

# Factors Affecting Antenatal Corticosteroid Administration from the Obstetricians' Viewpoint

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## ABSTRACT

**OBJECTIVE:** We aimed to investigate the factors affecting antenatal corticosteroid administration from the obstetricians' viewpoint.

**STUDY DESIGN:** The pregnant women who delivered between 24 and 34 weeks of gestation were divided into two groups: Group 1, pregnant patients given corticosteroid therapy; Group 2, pregnant patients who were not given corticosteroid therapy. The indications for delivery, gestational week at administration, dosing, residence and manner of transfer of the patients to the tertiary center, and the interval between admission to hospital and delivery were evaluated.

**RESULTS:** The percentage of patients who received antenatal corticosteroid treatment was 68.4%, whereas 31.6% of the pregnant women didn't receive corticosteroid therapy. The most common indications for preterm delivery were preterm labor and severe preeclampsia. The interval between admission to hospital and delivery was significantly higher in group 1.

**CONCLUSION:** Even though obstetricians are aware of the importance of corticosteroid treatment in preterm deliveries, indications for impending delivery can affect administration of the therapy.

**Keywords:** Preterm delivery, Antenatal corticosteroid administration, Affecting factors, Obstetrician, viewpoint

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## Introduction

Preterm delivery is still the most common cause of neonatal mortality and morbidity associated with complications such as respiratory distress syndrome (RDS), necrotizing enterocolitis and intraventricular hemorrhage.<sup>1,2</sup> Among these complications, RDS, which occurs in cases of lung immaturity and surfactant deficiency, is the major complication leading to neonatal loss.<sup>3</sup>

Antenatal corticosteroid treatment, which is administered to women at risk for preterm delivery between 28 and 34 weeks of gestation, was first reported by Liggins and Howie in

1972; it is believed to be the most effective intervention for reducing mortality and morbidity associated with RDS.<sup>4,5</sup> It is currently the standard treatment in cases in which preterm delivery (between 24 and 34 weeks of gestation) is suspected. However, since the introduction of this treatment, it has been a topic of debate among pediatricians and obstetricians.

The corticosteroid dose and interval between its administration and delivery are affected by several factors such as the indications for preterm labor and the hospitalization period.<sup>6</sup> The objective of this study was to investigate the factors affecting the features and the rate of antenatal corticosteroid administration from the obstetricians' viewpoint at a university hospital in Turkey.

## Material and Method

This retrospective study included 114 pregnant women who delivered between 24 and 34 weeks of gestation at Ondokuz Mayıs University Hospital between January 2012 and January 2013.

The subjects were divided into two groups based on the antenatal treatment given: Group 1, pregnant patients given corticosteroid therapy and tocolytic treatment (indomethacine for patients with 28-32 weeks of gestation, nifedipine for patients with 32-34 weeks of gestation) until the completion of

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corticosteroid therapy; group 2, pregnant patients who did not receive corticosteroid therapy and tocolytic treatment owing to impending delivery and informed about the risk/benefit for corticosteroid treatment. Data for the indications for preterm delivery, the place of administration, dosing (single or two doses) and completion of the corticosteroid therapy (it was considered to be complete 48 h after the first corticosteroid dose was administered), the gestation week at administration, residence and the manner of transfer of the patient to the hospital, the mode of delivery and the interval between corticosteroid administration and delivery.

A single course was defined as betamethasone given at a dose of 12 mg intramuscularly 24 h apart.<sup>7</sup> Preterm delivery and indications for preterm delivery were defined according to the guidelines of the American College of Obstetricians and Gynecologists (ACOG).<sup>8-14</sup>

Data analysis was performed by using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, United States). The Kolmogorov-Smirnov test was used to determine whether the distribution of continuous variables was normal or not. The homogeneity of variances was analyzed using the Levene test. Discriminative statistics and continuous and intermittent variables were expressed as mean ( $\pm$ standard deviation) or median (min–max), and categorical variables were expressed as case numbers and percentages (%).

