International Journal of Children and Adolescents

Original Article
IJCA, Vol. 2, No. 3, Jul, 2016.11-15.

Does antenatal Betamethasone improve neonatal outcome in late preterm births?

Fariba Almassinokiani: Obstetrician and Gynecologist, Professor, Minimally Invasive Surgery Research Center, Iran University of Medical Sciences, Tehran, Iran
Maryam Sabouteh: (**Corresponding author*) Pediatrician and neonatologist, Assistant Professor, Iran University of Medical Sciences, Tehran, Iran. sk12345@gmail.com
Fahimeh Soheilipour: Pediatrician endocrinologist, Assistant Professor, Minimally Invasive Surgery Research Center, Iran University of Medical Sciences, Tehran, Iran.
Maryam Kashanian: Obstetrician and Gynecologist, Professor, Iran University of Medical Sciences, Tehran, Iran
Peyman Akbari: Tehran University of Medical Sciences, Tehran, Iran.
Nahid Rahimzadeh: Pediatrician, Associate Professor, Minimally Invasive Surgery Research Center, Iran University of Medical Sciences, Tehran, Iran.

Received: 23 Feb 2016 Accepted: 11 May 2016

Abstract

Background and Objective: Preterm birth is a public health problem and late preterm birth (deliveries between 34-36 weeks of gestation) accounts for 75% of all preterm births. Antenatal Betamethasone can reduce the severity of respiratory distress in preterm infants and its effect is accepted in 24-34 weeks of gestation. Our goal was to determine the neonatal outcomes of Betamethasone prescription in late preterm births.

Methods: In a prospective cohort study in a tertiary teaching hospital, women at 34-36 weeks of gestation and at risk for imminent preterm delivery took one course of Betamethasone arbitrarily according to the on-call physician order (Betamethasone group) and the rate of neonatal respiratory distress and NICU admissions was assessed. Also, we compared the results with the results of late preterm deliveries without taken antenatal Betamethasone (Control group).

Results: We had 213 patients in control group and 187 in Betamethasone group. There was a significant difference between results, in two groups in 34 and 35 weeks deliveries. Frequency of need to respiratory support in Control group was 33.3% and in Betamethasone group was 9.6%. NICU admission in control group was 33.8% and in Betamethasone group was 10.7% (p=0.00).

Conclusion: In 34 and 35 weeks of gestation, one antenatal Betamethasone course, even a single dose of Betamethasone has a significant effect on reduction of the respiratory distress and NICU admission rate.

Keywords: Betamethasone, Neonatal Intensive Care Unit, Preterm Birth, Respiratory Distress Syndrome

Introduction

Preterm birth is one of the leading causes of perinatal death and disability and can lead to important public health problems (1-6). Administration of corticosteroids in cases of preterm labor can accelerate fetal lung maturity and reduces the severity of respiratory distress syndrome (RDS) in premature infants (1, 7-10). American College of Obstetricians and Gynecologists (ACOG) suggests the use of antenatal corticosteroid for fetal maturation in cases of preterm labor between 24-32 weeks of gestation with ruptured amniotic membranes and between 24-34 weeks with intact amniotic membranes (1,7-8). In a large study prescription of single course of Betamethasone before 34 weeks of gestation was associated with a significantly lower incidence of respiratory distress among those neonates born at 34-36 weeks of gestation (11). But, between 34-36 weeks of gestation the potential effect of steroids' prescription on neonatal outcome is unknown. Neonatal mortality and morbidity rate in deliveries at 34-36 weeks is higher than births at 39 weeks .In one study is reported that prescription of antenatal Betamethasone in elective cesarean sections can reduce the incidence of neonatal respiratory distress (12).

Is there any benefit after 34 weeks of gestation from antenatal corticosteroid therapy for preterm

newborns? As NICU (Neonatal Intensive Care Unit) is not provided in all maternity hospitals, especially in developing countries, answering to this question was our goal for this research.

Methods

In this prospective cohort study between Jan 2011-Feb 2012 in one tertiary teaching hospital, we analyzed the neonatal outcomes of prescription or not prescription of antenatal Betamethasone in late preterm [34(0.7)-36(6.7)] births. In this research 34 weeks means between 34 weeks plus one day to 34 weeks plus 6 days. Between 35 weeks and 35 weeks plus 6 days means 35 weeks. Between 36 weeks and 36 weeks plus 6 days means 36 weeks. In this teaching hospital in cases of late preterm labor some obstetricians believe to antenatal Betamethasone and others not (according to ACOG protocol). We put singleton vertex deliveries at 34-36 weeks of gestation that the mother took antenatal Betamethasone before delivery in B (Betamethasone) group and the deliveries that the mothers did not took Betamethasone in C (Control) group.

