

The Use of Betamethasone in Women at Risk of Preterm Delivery Associated with the Incidence of Neonates Respiratory Distress Syndrome (NRDS), A Systematic Review

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Abstract

Background: Neonatal Respiratory Disease Syndrome (NRDS) still become most causes of neonatal mortality and morbidity especially in premature infants. Antenatal betamethasone has positive effect on preventing NRDS. Objectives: We sought to perform a systematics review of the use of betamethasone in women at risk of preterm delivery associated with the incidence of NRDS articles over the past fifth years. Methods: A systematic review was performed on PubMed and Scopus search term "Pediatrics" and "Pregnancy". Results: Four articles identified between 2016 and 2019 specifically addressed for the use of betamethasone in women at risk of preterm delivery associated with the incidence of NRDS. A total 1800 patients were included in these four studies. The success rate ranges from 87,4% to 100%. Conclusion: Overall, the use of betamethasone in women at risk of preterm delivery decrease the incidence of respiratory distress syndrome in newborn significantly. Betamethasone administered success rates of RDS in newborn ranged from 87,4% to 100%. Overall, studies with a higher number of patients had higher success rates.

Keywords: *Betamethasone; Preterm Delivery; RDS; Systematic Review*

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Introduction

Neonatal Respiratory Distress Syndrome (NRDS) is one of neonatal's respiratory outcomes where evolution of lung is incomplete, commonly found in premature infants. Unfortunately, this syndrome can lead early neonatal mortality and the risk of short or long-term disabilities. Along with several factors, such as low birth weight, asphyxia, caesarean, and diabetic mothers that increase the risk of NRDS in infants, preterm birth has been considered as one of the most important risk factors of it, up to 50% of preterm births at 26-28 weeks, and 30% of them at 30-31 weeks end up in babies with NRDS. (Abbasalizadeh et al. 2020)

Administration of betamethasone before the 34th of the gestational age reduces the risk of severe neonatal outcomes including death, NRDS and other neonatal complications shows effectiveness on first randomized trial in 1972 (Olaloko, Mohammed, and Ojha 2018). Furthermore, administration of glucocorticoid in maternal with high risk of preterm labor became a consensus held by National Institutes of Health in 1994. (Gyamfi-Bannerman et al. 2016; Mirzamoradi et al. 2020) However, the use of these drugs in preterm labor after the 34th week of gestation is not recommended for two reasons; firstly, there is not sufficient evidence available and, secondly, it is believed that almost all babies at 34th–35th weeks of gestation survive and have a survival rate similar to term neonates. Nowadays, it is known that babies born in the late preterm period (34–36 weeks are more likely to have neonatal and childhood complications than babies born at or after 37 weeks. For this reason, in 2005, it was recommended to conduct studies to assess neonates born between the 34th and 36th week of gestation in order to find out whether the use of glucocorticoids can also be useful during this period. (McIntire and Leveno 2008; Yoder, Gordon, and Barth 2008) The most commonly used corticosteroids are betamethasone (BTM) and dexamethasone (DXM), which are able to cross the placental barrier and through the intramuscular (IM) route. This study aims to analyze the available evidence in systematic reviews that evaluated the efficacy of antenatal betamethasone administration in order to contribute to a prevention of NRDS.

Materials and method

A literature was performed using PubMed MeSH and Scopus search term “Pediatrics” and “Pregnancy”. We qualified all the journal with Sc imago. All articles were reviewed for inclusion such as pregnancy women with gestational age <37 weeks with a high probability of late preterm delivery and administered with betamethasone, betamethasone doses were 12 mg and 24 mg, using randomized trial and prospective observational study methodology. (Zannolli et al. 2012)

Pregnant women who administrated with other steroids except betamethasone, pregnant women with maternal medical illness and patient who had received antenatal glucocorticoids previously during the pregnancy were excluded. The aim of this study was to know the effect of administered betamethasone to pregnant women to reduce the incident of respiratory distress syndrome in newborn.

Results

From four studies that examined the use of betamethasone in women at risk of preterm delivery (<37 weeks gestational ages) associated with the incidence of respiratory distress syndrome (RDS) in neonates showed the incidence of RDS at all gestational ages was significantly lower in the betamethasone group than in the control group ($p < 0.05$).

