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(RESEARCH ARTICLE)

The effect of antenatal steroid administration on mortality and morbidity in newborns that 34 weeks and older

Atiye Fedakâr*

The Departments of Pediatrics, Afiyet Hospital. Ümraniye, İstanbul, Turkey.

Abstract

Objective: The effects of antenatal steroid (AS) administration on mothers during pregnancy were investigated on mortality and morbidity in newborns that 34 weeks' gestations and older.

Material and Method: Between January 2016 and June 2018, pregnant women who were followed-up from our hospital's gynecology and obstetrics outpatient clinic and children born from these pregnancies were included in the study. This study was conducted as prospective and retrospective. Patients included in the study were divided into three groups according to AS application: full cure, incomplete cure, and non-taking.

Results: A total of 727 pregnant women were included in the study, but 56 pregnant women were excluded from the study because they went to another hospitals to give birth. AS application on mothers; 251 (37.4%) complete dose, 176 (26.2%) incomplete cure and 244 (36.4%) was not applied at all. Newborn included in the study are 379 (56.5%) male, 292 (43.5%) female, 317 (47.2%) were between 34-36 weeks and 354 (52.7%) were between 37-39 weeks. There was also a statistically significant difference in the rate of hospitalization in the neonatal intensive care unit, intubation time, oxygen requirement period, maximum FiO_2, 5th minute Apgar score in children of women that AS not applied.

Conclusion: We may conclude that AS application will decrease respiratory problems especially in newborns over 34 weeks and thus affect the mortality and morbidity in the newborn. A single cure of AS may reduce the duration of intensive care unit and oxygen demand

Keywords: Pregnancy; Antenatal Steroid (AS); Administration; Morbidity; Newborn; Results

1. Introduction

Late preterm birth is defined as birth at 34 (0/7) and 36 (6/7) weeks of gestation starting from the first day of the mother's last menstrual period at first workshop held in july 2005 [1]. Late preterm infants are the most rapidly growing group in premature infant group and constitute 60-70% of premature births and 8% of all births [2, 3]. In recent years, increased number of assisted reproductive techniques, multiple pregnancies, increased elective cesarean section, increased late-age pregnancies, fear of vaginal delivery, and change of medical thresholds for cesarean delivery due to increased late preterm birth number [4]. It was stated that these babies had a high risk in terms of mortality and morbidity (especially respiratory distress, increased surfactant requirement, nutritional difficulties, hypoglycemia, hyperbilirubinemia, etc.[5, 6]. In the first 9 months of life, those born at 35 and 36 weeks of gestation have a higher rate of rehospitalization compared to those born at 37 weeks of age [7]. Good management of the respiratory system under rational conditions is of great importance [8, 9].

The administration of AS for the prevention of respiratory distress syndrome (RDS)in fetuses at < 34 weeks of gestation is widely supported since the National Institutes of Health Consensus statement in 1994 [10]. But nowadays the

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* Corresponding author: Dr Atiye Fedakâr

Armağan evler mah. Akdeniz cd. Sandra evleri c blok d-4. 34762 Ümraniye, İstanbul, Turkey.

evidence for use of AS at or after 34 weeks is still debatable [11]. The American College of Obstetricians and Gynecologists (AGOC) recommended AS only for women at risk of late premature delivery at greater than 34 weeks' gestation but not for women undergoing planned cesarean at term [12]. According to the Royal College of Obstetricians and Gynecologists AS should be given to all women with a planned elective cesarean section prior to 38 weeks' gestation [13].

The aim of this study was to investigate the effects of AS administration on mothers during pregnancy, on mortality and morbidity in newborns that 34 weeks and older.

2. Material and Methods

Between January 2016 and June 2018, pregnant women who were followed-up from our hospital's gynecology and obstetrics outpatient clinic and children born from these pregnancies were included in the study respectively. The study was approved by hospital ethics committee. We planned the study that it was a prospective and retrospective study. Records and evaluations of children were performed prospectively. The records of the mothers were retrospectively taken. Mothers' gestational age, maternal age, presence of chronic disease, dose of AS administration and the amount of application were recorded. The birth weight of the children, type of delivery, gender, 5-minute Apgar score, need for intensive care unit, intensive care stay, duration of oxygen support, need for oxygen support, intubation need, whether or not applied surfactant were recorded.

