15. PRETERM LABOR, CORTICOSTEROIDS FOR FETAL MATURATION

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This review is based primarily on the results of a National Institutes of Health (NIH) consensus development panel on the effect of corticosteroids for fetal maturation on perinatal outcomes (NIH Consensus Statement, 1994). This publication comprehensively reviews the available literature on antenatal corticosteroid administration, its risks and benefits, and makes specific treatment recommendations. It also contains a meta-analysis of available randomized trials of antenatal corticosteroid administration.

IMPORTANCE

Preterm birth (commonly defined as delivery prior to 37 weeks gestation) occurs in 7-10 percent of pregnancies and is a major cause of infant morbidity and mortality. Preterm births are associated with more than $2 billion in health care costs annually (NIH, 1994) and are the second leading cause of infant deaths in the United States. Neonatal complications such as respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC) contribute to morbidity and mortality. Multiple randomized controlled trials have demonstrated that the administration of corticosteroids to the mother prior to delivery when preterm birth is anticipated can result in significant reductions in these adverse outcomes. The NIH (1994) reports that only 12-18 percent of women who deliver preterm infants weighing 500-1500 grams actually receive this therapy.

EFFICACY AND/OR EFFECTIVENESS OF INTERVENTIONS

Data on the risks and benefits of antenatal steroid administration in preterm delivery come from two sources: meta-analysis of 15 randomized controlled trials (NIH, 1994) and a large observational data set. The observational data come from two large multi-center networks studying preterm birth, and from several randomized trials of neonatal surfactant administration after preterm delivery, in which data on
antenatal steroid administration were available. Data on more than 30,000 preterm infants are available.

The meta-analysis showed a reduction in the incidence of neonatal mortality (OR 0.6, 95 percent CI 0.5-0.8) and RDS (OR 0.5, 95 percent CI 0.4-0.6) when antenatal corticosteroids were administered to mothers of infants born at 24-34 weeks gestation. Similarly, results from the meta-analysis showed a decrease in IVH (OR 0.5, 95 percent CI 0.3-0.9) with antenatal steroid administration. These findings have been confirmed in the observational studies. Although the meta-analysis of randomized trials showed a reduction in NEC, the observational data showed no reduction in this outcome. The beneficial effects of antenatal steroids are seen consistently in babies of both sexes and in both white and nonwhite infants.

Dexamethasone and betamethasone, in doses of 6 mg every 12 hours for four doses, and 12 mg every 12 hours for 2 doses, respectively, have been shown to be effective. No other antenatal corticosteroid has been extensively studied. Maximum benefit to the infant appears to begin at 24 hours after the initiation of treatment, but some benefit begins even prior to this time. No benefit has been demonstrated in infants beyond 34 weeks gestation.

One possible explanation for the low prevalence of use of this intervention, despite its demonstrated efficacy, is the concern about adverse short and long term effects on both mother and infant. Several studies have followed infants for as long as 12 years following corticosteroid administration and have shown no adverse outcomes in the areas of motor skills, language, cognition, memory, concentration, or scholastic achievement. Because of the possible increased risk of neonatal and maternal infection, the use of antenatal steroids in preterm premature rupture of the membranes (PPROM) remains controversial. The risk of maternal infection after steroid administration may be increased in the case of PPROM; however, there is no evidence that steroid administration interferes with the ability to make the diagnosis. There is also concern about an increased risk of neonatal infection. In the meta-analysis cited above, the typical OR of neonatal infection in infants with PPROM after steroid administration
was 1.29, 95 percent CI 0.74-2.26. However, steroids are associated with a significant reduction in RDS in this group as well (OR 0.50, 95 percent CI 0.38-0.66). The NIH (1994) cites "...strong evidence from observational studies that even in the presence of PPROM, the incidence of neonatal mortality and IVH is reduced when antenatal corticosteroids are used. Although the risk of neonatal infection associated with antenatal corticosteroid use in the face of PPROM may be increased, the magnitude of the increase is small. Because of the effectiveness of antenatal corticosteroids in reducing mortality and IVH in fetuses of less than 30-32 weeks gestation, antenatal corticosteroid use is appropriate in the absence of chorioamnionitis." An American College of Obstetricians and Gynecologists (ACOG) committee opinion (ACOG Committee Opinion, 1994) states the support of the ACOG for all of the conclusions of the NIH panel, with the exception of the one pertaining to PPROM. The ACOG Committee (1994) feels that "...further research is needed to evaluate the risks and benefits of using corticosteroids in women who have preterm PROM" although they do not cite specific research questions to be addressed.
RECOMMENDED QUALITY INDICATORS FOR CORTICOSTEROIDS FOR FETAL MATURATION IN LABOR

The following criteria apply to all women admitted to the hospital for preterm labor or for delivery.

Treatment

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Quality of evidence</th>
<th>Literature</th>
<th>Benefits</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1. Women admitted to the hospital with labor, between 24 and 34 weeks gestation and without ruptured membranes, should receive antenatal steroids, even if delivery is anticipated in less than 24 hours.</td>
<td>I</td>
<td>Crowley, 1994; in NIH, 1994</td>
<td>Reduce neonatal mortality and intraventricular hemorrhage.</td>
<td>Currently, less than 20% of women who deliver preterm receive antenatal steroids. The use of antenatal steroids under these conditions results in a reduction in neonatal mortality (OR=0.6), RDS (OR=0.5), IVH (OR=0.5) and NEC. Serious adverse effects on mother and infant have not been proven, but each may be at an increased risk for infection if used in PPROM. We assume that fetuses of mothers admitted to the hospital for preterm labor at these gestational ages are at risk for preterm delivery.</td>
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<td>2. Steroid treatment should consist of either: - Betamethasone 12 mg. IM q24h x 2, or - Dexamethasone 6 mg. IM q12h x 4.</td>
<td>I</td>
<td>NIH, 1994</td>
<td>Reduce neonatal mortality and intraventricular hemorrhage.</td>
<td>These regimens have been proven to be effective.</td>
</tr>
<tr>
<td>3. Women admitted to the hospital at 24-32 weeks gestation with ruptured membranes should receive antenatal steroid administration.</td>
<td>II-2</td>
<td>NIH, 1994</td>
<td>Reduce neonatal mortality and intraventricular hemorrhage.</td>
<td>Reduction in infant mortality and IVH with a relatively small increase in the risk of neonatal infection. An ACOG committee feels that the available information does not provide a clear indication for the use of antenatal steroids in the presence of PPROM.</td>
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Quality of Evidence Codes:

I: RCT
II-1: Nonrandomized controlled trials
II-2: Cohort or case analysis
II-3: Multiple time series
III: Opinions or descriptive studies
REFERENCES — CORTICOSTEROIDS FOR FETAL MATURATION IN LABOR
