ORIGINAL ARTICLE

Effects of antenatal corticosteroids on maternal serum indicators of infection in women at risk for preterm delivery: A randomized trial comparing betamethasone and dexamethasone

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Objective: To compare the effect of betamethasone and dexamethasone on maternal white blood cell (WBC) and differential count, erythrocyte sedimentation rate (ESR), Apgar score, maternal and fetal plasma glucose and length of admission to delivery, gestational age at delivery in women at risk of preterm labor (PTL). **Study Design:** Two hundred and forty pregnant women at risk for PTL with intact membranes or preterm premature rupture of the membranes (PPROM) were randomly allocated to receive either two intramuscular injections of 12 mg betamethasone at 24-h intervals or 4 injections of 6 mg dexamethasone at 12-h intervals. Blood tests for WBC and differential count, ESR and fasting plasma glucose were drawn before betamethasone or dexamethasone injection and after injection every 24 h for two days. Pregnancy outcome was assessed as Apgar score, fetal plasma glucose and length of gestation. **Result**: In the preterm delivery group with intact membranes, no significant differences were found between the two groups in the maternal serum indicators of infection. The mean gestational age at delivery, 1- and 5-min Apgar score were higher in the dexamethasone group than in the betamethasone group. In the PPROM group, a significant rise in WBC count was occurred (12.4 cells/mm^3 vs. 10.5 cells/mm^3, $P < 0.001$), none of the other maternal serum indicators of infection and outcome variables showed significant differences between the dexamethasone and betamethasone groups. **Conclusions**: Dexamethasone compared to betamethasone significantly increased WBC count in women with PPROM, but in women at risk of PTL with intact membranes none of the maternal serum indicators of infection showed significant differences.

Key words: Betamethasone, dexamethasone, efficacy, gestational age. preterm premature rupture of membrane, pregnancy, preterm

INTRODUCTION

Preterm birth with or without intact membranes occurs in 5%-13% of all pregnancies, and intrauterine infection is a major threat to the preterm fetus and may increase neonatal morbidity and mortality.[1] The link between infection and preterm labor has long been recognized and at least 40% of preterm births are associated with intrauterine infection.[2] Antenatal corticosteroid therapy has become a standard management of women with preterm labor.[3-6] The recommended corticosteroids are either betamethasone or dexamethasone.[5-7] Both are the most potent agents in terms of their effect on the fetus, and both have minimal side effects compared with their benefits.[8] Although, they both have the same biological activity and adverse effects, there is considerable variation between countries as to whether dexamethasone or betamethasone is preferred by health practitioners, with many likely reasons for these differences including availability and cost (dexamethasone is cheaper than betamethasone),[9,10] the impact of inconsistent findings from observational studies[11] and the influence of opinion leaders.[12] A Cochrane review published in 2008[13] that included ten trials indicated that dexamethasone appears to decrease the incidence of intraventricular hemorrhage (IVH) compared to betamethasone. No statistically significant differences were seen for respiratory distress syndrome, bronchopulmonary dysplasia, severe IVH, preventricular leukemia, perinatal death or mean birth weight. The results for biophysical parameters have been inconsistent,[13,14] but most

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studies have reported no clinically important differences. The two most serious side effects of corticosteroid therapy are suppression of the hypothalamic-pituitary-adrenal axis, and predisposition to infection. Neither has been fully evaluated with specific reference to preterm labor. Nonetheless, the evidence of effects of dexamethasone and betamethasone on maternal indicators of infection is not sufficient to support dexamethasone or betamethasone, so the drug of choice for antenatal corticosteroid therapy is currently a topic of debate.

In the present trial, we compared the effects of the betamethasone and dexamethasone on maternal white blood cell (WBC) and differential count, erythrocyte sedimentation rate (ESR), maternal and fetal plasma glucose (PG), Apgar score, and length of gestation in women at risk of preterm birth with or without intact membranes.

