

The Possibility of Respiratory Distress Syndrome Prevention of Premature Born Children

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ABSTRACT

Pregnant women and premature born children were classified into four groups. In each group there were thirty of them. The first group included the pregnant women with premature rupture of membranes and amniotic fluid effluxed for 72 hours before the delivery. The second group included the pregnant women with amniotic fluid effluxing less than 72 hours before the delivery. The third group included the pregnant women who were given corticosteroids. The fourth group was a control group formed by those pregnant women (and their premature born children) whose amniotic fluid did not efflux long and those who weren't given corticosteroids during pregnancy. In all groups of pregnant women we observed: median age of pregnant women, the duration of pregnancy and mode of delivery (vaginal or cesarean section). In groups of premature born children we also observed: newborn birth weight, Apgar score in the first minute after delivery, Apgar score in the fifth minute after delivery, pH of the blood of umbilical cord, L/S ratio of amniotic fluid (lecithin-sphingomyelin ratio), RDS (neonatologist valuation in any degree of RDS developed in newborn child). Symptoms of RDS include tachypnoea, chest wall retraction and cyanosis and a 'ground glass' appearance of the chest on X-ray. Histopathological examinations of placentas compared the frequency of inflammatory or noninflammatory changes, also in all groups. No significant difference was found among groups of pregnant women for the following factors: the age of pregnant women, the duration of pregnancy and mode of delivery. No significant difference was found among the groups of children for the following factors: newborn birth weight, Apgar score in the fifth minute after delivery, blood pH of umbilical cord, L/S ratio of amniotic fluid. Significant difference was found among groups for the following factors: Apgar score in the first minute after delivery, the frequency of RDS and histology of placentas. The prevention of premature delivery is the most important. All the pregnant women with symptoms of the premature delivery must be transported to the centers with the well developed units of intensive neonatal care («transport in utero»).

Key words: premature born children, respiratory distress syndrome

Introduction

Respiratory distress syndrome (RDS) is a condition of pulmonary insufficiency that in its natural course commences at or shortly after birth and increases in severity over the first 2 days of life. If left untreated death can occur from progressive hypoxia and respiratory failure. In survivors resolution begins between 2 and 4 days. RDS is due to a lack of alveolar surfactant along with structural immaturity of the lung and it is mainly confined to preterm babies. Clinically RDS presents with early respiratory distress comprising cyanosis, grunting, retraction, and tachypnoea. Respiratory failure may develop and is indicated by blood gas analysis. Between 5 to 10 % of an-

nual births occurs preterm (before 37 weeks completed gestation)¹. Preterm infants represent 75% of all neonatal deaths¹. In conclusion, the prevention of the preterm birth is important but we must also focus on its treatment.

Patients and Methods

The aim of the study was to evaluate in which of the four groups of pregnant women preterm babies have greatest chances for survival.

The study was conducted from January 2000 through December 2002. The institutional review board approved this study.

Pregnant women and premature born children were classified into four groups. In each group there were thirty of them.

The first group included the pregnant women with premature rupture of membranes and amniotic fluid effluxed for 72 hours before the delivery. The second group included the pregnant women with amniotic fluid effluxing less than 72 hours before the delivery. The third group included the pregnant women who were given corticosteroids. All the mothers in the 3rd group received a complete course of dexamethasone steroids 48 hours after the first dose. The fourth group was a control group formed by those pregnant women (and their premature born children) whose amniotic fluid did not efflux long and those who weren't given corticosteroids during pregnancy. In all groups of pregnant women we observed:

- median age of pregnant women
- the duration of pregnancy
- mode of delivery (vaginal or cesarean section)

In groups of premature born children we also observed:

- newborn birth weight
- Apgar score in the first minute after delivery
- Apgar score in the fifth minute after delivery
- pH of the blood of umbilical cord
- L/S ratio of amniotic fluid (lecithin-sphingomyelin ratio)
- RDS (neonatologist valuation in any degree of RDS developed at newborn child). Symptoms of RDS include tachypnoea, chest wall retraction and cyanosis and a 'ground glass' appearance of the chest on X-ray.

Histopathological examinations of placentas compared the frequency of inflammatory or noninflammatory changes,

also in all groups. Kruskal-Wallis one-way analyses of variance, Kolmogorov-Smirnov test, Analysis of Variance (ANOVA) method and χ^2 -tests were used in this study.

