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Effect of antenatal steroid before elective cesarean section on prevention of respiratory morbidities of full-term neonates

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ABSTRACT

Background and Objective: Elective cesarean section (ECS) increases neonatal respiratory complications like transient tachypnea of the newborn (TTN) and respiratory distress syndrome (RDS). This pilot study examined the effect of antenatal steroids on the prevention of respiratory problems in full-term neonates born via ECS.

Methods: This experimental study was carried out on full-term neonates (39-42 weeks) born by ECS to the mothers admitted to Babol Clinic Hospital, northern, Iran in 2016. The intervention group received betamethasone (12 mg, intramuscular, once a day) for 2 days before ECS plus conventional care, but the control group received only conventional care. The rate of respiratory complication and the admission rate of the newborn ward and neonatal intensive care unit (NICU) were compared between two groups.

Findings: Overall, 200 full-term neonates (100 neonates in the experimental group and 100 neonates in the control group) were enrolled. Nine neonates (9%) in the experimental group and 8 neonates (8%) in the control group had TTN (P=0. 64), and one (1%) neonate in the experimental group and one neonate (1%) in the control group had RDS (P=1).

Conclusion: Antenatal corticosteroid administration to the mothers before ECS with gestational ages of 39-42 weeks does not reduce the incidence of respiratory complications. Thus, further studies are needed to determined its effects in gestational age group more than 39 weeks.

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Introduction

In recent years, cesarean section (CS) has become a widely popular way of delivery to the extent that official statistics report that this procedure is performed more frequently than vaginal delivery. So long as cesarean delivery is not performed according to the obstetrics recommendations, there might be accompanying risks, one of which involves respiratory problems including respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN) and persistent fetal circulation (PFC) [1].

Neonates born by CS are more likely to have difficulty breathing than babies born by vaginal delivery. In a regional study, the frequency of RDS and TTN was higher in newborns born by cesarean than those born by vaginal delivery. Moreover, the frequencies of both factors were higher in elective cesarean section (ECS) than emergency CS [2].

Pirjani et al. in a prospective cohort study showed that the rate of TTN and neonatal intensive care unit (NICU) admission was higher in neonates born by ECS delivery with 38-39 gestational weeks than those born with ECS performed after 39 completed gestational weeks [3]. In a recent study done by Khasawneh et al., the most common diagnoses for admitted term neonates delivered by ECS were TTN and RDS [4]. Moreover, Winovitch et al. reported a high rate of persistent pulmonary hypertension of the newborn following ECS [5].

The benefits of antenatal steroids in preterm birth have been well proven at gestational age of <34 weeks. No pharmacological agent in perinatal medicine has been as controversial as corticosteroid administration for perinatal and newborn babies [6]. It is advised by the majority of relevant literature to prescribe antenatal corticosteroids for all pregnant women in preterm labor conditions (24-34 weeks of gestation), whose delivery is more likely within one week [2, 7-10]. Previous guidelines recommended that antenatal corticosteroids be administered after 34 weeks of gestation only when there is evidence of pulmonary immaturity [11, 12]. Some other studies concerning the administration of antenatal corticosteroids; however, argued that antenatal corticosteroids should be given to all women experiencing a planned ECS before 38+6 weeks of pregnancy so as to curtail respiratory complications [9].

So, it is currently administered as a standard measure to prevent RDS in preterm birth less than 34 weeks of gestation [2]. The European consensus guideline released in 2019 recommend a single course of antenatal corticosteroids to all women at risk of preterm delivery, from when pregnancy is considered potentially viable up to 34 completed weeks of gestation. They also recommend that "antenatal steroids can also be considered for CS not in labor up to 39 weeks [13]. But there is no recommendation to apply this policy for pregnant mothers at 39-42 weeks, undergoing to an ECS. On the other hand, there have so far been few studies on the benefits of antenatal steroids to prevent respiratory morbidities before the birth of full-term babies through ECS.

Since birth by ECS may lead to increased prevalence of respiratory diseases such as RDS and TTN, it seems essential to take certain measures to prevent lung problems. Hence, this study intended to examine the effect of antenatal steroids on prevention of respiratory problems in full-term babies born by CS.