MATERIALS AND METHODS

A randomized trial was conducted to evaluate the effects of betamethasone and dexamethasone on maternal WBC and differential count, ESR, Apgar score, maternal and fetal PG and length of gestation in women at risk for preterm birth with or without intact membranes. The study protocol was approved by the Institutional Review Board of Isfahan University of Medical Sciences, Iran (project number 389484). Written informed consent was obtained.

Participants

Pregnant low parity women between 24 and 34 weeks gestation, who were hospitalized because they were at risk for preterm birth with or without intact membranes, were recruited from the obstetrics and gynecology departments of Isfahan University of Medical Sciences, Iran between February and November 2011. The inclusion criteria were low parity pregnant women 16-45 years of age, gestational age 24-34 complete weeks, low Bishop Score (≤ 5), nonsmoker, high risk of preterm labor (PTL) either with intact membranes or preterm premature rupture of membranes (PPROM) that justified preventive corticosteroid therapy, a singleton fetus, residence in Isfahan, and hospitalization planned to last at least 3 days. PTL was diagnosed in the presence of uterine contractions of four in 20 min or eight in 60 min plus progressive change in the cervix, cervical dilatation greater than 1 cm and cervical effacement of 80% or greater. [15] PPROM was diagnosed in the presence of a gush of fluid from the vagina followed by persistent, uncontrolled leakage, or polling of fluid on speculum examination with positive nitrazine and Fern testing.[16] Women were excluded if they had evidence of fetal distress, substantial abnormalities in neurological, psychiatric, cardiac, endocrinological, hematologic, hepatic, renal, or metabolic functions as determined by history, physical examination and blood screening tests. Other exclusion criteria were signs of infection (maternal temperature >37.5°C), positive urine culture and vaginal bleeding due to placenta previa or placental abruption.

Randomization scheme

A total of 260 pregnant women at risk for PTL with either intact membranes or PPROM were eligible for study. Twenty women were excluded because they declined to participate or did not meet the inclusion criteria. In all, 240 pregnant women were initially enrolled in the study, first treatment began with magnesium sulfate according to ACOG (American College of Obstetrics and Gynecology) committee protocol[17], then 120 women at risk for preterm delivery with intact membranes and 120 women with PPROM completed treatment without interruption and continued in the study until delivery. Women were randomized with a list of computer-generated numbers, and the group assignments were concealed in an opaque sealed envelope until just before entry into the study. The first treatment group received two intramuscular injections of 12 mg betamethasone at 24-h intervals as betamethasone sodium (produced by local pharmaceutical company Exir Pharmaceutical Lab., Tehran, Iran). The second group received four intramuscular injections of 6 mg dexamethasone at 12-h intervals as dexamethasone phosphate (produced by local pharmaceutical company Iranhormone Pharmaceutical Lab., Tehran, Iran). At enrolment, pretreatment evaluation in all women consisted of demographic data, complete medical history and physical examination. The allocation scheme is shown in Figure 1.

At enrollment, gestational age was determined by obstetric estimates from the last menstrual period, standard obstetric parameters and ultrasonography. Mean age of the women (SD) was 27.2 (5.4) years (range 16 to 43 years).

Evaluation

Before corticosteroids were injected, blood was drawn for peripheral WBC and differential count, ESR, hemoglobin (Hb) and maternal plasma glucose (PG). Blood was drawn again for the same tests at 24 and 48 h. Hemoglobin and WBC count were determined with a Coulter counter, and ESR was determined by the conventional mm/s sedimentation rate. Plasma glucose was measured with the glucose oxidase method. All the women who participated in the study were followed until delivery. After delivery cord blood was drawn for fetal plasma glucose measurement.

