Prolactin, cortisol and thyroxine levels and the premature infant

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Summary
The relationship of prolactin, cortisol and thyroxine values in cord and maternal plasma to fetal age and weight and to the incidence of hyaline membrane disease (HMD) was investigated in 80 neonates of whom 40 were born at more than 37 weeks gestation. Of the 40 born at less than 36 weeks 11 developed HMD. Serum cortisol has been shown to be a differentiating factor for HMD, but cord thyroxine and prolactin levels seem to be related more to age and weight than to the occurrence of HMD.

Hyaline membrane disease (HMD) is widely accepted as the major cause of morbidity and mortality in premature infants. This condition of functional immaturity of the lungs is thought to be associated mainly with inadequate alveolar surfactant, a surface-active material which lines the alveoli and reduces surface tension at the alveolar tissue/air interface. The regulatory mechanisms controlling lecithin synthesis, particularly those responsible for the surge in lecithin production in the late stages of gestation, are not fully understood.

The cortisol levels in amniotic fluid correlate well with gestational age. It has been shown by Murphy that mean cord cortisol levels in infants with HMD are significantly lower than those in infants of similar gestational age without HMD. Specific glucocorticoid receptors have been found in fetal lung, further suggesting that glucocorticoids are related to lung maturation.

It has been shown by Winters et al. that the concentration of prolactin in human fetal plasma increases throughout pregnancy, with a marked rise towards term. This finding suggests that plasma prolactin may be correlated with the presence or absence of HMD. Specific glucocorticoid receptors have been found in fetal lung, further suggesting that glucocorticoids are related to lung maturation.

The appearance of and progressive rise in fetal thyroxine take place at the same time as the earliest production of pulmonary surfactant and its subsequent increasing concentration. Since thyroxine has been shown to be an important regulator of lipid metabolism in vivo, several researchers have investigated the possibility that it may be involved in regulating the production or metabolism of surfactant.

The present study was designed to approach these problems by determining the prolactin, cortisol and thyroxine levels at delivery in maternal blood and cord blood of infants delivered preterm (before 36 weeks' gestation) and at term (after 37 weeks' gestation).

Patients, material and methods

The subjects were infants delivered at Coronation Hospital, Johannesburg, and their mothers. Of the 80 neonates studied 40 were judged to have gestational ages of more than 37 weeks (the mature group), whereas the other 40 had gestational ages of less than 36 weeks (the preterm group). In the preterm group 11 infants (27%) developed HMD, while the other 29 had normal lung function.

None of the patients in either group suffered any complications of pregnancy or labour. No pregnancy had been complicated by pregnancy-induced hypertension, diabetes, premature rupture of membranes, pyrexia or multiple pregnancy. No delivery was by caesarean section.

Prolactin, cortisol and thyroxine values were determined in maternal and mixed cord blood samples taken at the time of delivery. Prolactin levels were determined by a radio-immunoassay technique for the quantitative determination of prolactin in serum manufactured by Abbott Laboratories. Serum cortisol and thyroxine levels were both determined by radio-immunoassay kits manufactured by Clinical Assays.

Estimation of gestational age

Gestational age was estimated by dates, uterine size at the first antenatal visit and ultrasonography. Fetal age was also assessed by an experienced neonatologist using the Dubowitz score.

Diagnosis of hyaline membrane disease

The diagnosis of HMD was made by the neonatologist. His diagnosis was based on tachypnoea, inspiratory retraction, cyanosis, respiratory acidosis and chest radiographs. Those cases in which hyaline membrane disease could not be distinguished unequivocally from other forms of respiratory distress were not included in the study.

Results

The mean weights (± SD) of the mature group, the non-HMD group and the HMD group were 2961 ± 346.9 g, 1820 ± 328 g and 1448 ± 360 g. The difference between these groups was statistically significant (P < 0.01). The mean gestational age of the mature infants was 38.1 ± 1.1 weeks, while those of the non-HMD and HMD groups were 32.9 ± 1.3 and 31.5 ± 1.7 weeks respectively.