The exclusion criteria were:

- Multi fetal pregnancies
- Systemic diseases of mothers like diabetes mellitus, hypertension, connective tissue disorders and or known infectious or endocrine diseases of mothers
- Intra uterine fetal death
- Uncertain date pregnancies
- Non vertex presentation
- Major anomalies of the newborn

The decision to prescribe antenatal Betamethasone in late preterm deliveries or not was made by the on call obstetricians.

Inclusion criteria were: only the vertex deliveries with certain gestational age between 34 (0.7) and 36 (6.7) weeks of gestation that their gestational age were established based on mother's last menstrual period and confirmed by first or second trimester ultra sound. Immediately after delivery a data collection form was completed by resident of gynecology included maternal age, maternal parity, mode of delivery, and sex of newborn. The Apgar score in first and fifth minute of birth was given by pediatrician. Only the nurse of labor and resident of obstetrics knew that if the mother had taken antenatal Betamethasone and how long before delivery.

In each case if the responsible obstetrician decided to prescribe antenatal Betamethasone in 34-36 weeks of gestation, the nurse of labor started Betamethasone course (12mg Betamethasone intramuscular and if the mother did not deliver within next 24 hours, the second dose was injected 24 hours after first dose).

After delivery all newborns were visited by a neonatologist pediatrician every day and at the time of discharge of newborn a data collection form completed which was included newborn's weight in first day of life, starting of respiratory distress with need to respiratory support during the first 24 hours after delivery, need to ICU admission, the number of admission days or death after birth.

In our hospital for all preterm deliveries the pediatrician is in the delivery room at the time of vaginal delivery or cesarean section and the Apgar scores is given by him .The neonates were admitted to wellbeing nursery or neonatal intensive care unit (NICU) based on their respiratory and general condition. The incidence of need to respiratory support was defined as need for oxygen, ventilation and or intubation, continuous positive air way pressure or surfactant administration .The indications for admission in NICU were: need to respiratory support, possible sepsis, temperature instability, apnea, poor feeding, hyper bilirubinemia, and hypoglycemia.

We analyzed the data through SPSS v.13, using one sample Kolmogorov-Smirnov test (KS test) for normality of data distribution, Leven's test for equality of variances and independent samples, t-test for equality of means for comparing quantitative normal data between the 2 groups. Pearson Chi-square test for matching and comparing categorical variables between the 2 groups. According to the KS test, we compared the non-normal quantitative data by Mann-Whitney U non parametric test between the 2 groups.

Results

In this prospective cohort study on prescription or not prescription of antenatal Betamethasone in late preterm deliveries [34(0.7)-36(6.7)], between Jan 2013-Feb 2014, we had 400 deliveries with the mentioned criteria in our hospital, that 213 cases were in C group and 187 in B group. Most of patients in both groups had parity one (54% in C and 56.7% in B group). In both groups mode of delivery in most of patients was cesarean section (56.8% in C and 57.2 in B group). The mean newborn's weight in C group was 2452.1 gram and in B group was 2317.8.The frequency of boy infants was 57.7% in C and 50.8% in B group. The most frequent gestational age in C group was 34 weeks of gestation (47.4%) and in B group was 36 weeks

Table 1. Demographic data of the pregnancies.

Characteristics	Control Group (n=213)	Betamethasone Group (n=187)
Maternal age (years)	26.1 ± 5.7	26.6 ± 5.8
Gestational age 34(0.7)-34(6.7) weeks	101 (47.4%)	49 (26.2%)
Gestational age 35(0.7)-35(6.7) weeks	85 (39.9%)	60 (32.1%)
Gestational age 36(0.7)-36(6.7) weeks	27 (12.67%)	78 (41.7%)
Mean maternal parity	1.51	1.45
Incidence of parity 1	54%	56.7%
Rate of Cesarean section	121 (56.8%)	107 (57.2%)
Rate of vaginal delivery	92(42.8%)	80(42.8%)
Mean newborn's weight(gr)	2425.1 ± 491.6	2317.8 ± 381.1
Frequency of male newborn	123(57.7%)	95(50.8%)
Frequency of female newborn	90(42.3%)	92(49.2%)
Mean Apgar at first minute	8.4 ± 0.87	8.4 ± 0.79
Mean Apgar at 5thminute	9.5 ± 0.87	9.5 ± 0.66

Table 2. Prevalence of early complications of prematurity in two groups.