Statistical analysis

Outcomes in the betamethasone and dexamethasone groups were compared with Student's *t*-test for independent samples and analysis of variance with repeated measures over time; comparisons between baseline and post-treatment periods

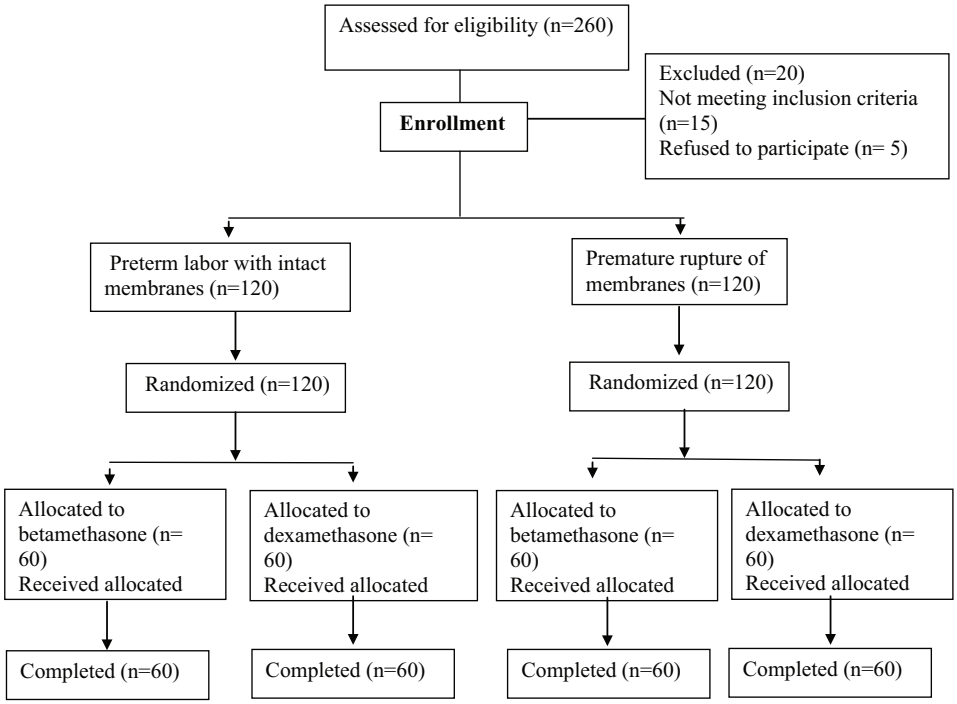

Figure 1: Design of the study

Table 1: Characteristics of pregnant women by treatment group at baseline

Characteristics	Treatment group		Difference (95% CI)
	Dexamethasone mean (SD)	Betamethasone mean (SD)	
Preterm delivery with intact membranes			
Number	60	60	-
Maternal age (years)	28.1 (5.3)	26.9 (5.7)	1.2 (-0.9, 3.1)
Gestational age at registration (weeks)	30.6 (2.3)	30.9 (2.8)	-0.3 (-1.2, 0.6)
Pulse rate (no.)	83.1 (4.9)	84.4 (4.8)	-1.3 (-3.1, 0.4)
Temperature (°C)	36.9 (0.2)	36.9 (0.2)	0.0 (-0.07, 0.08)
Fasting plasma glucose (mg/dL)	96.5 (13.4)	97.4 (19.6)	-0.9 (-7.0, 5.2)
WBC (cells/mm^3)	10.31 (1.90)	10.38 (2.72)	-0.07 (-0.09, 0.08)
Neutrophil count (%)	70.3 (7.6)	72.8 (7.8)	-2.5 9-5.3, 0.2)
Hemoglobin (g)	12.3 (1.2)	12.1 (1.1)	0.2 (-0.2, 0.6)
Platelet count (× 10^3/mm^3)	210.7 (46.5)	202.0 (51.7)	8.7 (-9.1, 26.5)
Erythrocyte sedimentation rate (mm/h)	21.6 (13.1)	26.3 (14.6)	-4.7 (-9.8, 0.5)
Systolic blood pressure (mm Hg)	98.7 (5.9)	98.8 (7.7)	-0.1 (-2.6, 2.3)
Diastolic blood pressure (mm Hg)	66.2 (6.1)	66.0 (6.4)	0.2 (-2.0, 2.5)
Preterm premature rupture of membranes			
Number	60	60	-
Age (years)	26.7 (5.2)	27.1 (5.3)	-0.4 (-2.2, 1.6)
Gestational age at registration (weeks)	30.1 (2.7)	30.0 (2.8)	0.1 (-0.9, 1.1)
Pulse rate (no.)	82.3 (5.0)	83.1 (5.0)	-0.8 (-2.5, 1.0)
Temperature (°C)	36.9 (0.2)	36.9 (0.2)	0.0 (-0.09, 005)
Fasting plasma glucose (mg/dL)	95.0 (12.7)	94.3 (12.5)	0.7 (-4.0, 5.3)
WBC (cells/mm^3)	10.60 (2.14)	9.39 (2.31)	1.21 (0.4, 2.0)**
Neutrophil count (%)	72.0 (8.3)	71.6 (9.3)	0.4 (-2.8, 3.5)
Hemoglobin (g)	11.9 (1.1)	12.1 (1.5)	-0.2 (-0.6, 0.3)
Platelet count (×10^3/mm^3)	203.3 (50.6)	205.4 (57.3)	-2.1 (-21.6, 17.3)
Erythrocyte sedimentation rate (mm/h)	29.0 (22.1)	21.9 (12.4)	7.1 (0.5, 13.5)*
Systolic blood pressure (mm Hg)	101.0 (7.7)	99.3 (7.7)	1.7 (-1.1, 4.4)
Diastolic blood pressure (mm Hg)	68.1 (5.9)	65.8 (5.9)	2.3 (0.2, 4.4)*