The mean differences between two independent groups were compared using the Student's t test while one-way analysis of variance (one-way ANOVA) was applied to compare the mean differences among more than two independent groups. The median differences between two independent groups were compared using the Mann-Whitney U test. The Kruskal-Wallis test was applied to compare the median differences among more than two independent groups. When the result of the Kruskal-Wallis test was found to be statistically significant, the factor causing the difference was searched using Conover's nonparametric multiple comparison test. Categorical variables were investigated by Pearson's chi-square, Fisher's exact or probability ratio tests.

A p value less than 0,05 was considered to indicate statistical significance.

## Results

The study included 114 pregnant women who delivered between 24 and 34 weeks of gestation. The most common indications for preterm delivery were preterm labor (n=29 [25.4%]), severe preeclampsia (n=29 [25.4%]) and preterm membrane rupture (n=26 [22.8%]), and cesarean section was much more common than vaginal delivery. The demographic and clinical features of the study group are shown in Table 1.

Table 1: Demographic and clinical features of the study group

Features	n = 114
<b>Age (y)</b>	29.6 $\pm$ 6.2
<b>Gravida</b>	1 (1-7)
<b>Parity</b>	0 (0-6)
<b>Multiple pregnancy</b>	<b>17 (14.9%)</b>
<b>Indications for preterm delivery</b>	
<i>Preterm labor</i>	29 (25.4%)
<i>Severe preeclampsia</i>	29 (25.4%)
<i>Preterm membrane rupture</i>	29 (25.4%)
<i>Fetal distress</i>	17 (14.9%)
<i>Eclampsia</i>	5 (4.4%)
<i>Placenta previa</i>	4 (3.5%)
<i>HELLP</i>	2 (1.8%)
<i>Intrahepatic cholestasis</i>	2 (1.8%)
<b>Gestational week</b>	30.8 $\pm$ 2.3
<b>Delivery mode</b>	
Vaginal delivery	6 (5.3%)
Cesarean section (C/S)	108 (94.7%)
<b>Residence of the patient</b>	
<i>Urban</i>	58 (50.9%)
<i>Rural</i>	56 (49.1%)
<b>Manner of transfer of the patient to the tertiary center (university)</b>	
<i>Self referred</i>	66 (57.9%)
<i>By ambulance</i>	48 (42.1%)

The percentage of patients who received antenatal corticosteroid administration was 68.4% (group 1, n=78), whereas 31.6% (group 2, n=36) of the pregnant women did not receive corticosteroid therapy. Tocolysis was administered to group 1 including patients with preterm labor (n=17), severe preeclampsia (n=18), preterm membrane rupture (n=29), fetal distress (n=11), placenta previa (n=4), intrahepatic cholestasis (n=2) until completion of the corticosteroid therapy, while group 2 including patients with preterm labor (n=12), severe preeclampsia (n=11), eclampsia (n=5), HELLP (n=2), fetal distress (n=6), did not receive tocolytic treatment due to the impending delivery. In group 1, a single dose was administered to 24 (21%) pregnant women, while two doses were administered to 54 (47.4%) patients. The rate of administration and completion of the therapy was higher at the university hospital than at the previous hospital from which the patient had been transferred (Table 2).

When the pregnant women who were administered corticosteroid therapy (group 1) were divided into three groups on the basis of gestational week at administration, no statistically significant difference was found in the features of the therapy (Table 3).

A significant difference was found between group 1 and group 2 with regard to the interval between steroid administration and delivery ( $p < 0.001$ ). The interval was 48 (0.3-336) h in

the former, whereas it was 0.5 (0.08-4) h in the latter. Although cesarean section (C/S) delivery was much more common than vaginal delivery in both groups ( $p < 0.001$ ), C/S was more common in group 1 than in group 2. No significant difference was found between the two groups with regard to the place of administration, the gestational week at administration, and the residence and manner of transfer of the patients to the hospital (Table 4).

When the group that received corticosteroid therapy was divided on the basis of the dose, the interval between corticosteroid administration and delivery was significantly shorter in the single-dose group than in the double-dose group ( $p < 0.001$ ). The incidence of C/S delivery was also found to be significantly higher in the single-dose group than in the double-dose group ( $p = 0.018$ ) (Table 5).