Betamethasone were administered two doses of 12 mg im at 24-hour intervals as AS. Patients included in the study were divided into three groups according to AS application.

Group 1: Patients who were born 24 hours after AS application.
Group 2: Patients who underwent AS application, but they were delivered before the cure was completed.
Group 3: Patients who non-taking any AS.

Exclusion criteria are congenital multiple anomalies newborn and AS initiated however, babies were born in another hospitals. Pregnant women who were excluded from the study because they went to another hospitals to give birth.

Transient tachypnea of the newborn (TTN) was defined as respiratory distress occurring in term or near-term babies, emerging within 4-6 hours of delivery, which generally is resolved within 3 days [14]. RDS was defined as tachypnea, chest wall retractions and cyanosis with room air, showing persistence or progression for the initial 48-96 hours, together with the characteristic reticulogranular appearance and air bronchograms in the chest X-ray [15]. Mortality rates, birth weight, sex, gestational week, Apgar scores, oxygen therapy, ventilator treatment, surfactant treatment, intubation need, maternal additional diseases and length of stay in the care unit were compared between the three groups included in the study.

The study was conducted in accordance with the Declaration of Helsinki Principles. Permission was obtained from patients or, if necessary, their legal representative.

Statistical Analyses

While evaluating the results obtained from the study, IBM SPSS Statistics 22 (SPSS IBM, Turkey) software was used for the statistical analyses. Kruskal Wallis test was used to comparison of the parameters that do not show normal distribution between groups. Mann Whitney U test was used to determine the group that caused the difference. Chi-square test and Fisher Freeman Halton test were used to compare qualitative data. A value of $p < 0.05$ was considered as the level of significance.

3. Results

A total of 727 pregnant women were included in the study. However, 56 pregnant women were excluded from the study because they went to another hospital to give birth. The mean age of the mothers was 29.03 ± 5.25 and the gestational week ranged from 34 to 39 weeks. Additional diseases seen in mothers of babies are shown in Table 1. Total 671 mothers and their children were evaluated. AS application on mothers; 251 (37.4%) complete dose, 176 (26.2%) incomplete cure and 244 (36.4%) was not applied at all.

Table 1 Additional diseases of mothers

Disease	n=%
Urinary tract infection	76(11.3%)
Gestational diabetes	42(6.2%)
Thyroid	31 (4.6%)
Oligohydroamnios	19 (2.8%)
Hypertension	12(1.7%)
Grippe	11 (1.6%)
Preeclampsia	6(0.8%)
Asthma	3 (0,4%)
Placental abruption	2 (0.2%)
Upper respiratory tract infection	2 (0.2%)
Anemia	2 (0.2%)
Pancreatitis	2 (0.2%)
Epilepsy	1 (0.1%)
Polihydroamniyos	1 (0.1%)

A total of 671 newborn data were examined. The sex distribution of the children was determined as 379 (56.5%) male and 292 (43.5%) female. In terms of gestational age, 317 (47.2%) were between 34-36 weeks and 354 (52.7%) were between 37-39 weeks, 492 (73.3%) were born by cesarean section and 179 (26.7%) by normal vaginal delivery. A total of 296 children had to be admitted to the neonatal intensive care unit. The patients who admitted neonatal intensive care unit were AS application data to their mother, respectively; 201 (82.4%) did not take AS at all, 59 (23.5%) had full doses of AS and 36 (20.5%) had incomplete cure. Demographic characteristics of children investigated in terms of the results of AS application are presented in Table 2.