*P < 0.05, **P < 0.01. CI=Confidence interval; WBC=White blood cell count

were done with paired-Student's *t*-tests. Comparisons between proportions were done with the chi-squared or Fisher's exact test. All analyses were done with SPSS version 18 software for Windows© (SPSS Inc., Chicago, IL). All tests for statistical significance were two-tailed, and were done assuming a type I error probability of <0.05.

RESULTS

Women's characteristics

All 240 women who completed treatment were available for follow-up at delivery. In women at risk for preterm delivery with intact membaranes, the two treatment groups were generally well matched at baseline with regard to age, gestational age, maternal PG level, WBC, neutrophil count, Hb concentration, blood pressure, and other characteristics. Women with PPROM in the dexamethasone group had slightly but significantly higher WBC, ESR and diastolic blood pressure ($P < 0.05$). A comparison of women at risk for preterm delivery with either intact membranes or PPROM detected no significant differences in pulse rate, temperature, or compliance between the two experimental groups. In women at risk for pretem delivery with intact membranes, mean (SD) gestational age was 30.6 (2.3) weeks in the dexamethasone group and 30.9 (2.8) weeks in the betamethasone group. In the PPROM group, mean (SD) gestational age was 30.1 (2.7) in the dexamethasone group and 30.0 (2.8) weeks in the betamethasone group [Table 1]

Table 2: Comparison of pregnancy outcome in 240 pregnant women at risk for preterm delivery with intact membranes or preterm premature rupture of membranes after treatment with betamethasone or dexamethasone