Results

In our study no significant difference was found among groups of pregnant women for the following factors: the age of pregnant women, the duration of pregnancy and mode of delivery (Table 1). Average time of gestation was 33 weeks in all four groups. The highest percentage of cesarean section was in the first group (26, 7%), while in the second and fourth group percentage was slightly lower (20%).

Average birth weight was between 2064 gr. (first group) and 2217 gr. (second group). There were no statistically significant differences in birth weight among four groups ($p < 0.05$).

Apgar score in first minute after delivery indicates that most endangered preterm babies (Apgar score 7 or lower) were in the first and third group and that there was statistically significant difference in comparison with second and fourth group ($p < 0.05$). However, there were

TABLE 1
OBSERVED PARAMETERS IN ALL GROUPS OF PREGNANT WOMEN

	Median age	Duration of pregnancy	Vaginal delivery	Cesarean section
I	26.9	33.4	22	8
II	26.6	34	24	6
III	28.9	33.9	23	7
IV	27.1	33.8	24	6
	NS	NS	NS	NS

There were no statistically significant differences in observed parameters among four groups ($p < 0.05$)

TABLE 2
OBSERVED PARAMETERS IN ALL GROUPS OF PREMATURE BORN CHILDREN

	I	II	III	IV	
Child mass	2064	2217	2084	2124	NS
Apgar score in the first minute after delivery ≤ 7	12	6	13	5	$p < 0.05$
Apgar score in the first minute after delivery ≥ 7	18	24	17	25	$p < 0.05$
Apgar score in the fifth minute after delivery ≤ 7	2	1	2	0	NS
Apgar score in the fifth minute after delivery ≥ 7	28	29	28	30	NS
pH of the blood of umbilical cord	7.24	7.23	7.25	7.25	NS
L/S ratio of amniotic fluid (lecithin-sphingomyelin ratio) ≤ 3	8	12	10		NS
L/S ratio of amniotic fluid (lecithin-sphingomyelin ratio) ≥ 3	7	4	4		NS
RDS	13	21	12	20	$p < 0.05$
Inflammatory changes on placentas	18/21	13/20	8/28	6/20	$p < 0.05$

Significant difference was found among groups for the following factors: Apgar score in the first minute after delivery, the frequency of RDS and histology of placentas ($p < 0.05$)

no statistically significant differences in Apgar score 5 minutes after delivery among four groups ($p < 0.05$).

Lowest PH of the umbilical cord blood was in the second group (7, 23 ± 0.040) and the highest was in the fourth group (7, 25 ± 0.031). There were no statistically significant differences in PH of umbilical cord blood among four groups ($p < 0.05$).

There were no statistically significant differences in L/S ratio of amniotic fluid, although the highest percentage of the preterm babies with L/S ratio higher than 3 was in the first group (46, 7%).

RDS was most frequent, according to our results, in second group. 70 % of preterm babies in second group had difficulties with breathing. The lowest frequency of RDS was in the third group (40, 0%). There were statistically significant differences in development of RDS among four groups ($p < 0.05$).

Histopathological examinations of placentas have shown the highest percentage of inflammatory changes in the first group (85.7%). In the second group percentage of inflammatory changes was 58.8 % and in the third group 35.7 %. The lowest percentage of inflammatory changes was in the fourth group (30%). There were statistically significant differences in the frequency of inflammatory or noninflammatory changes on the histopathological examinations of placentas ($p < 0.05$) (Table 2).

Discussion

Preterm babies at risk of RDS should be born in centers where appropriate skills are available for stabilization and ongoing respiratory support, including intubation and mechanical ventilation. There is often prior warning of impending preterm delivery, allowing time for interventions to be considered including *in utero* (maternal) transfer where appropriate. Preterm delivery can be delayed by using antibiotics in the case of preterm, pre-labor rupture of the membranes², and tocolytic drugs can be used in the short-term to delay birth^{3–5} to allow safe transfer to a perinatal center and to enable prenatal corticosteroids to take effect.

Prenatal corticosteroid therapy is recommended in all pregnancies with threatened preterm labor below 35 weeks' gestation. Improved neurological outcome has been demonstrated for even the tiniest babies^{6,7}. The optimal treatment to delivery interval is more than 24 h and –7 days after the start of steroid treatment⁷.