	Control group	Betamethasone group
need to respiratory support	71(33.3%)	18(9.6%)
ICH	3(1.4%)	3(1.6%)
Need to sepsis works up	61(28.6%)	20(10.7%)
Newborn's death	4(1.9%)	3(1.6%)
NICU admission	72(33.8%)	20(10.7%)
Delivery during 24 hours after admission	213(100%)	191(90.1%)
Newborn's hospitalization for 5 days or less	67.1%	79.7%

(34.8%).The mean first minute Apgar score in both groups was 8.4 and for fifth minute was 9.5. Frequency of need to respiratory support in C group was 33.3% and in B group was 9.6%. NICU admission in C group was 33.8% and in B was 10.7% (Table 1 and 2).

Table 3 compares the findings of B and C group in different gestational ages. The rate of need to respiratory support and NICU admission in 34 and 35 weeks of gestation had significant difference between B and C group. Days of hospitalization and boy/girl ratio had not significant difference in the 2 groups. About 90.1% of patients in B group took only one dose of Betamethasone (12mg-intramuscular) less than 24 hours before delivery and the rate of need to respiratory support in them was lower than C group (Table 3).

Discussion

In our prospective cohort study, antenatal prescription of Betamethasone in women at 34-36 weeks pregnancies and at risk to preterm delivery was effective in reducing of need to respiratory support and NICU admission of newborns in 34 and 35 weeks gestation. Death rate in 2 groups had not significant difference.

Preterm birth rate was 12.3% in the USA in 2003 and late preterm birth accounts for approximately 75% of all preterm births (1). It may be a regional variation in late preterm birth rate, due to socio demographic and medical risk factors (13-14). Such a large number of births must receive increased attention in obstetrical and neonatal management. In one prospective cohort study the respiratory function in healthy late preterm infants delivered at 33-36 weeks of gestation (n=31) was compared with term infants matched for race and

Table 3. Comparison between 2 groups in different gestational ages

Gestational Age (weeks)	Number in B group	Number in C group	need to respirato-ry support in B	need to respirato-ry support in C	P value	NICU in B	NICU in C	P value	Boy/Girl In B	Boy/Girl In C	P value	Mean weight in B	Mean weight In C
34(0.7)-34(6.7)	49 26.2%	101 47.4%	8	36	0.00	9	37	0.00	27/22	61/40	0.165	2218	2040
35(0.7)-35(6.7)	60 32.1%	85 39.9%	6	27	0.00	7	27	0.04	29/31	49/36	0.165	2336	2466
36(0.7)-36(6.7)	78 41.7%	27 12.67%	4	8	0.13	4	8	0.13	39/39	13/14	0.165	2620	2623

sex (n=31). In comparison with the term infants, the late preterm infants had decreased respiratory compliance and decreased time to peak tidal respiratory flow to expiratory time. Late preterm infants also had an increased respiratory resistance ($p<0.01$)(15). In one study on infants admitted to a Canadian NICU (n=6636), 44.2% were late preterm (16).Neonatal morbidity in late preterm infants is higher than term infants and the frequency of respiratory morbidity decreases by approximately 50% for week from 34-37 completed weeks (1,17,18). In one study on 188 near term infants, the rate of need to respiratory support or oxygen therapy after elective cesarean section, in late preterm deliveries was 44% (n=55) and in [37(0.7)-37(6.7)] age infants was 15.9% (n=10) ($p<0.01$) and the incidence of admission in the NICU was 13.6% in first group (n=17) and 3.2% in second group (n=2) (19). In another study on late preterm births 33% were admitted in NICU compared with 7% for term births ($p<0.05$). The overall incidence of respiratory distress syndrome was 9%, 4%, 3%, 0.7%, 0.2% and 0% in 34 weeks, 35 weeks, 36 weeks, 37 weeks, 38-39 weeks and 40 weeks (20). One systematic review in 2012 suggests that administration of antenatal glucocorticoids to women at risk of preterm birth has major benefits for infants but the use of repeat doses is controversial (21). In another research 5% of doctors use corticosteroids at gestational age more than 34 weeks (22).

In one study in Brazil, antenatal corticosteroid in women at 34-36 weeks of pregnancy was ineffective in reducing the rate of RDS in newborns (23). A systematic review in 2009 suggests that future studies are needed to investigate the effectiveness of antenatal corticosteroids on neonatal outcomes (24). In a study, early neonatal sepsis was significantly associated with multiple courses of corticosteroids, but a single course of corticosteroid administration was not significantly associated with any maternal and neonatal infectious complications (25).

