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Prevention of respiratory distress syndrome by antenatal maternal steroid treatment

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A total of 107 women at risk of premature delivery received antepartum 45 to 60 mg prednisolone medication. Their babies were matched with comparable neonates of untreated mothers. The frequency of respiratory distress syndrome was 6/107 in the steroid-treated, and 33/107 in the control group. No maternal complications were seen. Neonatal mortality was lower in the pretreated group in which, however, a higher number of bronchopneumonia was observed. In 58 prednisolone-treated women labour could be delayed, and their infants were born at term. No stillbirth or intrauterine growth retardation occurred among them.

Since the first attempt to prevent neonatal respiratory distress (RDS) by ante-partum administration of glucocorticoids [12], several studies have demonstrated that steroids are capable of inducing surfactant production [2, 3, 4, 14], and of lowering the incidence of RDS [1, 5, 6, 10, 18].

We report below on our own experience with prednisolone premedication of pregnant women at risk of premature birth.

Patients and Methods

Altogether 245 women at risk of premature delivery received premedication. Their period of gestation ranged from 28 to 36 weeks. Additional 8 patients, in whom Caesarean section was performed because of maternal diabetes or Rh-isoimmunization in the 37th and 38th week of gestation were also included. Prednisolone was given orally in an amount of 3×10 mg daily for two days. Patients with hypertension or proteinuria were excluded from the study. Labour was delayed with either alcohol-infusion or salbutamol.

In 80 cases delivery occurred within 36 hours after admission; these patients were also excluded from the study. Thus only 165 women received prednisolone in a total amount ranging from 45 to 60 mg in a period of 36—48 hours. Of the 165 woman, 107 delivered a baby within a week's time. Each newborn infant was matched with the next consecutively born infant of the same gestational age, route of delivery and similar birth weight. The frequency of RDS in the two groups of neonates was compared. The diagnosis of RDS was based on clinical and laboratory signs tachypnoea, subcostal retraction, grunting, cyanosis, combined respiratory and metabolic acidosis. Chest X-rays were also done in part of the newborns.

In 58 cases the labour could be delayed until the 36th to 41st week of gestation. The intrauterine growth rate was compared to a Hungarian growth chart [9].

In 17 cases the surfactant content of amniotic fluid was estimated by the bubble stability test [7] and quantitative measurement of palmitic acid concentration [17]

before and after prednisolone administration.

Necropsy and histological examination were carried out in all infants who had died.

Results

Results are summarized in Table I.

Only 6 of the 107 newborns with antenatal prednisolone-treatment had respiratory distress, in contrast to 33 of the 107 neonates born to untreated mothers. The difference was highly significant statistically ($\chi^2 = 22.99$; d.f. $= 1$; $p < 0.001$). The protective effect of maternal steroid medication was quite striking in the infants born after the 32nd week of gestation. Only a single case of RDS occurred among these neonates, and even this baby survived. In contrast, among those born between the 28th and 32nd week, five infants showed clinical signs of RDS. One of them died within 14 hours, the other 4 recovered, but two of them succumbed later to bronchopneumonia. However, as compared to the high morbidity and mortality rates of prematures with a similar gestational age, prednisolone premedication proved useful also under the 32nd week of pregnancy.

Perinatal mortality rate was 6% less in the prednisolone-treated group, but because of the small number of cases, the difference was not significant ($\chi^2 = 1.06$; d.f. $= 1$; $p \sim 0.30$). As regards pulmonary pathology, it was conspicuous that while, except

Table I

Frequency of RDS and causes of neonatal death in newborns of prednisolone-treated and untreated mothers

Gestational age	Prednisolone-treated		Control	
	n	RDS	n	RDS
28–32 weeks	38	5	38	13
33–36 weeks	61	1	61	17
> 36 wk (Caesarean section)	8	0	8	3
Total	107	6	107	33
Neonatal mortality				
Intraventricular haemorrhage	6		6	
RDS	1		13	
RDS + meconium aspiration + intracranial haemorrhage	0		3	
Meconium aspiration + bronchopneumonia	3		0	
Bronchopneumonia	7		1	
Pulmonary haemorrhage	0		1	
Spina bifida aperta	1		0	
Total	18		24	
Mean survival time	5.4 days		1.2 days	

for one case, no hyaline membrane was found in the prednisolone-treated group, bronchopneumonia appeared to be the primary cause of death in 10 of these infants. On the contrary, in the control group necropsy revealed characteristic RDS in 16 neonates, but only one case of bronchopneumonia was recorded. Survival time of newborns with fatal outcome was significantly different: 5.4 days in the prednisolone-treated versus 1.2 days in the control group.

The benefit of steroid therapy was demonstrated by the simple shake test or determination of palmitic acid concentration in the amniotic fluid. In all the cases showing negative or transitional bubble stability or a low palmitic acid concentration, positive shake test and/or high concentrations were obtained after 48 hours prednisolone treatment.

In 58 cases, delivery could be delayed and it occurred at term. All the infants born from these pregnancies were mature and appropriate for date. They did not show physical signs suggestive of intrauterine growth retardation, the position of their birth weight was between the 25th and 90th percentile of the growth chart [9].

Discussion

The results so far suggest that maternal steroid medication is a useful method in the prevention of neonatal RDS. Choice of an adequate control group is, however, difficult; in this study special care was paid to match the babies of prednisolone-treated mothers with comparable untreated infants. Had we failed to do so in some of the cases, the difference between the two groups was so great that it could not have essentially altered the results. The beneficial effect of prednisolone-pretreatment was shown also by the cases not included in this study because the therapy could not be completed. Still, RDS occurred less frequently and was milder in these cases too.

A common argument against steroid administration is that knowledge is still scarce concerning its possible complications [13, 15]. In the present series no maternal side-effects were observed. In contrast to findings in animal experiments [8] and observations on pregnant women receiving prolonged steroid therapy [11, 16], neither intrauterine growth retardation, nor stillbirths occurred. This may have been due to the short duration of the therapy.

The high incidence of bronchopneumonia in the prednisolone-treated and died neonates may have been due to two major mechanisms. First, the increased number of bronchopneumonias may have been a direct consequence of the increased susceptibility to infections caused by the steroids. Second, since in the fatal cases survival was much longer in the premedicated than in the untreated group, these infants might have had time to develop bronchopneumonia, while the untreated ones had died before the consequences of infection could develop. This adverse effect as

well as the possible transient or permanent metabolic changes need further examination.

Although the present observations do not permit definite conclusions, they still seem to indicate the beneficial effect of steroid treatment in the prevention of RDS.

Results

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