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Antenatal corticosteroid administration before elective caesarean section at term to prevent neonatal respiratory morbidity: a randomized controlled trial

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ABSTRACT

Objective: To assess the effect of prophylactic corticosteroid administration before elective caesarean section at term (between 38 and 38^{+6} weeks) in reducing neonatal respiratory morbidity and admission to a neonatal intensive care unit (NICU) with respiratory complications.
Methods: Women in this study ($n = 1290$) were randomized into two groups: the dexamethasone group ($n = 645$) and the control group ($n = 645$). Women in the dexamethasone group received three doses of intramuscular dexamethasone 8 mg, 12 h apart, 48 h before caesarean section. Women in the control group received intramuscular saline as a placebo in the same dosage as the dexamethasone group.
Primary outcome: Comparison of NICU admission rates and the occurrence of neonatal respiratory morbidity between the two groups.
Results: The NICU admission rate for respiratory morbidity was significantly lower in the dexamethasone group compared with the control group [10/616 (1.6%) vs 24 (3.9%), respectively; $p = 0.014$]. Antenatal administration of dexamethasone was significantly associated with almost 2.5-fold reduction in the risk of NICU admission for respiratory morbidity (relative risk 0.41, 95% confidence interval 0.2–0.86; number needed to treat ≅43).
Conclusion: Antenatal corticosteroids reduce the incidence of NICU admission with respiratory morbidity after elective caesarean section at term.

Introduction

Infants born preterm are at high risk of neonatal lung disease and associated complications [1]. Respiratory distress syndrome, a consequence of immature lung development, is the primary cause of early neonatal mortality [2] and long-term morbidity in survivors [3].

Maternal steroid treatment before preterm delivery is one of the best documented and most cost-effective life-saving treatments in prenatal medicine [4,5].

In comparison with intended vaginal delivery, elective caesarean section has a two- to four-fold higher risk of overall neonatal respiratory morbidity, and even higher relative risks (RR) of serious respiratory morbidity in term newborns. Hansen et al. suggested that a significant reduction in neonatal respiratory morbidity may be obtained if elective caesarean section is postponed to 39 weeks of gestation [6].

The risk of respiratory complications, mainly respiratory distress syndrome and transient tachypnoea, decreases from 37 weeks to 39 weeks of gestation. Maternal corticosteroid injections have been shown to reduce the risk of breathing problems in babies born before 34 weeks of gestation [7].

Randomized trials regarding maternal administration of steroids before elective caesarean section at term are sought to evaluate whether giving the recommended dose of corticosteroids before delivery may lead to a reduction in respiratory morbidity in babies [7].

As such, a large randomized clinical trial was undertaken to study the effectiveness of corticosteroids on the prevention of

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neonatal respiratory complications in babies born at term by elective caesarean section.

Materials and methods

This randomized prospective placebo control trial was conducted at Ain Shams University Maternity Hospital between November 2011 and December 2014 to assess the role of prophylactic antenatal dexamethasone administration before elective caesarean section at term (between 38 and 38^{+6} weeks).

Protocol approval

Before commencement of the study and in accordance with local regulations, the protocol and all corresponding documents received ethical and research approval from the Council of the Obstetrics and Gynaecology Department, Ain Shams University on 1 November 2011.

Patient selection

The study population was divided into two groups: the dexamethasone group and the control group. The dexamethasone group consisted of 645 women who received intramuscular prophylactic dexamethasone 8 mg every 12 h for 2 days, 48 h before elective caesarean section. The control group consisted of 645 women who received intramuscular saline as a placebo before elective caesarean section. All patients attended the Maternity Hospital of Ain Shams University for routine antenatal care prior to delivery.

All cases underwent elective caesarean section 48 h after completion of the antenatal steroid course (or placebo). Neonatal outcomes were examined for respiratory or non-respiratory morbidities, and the results were analyzed using Statistical Package for the Social Sciences Version 16 (IBM Corp., Armonk, NY, USA).

