Does Antenatal Dexamethasone before FullTerm Planned Cesarean Section Affect the Incidence or Severity of neonatal Jaundice? A Randomized Controlled Trial

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Abstract

Objectives: Toevaluate the effectiveness of antenatal dexamethasone before elective caesarean section at 37-39 weeks of gestation in reducing incidence and/or severity of neonatal jaundice.Patients and.

Methods: A randomized controlled study was done in the Department of Obstetrics and Gynecology, Mansoura University Hospital. The study group received three doses of intramuscular dexamethasone 8 mg ampoules at 8-hourly interval over 24 hours ended 48 hours before time of elective CS. Control group received the usual management without dexamethasone. Neonates were followed up and those who presented with neonatal jaundice within the first 72 hour of delivery (physiologic jaundice) the level of total bilirubin was measured.

Results: The study included 200 cases. Hundred cases (50 %), received single course of antenatal dexamethasone and 100 control cases (50%). the incidence of neonatal jaundice (group 1 was 34% and group 2 was 38%) and the mean level of bilirubin in neonates who develop jaundice (group1 was 11.52±0.56 mg/dl) and (group 2 was 13.08±0.72 mg/dl). No significant difference were found between the intervention and the control groups regarding the incidence of jaundice ($p=0.56$) while there was a significant difference in bilirubin level in neonates who developed jaundice ($P<0.001$).

Conclusion: Administration of antenatal dexamethasone before elective CS at 37-39 gestational weeks was associated with reduced incidence of neonatal jaundice and lower level of bilirubin in cases that developed jaundice.

Keywords: Words: Elective CS; Antenatal corticosteroids; Neonates. Neonatal jaundice .

INTRODUCTION

Neonatal jaundice that classically appear on the first few days after delivery resulted from higher production of bilirubin since the relatively larger circulating red cell mass with short life span. Moreover, there is slight decrease in the concentration of hepatocyte binding protein and limited activity of some liver enzymes that normally occurs in the newborn babies[1].

Corticosteroids have been studied in many clinical trials for their benefit regarding lung maturation and consequently reducing neonatal morbidity and mortality[2].

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Steroids act as promoters of maturation in different organs of the fetus is widelyevidenced.The principle mechanism supporting the use of antenatal corticosteroids is attributed to alteration of a large number of genes associated with surfactant protein synthesis and different antioxidant enzyme production affecting as well as the expression of vascular endothelial growth factors[3].

Several other differentiating organs like liver, pancreas, kidney, and heart have been shown to be affected by the promoting effect of Corticosteroids-This was proved through many animal studies [4,5].

Two doses betamethasone given antenatally for full term pregnant women before elective cesarean section was studied by Stutchfield et al in 2005 on 998 pregnant women. They described their results as " antenatal betamethasone reduced the incidence of transient tachypnea of the newborn from 4% of elective caesarean sections to 2.1% and that of respiratory distress syndrome from 1.1% to 0.2%"[6].

Many studies lasting between 3 and 20 years, have studied the potential unfavorable side effects of a single course of antenatal corticosteroids. However differences in results , data points to that there is no increase in frequency of infection of fetus or mother or long-term neurological or intellectual effects [7,8]as well as other reveled the potential increase in the placental and fetal blood flow after administration[9].

Eighty four percent of full term babied is diagnosedwith mold neonatal jaundice where total bilirubin is less than 15 mg per dL(10)and is the most common cause of admission to neonatal care unit in the early neonatal period. Severe hyperbilirubinemia (total serum bilirubin more than 20 mg per dL) affects less than 2% of full-term babies and may cause kernicterus and permanent neurological and developmental delay[11].

The aim of our study was to evaluate the proposed enhancing effect of corticosteroids on fetal liver maturation and the effect of antenatal corticosteroids before elective CS at term on the incidence and severity of neonatal hyperbilirubinemia.

Patients and method

This randomized controlled trial was done in, Mansoura University Hospitals, Department of Obstetrics and Gynecology during the period from 1/1/2016 to 31/12/2017 (24 months). It included the admitted pregnant women planned for elective caesarean section at 37 to 39 completed weeks of gestation.

