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IMPACT OF CORTICOSTEROID USE ON GESTATIONAL OUTCOMES

IMPACTO DO USO DE CORTICOSTEROIDES NOS DESFECHOS GESTACIONAIS

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ABSTRACT: **Objective:** To assess the impact of corticosteroids on gestational outcomes. **Method:** This cross-sectional study included 257 pregnant women with newborns aged 34 weeks or less, who either received or did not receive a corticosteroid cycle. Outcomes assessed: admission to neonatal intensive care unit (NICU), respiratory distress syndrome (RDS), mechanical ventilation (MV), neurological impairment (NI), and death. **Results:** We found significant differences in NICU admission (70.8% vs. 91.4%, p=0.000) and mechanical ventilation (60.5% vs. 81.7%, p=0.000). However, we observed no significant differences in respiratory distress syndrome (55.4% vs. 64.8%, p=0.129), neurological impairment (3.1% vs. 7.1%, p=0.167), or neonatal death (0.8% vs. 3.2%, p=0.211) between the corticosteroid and non-corticosteroid groups. **Conclusion:** Corticosteroid use significantly reduced the need for NICU admission and mechanical ventilation, highlighting its importance in improving preterm infant outcomes. **Keywords:** Corticosteroids. Preterm Birth. Respiratory Distress Syndrome. Morbidity.

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RESUMO: **Objetivo:** Avaliar o impacto do uso de corticosteroides nos desfechos gestacionais. **Método:** Estudo de corte transversal, com 257 gestantes, com recém-nascidos de 34 semanas ou menos, que fizeram ou não ciclo de corticoide. Desfechos avaliados: ingresso em UTI neonatal (UTIneo), síndrome do desconforto respiratório (SDR), ventilação mecânica (VM), prejuízo neurológico (PN) e morte. **Resultados:** Diferiram quanto ingresso em UTI neonatal (70,8% vs 91,4% p=0,000) e necessidade de ventilação mecânica (60,5% vs 81,7% p=0,000). Não foi encontrada diferença na síndrome do desconforto respiratório (55,4% vs 64,8% p=0,129), prejuízo neurológico (3,1% vs 7,1% p=0,167) e morte neonatal (0,8% vs 3,2%p=0,211), com e sem uso de corticoide respectivamente. **Conclusão:** O corticoide teve impacto positivo na diminuição do tempo de internação em UTI neonatal e ventilação mecânica, enfatizando a importância dos corticoides para melhor evolução do prematuro.

PALAVRAS-CHAVE: Corticoides. Morbidade. Prematuridade. Síndrome do Desconforto Respiratório.

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INTRODUCTION

Administering corticosteroids before preterm birth is one of the most important and effective prenatal therapies available to improve gestational outcomes and neonatal prognosis[1]. It has been used since 1972 to accelerate fetal lung maturation and reduce the incidence of neonatal respiratory distress syndrome. This practice is considered the standard treatment and has been increasingly used over the years[2].

Respiratory distress syndrome (RDS) is a severe complication of preterm birth and the leading cause of early neonatal death and disability. It affects up to half of the babies born before 28 weeks and one-third born before 32 weeks[3].

Respiratory failure in these infants results from surfactant deficiency, poor anatomical lung development, and immaturity in other organs[3]. Fetal lung development has five stages: embryonic, pseudoglandular, canalicular, saccular, and alveolar. The lung first appears as an extension of the primitive gut 22 to 26 days after conception. Mature lungs contain over 40 different cell types derived from this initial tissue. From 8 to 16 weeks of gestation, the main bronchial airways and associated pulmonary respiratory units progressively form. At this time, pulmonary blood vessels also begin to grow in parallel. From 17 to 25 weeks of gestation, the airways develop, forming the terminal bronchioles, which subsequently give rise to the terminal sacs (primitive alveoli). These are the functional units of the lung[4].

In this stage, the air-blood interface begins—a crucial process for effective air exchange, which only occurs in the terminal bronchioles. From 28 to 35 weeks of gestation, alveoli can be counted, and as gestational age increases, they become more mature. Lung volume increases fourfold between 29 weeks and term. At birth, there are approximately 150 million alveoli, representing half the number expected in an adult. Alveoli, in turn, produce surfactant. The low alveolar count likely contributes to respiratory dysfunction in a preterm newborn[4].

The fetal lung also matures biochemically throughout gestation. Lamellar bodies, responsible for storing surfactants, appear between 22 and 24 weeks. Surfactant is a complex mixture of lipids and proteins that maintains stability during expiration, preventing alveolar collapse. Preterm infants present both qualitative and quantitative surfactant deficiencies, predisposing them to RDS. With low lung volume during expiration, surface tension becomes too high, leading to atelectasis, subsequent intrapulmonary shunting, ventilation-perfusion mismatch, and eventually respiratory failure[4].