Cord thyroxine values in the mature, non-HMD and HMD groups were 15.3 ± 4.2, 11.9 ± 7.7 and 9.9 ± 3.3 nmol/l. There...
was a statistically significant difference between the mature and preterm groups \( (P < 0.01) \) but not between the non-HMD and HMD groups. Maternal thyroxine levels for the three groups were 13.3 ± 14.5, 8.8 ± 4.7 and 11.43 ± 2.01 nmol/L.

Cord cortisol levels were 19.3 ± 9.2, 19.2 ± 19.2 and 13.1 ± 10.8 mg/ml in the mature, non-HMD and HMD groups. There was a statistically significant difference between the mature and HMD groups \( (P < 0.05) \). Maternal cortisol values were 54.4 ± 28.4, 43.5 ± 25.5 and 38.6 ± 25.4 mg/ml in the mature, non-HMD and HMD groups.

Cord prolactin values were 281.6 ± 134.5, 198.0 ± 140.7 and 225.1 ± 119.9 mg/ml in the mature, non-HMD and HMD groups. There was a statistically significant difference \( (P < 0.01) \) between the mature group and the combined preterm group as well as between the mature and HMD groups. Maternal prolactin levels were 225.7 ± 183.4, 158.3 ± 137.7 and 141.0 ± 87.3 mg/ml; there were statistically significant differences between the mature group and the combined preterm group \( (P < 0.04) \) and between the mature and HMD groups \( (P < 0.03) \).

Cord blood prolactin levels have been shown by Hauth et al.\(^7\) and Smith et al.\(^11\) to correlate significantly with the weights of the newborn infants as well as with their gestational ages. They also showed that cord plasma prolactin levels in infants who developed HMD were low.

Our results showed that mean cord prolactin levels were lower in both preterm groups than in the mature group. However, only the differences between the mature group and the combined preterm group and between the control group and the non-HMD group reached statistical significance. The difference between the mature and HMD groups alone was not statistically significant. This shows that the lower cord prolactin levels in the preterm group are related only to prematurity (weight and age) and not specifically to HMD. These results are similar to those of Hauth et al.\(^7\) and Smith et al.\(^11\)

Maternal prolactin levels were markedly lower in the preterm group than in the mature group. There is a significant difference between the mature group and both the HMD group and the combined preterm group, but none between the mature group and the non-HMD group. This indicates that the maternal serum prolactin level is related to prematurity as a whole, and in addition is specifically related to the respiratory distress syndrome.

When the HMD group and the non-HMD groups are compared, statistically significant differences are only seen between the cord cortisol levels in the HMD group and those in the mature group. A statistically significant increase in serum cord thyroxine and prolactin values with an increase in weight has also been demonstrated.

Although not statistically significant, there was a mean fall in cord cortisol and thyroxine levels between the HMD and non-HMD groups, with an increase in cord prolactin between these two groups.

Low serum cord cortisol values are therefore a differentiating factor for HMD, but cord thyroxine and cord prolactin levels seem to be related more to weight and gestational age than to the presence of HMD.

**Discussion**

Mean weights and ages were significantly lower in the preterm group than in the mature group; furthermore, the infants with HMD weighed significantly less than the preterm infants without HMD. Mean cord serum thyroxine levels rose significantly with age and weight (preterm v. mature), but not within the preterm group. This supports the work of Fisher et al.\(^10\) indicating a rise in fetal thyroxine values with weight and age. Maternal serum thyroxine values did not differ significantly between any of the groups studied.

Klein et al.\(^12\) and his associates found higher cortisol levels in infants with HMD than in controls; in contrast Murphy\(^3\) described significantly lower cord cortisol levels in infants with HMD than in controls.

In our study there was no difference between cord cortisol levels in the mature and the non-HMD preterm groups. However, there was a statistically significant reduction in level in the HMD group compared with the mature group. This contradicts the findings of Klein et al.\(^12\) but supports those of Murphy.\(^3\)

There is no statistically significant relationship between maternal cortisol values.

**REFERENCES**

5. Giannopoulous G. Variations in the levels of cytoplasmic glucocorticoid receptors in lungs of various species at different developmental stages. Endocrinology 1974; 94: 540-548.