Table 2: Features of the corticosteroid therapy

Features	n = 114
<b>Corticosteroid administration</b>	
Yes (group 1)	78 (68.4%)
Single dose	24 (21.0%)
Two doses	54 (47.4%)
No (group 2)	36 (31.6%)
<b>Dose status</b>	
Incomplete	3 (5.6%)
Complete	51 (94.4%)
<b>Place of administration</b>	
University hospital	59 (75.6%)
Previous hospital	19 (24.4%)
<b>Place of completion of the dose</b>	
University hospital	38 (74.5%)
Previous hospital	13 (25.5%)

Table 3: Relationship between the features of the corticosteroid therapy and gestational week at administration

	24-28 (n= 9)	28-32 (n=44)	32-34 (n=25)	p-value
Corticosteroid administration				0.277
	9 (52.9%)	44 (73.3%)	25 (67.6%)	
<b>Dosing</b>				0.719
Single dose	2 (22.2%)	13 (29.5%)	9 (36.0%)	
Two doses	7 (77.8%)	31 (70.5%)	16 (64.0%)	
<b>Dose status</b>				0.651
Incomplete	-	2 (6.5%)	1 (6.3%)	
Complete	7 (100.0%)	29 (93.5%)	15 (93.7%)	
<b>Interval between corticosteroid administration and delivery (h)</b>	3 (0.33-96)	24 (0.17-336)	8 (0.08-120)	0.241

Table 4: Comparison of the demographic and clinical features of Group 1 and Group 2

Features	Group 1 (with steroid therapy)n = 78	Group 2 (without steroid therapy) n = 36	p-value
Age (y)	29.9±6.1	29.0±6.4	0.523
Gravida	1 (1-7)	2 (1-6)	0.919
Parity	0 (0-6)	0 (0-4)	0.586
<b>Gestational week</b>	30.9±2.2	30.6±2.6	0.667
			0.277
24-28	9 (11.5%)	8 (22.2%)	
28-32	44 (56.4%)	16 (44.4%)	
32-34	25 (32.1%)	12 (33.3%)	
<b>Interval between admission to hospital and delivery (h)</b>	48 (0.3-336)	0.5 (0.08-4)	<b>&lt;0.001</b>
<b>Mode of delivery</b>			<b>0.012</b>
Vaginal	1 (1.3%)	5 (13.9%)	
C/S	77 (98.7%)	31 (86.1%)	
<b>Residence of the patient</b>			0.783
Urban	39 (50.0%)	19 (52.8%)	
Rural	39 (50.0%)	17 (47.2%)	
<b>Manner of transfer of the patient to the tertiary center (university)</b>			0.731
Self referred	46 (59.0%)	20 (55.6%)	
By ambulance	32 (41.0%)	16 (44.4%)	

Table 5: Comparison of the demographic and clinical features of the single-dose and double-dose corticosteroid therapy group

Features	One dose (n = 24)	Two doses (n = 54)	p-value
Age (y)	29.1±6.6	30.2±5.9	0.643
Gravida	1 (1-7)	2 (1-7)	0.421
Parity	0 (0-6)	1 (0-5)	0.489
Gestational week	31.4±1.8	30.8±2.3	0.453
			0.532
24-28	2 (8.3%)	7 (13.0%)	
28-32	13 (54.2%)	31 (57.4%)	
32-34	9 (37.5%)	16 (29.6%)	
Interval between corticosteroid administration and delivery	4 (0.33-24)	48 (3-336)	<b>&lt;0.001</b>
Mode of delivery			<b>0.018</b>
Vaginal	-	1 (1.9%)	
C/S	24 (100.0%)	53 (98.1%)	
Residence of the patient			0.963
Urban	12 (50.0%)	27 (50.0%)	
Rural	12 (50.0%)	27 (50.0%)	
Manner of transfer of the patient to the tertiary center (university)			0.112
Self referred	10 (41.7%)	36 (66.7%)	
By ambulance	14 (58.3%)	18 (33.3%)	
Place of corticosteroid administration			0.629
University hospital	19 (79.2%)	40 (74.1%)	
Previous hospital	5 (20.8%)	14 (25.9%)	

## Discussion

Despite all the advances in maternal and neonatal care, preterm birth is the leading cause of neonatal mortality and morbidity around the world. Antenatal corticosteroid treatment is currently the most effective treatment that is used to reduce the mortality and morbidity resulting from direct complications of preterm delivery.<sup>5</sup>

Several studies have investigated the maternal and neonatal effects of antenatal steroid therapy.<sup>15</sup> The features of the treatment, such as dosing, choice of drug, timing before delivery, and additional therapy, were evaluated in order to find the association of these factors with the outcomes. This topic has never been examined from the obstetricians' viewpoint. In this study, we investigated the patient-, physician-, and hospital-related factors that affect the outcome of antenatal corticosteroid therapy and discuss the findings from the viewpoint of obstetricians.