Studies have demonstrated that antenatal corticosteroids, such as intramuscular dexamethasone or betamethasone, cross the placenta and induce fetal lung maturation[3]. These medications accelerate the appearance of the pulmonary surfactant. The hypothesis is that corticosteroids trigger ribonucleic acid synthesis, which encodes specific proteins involved in the biosynthesis of phospholipids or glycogen breakdown[4].

Given the prevalence of preterm births and the high need for corticosteroid administration during pregnancy, which frequently affects gestational outcomes, it is essential to gather data supporting this theory. Therefore, this study aims to evaluate the impact of corticosteroid administration on gestational outcomes.

METHODOLOGY

We conducted a cross-sectional study with a sample of postpartum women from Maternidade Darcy Vargas in Joinville (SC), divided into two groups based on the use or non-use of corticosteroids during the prenatal period. The study followed the requirements of CNS Resolution 466/2012, ensuring

the principles of data confidentiality. With the maternity hospital's approval, we submitted this study to the Research Ethics Committee (CEP) and the Brazil platform (CAAE) 58076122.1.0000.5366. The researchers signed the commitment agreement for data use.

The inclusion criteria were postpartum women with newborns of 34 weeks or less, who either completed or did not complete the full cycle of corticosteroids during the prenatal period. We excluded records with incomplete data.

We extracted data on outcomes and sociodemographic variables, including age, marital status, race, adequacy of prenatal care, associated pathologies, alcohol use, and smoking habits, from the hospital's records between 01/31 and 03/03 of 2023. Additionally, we collected information on neonatal characteristics and adverse outcomes, such as admission to the neonatal intensive care unit (NICU), occurrence of respiratory distress syndrome (RDS), need for mechanical ventilation (MV), neurological impairment (NI), and death.

We analyzed the data using the Statistical Package for the Social Sciences (SPSS) version 21.0 software. Quantitative variables were presented as means and standard deviations, while qualitative variables were presented as absolute and relative frequencies. We evaluated qualitative variables using the chi-square test, and when the subjects were equal to or less than 5, we applied Fisher's exact test. For quantitative variables, we used the Kolmogorov-Smirnov normality test. For normally distributed variables, we applied the Student's t-test, and for non-normally distributed variables, we used the Mann-Whitney test. We considered p-values less than 0.05 to be significant.

RESULTS

In this study, we included 257 pregnant women, taking into account the inclusion criteria. Table 1 presents the maternal characteristics, including maternal pathologies, where we predominantly observed hypertensive disorders of pregnancy (HDP), gestational diabetes mellitus (GDM), urinary tract infection (UTI), and chronic arterial hypertension. The predominant maternal age range in both groups was 25 to 29 years.

Table 1 – Maternal characteristics

	Corticosteroid Yes N=129	**Corticosteroid No N=128**	**P**
Age (years)			0,650*
<20	11 (8,5%)	10 (7,8%)	
20 – 24	32 (24,6%)	31 (24,2%)	
25 – 29	36 (27,7%)	25,8%)	
30 – 34	27 (20,8%)	26 (20,3%)	
35 – 39	15 (11,5%)	20 (15,6%)	
40 – 44	6 (4,6%)	8 (6,3%)	
>40	3 (2,3%)	0	
Marital status	0,693*		
Married	19 (14,7%)	26 (20,3%)	
Single	99 (76,7%)	92 (71,9%)	
Common-law marriage	5 (3,9%)	4 (3,1%)	
Divorced	6 (4,7%)	6 (4,7%)	
Race	0,082*		
White	97 (73,8%)	110 (85,9%)	
Black	7 (5,4%)	8 (6,3%)	
Indigenous	1 (0,8%)	0	
Prenatal care completed	127 (98,4%)	126 (98,4%)	0,507*
Associated conditions			
GDM	23 (17,7%)	31 (24,2%)	0,222*
Pre-existing DM	4 (3,1%)	3 (2,3%)	1,000**
HDP	28 (21,5%)	41 (32,0%)	0,068*
Chronic Hypertesion	15 (11,5%)	18 (14,1%)	0,580*
COVID-19	8 (6,2%)	3 (2,3%)	0,217**
UTI	40 (30,8%)	44 (34,4%)	0,596*
Alcohol use	7 (5,4%)	4 (3,1%)	0,279**
Smoking	18 (13,8%)	14 (10,9%)	0,302*

Source: Author. * Chi-square test; ** Fisher's exact test; *** Mann-Whitney test

Table 2 shows the characteristics of the newborns, where the average gestational age was slightly higher in the group of women who received corticosteroids compared to those who did not. We observed a higher incidence of vaginal births in the group that received corticosteroids compared to the group that did not. The average birth weight of newborns was higher in the pregnancies where corticosteroids were administered and lower in those without corticosteroid administration. Regarding magnesium sulfate, we observed a significantly higher usage among women who received corticosteroids than those who did not.