One systematic review suggests that prescription of one course of antenatal corticosteroids in 24-34 weeks of gestation reduced the risk of neonatal death and intraventricular hemorrhage and necrotizing enter colitis, need to respiratory support and intensive care admissions significantly compared with no treatment or placebo (26). Antenatal corticosteroid use is associated with a significantly decreased need to use surfactant, but there is an increased rate of gastrointestinal reflux in the neonates (27). Betamethasone causes profound, but transient suppression of FHR parameters which can mimic fetal distress. Doctors need to be aware of this phenomenon in order to avoid unwanted iatrogenic delivery (28). In one study, administration of corticosteroids at 24-34 weeks made delay in the onset of lacto genesis in the mother and reduction of milk volume (29). Long-term follow up of survivors from randomized trials of antenatal corticosteroid therapy through childhood to adulthood (up to 30 years of age) showed no clear neurological or congenital adverse effects (30).

In one 18 years study, neonatal mortality and morbidity rate in 34-36 weeks deliveries was analyzed and concluded that neonatal mortality and morbidity in late preterm births (34-36 weeks gestation) is higher than birth at 39 weeks (31). As there had not found any important side effects of one course of antenatal corticosteroids, but its benefit is shown, we suggest antenatal Betamethasone in late preterm deliveries to reduce the risk of need to respiratory support and NICU admission.

Conclusion

In 34 and 35 weeks preterm deliveries, prescription of one course Betamethasone to mothers has good effects on decreasing the need to respiratory support in newborn infants. Especially in developing countries that NICU is not provided in all maternity hospitals, it can reduce the need to NICU admission.

Financial Support

This study was founded and supported by Iran University of Medical Sciences. Grant no. 91-02-30-14880

Conflicts of interest: We attest that we have herein disclosed any and all financial or other relationships that could be construed as a conflict of interest.

References

1. Cunningham FG, Leveno Jk, Bloom SL, Hauth JC, Rouse DJ, Spong C.Y. Williams Obstetrics. 24th ed. NY:McGraw Hill, 2014; pp.653-660.
2. Bonanno C, Wapner RJ. Antenatal corticosteroids in the management of preterm birth: are we back where we started? Obstet Gynecol Clin North Am. 2012;39(1):47-63.
3. Power ML, Henderson Z, Behler JE, Schulkin J. Attitudes and practices regarding late preterm birth among American obstetrician-gynecologists. J Women Health (Larchmt). 2013;22(2):167-72.
4. Raju TN. Moderately preterm, late preterm and early