Gyamfi et al reviewed the primary outcome occurred in 165 of 1427 infants (11.6%) in the betamethasone group and 202 of 1400 (14.4%) in the placebo group (relative risk in the betamethasone group, 0.80; 95% confidence interval [CI], 0.66 to 0.97; $P=0.02$). Severe respiratory complications, transient tachypnea of the newborn, surfactant use, and bronchopulmonary dysplasia also occurred significantly less frequently in the betamethasone group. (Gyamfi-Bannerman et al. 2016)

Komal Gaur and Barna Ganguly reported Out of 111 newborn babies, 71 newborns delivered within 24 hours of betamethasone administration and rest 40 delivered after 24 hours. Out of these 71, 51(71.8%) deliveries were preterm while 20 (28.7%) full term, 71 were born within 24 hours and rest were born after 24 hours of betamethasone administration. RDS at birth was recorded in only 14 neonates out of whom, 12 were born within 24 hours of betamethasone administration. The other recorded diagnoses were Transient Tachypnoea of Newborn (TTN), Birth Asphyxia (BA) (Gaur and Ganguly 2017).

Fatemeh et al reviewed the incidence of NRDS was significantly lower in infants of betamethasone group than the ones in the control group (4.9% vs 18.1%, $P=0.034$) while it did not show a significant reduction in preterm infants compared to mature ones. Also, the intervention group presented a significant lower neonatal ventilation than the control group (47.2% vs 63.2%, $P=0.041$) (Abbasalizadeh et al. 2020).

Masoumeh et al reported in general the incidence of respiratory morbidities at all gestational ages was significantly lower in the betamethasone group than in the control group ($p < .05$). The need for oxygen for more than an hour was the most frequently observed morbidity (in 34 neonates, 14%). Furthermore, the incidence of NRDS was 0 and the need for surfactant were significantly lower in betamethasone group than in the control group ($p < .05$) (Mirzamoradi et al. 2020).

Discussion

Betamethasone is used to accelerate fetal lung maturation in women with preterm birth, but its efficacy is variable and limited by the lack of patient individualization in its dosing and administration (Kinney et al. 2021). To determine sources of variability and potential opportunities of therapy, this study was to evaluate development of neonatal respiratory distress syndrome (RDS) in women who received betamethasone (Kinney et al. 2021).

In the randomized, multicenter trial, Gyamfi et al found that antenatal administration of betamethasone to women at risk for late preterm delivery decreased the need for substantial respiratory support during the first 72 hours after birth (Gyamfi-Bannerman et al. 2016). From 1427 infants in betamethasone group 165 become RDS it means only 11,6% infants had RDS meanwhile the success rate was 89,4% (Alhassen et al. 2021).

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Another study by Komal Gaur and Barna Ganguly reported Out of 111 newborn babies, 71 were born within 24 hours and rest were born after 24 hours of betamethasone administration. RDS at birth was recorded in only 14 neonates out of whom, 12 were born within 24 hours of betamethasone administration. The other recorded diagnoses were Transient Tachypnoea of Newborn (TTN), Birth Asphyxia (BA) (Gaur and Ganguly 2017). From their study we can concluded that the success rate was 87,4 %

The findings of the study by Fatemeh et al showed the efficacy of prenatal maternal administration of two doses of betamethasone 12 mg in multifetal pregnancies which are at high risk of preterm delivery, showed a significant reduction in occurrence of NRDS (Abbasalizadeh et al. 2020) from 142 infants they reported only 7 who had incidence of RDS, it means the success rate was 95,1 %.

In the randomized clinical trial performed on 240 women with single pregnancy that was at high risk of late preterm delivery (34–37 weeks), Masoumeh et al reported the incidence of respiratory morbidities at all gestational ages was significantly lower in the betamethasone group than in the control group ($p < 0.5$) (Mirzamoradi et al. 2020). Furthermore, the incidence of NRDS was 0 it means the success rate was 100%.

The outcomes found in this overview also enhance the positive evidence that the use of betamethasone in pregnant women at risk of preterm delivery is actually effective in reducing the risk of RDS. Overall, success rates with betamethasone administered range from 87,4% to 100% in four studies that we used as a reference (Schiffman et al. 2014). There are differences in success rates which can be caused by several things, one of which is the number of samples, maternal factors, and other possible causes that are not yet known. it is necessary to do further research on the factors that influence the incidence of RDS in premature newborns who have previously received betamethasone (Liggins and Howie 1972).

Author	Journal	Year	Betamethasone Group	NRDS Incidence	Success Rate
Gyamfi-Bannerman et al. 2016	NEJM	2016	1427	165 (11,6 %)	89,4 %
Gaur and Ganguly 2017	Journal of Clinical and Diagnostic Research	2017	111	14 (12,6%)	87,4%
Fatemeh et al	Current Clinical Pharmacology	2019	142	7 (4,9 %)	95,1%
Mirzamoradi et al. 2020	The Journal of Maternal-Fetal & Neonatal Medicine	2019	120	0 (0 %)	100%

Table 1. Success Rates of Betamethasone

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Conclusion

In a systematic review of betamethasone administered in pregnant women with high probability of late preterm delivery, four studies with 1800 total patients were identified. Betamethasone administered success rates of RDS in newborn ranged from 87,4% to 100%. Overall, studies with a higher number of patients had higher success rates.

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