History taking and full examination initiallywas done for evaluation of the patients. Ultrasound was performedto assessfetal well-being. Routine laboratory investigations were done. A written informed consent was obtained from all participating women. The local ethical committee of Mansoura University Hospitals approved the study.

Inclusion criteria were, pregnant women at 37-39 weeks of gestation who were planned for elective C. S and accepted to be enrolled in the study.

- Exclusion criteria were:
- Multiple pregnancies.
- Premature rupture of membranes.
- Presence of fetal congenital malformations or intrauterine growth restriction.
- Women with medical disease with pregnancy (DM, hypertensive disorders or cardiac disease, viral or non viral hepatitis).
- History of neonatal jaundice in previous deliveries

Eligible patients were randomized by asking her to choose one of 2 closed envelopes, one of them for the study and the other for the control group. The study group received 3 doses of intramuscular dexamethasone 8 mg ampoules (Elamrya co., Egypt) at 8-hourly interval over 24 hours to be ended 48 hours before time of elective CS. Neonatal resuscitation and management was performed by a specialized neonatology team.

Neonates were followed up and those who presented with neonatal jaundice within the first 72 hour of delivery (physiologic jaundice) the level of total bilirubin was measured.

Results

The study included 200 cases. Group 1 (n= 100 cases) received single course of antenatal dexamethasone and Group 2 (n= 100 controls) control cases who did not receive antenatal Dexamethasone.

The mean maternal age, gravidity, parity, gestational age (GA), and neonatal gender of the studied cases were shown in table (1).

These criteria showed that both groups were comparable regarding maternal age, gravidity, parity, gestational age (GA), and neonatal gender (p = 0.26, 0.76,0.14,0. 0.19 and 0.78 respectively).

Table (1) Demographic criteria of the intervention and control group.

	Group 1 N=100	Group 2 N=100	Test of significance
Maternal Age /year mean±SD	28.0±4.83	27.22±4.94	t=1.13 P=0.26
Gravidity mean ± SD	2.48±0.93	2.44±0.95	t=0.30 P=0.76
Parity mean ± SD	1.36±0.96	1.16±0.95	t=1.48 p=0.14
Gestational age mean ± SD	38.26±0.72	38.12±0.74	t=1.35 ,P=0.19
Newborn gender Male Female	N(%) 54(54.0) 46(46.0)	N(%) 56(56.0) 44(44.0)	χ^2=0.08 p=0.78

Table (2) summarizes the impact of antenatal dexamethasone on the incidence of neonatal jaundice (group 1 was 34% and group 2 was 38%) and the mean level of bilirubin in neonates who develop jaundice (group1 was 11.52±0.56 mg/dl) and (group 2 was 13.08±0.72 mg/dl).

As can be noted,no significant difference were found between the intervention and the control groups regarding the incidence of jaundice (p=0.56) while there was a significant difference in bilirubin level in neonates who developed jaundice (P<0.001). Administration of antenatal dexamethasone before elective CS at 37-39 gestational weeks was associated with reduced incidence of neonatal jaundice and lower level of bilirubin in cases that developed jaundice.

Table (2) neonatal jaundice and bilirubin level

Jaundice -VE +VE	Group 1 N=100(%) 66(66.0) 34(34.0)	Group 2 N= 100(%) 62(62.0) 38(38.0)	χ^2=0.35 p=0.56
Jaundice level mg/dl Mean ± SD	11.52±0.56	N13.08±0.72	t=10.22 , P<0.001*

