS was 30% at gestational age of 36 weeks, and 100% below this gestational age. This finding gives support to the concept that the premature infant develops RDS because they lack the ability to synthesise lecithin at the required rapid rate.36

Total cholesterol of amniotic fluid in premature infants also showed a significant decrease compared with that of the controls. This decrease paralleled the decrease in total lipids and phospholipids. Low total cholesterol content of the amniotic fluid may be explained on the same basis as decreased total lipids. The ratio of mean values of cholesterol to total lipids was found to be less than 0.5, which agrees with the results reported by Pomerance et al.35

The insignificant decrease found in the inorganic phosphorus of the premature infants when compared with that of controls may be owing to some extent to the decrease in the osmolality with advancing gestational age reported by Lind et al.34 and Miles and Pearson.35 Lind et al. attributed this to the fact that the liquor sodium chloride level fell, whereas the values for both potassium and phosphate did not show alteration.

From the present study it is apparent that it is possible to detect definite changes in total lipids, lipid phosphorus, phospholipids and total cholesterol in amniotic fluid in abnormal pregnancies. These contents were significantly decreased in stillborn infants, as well as in infants with RDS.

We wish to thank Prof. Dr M. R. Sakr and Prof. Dr A. F. Youssef for their help in the clinical manifestation of the cases.

REFERENCES


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TABLE II. THE AMNIOTIC FLUID DATA (MG/100 ML) UNDER PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS

<table>
<thead>
<tr>
<th>Group</th>
<th>Total lipids</th>
<th>Lipid phosphorus</th>
<th>Phospholipids</th>
<th>Cholesterol</th>
<th>Inorganic phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-term mature</td>
<td>Range 30.0 - 96.7</td>
<td>0.19 - 1.47</td>
<td>4.47 - 34.5</td>
<td>8.6 - 19.6</td>
<td>0.5 - 7.2</td>
</tr>
<tr>
<td>controls (29 infants)</td>
<td>Mean 57.4</td>
<td>0.44</td>
<td>10.89</td>
<td>14.75</td>
<td>2.25</td>
</tr>
<tr>
<td>Small-for-term</td>
<td>Range 36.0 - 75.0</td>
<td>0.19 - 0.8</td>
<td>4.47 - 18.6</td>
<td>7.0 - 15.0</td>
<td>1.2 - 6.0</td>
</tr>
<tr>
<td>controls (9 infants)</td>
<td>Mean 53.6</td>
<td>0.33</td>
<td>7.55</td>
<td>11.58</td>
<td>3.12</td>
</tr>
<tr>
<td>Total controls (38 infants)</td>
<td>Mean 55.7</td>
<td>0.43</td>
<td>10.31</td>
<td>14.14</td>
<td>2.42</td>
</tr>
<tr>
<td>SE 11.28</td>
<td></td>
<td>0.30</td>
<td>7.50</td>
<td>3.18</td>
<td>1.68</td>
</tr>
<tr>
<td>Preterm infants</td>
<td>Mean 1.88</td>
<td>0.05</td>
<td>1.25</td>
<td>0.53</td>
<td>0.28</td>
</tr>
<tr>
<td>Stillbirths (3 infants)</td>
<td>Mean 10.9</td>
<td>0.033</td>
<td>0.79</td>
<td>5.2</td>
<td>2.42</td>
</tr>
<tr>
<td>Alive with RDS (5 infants)</td>
<td>Mean 9.98</td>
<td>0.057</td>
<td>1.32</td>
<td>3.76</td>
<td>3.26</td>
</tr>
<tr>
<td>Alive (2 infants)</td>
<td>Mean 26.7</td>
<td>0.275</td>
<td>6.47</td>
<td>8.65</td>
<td>3.05</td>
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<td>Total preterm (10 infants)</td>
<td>Mean 16.30</td>
<td>0.094</td>
<td>2.191</td>
<td>5.07</td>
<td>2.99</td>
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<tr>
<td>(10 infants)</td>
<td>SD 7.68</td>
<td>0.09</td>
<td>2.340</td>
<td>2.31</td>
<td>1.68</td>
</tr>
<tr>
<td>SE 2.43</td>
<td></td>
<td>0.03</td>
<td>0.740</td>
<td>0.73</td>
<td>0.53</td>
</tr>
</tbody>
</table>

P value

<0.01 <0.01 <0.01 <0.01 NS

SB = stillbirth; RDS = respiratory distress syndrome; NS = not significant.