VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska
2022, vol. 93, no. 6, 478–481

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/GP.a2022.0012

Influence of prenatal steroid therapy on the incidence of respiratory disorders in late premature infants

Natalia Czaplinska[1], Monika Gruszfeld[1], Joanna Schreiber-Zamora[1], Natalia Goluchowska[1], Piotr Rzepniewski[1], Bronislawa Pietrzak[2], Miroslaw Wielgos[2], Bozena Kociszewska-Najman[1]

[1]Department of Neonatology, Medical University of Warsaw, Pediatric Hospital, Warsaw, Poland
[2]1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland

ABSTRACT

Objectives: This study was conducted because of conflicting data on the role of corticosteroids administered before delivery in the late premature period. The aim of the study was to assess the frequency of respiratory disorders in 'late premature infants' and the impact of using prenatal steroid therapy.

Material and methods: The study included 513 newborns born between the 34–36 week of pregnancy. They were divided into two groups. In the first group, there were 439 newborns (85.58%) who did not receive prenatal steroid therapy, and in the second group, there were 74 newborns (14.42%) born after the prenatal steroid course. The frequency of occurrence of respiratory disorders requiring the use of non-invasive respiratory support methods as well as intubation and mechanical ventilation was compared in both groups.

Results: In the group of premature infants after steroid therapy 43/74 (58.12%) did not require respiratory support compared to the group of infants without prenatal steroid therapy where in 368/439 (83.8%) cases no respiratory disorders were found.

Conclusions: If there is a risk of preterm labor in the 34–36 week of pregnancy, the use of steroid therapy should be considered. Steroidotherapy at this moment of gestation may not be such beneficial, like in the more premature delivery, before 34 weeks of pregnancy.

Key words: prenatal steroid therapy; late preterm; RDS; respiratory support

Ginekologia Polska 2022; 93, 6: 478–481

INTRODUCTION

Preterm labor is a serious health problem around the world and is associated with other challenges to doctors, in comparison to the cases of term newborns [1]. Late preterm labors between 34–36 week account for approximately 75% of all preterm labors and are the fastest-growing subgroup of premature infants [2]. Fortunately, the increase in the incidence of late preterm deliveries has stalled in recent years, and the estimated frequency of occurrence in 2013 was 8.0% and remains on a similar level until now [3]. Preterm infants stay longer in hospital and generate higher care costs. They are also at higher risk of developing some diseases (hypoglycemia, hypothermia, eating problems, sudden infant death syndrome), as well as three times higher mortality compared to full-term newborns. More than 1/3 of premature infants requires a stay in the neonatal intensive care unit, mainly due to respiratory system diseases [5].

Hence, the potential public health effects as well as the economic effects of reducing the incidence of late prematurity complications by administering glucocorticoids before labor, are worth investigating.

Compared with infants delivered between the 39 and 40 week of pregnancy, infants delivered in the 34 week are at higher risk for respiratory complications, including RDS/hyaline disease of the newborn [odds ratio (OR): 40.1; 95% CI: 32.0–50.3], transient tachypnea of the newborn (OR: 14.7; 95% CI: 11.7–18.4), pneumonia (OR: 7.6; 95% CI: 5.2–11.2), respiratory failure (OR: 10.5; 95% CI: 6.9–16.1),

Corresponding author:
Natalia Goluchowska
Department of Neonatology, Medical University of Warsaw, Pediatric Hospital, Warsaw, Poland
e-mail: goluchowskan@gmail.com

Received: 5.08.2021 Accepted: 7.02.2022 Early publication date: 7.04.2022

and the need to assist breathing with a respirator (OR: 13.9; 95% CI: 11.0–17.6). The risk of lung disease incidence decreases with increasing gestational age at delivery [6].

In 1972 Liggins and Howie started looking for a method to reduce the occurrence of respiratory diseases in the group of premature newborns. They published a study, in which they proved the beneficial effect of prenatal corticosteroid therapy in cases of inevitable deliveries before the 32nd weeks of pregnancy [7]. The premise of the therapy is to stimulate faster development of the newborn's lungs so that they reach the level of maturity sufficient for efficient work in the extrauterine environment. Such treatment reduces the incidence of the respiratory distress syndrome (RDS) and the incidence of intraventricular bleeding or necrotizing enterocolitis (NEC) [8].

The use of corticosteroids in the prenatal period, in cases of risk of preterm labor, gained popularity after the National Institute of Child Health and Human Development (NICHD) consensus meeting in 1994 [9]. There have been recommendations that corticosteroids should be given to all women with a gestational age of 24–34 at risk of preterm labor, which is now the standard of antenatal care. However, there is no unambiguous data to support treatment with corticosteroids in the late premature period [2].