Methods

Subjects and Protocol

This clinical trial was conducted on newborn infants born to mothers referred to Babol Clinic Hospital, Northern Iran, who were admitted for ECS from 39 to 42 weeks gestation of pregnancy due to repeated CS.

The study protocol was registered under the code of IRCT2015090923963N1in www.irct.ir and was approved by the Ethics Committee of Babol University of Medical Sciences under serial no. 5808-30/J/P. Moreover, informed consent was obtained from parents. Inclusion criteria for mothers were the full gestational age of ≥39 weeks based on ultrasound images, no history of cesarean indications other than repeated CS. The exclusion criteria were applied to mothers who had obstetrical or underlying diseases such as placental abruption, cephalopelvic disproportion and macrosomia. Similarly, mothers with a history of infection, diabetes,

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prolonged rupture of membranes and taking antenatal steroids for any other reason prior to delivery were excluded.

Inclusion and exclusion criteria

Inclusion criteria for mothers and infants were gestational age of ≥39 weeks based on perinatal ultrasounds plus physical characteristics of neonates based on New Ballard Score (NBS) performed by the researcher. Neonates with diseases such as intrauterine growth retardation, macrosomia or perinatal infections and congenital anomalies were excluded.

Intervention

Mothers were randomly divided into two intervention and control groups. The mothers in the intervention group received betamethasone (12 mg, intramuscular, every 24 hours and two doses) within 48 hours prior to delivery plus conventional care while the control group only received conventional care.

Outcome variables

The outcome variables included;

a) Primary outcome: Signs of any respiratory distress during the hospital stay, like tachypnea, retraction, grunting and cyanosis.

b) Secondary outcome: need for oxygen administration, admission of babies to the neonatal ward or NICU, sepsis, neonatal death and maternal complications of steroids such as hyperglycemia and increased blood pressure.

Sample size

Considering this is the Phase I of a clinical trial, the sample size was calculated to be 100 for each group. After obtaining the sample size, the two groups were compared in terms of outcome variables including the incidence of antenatal respiratory problems, identifying the underlying causes of distress, need of hospitalization, duration of hospital stay and need for oxygen. Statistical analysis was performed using SPSS 20. The Chi-square test, Fisher's exact test and logistic regression were used with the significant level of <0.05.

Results

This study involved a total of 200 infants with the age of 39-42 weeks in two groups of control group (n=100) and betamethasone group (n=100). There were no significant differences between these two groups in terms of gender, mean birth weight, gestational age, admission age, age at the time of discharge and duration of hospital stay (table 1)

In both groups, there were 19 cases with respiratory diseases, all of which were hospitalized and required supplemental oxygen. There were 2 cases of RDS hospitalized in NICU and 17 cases of TTN admitted to the special care nursery. All neonates with TTN did not need to transfer to in NICU over the course of treatment. There were no PFC cases identified in both groups.

One of 2 diagnosed RDS cases (1%) was found in the control group while the other case (1%) was observed in the betamethasone group, indicating no statistically significant difference between two groups (P =1) (table 1). Out of the 17 cases of TTN, 9 (9%) and 8 (8%) infants were in the control and betamethasone groups, respectively (P=0. 64).

All patients with RDS and TTN were admitted, since all needed to receive intravenous fluids, antibiotics and supplemental oxygen via head box. Moreover, none of the patients required surfactant replacement therapy,

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continuous positive airway pressure therapy and mechanical ventilation. All of the patients were discharged after treatment measures with desirable general health status without any cases of infant mortality. There were no maternal complications in the present study associated with the administration of betamethasone.

Table 1. Comparison of baseline characteristics and outcome variables between bethamehasone and control groups.