	Treatment group		Difference (95% CI)
	Dexamethasone mean (SD)	Betamethasone mean (SD)	
Preterm delivery with intact membranes			
Number	60	60	-
Gestational age at delivery (weeks)	36.3 (3.5)	34.0 (3.6)	2.3 (0.97, 3.53)**
Fetal plasma glucose (mg/dL)	95.3 (11.9)	91.0 (15.2)	4.3 (-0.57, 9.30)
NICU stay (days)	3.0 (1.7)	5.2 (3.6)	-2.2 (-4.52, 0.19)
1-min Apgar score	8.6 (6.9)	7.9 (1.4)	0.7 (0.31, 1.16)**
5-min Apgar score	9.7 (0.8)	9.1 (1.1)	0.6 (0.24, 0.93)**
Neutrophil count (%)	79.9 (7.8)	77.6 (7.4)	-2.3 (-0.45, 5.05)
ESR (mm/h)	27.0 (12.5)	30.6 (13.2)	-3.6 (-8.25, 1.05)
Maternal fasting plasma glucose (mg/dL)	103.9 (13.3)	101.1 (10.7)	2.8 (-1.56, 7.16)
WBC (cells/mm^3)	12.09 (2.86)	11.21 (2.29)	0.88 (-0.06, 1.82)
Hemoglobin (g)	11.4 (0.8)	11.6 (1.4)	-0.2 (-0.61, 0.21)
Platelet count (× 10^3/mm^3)	198.8 (52.1)	191.5 (43.6)	7.3 (-10.1, 24.7)
Length of gestation (weeks), no. (%)			
≥37	34 (56.7)	14 (23.3)	33.4 (-49.8, -16.8)***
<37	26 (43.3)	46 (76.7)	-
Length of admission to delivery (days)	21.0 (4.4)	14.0 (3.6)	7.0 (5.6, 8.5)**
Infant transferred to NICU, no. (%)	9 (15.0)	12 (20.0)	-5.0 (-18.6, 8.6)
Preterm premature rupture of membranes			
Number	60	60	-
Gestational age at delivery (weeks)	32.7 (4.1)	33.0 (4.7)	-0.3 (-1.9, 1.3)
Fetal plasma glucose (mg/dL)	93.3 (14.4)	95.3 (17.3)	-2.0 (-7.8, 3.7)
NICU stay (days)	2.9 (1.6)	3.6 (1.7)	-0.7 (-1.6, 0.3)
1-min Apgar score	7.9 (1.5)	7.7 (1.3)	0.2 9-0.3, 0.7)
5-min Apgar score	9.0 (1.4)	8.9 (1.2)	0.1 (-0.3, 0.6)
Neutrophil count (%)	78.0 (7.9)	75.9 (8.8)	2.1 (-0.92, 5.12)
ESR (mm/h)	30.6 (13.8)	27.3 (12.5)	3.3 (-1.46, 8.06)
Maternal fasting plasma glucose (mg/dL)	100.9 (10.4)	99.6 (11.8)	1.3 (-2.72, 5.32)
WBC (cells/mm^3)	12.42 (2.61)	10.50 (2.41)	1.9 (1.01, 2.83)***
Hemoglobin (g)	11.7 (1.0)	12.0 (1.6)	-0.3 (-0.78, 0.18)
Platelet count (× 10^3/mm^3)	212.5 (53.2)	211.0 (62.4)	1.5(-19.5, 22.5)
Length of gestation (weeks), no. (%)			
≥37	11 (18.3)	19 (31.7)	-13.4 (-28.6, 2.0)
<37	49 (81.7)	41 (68.3)	-
Length of admission to delivery (days)	7.1 (2.9)	7.1 (2.6)	0.0 (-1.0, 1.0)
Infant transferred to NICU, no. (%)	25 (41.7)	24 (40.0)	1.7 (-15.9, 19.3)

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. CI=Confidence interval; NICU=Neonatal intensive care unit

Women at risk for preterm delivery with intact membranes

Table 2 shows the results of blood test and pregnancy outcomes in dexamethasone and betamethasone groups. In this group, neutrophil count and ESR significantly increased and Hb decreased 24 h after treatment. Mean neutrophil count increased from the baseline value by 9.6 (95% CI: 6.8, 12.4) in the dexamethasone group and by 4.8 (95% CI: 2.1, 7.6) in the betamethasone group. ESR increased by 5.4 (95% CI: 0.8, 10.6) in the dexamethasone group and by 4.3 (95% CI: 0.7, 9.3) in the betamethasone group. Mean Hb concentration decreased from baseline by 0.9 g (95% CI: 0.5, 1.3) in the dexamethasone group and by 0.5 g (95% CI: 0.04, 1.0) in the betamethasone group. The overall analysis with repeated measure ANOVA revealed no significant differences between the two treatment groups.

In women at risk for preterm delivery with intact membranes, mean gestational age at delivery, 1- and 5-min Apgar score and length of admission to delivery were significantly higher in the dexamethasone group. In the dexamethasone group, gestational age at delivery ranged from 25.4 weeks to 40.0 weeks. In the betamethasone group, gestational age at delivery ranged from 25.9 weeks to 39.0 weeks. There were 72 (60%) preterm newborns (<37 weeks gestational age): 26 (43.3%) in the dexamethasone and 46 (76.7%) in the betamethasone group. We could not reject the null hypothesis that this was more than a chance finding (RR 0.57; 95% CI: 0.41, 0.78). There were statistically significant but clinically nonsignificant differences in Apgar scores between the two treatment groups. No difference in mean fetal plasma glucose observed.