Table 2 Evaluation of demographic characteristics of antenatal steroid administration groups

	Antenatal steroid administration			Total	p
	Full cure, and	Incomplete cure,	Never administrated		
	mean±SS	mean±SS	mean±SS	mean±SS	
Weight	2891.75±453.84	3025.67±474.36	2848.11±493.94	2911.01±478.7	[1]0.001*
Mother age	28.92±5.12	29.16±5.21	29.05±5.44	29.03±5.25	[1]0.901
Week of pregnancy	36.58±1.37	37.07±1.23	35.99±1.19	36.5±1.34	[1]0.000*
Pregnancy count *(median)*	2.22±1.28 (2)	2.01±1.04 (2)	2.25±1.36 (2)	2.17±1.,25 (2)	[2]0.264
Hospitalization time (days)*(median)*	1.6±3.29 (0)	1.38±3.23 (0)	5.48±4.39 (5)	2.95±4.18 (0)	[2]0.000*
Oxygen supply time *(median)*	0.93±2.14 (0)	0.91±2.23 (0)	3.36±3.54 (2)	1.81±2.99 (0)	[2]0.000*
İntubated *(median)*	0.14±0.7 (0)	0.11±0.62 (0)	0.43±1.48 (0)	0.24±1.05 (0)	[2]0.001*
CPAP*(median)*	0.34±1.01 (0)	0,4±1,92 (0)	1±1.75 (0)	0,6±1,6 (0)	[2]0.000*
Hood*(median)*	0.45±1.02 (0)	0,52±1,19 (0)	2±1,73 (2)	1.03±1.54 (0)	[2]0.000*
Max Fio2*(median)*	13.8±26.29 (0)	12.1±24.37 (0)	47.3±24.91 (50)	25.52±30.16(0)	[2]0.000*

APGAR5(median)	8.95±0.44 (9)	8.95±0.39 (9)	8.73±0.81 (9)	8.87±0.6 (9)	[2]0.001*
Gender n(%)					
Male	131 (52.2%)	97 (55.1%)	151 (61.9%)	379 (56.5%)	[3]0.086
Female	120 (47.8%)	79 (44.9%)	93 (38.1%)	292 (43.5%)	
Type of Delivery (%)					
Caesarean	184 (73.3%)	122 (69.,3%)	186 (76.2%)	492 (73.3%)	[3]0.287
Normal	67 (26.7%)	54 (30.7%)	58 (23.8%)	179 (26.7%)	
Maternal Sickness n(%)					
Yes	59 (23.5%)	28 (15.9%)	]124 (50.8%)	211 (31.4%)	[3]0.000*
No	192 (%76.5)	148 (84.1%)	120 (49.2%)	460 (68.6%)	
Surfactant (%)					
Yes	243 (%97.2)	172 (%97.7)	230 (%94.7)	645 (%96.4)	[3]0.173
No	7 (%2.8)	4 (%2.3)	13 (%5.3)	24 (%3.6)	
ICU Admission n(%)					
No admission	192 (76.5%)	140 (79.5%)	43 (17.6%)	375 (55.9%)	[3]0.000*
Need admission	59 (23.5%)	36 (20.5%)	201 (82.4%)	296 (44.1%)	

[1]Oneway Anova Test   [2]Kruskal Wallis Test[3]Ki Kare Test [4]Fisher FreemanHalton Test*p<0.05

No side effects of AS application were observed in mothers and infants. Our mortality was zero. The most common reason to hospitalization of the patients in the neonatal intensive care unit was preterm + TTN. The diagnoses of admission to the neonatal intensive care unit are shown in Table 3.

Table 3 Diagnosis of patients

Antenatal steroid (AS) administration n=296(%44,1)	Full Cure 59(%23,5)	Incomplete Cure 36(%20,5)	Non-Taking any AS 201(%82,4)
Premature + TTN	43 (14.5%)	25(8.4%)	130(43.9%)
TTN	5 (1.6%)	6 (2%)	37(12.5%)
TTN+ sepsis	7 (2.3%)	3 (0.3%)	23(7.7%)
RDS	4(1.3%)	2 (0.6%)	10(3.3%)
Meconium aspiration	0	0	1 (0.3%)

TTN: Transient tachypnea of newborn RDS: Respiratory distress syndromes

AS was evaluated according to gestational week. There were statistically significant differences between the groups in terms of gestational week averages (p: 0.000; p <0.05). As a result of the paired comparisons to determine the difference; the mean gestational week of the group who received incomplete curing AS was statistically significantly higher than the group who received full dose of AS and never applied (p: 0.000; p <0.05). The mean gestational week of the group receiving full dose AS was found to be statistically significantly higher than the group without any treatment (p: 0.000; p <0.05).

