Antenatal Late Preterm Steroids (ALPS): Benefits & Barriers

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March 2017

This activity is jointly-provided by SynAptiv and the Colorado Hospital Association
Disclosures

• No disclosures regarding commercial interests
• I was the Principal Investigator at the University of Colorado site for the NIH ALPS trial.

Objectives

• Cite the excess morbidity of infants delivering at 34-36 weeks.
• Cite the primary benefit demonstrated in the ALPS study.
• Cite one neonatal complication of ALPS.
• State ACOG/SMFM recommendations for ALPS.
• Implement ALPS recommendations in your practice by identifying and overcoming barriers.
Have you cared for one or more patients who have received ALPS?

Yes _____  No _____
Antenatal Late Preterm Steroids

Do you feel confident about when to use and when not to use ALPS?

Yes _____  No _____

US preterm births: Change 1992-02

MOD: Davidoff 2005
### US Late Preterm Singleton Births

- <32 weeks: 40%
- 32 weeks: 14%
- 33 weeks: 5%
- 34 weeks: 7%
- 35 weeks: 13%
- 36 weeks: 22%

**75% of all pts!**

Source: NCHS, final natality data
Prepared by March of Dimes Perinatal Data Center, April 2006.

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### Adjusted Odds of RDS by GA at Birth

- 34 weeks: 40.1
- 35 weeks: 21.9
- 36 weeks: 9.1
- 37 weeks: 3.1
- 38 weeks: 1.1
- 39-40 weeks: 1

The Consortium on Safe Labor, JAMA 2010;304:419-425.
Morbidity in Late Preterm Infants

- Significant increases compared to 39 weekers in:
  - IVH, grade 1 or 2
  - Culture-proven sepsis
  - Necrotizing Enterocolitis (NEC)
  - Ventilator use

McIntyre & Leveno, *Obstetrics and Gynecology* 2008; 111:35-41

Mortality in Late Preterm Infants

- Late Preterm births: 2,221,545 (7.3%)
- Late Preterm deaths: 18,484 (9.8%)
- Mortality in late preterm infants:
  - Early Neonatal (0-6 d) Mortality: 6 x Term
  - Late Neonatal (7-28 d) Mortality: 2 x Term
  - Infant Mortality (birth – 1 year): 3 x Term
- Higher risk persists even after excluding congenital anomalies

Antecedents to Late Preterm Delivery

<table>
<thead>
<tr>
<th>Spontaneous (PTL, PPROM)</th>
<th>Indicated (NRFHT, severe preeclampsia/HELLP, abruption, previa)</th>
<th>Elective (NS/NI) (Repeat C/S, IUGR w/ normal testing, oligo, multiples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1821/2693</td>
<td>378/2693</td>
<td>494/2693</td>
</tr>
<tr>
<td>67.6%</td>
<td>14.0%</td>
<td>18.3%</td>
</tr>
</tbody>
</table>

Gyamfi-Bannerman et al, AJOG. 2011;205:456.e1-6

The NEW ENGLAND JOURNAL of MEDICINE

Antenatal Betamethasone for Women at Risk for Late Preterm Delivery


Objective

To assess whether administration of betamethasone to women likely to deliver in the late preterm period decreased respiratory and other neonatal morbidities

Methods

• Multicenter double-blind randomized, placebo-controlled trial

• 17 MFMU university-based medical centers
  – Both academic and community hospitals

• 2010-2015
Eligibility

• Women with a high likelihood of delivery from 34 0/7 to 36 6/7 weeks

• Specific criteria:
  – Preterm Labor Intact Membranes
    • At least 3 cm dilated or 75% effaced
  – Preterm PROM
  – Indicated preterm delivery
    • Indication at the discretion of the provider
    • Between 24 hours and <7 days after randomization

Exclusion Criteria

• PPROM with active labor
  – ≥6 CTX/hour or ≥3 cm dilated
• Chorioamnionitis
• Cervical dilation ≥8cm
• Non-reassuring fetal status requiring delivery
• Delivery expected within 12 hours
Exclusion Criteria

- Previous course of antenatal corticosteroids
- Pre-gestational diabetes
  - Unblinding
- Candidate for stress-dose steroids
- Known major fetal anomaly
- Other contraindication to betamethasone

Randomization

- Randomly allocated 1:1 ratio

  - Betamethasone (12mg)
    - 2mL IM x 2 doses
    - 24 hours apart
  - Identical placebo
    - 2mL IM x 2 doses
    - 24 hours apart

- Tocolysis was not employed as part of this trial
Primary Outcome

• Composite describing need for respiratory support
  – Oxygen with FiO₂ ≥30% for at least 4 hrs
  – CPAP or high flow nasal cannula for at least 2 hrs
  – Mechanical ventilation
  – ECMO

• All within 72 hrs of birth
• Stillbirth and neonatal death before 72 hrs

Secondary Outcomes

• Severe respiratory morbidity
  – Same composite as primary outcome
    • Oxygen with FiO₂ ≥30% for at least 24 hrs
    • CPAP or high flow nasal cannula for at least 12 hrs
Primary Outcome

• Composite of Need for Respiratory Support

Relative Risk 0.80, 95% CI 0.66-0.97
P=0.02
The number needed to treat = 35

Secondary Outcome

• Severe Respiratory Morbidity

Relative Risk 0.67, 95% CI 0.53-0.84
P<0.001
The number needed to treat = 25
Antenatal betamethasone given to women at high risk for late preterm delivery significantly decreased the need for respiratory support.