Currently, numerous studies on the influence of betamethasone administration before parturition on the incidence of late prematurity complications from the respiratory system in newborns are being developed [10]. C. Gyamfi-Bannerman et al. [10] investigated the effect of administering betamethasone in two injections at a dose of 12 mg to pregnant patients from 34–36 weeks, who were at high risk of late preterm delivery, on the incidence of complications in newborns. Severe respiratory complications, transient neonatal rapid breathing, the need for surfactant and bronchopulmonary dysplasia were less common in the betamethasone treatment group compared to the placebo. However, it was associated with a higher incidence of hypoglycaemia in newborns in the test group.

Objectives

This study was conducted because of conflicting data on the role of corticosteroids administered before delivery in the late premature period. The aim of the study was to assess the frequency of respiratory disorders in 'late premature infants' and the impact of using prenatal steroid therapy.

MATERIAL AND METHODS

The study included 513 newborns born between the 34–36 week of pregnancy. They were divided into two groups. In the first group, there were 439 newborns (85.58%) who did not receive prenatal steroid therapy, and in the second group, there were 74 newborns (14.42%) born after the prenatal steroid course. The frequency of occurrence of respiratory disorders requiring the use of non-invasive respiratory support methods as well as intubation and mechanical ventilation was compared in both groups.

RESULTS

In the group of premature infants after steroid therapy 43/74 (58.12%) did not require respiratory support. In 27/74 newborns (36.49%), respiratory disorders requiring non-invasive ventilation were found. 4/74 (5.41%) of the infants required intubation and mechanical ventilation.

In the group of infants without prenatal steroid therapy 368/439 (83.8%) no respiratory disorders were found. 55/439 (12.53%) infants had breathing disorders requiring the use of non-invasive breathing support methods (CPAP, Duopap), and 16/439 (3.65%) infants had respiratory failure requiring intubation and mechanical ventilation (Tab. 1).

DISCUSSION

The effect of the administration of antenatal corticosteroids in the late premature period is controversial. Data concerning lack of a beneficial effect of prenatal steroid therapy in 'late premature infants' might be found in literature.

Mohammad K. Ramadan et al. [2] described 295 children who were divided into two groups: the test group

Table 1. Incidence of respiratory disorders

	Steroids		No steroids	
	n	%	n	%
No respiratory distress	43	58.1	368	83.8
Non-invasive ventilation	27	36.5	55	12.5
Mechanical ventilation	4	5.4	16	3.6
Total	74	100.0	439	100.0

Chi 2 = 28.471; p = 0.0000

(n = 74 patients) of neonates who received corticosteroids and the control group (n = 221) of patients who did not receive treatment. There was no statistically significant difference in the incidence of any adverse neonatal morbidity (47.3% vs to 40.7%) or in the percentage of neonatal morbidity composite (34.4% vs to 37.8%) between those two groups. Moreover, there was no statistically significant difference in the frequency of admitting newborns to the intensive care unit, and in the occurrence of acute respiratory distress syndrome, transient neonatal tachypnea, hypothermia, and the need for phototherapy. The presented studies clearly showed that administering corticosteroids before delivery to patients with late preterm labor does not reduce the incidence of short-term complications in newborns [14]. Porto et al. [11] also investigated the effect of corticosteroid treatment at 34–36 week of pregnancy. Their analysis included 143 treated patients and 130 of control group participants. Conclusions drawn from their research clearly indicated no reduction in the incidence of respiratory disorders in newborns whose mothers received corticosteroids [11].

The use of antenatal corticosteroids in LPP is supported by a retrospective cohort study of women conducted by Yinon et al. [12]. Women underwent amniocentesis to determine fetal lung maturity at 34–37 weeks of gestation [12]. Patients with negative results were divided into two groups: the test group treated with betamethasone (n = 83 women) and the control group in which the patients did not receive betamethasone therapy (n = 84 women). The study showed that the administration of steroids in the antenatal period after 34 weeks of pregnancy resulted in an improvement in neonatal results and should be considered, if the fetal lung immaturity is documented. The influence of prenatal steroids use was also investigated by Kamatkar S et al. [13]. Pregnant women were given two intramuscular injections containing 12 mg of betamethasone (equal parts of betamethasone sodium phosphate and betamethasone acetate) to the group after antenatal steroid therapy or its equivalent in form of placebo given 24 hours apart (placebo group). Researchers in their study showed that the use of noninvasive ventillation high-flow nasal cannula for at least two consecutive hours, or oxygen therapy of at least 0.30 for at least four uninterrupted hours, or mechanical ventilation was lower in the treatment group compared to placebo. Their studies show that the benefits of treating premature babies up to 34 weeks gestation clearly outweigh the risks of ACS. Still, this conclusion is less certain for premature babies between 34- and 37-weeks gestation due to the direct side effect of late steroid use, which was transient hypoglycaemia in the treatment group. Gyamfi-Bannerman C et al. [10] also observed a more frequent occurrence of hypoglycaemia in the newborns of the betamethasone group — hypoglycaemia occurred in 24.0% of newborns from the research group, while in the placebo group it was found in 15.0% [15].