The incidence of newborn intensive care admission was statistically significantly higher in the group with no AS application (p: 0.000; p <0.05) (Figure1). There was no statistically significant difference between complete dose and incomplete cure groups (p> 0.05).
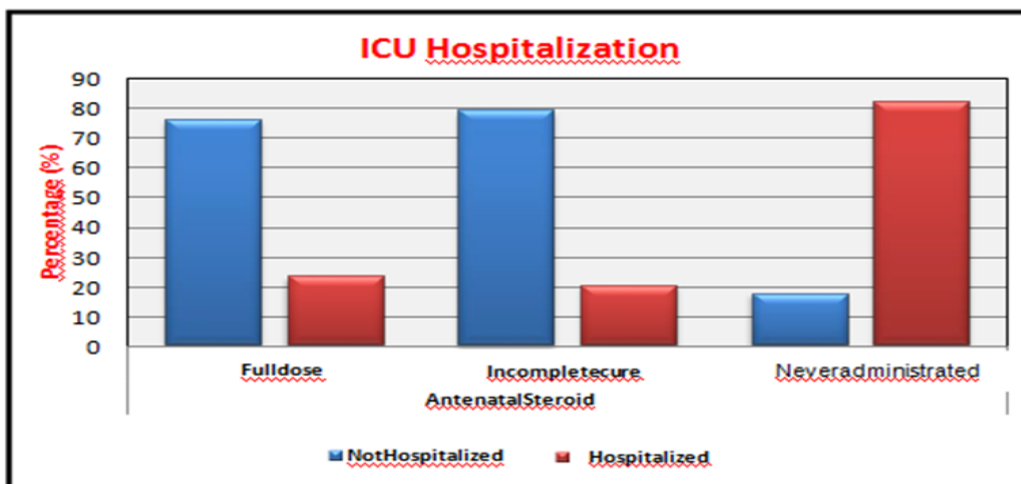
Figure 1 Hospitalization rate of patients in the neonatal intensive care unit

The incidence of additional disease in the mother was evaluated. Incidence of additional disease in the mother in the group with no AS applied was found to be significantly higher than complete dose and incomplete cure groups (p: 0.000; p <0.05). There was no statistically significant difference between complete dose and incomplete cure groups (p> 0.05). There was no statistically significant difference between the AS groups in terms of maternal age, number of pregnancies, and gender (p> 0.05). There was no statistically significant difference between the groups in terms of surfactant application and delivery type (p> 0.05).

There was a statistically significant difference between the groups in terms of CPAP application, hood initiation, max FiO2 mean (p: 0.000; p <0.05) (Figure2). There was statistically significant difference between the patients who had not been treated with AS than full cure and incomplete cure groups (p: 0.000; p <0.05). There was no statistically significant difference between complete dose and incomplete cure groups (p> 0.05).
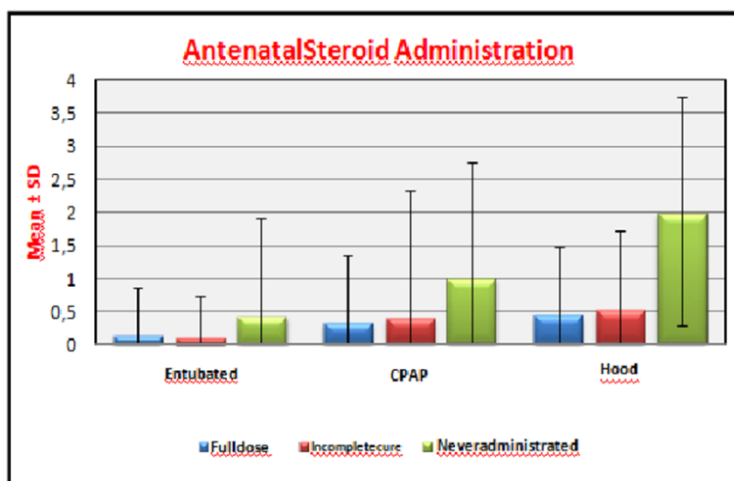
Figure 2 Duration of hospitalization and oxygen treatment