Inclusion criteria included women with singleton pregnancies, pregnant women between 38 and 38^{+6} weeks of pregnancy (as calculated from the first day of the last menstrual period), age between 20 and 40 years, absence of any medical problem that could affect fetal well-being, absence of uterine contractions, and tenderness (which can be a sign of intrauterine infection).

Each woman underwent an ultrasound examination to ensure the date, and the absence of multifetal pregnancy, intrauterine growth restriction, oligohydramnios, hydramnios or fetal congenital malformations. Women who developed spontaneous labor were excluded from this study.

Consent process

Patients were recruited during routine antenatal visits and counseled about the study at 36 weeks of gestation.

The population sample under study was instructed about the research protocol, and verbal informed consent was received from each participant before randomization. Patients were randomized using computer-based tables, and allocation was performed using the closed envelope technique.

Elective caesarean sections were performed by senior residents, and the neonates were managed by a senior neonatologist. Neonates were assessed by recording: the incidence of NICU admission with respiratory distress; the incidence of transient tachypnoea of the newborn; the incidence of respiratory distress syndrome; the need for mechanical ventilation; and Apgar scores at 1 and 5 min.

Outcome measures

Primary outcome

The primary outcome was NICU admission with respiratory distress.

Secondary outcomes

Secondary outcomes were: respiratory distress syndrome; transient tachypnoea of the neonate; development of neonatal respiratory complications (pneumonia, air leak syndrome); perinatal death (within first 24 h); and need for mechanical ventilation.

Sample size justification

The sample size was calculated using EpiInfo Version 6.0, with type 1 (α) error of 0.05 and power (1-β) of 0.8. Data from previous studies showed that administration of corticosteroids decreased the incidence of NICU admission with respiratory distress following elective caesarean section at term from 22/464 (4.9%) to 7/373 (1.9%). Calculations according to these values indicated a minimal sample size of 611 women in each group. Assuming a drop-out rate of 5%, the total sample size was 1290 women.

Statistical methods

Descriptive statistics for measured variables were expressed as range, mean and standard deviation (SD) for metric data; range, median and interquartile range for discrete data; and number and proportions for categorical data. Demographic data, and primary and secondary outcomes of both groups were compared using Student's *t*-test for quantitative parametric measures, Mann–Whitney's *U*-test for quantitative non-parametric measures, and Chi-squared and Fischer's exact tests for categorical measures. Associations between variables were assessed using Pearson's correlation coefficient for metric variables, and Spearman's correlation coefficient for rank variables. RR of respiratory distress was calculated for both groups, with the corresponding 95% confidence interval (CI). Excel Version 2007 (Microsoft Corp., Redmond, WA, USA) and Statistical Package for the Social Sciences Version 16.0 (IBM Corp.) were used for data presentation and statistical analysis.

Results

This study recruited 1290 women planned for elective caesarean section at gestations between 38 and 38^{+6} weeks.

The mean age of study participants was 28.87 (SD 4.92) years (range 20–40 years). Median parity was 1 (range 0–5, interquartile range 1–3). The mean gestational age was 38^{+4} weeks (SD 3 days) (range 38–38^{+6} weeks).

No significant differences in age, parity and gestational age were found between the women in the two groups (Table 1).

Indications for elective caesarean section in the recruited women included previous caesarean section [$n = 1180$ (91.5%)], malpresentation [$n = 67$ (5.2%)], and infertility or advanced maternal age [$n = 43$ (3.3%)] (Table 1).

No significant differences in indications for caesarean section and type of anesthesia were found between the women in the two groups (Table 1). In addition, no significant differences in neonatal sex, birth weight, and 1- and 5-min Apgar scores were found between the two groups (Table 2).

The NICU admission rate was significantly lower in the dexamethasone group compared with the control group [19/616 (3.1%) vs 41 (6.7%), respectively; $p = 0.003$]. Antenatal administration of dexamethasone was significantly associated with almost