Variables	Bethamethasone group (N=100)	Control group (N=100)	P-Value
Birth weight (g) Mean±SD	3406±352	3450±386	0.403
Gestational age (w) Mean±SD	39.73±1.49	39.48±0.35	0.109
Sex:			
Female	50 (50%)	53 (53%)	0.18
Male	50 (50%)	47 (47%)	
Age at admission (day) Mean±SD	2.14±1.2	3.89±2.12	0.884
Age at discharge (day) Mean±SD	4±1.11	3.9±1.6	0.868
Duration of Hospital stay (day) Mean±SD	3.78±0.97	3.89±1.61	0.862
Special Care Nursery Admission (%)	8 (8%)	9 (9%)	0.99
NICU Admission (%)	1 (1%)	1 (1%)	1
TTN (%)	8 (8%)	9 (9%)	0.64
RDS (%)	1 (1%)	1 (1%)	1

Abbreviation, NICU: Neonatal Intensive Care Unit, TTN: Transient Tachypnea of Newborn, RDS: Respiratory Distress Syndrome.

Discussion

The results of the present study indicated that the antenatal administration of steroids in full term babies left no impact on the incidence of respiratory problems including TTN and RDS.

The frequency of RDS in infants over 39-42 weeks in the current study was roughly equivalent to 1%. Anandkat et al. reported the incidence of RDS <1% within 37 weeks of gestational age [2]. In present study, the incidence of RDS in both experimental and control groups was approximately 1%. In fact, there was no statistically significant relationship between two groups.

The incidence of RDS decreases at later gestational ages [8]. The present study could provide evidence that antenatal corticosteroid injections for full-term infants had no effect on decreasing the risk of respiratory problems. That is because there is no higher incidence of RDS in full-term infants expected to have experienced lung maturation at this age. Hence, antenatal administration of corticosteroid can hardly reduce the risk of RDS.

The incidence of TTN is generally 5.7 per 1,000 full-term deliveries [14]. Nevertheless, the incidence of TTN in CS tends to be 2-3 times higher than that in vaginal deliveries [2]. The frequency of TTN in this study was far higher than reported one. This may be associated with the high incidence of TTN in the region under study. A local study conducted in Babol in 2008 reported that the frequency of TTN in CS was greater than that in vaginal deliveries (10% vs. 5.8%) [2]. Previous studies already acknowledged that the incidence of TTN tended to be higher in infants born by CS than vaginal deliveries [2, 8].

As the present study involved only ECS, it has been impractical to make any comparison TTN frequencies among full term newborns of normal delivery. What is obvious; however, is the high incidence of TTN in CS versus vaginal delivery as well as the need to find strategies to reduce the risk of complications.

In addition, in the ongoing study, 9 (9%) and 8 (8%) TTN cases were found in the experimental and control groups, respectively. Although the frequency of TTN in the experimental group was lower by about 1%, this relationship was not statistically significant.

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It is believed that the TTN leads to slow absorption of fluid in the lungs, which, in turn, reduces the lung capacity, tidal volume and greater dead space [8]. On the other hand, it is well-known that corticosteroids affect amiloride-sensitive epithelial sodium channel, accelerating the water re-absorption within the alveolar space [2].

A study has demonstrated that if antenatal corticosteroids are prescribed before a planned ECS during 37-39 weeks, there will be a lower risk of respiratory distress by 50%. In this respect, Royal Australian and New Zealand College of Obstetricians and Gynecologist (RANZCOG) recommended that physicians should take that particular measure [15].

In a study by Stutchfield et al. titled "antenatal betamethasone and incidence of neonatal respiratory distress after elective cesarean section", the incidence of TTN was 4 and 2.1% in the control and treatment groups, respectively. The incidence of RDS was 1.1 and 0.2% in the control and treatment groups while the severity of respiratory distress in newborns hospitalized in the ICU was similar in both groups. They concluded that both antenatal betamethasone and delaying delivery until 39 weeks can reduce the risk of admission to the ICU with respiratory distress after ECS in full-term infants. Their study also demonstrated that the risk of hospitalization for newborns with respiratory distress in control group reduced with increasing gestational age. In fact, the probability of hospital admission in control group was11. 4% during 37 weeks, 6.2% for 38 weeks and 1.5% during 39 weeks, indicating recommendations to delay ECS up to 39 weeks [16].