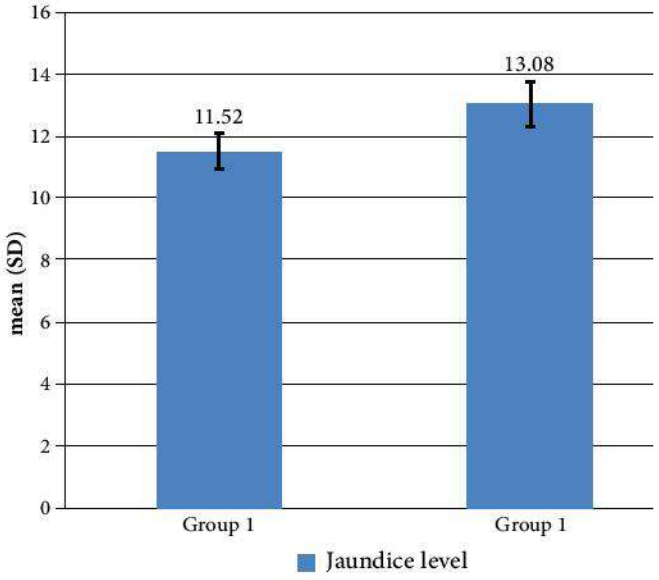

Figure (1): Mean level of bilirubin in neonates who developed jaundice (group1 where mothers received dexamethasone) (group 2 where mothers did not receive dexamethasone).

Discussion

Neonatal jaundice affects more than 2/3 of term newbornsand is the commonest cause of hospital readmission in the neonatal period. Therefore, it is important to systemically appraise the possibility to reduce the incidence of hyperbilirubinemia prenatally and early postnatal evaluation of all infants.

The potential effect of corticosteroids on maturation of fetal organs made them widely used in women with threatened preterm labor, who usually gain a significant beneficial effect on morbidity and mortality in premature neonates(3).

The mechanism that is played by antenatal corticosteroid in enhancement lung maturity was studied many years ago. Expression of certain genes was found to be involved in surfactant protein synthesis. However stimulation of other organs in the fetus like liver, pancreas, kidney was also evaluated (4,5).

In the current study, the comparison was done between100 full term pregnant women received dexamethasone 48 hours before performing elective Cs and those who did notreceive steroids as regard the development of neonatal jaundice. Although the number of delivered neonates who developed jaundice are higher than those who their mother did not receive corticosteroid but the difference in incidence was found to be notsignificant.These results could be explained by a study done by Khulan al 2016 that was concerned with an animal rat model study. They suggested that glucocorticoids associate with alterations in DNA methylation thatmay facilitate gene transcription(5).In addition, another study showed thatglucocorticoids induce demethylation of the hepatic tyrosineaminotransferase gene promoter in late gestation, which is permissive fortranscription bindingfactor , isin agreement also with our results(12).

Data showed that prenatal glucocorticoids induce transient changes in gene expression and DNA methylation as key genes in the heme biosynthesis pathway made authors suggested a mechanism through which glucocorticoids associate with accelerated maturation that may prevent neonatal hyperbilirubinemia. Since the high safety of providing antenatal corticosteroids even in term pregnancy for different issues, our study was based on the rational of that it may favor prevention of high postnatal bilirubin

Although , non-significant difference in the incidence of neonatal jaundice between both groups was found (group 1 was 34% and group 2 was 38%, p0.56),authors in the current study found that the mean level of bilirubin is significantly higher in those who their mothers did notreceivecorticosteroids prior to delivery, (the mean level of bilirubin in neonates who develop jaundice (group1 was 11.52±0.56 mg/dl) and (group 2 was 13.08±0.72 mg/dl).

Alternatively, Pettit et al 2016(13), found thatsignificantly higher rates of neonatal hypoglycemia in neonates exposed to antenatal betamethasone(5.7% versus 4.2%, $p<0.05$) and hyperbilirubinemia (45.9% versus 24.1%, $p<0.05$) were also observed. They assess the effect of betamethasone on 6675 preterm deliveries. These findings persisted with betamethasone-exposed neonates, 1.6 times more likely to have hypoglycemia and 3.2 times more likely to have hyperbilirubinemia.Higherincidence of hyperbilirubinemia can be explained by smaller gestational age at deliveries(13). Further studies to determine whether this association is related to maternal hyperglycemia, neonatal immaturity should behandled.

Conclusion

Neonatal jaundice, being one of the commonest neonatal disoreders confronting neonatologists and proved to be linked greatly to organs maturity,provoke the idea of using corticosteroids in term pregnancy before delivery to limit its development.

To our knowledge, this is the first randomized trial concerning the use of such protocol of management to appraise its effect on neonatal jaundice. Further studies including larger numbers and different groups of patients.

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BRIEFREPORT

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