The number of infants admitted to the neonatal intensive care unit (NICU) because of respiratory distress syndrome was 9 (15.0%) in the dexamethasone group and 12 (20.0%) in the betamethasone group [Table 2]. There was no statistically significant difference between groups in the number of infants transferred to the NICU. Although the duration of stay in the NICU was shorter in the dexamethasone group (3.0 days) than in the betamethasone group (5.2 days), the difference was not statistically significant.

Women at risk for preterm premature rupture of the membranes

In this group, none of the following outcomes differed significantly between the dexamethasone and betamethasone groups: Gestational age at delivery, 1- and 5-min Apgar scores, length of admission to delivery, fetal plasma glucose, ESR, number of infant admitted to the NICU, and duration of stay in the NICU [Table 2]. Neutrophil count, maternal PG and WBC increased significantly 24 h after treatment. Mean neutrophil count increased from baseline by 6.0 (95% CI: 3.1, 8.9) in the dexamethasone group, and by 4.3 (95% CI: 1.0, 7.6) in the betamethasone group. Erythrocyte sedimentation rate increased by 5.4 (95% CI: 0.9, 9.9) in the dexamethasone group, and no increase was seen in the betamethasone group. Mean WBC count increased from baseline by 1.8 (95% CI: 0.9, 2.7) cells/mm^3 in the dexamethasone group, and by 1.1 (95% CI: 0.3, 1.9) cells/mm^3 in the betamethasone group. Mean maternal PG increased from baseline by 5.9 (95% CI: 1.7, 10.1) mg/dL in the dexamethasone and by 5.3 (0.9, 9.7) mg/dL in the betamethasone group. The overall analysis with repeated measure ANOVA revealed significance differences in WBC ($P < 0.001$) between the two treatment groups.

Both, dexamethasone and betamethasone treatment was tolerated well and most of the adverse events reported were mild in severity.

DISCUSSION

In the current trial, although both treatment groups during pregnancy showed a transient rise in total WBC count with neutrophil, ESR and PG and decrease in Hb, no significant difference was found between the two treatment groups in women at risk for PTL**.** The dexamethasone treatment increased length of gestation, length of admission to delivery and Apgar score in women at risk for preterm delivery with intact membranes. In the PPROM group, none of the outcomes showed significant differences between the two treatment groups except WBC count, which was slightly higher in the dexamethasone group. No unusual or unexpected safety risks were found with dexamethasone or betamethasone therapy in these pregnant women. The spectrum of most frequent adverse events was similar to that reported in previous research with dexamethasone or betamethasone, which has shown both drugs to be fairly safe[8].

Our findings are consistent with those of others[18-20] who found increases in total WBC count in women who received corticosteroids during pregnancy. Ferguson *et al*.[21] claimed that the changes in WBC count were related to PTL, and found no additional increase in WBC count in women with PTL who were treated with betamethasone. We found a significant increase in WBC count in women at risk for PTL either with intact membranes or PPROM. Awareness of the possibility of post-corticosteroid leukocytosis is important in order to avoid misinterpreting leukocytosis as a sign of infection in women with PPROM or PTL with intact membranes. In most of our patients, WBC count and ESR returned to baseline on day three following betamethasone or dexamethasone treatment. Therefore, we suggest that if WBC count or ESR remains elevated beyond day three, the women should be monitored carefully for other signs of infection.

ESR is a limited blood test during pregnancy because it is variably affected by physiologic changes in fibrinogen and erythrocyte count occurring often in pregnancy. Although

it is specific for infection, it has low sensitivity (65%) when normal results were considered as ESR <60 mm/h.[22] ESR is not affected by dexamethasone or betamethasone administration. However, it remains to be elucidated whether a day-to-day change in ESR can be a sensitive predictor of chorioamnionitis.