There is continuing controversy over the use of repeated courses of prenatal corticosteroids. Although there may be clinical benefits of giving a second course in cases where delivery has not occurred in terms of further

reducing RDS⁸, long-term follow up data are not yet available. In animal studies there are changes in brain myelination following repeated exposure to prenatal steroids^{9,10} and in a large cohort study a decrease in newborn head circumference has also been observed with increasing prenatal steroid exposure¹¹. The recent Cochrane systematic review does not recommend routine repeat courses of prenatal steroids¹².

Evidence from experimental studies in animals indicates that corticosteroid-induced functional 'maturation' of the preterm lungs is caused primarily by structural changes and that increases in surfactant are relatively slower to occur and exist only transiently after corticosteroid treatment¹³. Thus, surfactant deficiency (the principal contributor to RDS) may not be adequately treated by antenatal corticosteroids; this is reflected by the fact that RDS is prevented by antenatal corticosteroids in only 50% of cases.

The structural changes induced by antenatal corticosteroid treatment result in thinner alveolar walls and fewer, larger alveoli than normal¹⁴. Although beneficial in the immediate neonatal period, these structural effects may have longer-term adverse consequences because this phenotype is characteristic of the chronic neonatal lung disease bronchopulmonary dysplasia (BPD).

The recent realization are that many preterm births are associated with intrauterine inflammation and that intrauterine infection /inflammation is associated with a reduced risk of RDS in some cohorts of infants^{15,16}.

Exploitation of inflammatory pathways for inducing preterm lung 'maturation' in humans appears as a possibility. The reduced risk of RDS associated with inflammation is accompanied by an increased risk of BPD in humans¹⁶. BPD-like changes in lung structure and the surfactant system in preterm lambs after exposure to intrauterine inflammation have been observed¹⁷.

Conclusion

We can conclude that, in the pregnant women with premature rupture of membranes and amniotic fluid efflux, there is increased risk of infection as time goes by until delivery, but there is significantly lower incident of RDS in preterm babies. Corticosteroids can be administered if there is risk of preterm delivery, but only if there is no sign of infection.

The prevention of premature delivery is the most important. All the pregnant women with symptoms of the premature delivery must be transported to the centers with the well developed unites of intensive neonatal care (>transport *in utero*<).

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MOGUĆNOST PREVENCIJE RESPIRATORNOG DISTRES SINDROMA U PRIJEVREMENO ROĐENE DJECE

SAŽETAK

Trudnice i prijevremeno rođena djeca svrstani su u četiri skupine. U svakoj skupini bilo ih je 30. U prvu skupinu uključene su trudnice kod kojih je došlo do prijevremenog prsnuća vodenjaka i plodova voda je otjecala više od 72 sata prije porođaja. Drugu skupinu činile su trudnice kod kojih je plodova voda otjecala manje od 72 sata prije porođaja. Treću skupinu činile su trudnice koje su u trudnoći primale kortikosteroide. Četvrta skupina je bila kontrolna i činile su je trudnice (i njihova prijevremeno rođena djeca) kod kojih plodova voda nije otjecala, a nisu niti dobivale kortikosteroide u trudnoći. Kod trudnica smo po skupinama određivali: prosječnu dob trudnica, trajanje trudnoće, način dovršenja porođaja (vaginalno ili carskim rezom). Kod novorođenčadi smo, također po skupinama, određivali: porođajnu težinu djeteta, Apgar indeks u prvoj i petoj minuti nakon porođaja, pH krvi iz pupkovine, L/S omjer iz plodove vode /omjer lecitina i sfingomijelina, RDS /procjena neonatologa da li se razvio bilo koji stupanj RDS-a kod novorođenčeta. Na posteljicama je patohistološkim pregledom uspoređivana učestalost upalnih neupalnih promjena, također po skupinama. Nije nađena značajna razlika među skupinama trudnica za varijable: dob roditelja, trajanje trudnoće, način dovršenja porođaja. Kod novorođenčadi nije nađena značajna razlika među skupinama za varijable: porođajna težina, Apgar indeks u petoj minuti, pH krvi iz pupkovine, L/S omjer iz plodove vode. Nađena je značajna razlika među skupinama za varijable: Apgar indeks u prvoj minuti, učestalost pojave RDS-a, PHD posteljice. Važna je prevencija prijevremenog porođaja. Sve trudnice sa znacima prijevremenog porođaja treba uputiti u centre sa dobro razvijenom jedinicom intenzivne skrbi za malo dijete (»transport in utero«).