Our study found a significantly higher incidence of respiratory disorders requiring treatment in the group of children after prenatal steroids when compared to the control group (83.8 vs 58.1%).

Respiratory disorders requiring the use of non-invasive methods of ventilation were more frequent in newborns from the steroid treatment group ($p < 0.05$). In this group, severe respiratory disorders requiring intubation and mechanical ventilation were also more frequent (5.4 vs 3.6%), taking that into consideration, the difference was also statistically significant $p < 0.05$).

CONCLUSIONS

If there is a risk of preterm labor in the 34–36 week of pregnancy, the use of steroid therapy should be considered. Steroidotherapy at this moment of gestation may not be such beneficial, like in the more premature delivery, before 34 weeks of pregnancy.

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

1. Blencowe H, Vos T, Lee ACC, et al. Estimates of neonatal morbidities and disabilities at regional and global levels for 2010: introduction, methods overview, and relevant findings from the Global Burden of Disease study. Pediatr Res. 2013; 74(Suppl 1): 4–16, doi: 10.1038/pr.2013.203, indexed in Pubmed: 24366460.
2. Ramadan MK, Hussein G, Saheb W, et al. Antenatal corticosteroids in the late preterm period: A prospective cohort study. J Neonatal Perinatal Med. 2016; 9(1): 15–22, doi: 10.3233/NPM-16915086, indexed in Pubmed: 27002271.
3. Child Trends. Databank (2014). Preterm births. http://www.childtrends.org/?indicators=preterm-births (16.10.2020).
4. Raju TNK, Higgins RD, Stark AR, et al. Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development. Pediatrics. 2006; 118(3): 1207–1214, doi: 10.1542/peds.2006-0018, indexed in Pubmed: 16951017.
5. Mally PV, Bailey S, Hendricks-Muñoz KD. Clinical issues in the management of late preterm infants. Curr Probl Pediatr Adolesc Health Care. 2010; 40(9): 218–233, doi: 10.1016/j.cppeds.2010.07.005, indexed in Pubmed: 20875895.
6. Hibbard JU, Wilkins I, Sun L, et al. Consortium on Safe Labor. Respiratory morbidity in late preterm births. JAMA. 2010; 304(4): 419–425, doi: 10.1001/jama.2010.1015, indexed in Pubmed: 20664042.
7. Avery CM, Liggins GC, Howie RN. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. Pediatrics. 1972; 50(4): 515–525, indexed in Pubmed: 4561295.
8. Dixon CL, Too G, Saade GR, et al. Past and present: a review of antenatal corticosteroids and recommendations for late preterm birth steroids. Am J Perinatol. 2018; 35(13): 1241–1250, doi: 10.1055/s-0038-1653944, indexed in Pubmed: 29791953.
9. Chien LY, Ohlsson A, Seshia MMK, et al. Canadian Neonatal Network. Variations in antenatal corticosteroid therapy: a persistent problem despite 30 years of evidence. Obstet Gynecol. 2002; 99(3): 401–408, doi: 10.1016/s0029-7844(01)01732-x, indexed in Pubmed: 11864666.

10. Gyamfi-Bannerman C, Thom E, Blackwell S, et al. Antenatal Betamethasone for Women at Risk for Late Preterm Delivery. New England Journal of Medicine. 2016; 374(14): 1311–1320, doi: 10.1056/nejmoa1516783.
11. Porto AM, Coutinho IC, Correia JB, et al. Effectiveness of antenatal corticosteroids in reducing respiratory disorders in late preterm infants: randomised clinical trial. BMJ. 2011; 342: d1696, doi: 10.1136/bmj.d1696, indexed in Pubmed: 21487057.
12. Yinon Y, Haas J, Mazaki-Tovi S, et al. Should patients with documented fetal lung immaturity after 34 weeks of gestation be treated with steroids? Am J Obstet Gynecol. 2012; 207(3): 222.e1–222.e4, doi: 10.1016/j.ajog.2012.06.019, indexed in Pubmed: 22749409.
13. Kamatkar S, Jobe A. Antenatal Late Preterm Steroids (ALPS): are we ready to accept it? J Perinatol. 2017; 37(6): 624–625, doi: 10.1038/jp.2017.25, indexed in Pubmed: 28333158.
14. Gyamfi-Bannerman C, Thom EA, Gyamfi-Bannerman C, et al. NICHD Maternal–Fetal Medicine Units Network. Antenatal betamethasone for women at risk for late preterm delivery. N Engl J Med. 2016; 374(14): 1311–1320, doi: 10.1056/NEJMoa1516783, indexed in Pubmed: 26842679.