In the present study, dexamethasone prolonged the average duration of pregnancy compared to betamethasone in women with preterm delivery with intact membranes, but not in women with PPROM. Similar increases in length of gestation after dexamethasone treatment have been reported in other studies, but these differences failed to reach statistical significance because of the limited statistical power.[23-28] The longer treatment period for dexamethasone might to some extent explain the higher gestational age at birth found in dexamethasone group. The finding of an increase in mean duration of pregnancy in our dexamethasone group warrants further investigation.

We found that the mean duration of stay in the NICU was reduced in the dexamethasone group, but this difference was not statistically significant. In contrast, one trial, which included 105 infants, found that significantly more infants were admitted to the NICU in the dexamethasone group compared to the betamethasone group.[29] The finding of a nonsignificant reduction in the duration of stay in the NICU for infants born to women in the dexamethasone group who were at risk for preterm delivery and had intact membranes warrants further investigation in a larger sample.

Another finding that requires elaboration is the higher 1- and 5-min Apgar score in our dexamethasone treatment group. No statistically significant differences between neonates exposed to betamethasone or dexamethasone were seen for Apgar score at 5 min in one trial,[30] or in 5-min Apgar scores less than 7 in other two trials.[23,25] Further studies are needed to solve this issue.

The mechanisms by which corticosteroids might predispose to infection are not clear. Several studies have shown little or no increase in the incidence of infection among corticosteroid treated patients compared with control.[31-33]

The mechanisms that may account for the more favorable pregnancy outcomes after dexamethasone treatment compared to betamethasone also are not clear. Both, corticosteroids are similar in their binding with blood proteins, half-life in the maternal circulation, metabolic clearance and placental crossing. The chemical composition of betamethasone and dexamethasone is virtually identical except for the configuration of a methyl group in position 16.[34] Therefore, the physiological basis for the difference in their effect on pregnancy outcomes remains an enigma. One possible explanation is the preservative used with dexamethasone but not with betamethasone. The dexamethasone regimen may lead to a lower peak level but a longer time to biological activity, and more rapid passage through the blood-brain barrier, compared to the betamethasone regimen.

This trial could draw criticism because of the un-blind design and the short follow-up. Albeit the value of the double blind, controlled trial is widely recognized, this design is not always appropriate or indicated. Because of the different injection frequency and treatment period of dexamethasone and betamethasone, it would have been impossible to keep patients blinded in a study of this nature. Similarly, the treating physicians dealing with clinical and laboratory adverse events can easily become un-blinded. However, Schultz and co-workers reported that, to avoid bias in clinical trials, careful randomization is more important than a double-blind design.[35] Trials with inadequate randomization yield an assessment of treatment effects exaggerated by 30-41% when compared with trials that use adequate concealment of treatment allocation. By contrast, trials without double blinding yield an assessment of treatment effects exaggerated, on average, by only 17% compared with double-blinded trials. In this study, selection bias was controlled for by randomization, with concealed treatment allocation, and observation bias was probably marginal because clinical results were un-blinded analysis. The WBC count and ESR differed between the two treatment groups in women with PPROM. These measures were more favorable in the dexamethasone treatment group, and it could be argued that the slightly higher WBC in this group was related to the higher WBC count at baseline. Another limitation could be small number of women studied for evaluating the impact of such drugs as dexamethasone and betamethasone, but the effect was robust. The present results clearly need to be replicated and extended across multiple centers and investigators in long-term follow-up studies.

In conclusion, the results showed that dexamethasone increased gestational age at delivery and Apgar score significantly more than betamethasone did in women at risk for PTL with intact membranes. Dexamethasone might therefore be preferred for the induction of lung maturity in women at risk for PTL with intact membranes. However, in women with PPROM the pregnancy outcome measures were similar in our betamethasone and dexamethasone groups. Our results highlight the need for randomized controlled trials with larger sample sizes and longer follow-up periods to determine whether dexamethasone should be the treatment of choice for women with PTL.

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