In general, Stutchfield et al. reported a decrease in the risk of TTN by 50%. However, they observed such effect of corticosteroids in 37-39 week infants through pregnancy. In fact, they suggested that elective cesarean delivery should be delayed until 39 weeks; otherwise, antenatal corticosteroid should be administered. Nonetheless, pregnant women in the current study took more than 39 weeks. Based on Stutchfield et al.'s study, it can be concluded that the administration of antenatal corticosteroids may be effective in reducing the incidence of TTN from 37 to 39 weeks. This effect may not be statistically significant after 39 weeks, as observed in the current study [16].

Furthermore, in a cohort study by Hansen et al. (2008) in Denmark titled "the risk of respiratory complications in neonates with elective cesarean section", a total of 2687 babies born by ECS in Aarhus Hospital, Denmark were compared with infants born by vaginal delivery. It was found that there was a greater overall risk of respiratory complications in neonates of cesarean and those of natural delivery, aggravating at higher gestational ages. In fact, ECS compared with vaginal delivery leads to 2-4 times increased risk of respiratory complications and even serious respiratory morbidity in full-term infants. Moreover, the results have displayed that if ECS is postponed until the 39th week of pregnancy, there will be a significant reduction in neonatal respiratory complications [14].

Ahmed et al. in Egypt (2015) assessed the effect of prophylactic corticosteroids at 37 weeks before ECS for reducing neonatal respiratory morbidity and NICU admission. To do so, the pregnant women at 37 weeks were divided into two groups so that the experimental group received two doses of 12 mg intramuscular dexamethasone 24 hours earlier, and the control group received routine care. Then, the respiratory consequences of RDS and TTN and admission to the NICU were examined. The overall incidence of RDS was lower in the experimental group than control group (7.9% vs. 23%). The main complication was TTN (7% vs. 19.6%). This represented a significant reduction in the incidence of mild and moderate respiratory distress in the experimental group (7% and 0.9%) compared with 17% and 5.3% in the control group, indicating the most dramatic benefit of steroids in children 37 (+6) weeks. They concluded that the administration of antenatal steroids at 37 weeks appeared to reduce neonatal respiratory complications in women undergoing ECS [17].

In a Cochrane review by Sotiradis et al. titled "corticosteroids for the prevention of neonatal respiratory morbidity after elective cesarean section', it was found that the prophylactic betamethasone was associated with a significant reduction in the risk of hospitalization in the NICU due to the respiratory complications at 37-39 weeks of pregnancy. However, there was no statistically significant reduction in the incidence of RDS and TTN, need for mechanical ventilation and duration of hospital stay in the NICU, which is consistent with the current

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study. There was no reported evidence of neonatal sepsis, perinatal deaths or maternal infection, which is similar to the current study [1].

There was a lower risk of respiratory complications in infants at later gestational ages. Between 37+0 and 37+6 weeks, the risk of developing respiratory complications was 1.7 times higher than 38-0 and 38+6 weeks, which was, in turn, 2.4 times higher than babies born between 39+0 and 39+6 weeks [18]. This trend was curtailed especially for RDS, where the risk was about 39 in 1000 for the period between 37+0 and 37+6 down to about 8 in 1000 for the period between 39+0 and 39+6 weeks. That was the same as the incidence of RDS in the current study in which about 1% of infants had achieved full-term [19]. Given this evidence, it is recommended that the ECS should be delayed until 39 weeks [1].

A cohort study suggested that childbirth at 37 weeks and 38 weeks of pregnancy compared to ECS at 39 weeks of pregnancy was associated with increased risk of the combined outcomes such as neonatal death or respiratory complications, treated hypoglycemia, neonatal sepsis and admission to the NICU [20]. None of these complications were observed in the current study.

According to the findings of the present study, it was concluded that the administration of antenatal corticosteroids at gestational age of 39-42 weeks did not significantly reduce respiratory complications. Hence, it seems illogical to prescribe corticosteroid in gestational ages >39 weeks.

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Conflict of interest

The authors declare no conflict of interest.

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