Antenatal Corticosteroids
Who Should We Be Treating?

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KEYWORDS

• Antenatal corticosteroids • Prematurity • Preterm birth • Preterm labor
• Respiratory distress syndrome

KEY POINTS

- Antenatal corticosteroids are a crucial treatment in improving neonatal outcomes for those patients at risk for preterm birth.
- Reduction in neonatal morbidities include respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis.
- Therapeutic benefits have been demonstrated as early as 23 weeks' gestation, and recent data have supported neonatal benefit through the late preterm period.

INTRODUCTION

One of the most important antenatal therapies to improve outcomes for patients at risk for preterm birth is antenatal corticosteroids.[1,2] As early as 1969, Liggins[2] noted that lambs who received glucocorticoids and then delivered prematurely had lungs that remained partially expanded. This preliminary evidence led to a randomized, controlled trial of betamethasone therapy on 282 mothers who were at risk for preterm delivery, to assess the effect of steroids on neonatal morbidity and mortality. They found that in pregnancies at risk for premature delivery, when treated with corticosteroids, infants demonstrated a decreased risk of respiratory distress syndrome (RDS) compared with those not treated with steroids.[3] Additionally, they found that early neonatal mortality was 3.2% in the antenatal corticosteroid treated group and 15.0% in the controls ($P = .01$). From these early studies, Liggins[3] hypothesized that glucocorticoids caused premature liberation of surfactant into the alveoli, by induction of an enzyme related to the biosynthesis of surfactant.

The authors of this article have no commercial or financial conflicts of interests, and no funding sources were used in the composition of this article.
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Clin Perinatol ■ (2018) ■–■
https://doi.org/10.1016/j.clp.2018.01.002
perinatology.theclinics.com

Mechanism of Action

Antenatal corticosteroids affect the fetal lungs through multiple processes (**Box 1**). They stimulate development of both type I and type II pneumocytes, which are surface epithelial cells of the lung alveoli. Type II pneumocytes contain phospholipid multilamellar bodies, the precursors to pulmonary surfactant.[4] The saccular stage of lung development begins at 24 to 28 weeks' gestation and is when type II pneumocytes first appear. It is at this phase that steroid administration has the clear capability to induce type II pneumocytes to increase surfactant production.[5] Additionally, glucocorticoids act to increase lung compliance and maximal lung volume, as well as to reduce protein extravasation from the pulmonary vasculature to the airspace, thereby helping to clear lung fluid before delivery. These biochemical and structural effects on the lung are the basis for improved clinical outcomes after glucocorticoid treatment.[4]

Clinical Efficacy

RDS is a syndrome most commonly diagnosed in premature neonates, clinically characterized by tachypnea, tachycardia, chest wall retractions, expiratory grunting, and nasal flaring. It likely occurs owing to insufficient production of pulmonary surfactant and structural immaturity of the lungs. The incidence of RDS increases with earlier gestational ages, and is highest in infants before 28 weeks' gestation.[6] Approximately 1% of newborn infants are affected by RDS and it is the leading cause of death in babies who are born prematurely.[6,7] The introduction of antenatal steroids for the acceleration of fetal lung maturity and the development of exogenous surfactant has demonstrated reduced rates of RDS in randomized trials worldwide.[8] A recent 2017 Cochrane review of all randomized trials comparing treatment with antenatal corticosteroids versus placebo in patients at risk for preterm birth demonstrated a significant

Box 1
Effects of antenatal corticosteroids on fetal lungs

Anatomy and biochemistry
- Thinning of the mesenchyme of the alveolar-capillary structure
- Increased saccular and alveolar gas volumes
- Decreased alveolar septation
- Increased antioxidant volumes
- Increased surfactant

Physiology
- Increase compliance
- Improved gas exchange
- Decreases epithelial permeability
- Protection of the preterm lung from injury during resuscitation

Interactions with exogenous surfactant
- Improved surfactant treatment responses
- Improved surfactant dosage–response curve
- Decreases inactivation of surfactant

Clinical
- Decreases incidence of respiratory distress syndrome
- No effect on the incidence on bronchopulmonary dysplasia
- Decreased mortality

(*From* Jobe AH, Kamath-Rayne BD. Fetal lung development and surfactant. In: Creasy RK, Resnik R, Greene MF, et al, editors. Creasy and Resnik's maternal-fetal medicine: principles and practice. Philadelphia: Elsevier/Saunders; 2014. p. 184; with permission.)