Certain indications require emergency delivery, such as severe preeclampsia, eclampsia and fetal distress; it may be difficult and sometimes impossible to administer and complete corticosteroid therapy in such cases. In this study, we found that preterm labor, severe preeclampsia and preterm membrane rupture are the most common indications for preterm delivery, and our administration rate was 68.4%. Betamethasone given at a dose of 12 mg intramuscularly 24 h apart was the treatment administered to our study group; 21% of the patients in

the group were treated with a single dose and 47.4% were given two doses. In the subgroup given two doses, the dose was completed in 94.4% of the patients.

The features of the patients were evaluated in order to determine whether they had an effect on the treatment rates and dosing. The study group was divided on the basis of the treatment status. There was no significant difference in gestational weeks in terms of treatment status. The residence (urban or rural) was not found to have a significant effect on the therapy either. Since preterm neonates require intensive care, such cases should be transferred to tertiary care centers. Therefore, we investigated corticosteroid administration and completion of the therapy outside our tertiary university hospital, but found no statistically significant difference. In addition, the manner of transfer of the patients was found to be important, because it is likely that in cases of self-referral, there may have been some delay in the corticosteroid treatment. However, we did not find a significant difference between the patients who came by themselves and those who were brought in by an ambulance.

The duration of the interval between corticosteroid administration and delivery has been also investigated in order to determine the optimal treatment-delivery interval.<sup>16-20</sup> In vitro studies have shown that choline begins to get incorporated into phospholipids at 6 h and peaks at 48 h after the first dose of antenatal corticosteroid is administered.<sup>21</sup> The optimal

treatment-delivery interval for administration of antenatal corticosteroids has been found to be more than 24 h but >7 days after the start of treatment.<sup>22</sup> In the present study, this interval was only 30 min in the group without therapy whereas it was 48 h in the group administered treatment.

In conclusion, this study shows that indications for preterm delivery, particularly impending delivery, seem to be the most influential factors that determine the effectiveness of antenatal corticosteroid administration. Despite the fact that obstetricians are aware of the importance of corticosteroid therapy in preterm deliveries, certain indications can affect administration of the therapy.

## Obstetrisyenlerin Bakış Açısıyla Antenatal Kortikosteroid Uygulamasını Etkileyen Faktörler

### ÖZET

**AMAÇ:** Obstetrisyenlerin bakış açısıyla, antenatal kortikosteroid uygulamasını etkileyen faktörleri araştırmayı hedefledik.

**GEREÇ VE YÖNTEM:** Ondokuz Mayıs Üniversitesi'nde 24-34 gebelik haftaları arasında doğum yapmış olan hastalar iki gruba ayrıldı: Grup 1, kortikosteroid tedavisi verilenler; Grup 2: kortikosteroid tedavi verilmeyenler. Doğum endikasyonları, steroid uygulama sırasındaki gebelik haftası, kortikosteroid dozu, uygulama yeri, hastaların tersiyer merkeze transfer şekilleri ve hastaneye kabul ile doğum arasında geçen süre değerlendirildi.

**BULGULAR:** Antenatal kortikosteroid tedavisi alanlar %68,4, almayanların yüzdesi ise %31,6 idi. En sık görülen preterm doğum endikasyonları, preterm eylem ve şiddetli preeklampsiydi. Hastaneye kabul ile doğum arasındaki süre grup 1'de grup 2'den daha uzundu.

**SONUÇ:** Obstetrisyenler antenatal kortikosteroid uygulamasının öneminin farkında olmalarına rağmen, doğumun kaçınılmaz olduğu endikasyonlar tedaviyi etkileyebilmektedir.

**Anahtar Kelimeler:** Preterm doğum, Antenatal kortikosteroid uygulaması, Etkili faktörler, Obstetrisyen, Bakış açısı

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