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Table 2 – Newborn characteristics

Newborn	**Corticosteroid Yes N=129**	**Corticosteroid No N=128**	**P**
Gestational age	32,1 (±2,72)	30,9 (±2,8)	0,000***
Vaginal birth	79 (60,8%)	60 (46,9%)	0,017*
Weight	1982,6gr (±580)	1589,2 (±611)	0,000***
Weight classification	0,099*		
PIG	18 (12,4%)	33 (24,0%)	
AIG	106 (82,2%)	87 (69,6%)	
GIG	5 (3,9%)	5 (4,0%)	
Malformation	1 (0,8%)	3 (2,3%)	0,370***
Magnesium sulfate	77 (60,6%)	10 (7,7%)	0,000*

Source: Author. SGA - Small for gestational age; AGA - Appropriate for gestational age; LGA - Large for gestational age; * Chi-square test; ** Fisher's exact test; *** Mann-Whitney test.

Table 3 outlines the neonatal outcomes in both groups, with and without corticosteroid use during pregnancy. We found that the rate of NICU admission was significantly higher in the group that did not receive corticosteroids. Additionally, we observed a higher rate of mechanical ventilation in newborns from the group without corticosteroid administration compared to the corticosteroid group. Regarding the rates of RDS, neurological impairment, and neonatal death, there was no statistical significance, making it impossible to compare these factors in this study.

Tabela 3 – Adverse neonatal outcomes

	Corticosteroid Yes N=129	**Corticosteroid No N=128**	**P**
NICU	92 (71,3%)	117 (91,4%)	0,000*
RDS	72 (55,4%)	83 (64,8%)	0,129*
Mechanical ventilation	78 (60,5%)	103 (81,7%)	0,000*
Neurological impariment	4 (3,1%)	9 (7,1%)	0,167**
Death	1 (0,8%)	4 (3,2%)	0,211**

Source: Author. NICU - Neonatal Intensive Care Unit; RDS - respiratory distress syndrome; * Chi-square test; ** Fisher's exact test; *** Mann-Whitney test.

DISCUSSION

Administering corticosteroids during pregnancy has proven to be an important tool in caring for and ensuring the proper development of preterm infants. Corticosteroids play a key role in intrauterine development, especially toward the end of gestation, by supporting the development of organs and tissues that enable the newborn to survive outside the womb[10], with the lungs being one of the most critical organs for immediate survival[11]. Consistent with this, the results presented in this study highlight that corticosteroid use in preterm infants reduces the risk of NICU admission. This likely occurs because corticosteroid therapy promotes fetal lung maturation, regulated by cortisol secretion[14]. Its mechanism involves the release or increase of surfactant, along with accelerating fluid absorption in the lungs[13].

This study also showed a reduced need for mechanical ventilation in newborns who received corticosteroids. This finding aligns with the 2019 European Consensus Guidelines on the Management of Respiratory Distress Syndrome, which report that corticosteroid administration up to the 34th week of gestation in twin pregnancies reduced the need for mechanical ventilation by approximately 50%[8]. Moreover, corticosteroid administration can sometimes prevent intubation[8], contributing positively to the recovery of preterm infants.

We did not find statistically significant differences in the occurrence of RDS between the groups with and without corticosteroid use. However, further studies are needed to investigate whether corticosteroid use prevents severe forms of the condition, as the pathophysiology of RDS involves lung immaturity and a deficiency in endogenous surfactant production[9]. It is known that corticosteroid therapy is based on the premise that preterm infants lack adequate exposure to endogenous corticosteroids for organ maturation[14]. Thus, exogenous administration mimics the increase in endogenous corticosteroids that would naturally occur in a full-term pregnancy, preparing the fetus for life outside the womb[12].

This study did not find statistically significant associations between corticosteroid non-use and neurological impairment. However, some studies have observed a positive impact on the neurological development of infants exposed to corticosteroids during pregnancy[13,15], indicating the need to further investigate this hypothesis.

We did not find statistically significant results when comparing neonatal death rates between those who received corticosteroids and those who did not. This is likely due to the small sample size, which limited the ability to effectively compare this outcome.

Corticosteroids are accessible, easy to administer, and effective during pregnancy. Their benefits include promoting intrauterine lung development, reducing respiratory complications, and decreasing the need for mechanical ventilation in newborns, which positively affects neonatal morbidity and mortality. Additionally, their use may yield economic benefits and positively influence global health systems. Nevertheless, further studies are required to investigate the effects of corticosteroids, particularly regarding their influence on growth, the hypothalamic-pituitary-adrenal axis, and neuropsychomotor development

CONCLUSION

This study demonstrated worse neonatal outcomes when corticosteroids were not administered during pregnancy, emphasizing the importance of this medication in preventing morbidity in preterm infants. Proper and well-indicated use of corticosteroids improves respiratory support and assists in the

appropriate development of preterm newborns. While the benefits are well-established, further studies to confirm their effects on the fetus, particularly in neurological development, are crucial to enhancing the safety of their use in practice and assuring healthcare professionals of the appropriateness of their administration. It should also be noted that this study faced some limitations, particularly the small final sample size due to the inclusion and exclusion criteria applied.

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