term infants: research needs. Clin Perinatol. 2013;40(4):791-7.
5. Scheuchenegger A, Lechner E, Wiesinger-Eidenberger G, Weissensteiner M, Wagner O, Schimetta W, et al. Short-term morbidities in moderate and late preterm infants. Klin Padiatr.2014;226(4):216-20.
6. Ananth CV, Friedman AM, Gyamfi-Bannerman C. Epidemiology of moderate preterm, late preterm and early term delivery. Clin Perinatol. 2013;40(4):601-10.
7. Committee on Obstetric Practice. ACOG committee opinion. Antenatal corticosteroid therapy for fetal maturation. American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet.2002;78(1):95-7.
8.ACOG Committee on Obstetric Practice. ACOG Committee Opinion No. 475: Antenatal corticosteroid therapy for fetal maturation. Obstet Gynecol.2011 Feb;117(2 Pt 1):422-4.
9.Wang YC, Tseng HI, Yang SN, Lu CC, Wu JR, Dai ZK, et al. Effects of antenatal corticosteroids on neonatal outcomes in very-low-birth-weight preterm newborns: a 10-year retrospective study in a medical center. Pediatr Neonatol.2012;53(3):178-83
10. Leviton LC, Goldenberg RL, Baker CS, Schwartz RM, Freda MC, Fish LJ, et al. Methods to encourage the use of antenatal corticosteroid therapy for fetal maturation: a randomized controlled trial. JAMA.1999; 6;281(1):46-52.
11-Ventolini G, Neiger R, Mathews L, Adragna N, BelcastroM.Incidence of respiratory disorders in neonates born between 34 and 36 weeks of gestation following exposure to antenatal corticosteroids between 24 and 34 weeks of gestation. Am J Perinatol. 2008 Feb;25(2):79-83.
12.Stutchfield P, Whitaker R, Russell I; Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomized trial. BMJ. 2005; 24;331(7518):662.
13.Aliaga SR, Smith PB, Price WA, Ivester TS, Boggess K, Tolleson-Rinehart S, et al. Regional variation in late preterm births in North Carolina. Matern Child Health J. 2013 Jan;17(1):33-41.
14. Zou L, Wang X, Ruan Y, Li G, Chen Y, Zhang W. Preterm birth and neonatal mortality in China in 2011. Int J Gynaecol Obstet. 2014;127(3):243-7.
15. McEvoy C, Venigalla S, Schilling D, Clay N, Spitale P, Nguyen T. Respiratory function in healthy late preterm infants delivered at 33-36 weeks of gestation. J Pediatr.2013;162(3):464-9.
16. Bassil KL, Shah PS, Shah V, Ye XY, Lee SK, Jefferies AL. Canadian Neonatal Network. Impact of late preterm and early term infants on Canadian neonatal intensive care units. Am J Perinatol. 2014;31(4):269-78.
17.Petrini JR, Dias T, McCormick MC, Massolo ML, Green NS, Escobar GJ. Increased risk of adverse neurological development for late preterm infants. J Pediatr.2009 Feb;154(2):169-76.
18- Engle WA, Kominiarek MA. Late preterm infants, early term infants, and timing of elective deliveries. Clin Perinatol.2008;35(2):325-41.
19.Berthelot-Ricou A, Lacroze V, Courbiere B, Guidicelli B, Gamerre M, Simeoni U. Respiratory distress syndrome after elective caesarean section in near term infants: a 5-year cohort study. J Matern Fetal Neonatal Med.2013;26(2):176-82.
20. Mally PV, Hendricks-Muñoz KD, Bailey S. Incidence and etiology of late preterm admissions to the neonatal intensive care unit and its associated respiratory morbidities when compared to term infants.Am J Perinatol. 2013;30(5):425-31.
21. McKinlay CJ, Crowther CA, Middleton P, Harding JE. Repeat antenatal glucocorticoids for women at risk of preterm birth: a Cochrane Systematic Review. Am J Obstet Gynecol.2012;206(3):187-94.
22.Cosmi E, Bevilacqua G, Maranghi L, Anceschi MM. The policy of antenatal corticosteroid administration in Italy vs. other European countries. J Matern Fetal Neonatal Med.2004;16 Suppl 2:1-3.
23. Porto AM, Coutinho IC, Correia JB, Amorim MM. Effectiveness of antenatal corticosteroids in reducing respiratory disorders in late preterm infants: randomized clinical trial. BMJ.2011;12;342:d1696.
24. Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis JP. Corticosteroids for preventing neonatal respiratory morbidity after elective caesarean section at term. Cochrane Database Syst Rev.2009; (4):CD006614.
25.Vermillion ST, Soper DE, Chasedunn-Roark J. Neonatal sepsis after betamethasone administration to patients with preterm premature rupture of membranes. Am J Obstet Gynecol. 1999;181(2):320-7.
26. Miracle X, Di Renzo GC, Stark A, Fanaroff A, Carbonell-Estrany X, Saling E; Coordinators Of World Association of Perinatal Medicine Prematurity Working Group. Guideline for the use of antenatal corticosteroids for fetal maturation. J Perinat Med.2008;36(3):191-6.
27. Chin SO, Brodsky NL, Bhandari V. Antenatal steroid use is associated with increased gastroesophageal reflux in neonates. Am J Perinatol.2003;20(4):205-13.
28. Rotmensch S, Lev S, Kovo M, Efrat Z, Zahavi Z, Lev N, et al. Effect of betamethasone administration on fetal heart rate tracing: a blinded longitudinal study. Fetal DiagnTher. 2005 ;20(5):371-6.
29. Henderson JJ, Hartmann PE, Newnham JP, Simmer K. Effect of preterm birth and antenatal corticosteroid treatment on lactogenesis II in women. Pediatrics. 2008;121(1):e92-100.
30. Dalziel SR, Walker NK, Parag V, Mantell C, Rea HH, Rodgers A, et al. Cardiovascular risk factors after antenatal exposure to betamethasone: 30-year follow-up of a randomized controlled trial. Lancet.2005;365(9474):1856-62.
31. McIntire DD, Leveno KJ. Neonatal mortality and morbidity rates in late preterm births compared with births at term. Obstet Gynecol. 2008;111(1):35-41.