4. Discussion

Late preterm neonates (especially between 34 and 36 weeks) are significantly higher rates of respiratory complications than neonates born at term [16]. İn this study, we found that AS administration of women at risk for late preterm delivery decreased neonatal respiratory complications. AS applied group showed that hospitalization rate and length of stay, oxygen duration, intubation time, CPAP application, oxygen supply requirement with hood were lower than those patients who non-taking any AS. The Apgar 5th goal score was significantly higher at AS applied group. Our meta-analysis showed the benefit of a newborn with a single dose of AS before delivery in women with late preterm delivery. Our findings are similar with the results of the study by Gyamfi-Bannerman et al. In the study by Gyamfi-Bannerman et

al. randomized placebo-controlled trial examined the effectiveness of betamethasone in preventing neonatal respiratory complications for 2831 women at high probability of preterm delivery (between 34 weeks and 36 weeks, 6 days of gestation). This study showed that the need for respiratory support treatment (especially CPAP and HFNC) decreased statistically, but the risk of hypoglycemia increased [17]. Unlike her study, our patient group did not show hypoglycemia. Hypoglycemia can be tolerated more easily.

In terms of the use of surfactant, no statistically significant difference was found between the groups. The rate of did not require admission to the neonatal intensive care unit babies .Using full dose and incomplete dose are 76.5% and 79.5%, respectively. In our study, hospitalization time was 1.6 days in full dose AS patients, 1.3 days in those with incomplete curing AS, and 5.4 days in those who did not use AS. Statistically   significant decrease for hospıtalısation after AS administration. In late premature infants, hospital stay is and 10-13 days for 34 weeks infants, and this period may be 3-4 days for term babies [18]. In the study performed by Raju, the costs of babies born at 34, 35, 36 weeks gestation were reported as $ 7200, $ 4200, and $ 2600, respectively [19, 20, 21]. We believe that shortening the length of stay will contribute to the national economy.

Premature births constitute the most important place in neonatal intensive care services. On the other hand, the separation of the mother from her baby increases the mother's potential postpartum depression. This is of great importance in the management of infants in terms of the respiratory system and the complications waiting for them. We believe that AS application can decrease the respiratory problems especially in newborns and thus can affect the mortality and morbidity positively in newborn in both short and long term.

It is a handicap that the results of long-term adult use of AS are unknown. The Antenatal Steroids for Term Elective Caesarean Section (ASTECS) trial reported that antenatal betamethasone did not result in any adverse long term neurological or cognitive outcomes at age 8-15 years [21] .In a study on the cardiovascular system, there was no difference detected in blood lipid level, diabetes incidence, blood pressure which were performed at 30th age, but an increase in insulin resistance was observed [22]. Our study yet more new .We do not know what will be the long-term results.

Conclusion

Premature deliveries have the most important place in newborn intensive care services. It imposes a burden for the country's economy, and long-term hospitalization and development of complications cause the cost to increase further. On the other hand, separating infants from their mothers increases potential postpartum depression of mother further. In addition, hospitalization to the intensive care unit, disease periods cause serious concern for parents. Therefore, it is crucial that these infants should be managed in rational conditions in terms of respiratory system and complications. For this reason, we believe that AS application will especially minimize respiratory problems in newborns, thus, it can positively affect mortality and morbidity in newborns both in the short-term and long-term.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of ethical approval

The study was approved by the special Afiyet Hospital Ethics Committee.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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