Also decreased relative risk for:

- Prolonged stay in the NICU: 11%
- Transient tachypnea of the newborn: 33%
- The need for surfactant: 41%
- Bronchopulmonary dysplasia: 78%
  - Prognostic of childhood chronic lung disease

- No difference in maternal or neonatal infectious morbidity
- No difference in birth weight or SGA
- Beneficial in the absence of tocolysis
- Hypoglycemia, a known late preterm complication, occurred more frequently after betamethasone exposure
- Associated with shorter Intermediate/NICU stays
- Suggest postnatal glucose assessment
  - Already recommended by the AAP
Antenatal corticosteroids for maturity of term or near term fetuses: systematic review and meta-analysis of randomized controlled trials

Gabriele Saccione, Vincenzo Berghella

ABSTRACT
OBJECTIVE
To evaluate the effectiveness of antenatal corticosteroids given at 25-4 weeks' gestation.

DESIGN
Systematic review with meta-analysis.

DATA SOURCES
Electronic databases were searched from their inception to February 2016.

Eligibility criteria for study selection
Randomized controlled trials comparing antenatal corticosteroids with placebo or no treatment in women with a singleton pregnancy at 25-4 weeks' gestation. Trials on antenatal steroids in women expected to deliver preterm (34-36 weeks) and trials given before planned cesarean delivery at term (37 weeks) and to <1.95, lower maximum inspired oxygen concentration (0.06-0.6%), shorter stay in a neonatal intensive care unit (7.4 days), and higher APGAR scores compared with controls. Infants of mothers who received antenatal betamethasone at 34-36 weeks' gestation had a significantly lower incidence of transient tachypnea of the newborn relative risk 0.22, 95% confidence interval 0.16 to 0.29, severe RDS (0.40, 0.33 to 0.54), and use of surfactant (0.61, 0.38 to 0.99). Infants of women undergoing planned cesarean delivery at 37 weeks' gestation who received prophylactic antenatal corticosteroids 48 hours before delivery had a significantly lower risk of RDS (0.40, 0.27 to 0.60), mild RDS (0.43, 0.36 to 0.53), moderate RDS (0.46, 0.18 to 0.88), transient tachypnea of the newborn (0.38, 0.25 to 0.57), and

Obstetric Societies
Implementation of the use of antenatal corticosteroids in the late preterm birth period in women at risk for preterm delivery

Society for Maternal-Fetal Medicine (SMFM) Publications Committee

Committee Opinion
Antenatal Corticosteroid Therapy for Fetal Maturation

SMFM Statement
smfm.org

The American College of Obstetricians and Gynecologists
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Committee on Obstetric Practice
This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Obstetric Practice in collaboration with members of the Committee on Perinatal Nutrition and the Committee on Fetal Homeostasis Committee on Perinatal Nutrition.

The information and conclusions or recommendations expressed in this statement are those of the authors and do not necessarily reflect the opinion or policies of the American College of Obstetricians and Gynecologists. This statement should not be construed as an endorsement of a particular product or service.

Antenatal Corticosteroid Therapy for Fetal Maturation

Number 677 • October 2016

Committee on Obstetric Practice
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Considerations and Challenges

• ACOG 2016
  – Not indicated in women diagnosed with an intrauterine infection
  – Tocolysis should not be used to delay delivery for antenatal steroids in LP
  – Indicated preterm delivery (i.e. severe preeclampsia) should not be delayed

Considerations and Challenges

• ACOG 2016
  – Groups not studied and so unknown benefit
    • Multiple gestation
    • Pregestational diabetes
    • Previous steroid course
  – Overuse of steroids
    • Optimal therapeutic window is 2-7 days
    • Only 20-40% of women delivered in that window following steroids – Adams et al AJOG 2015
**SMFM recommendations**

1. In women with a singleton pregnancy between 34 weeks 0 days and 36 weeks 6 days of gestation who are at high risk for preterm birth within the next 7 days (but before 37 weeks of gestation), we recommend treatment with betamethasone (2 doses of 12 mg intramuscularly 24 hours apart).

2. In women with preterm labor symptoms in the late preterm period, we recommend waiting for evidence of preterm labor, such as a cervical dilatation of at least 3 cm or effacement of at least 75%, before treatment with betamethasone.

3. In women with late preterm pregnancies receiving betamethasone, we recommend against the use of tocolysis in an attempt to delay delivery to complete the steroid course because it is unclear whether the benefits of betamethasone administration are outweighed by the risks of attempts to delay delivery.

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**SMFM recommendations**

4. In women with late preterm pregnancies with a potential medical indication for delivery, we recommend betamethasone not be given unless there is a definitive plan for late preterm delivery.

5. We recommend that institutions utilize standard guidelines for the assessment and management of neonatal hypoglycemia in late preterm newborns.

6. We recommend against implementation of the Antenatal Late Preterm Steroids protocol for conditions not studied in the randomized controlled trial unless performed as part of research or quality improvement.
A reasonable assessment of delivery imminence should guide administration of antenatal steroids in the late preterm period

- PTL - 3cm, 75% effaced
- and/or
- Within 7 days but not for 8-12 hours

Have you cared for one or more patients who have received ALPS?

Yes _____  No _____
Antenatal Late Preterm Steroids

Do you feel confident about when to use and when not to use ALPS?

Yes _____     No _____

Antenatal Late Preterm Steroids

Does your obstetrical unit have a formal policy about use of ALPS?

Yes _____     No _____     Don’t Know _____
What are/were the barriers to implementing ALPS?

- Remembering who are the candidates for ALPS
- Identifying exactly who is a candidate; judging who is likely to deliver in the “window”
- Worry about side effects
- Too busy with other priorities
- Insurance payment
Antenatal Late Preterm Steroids

How can or did you or your obstetrical service overcome these barriers?

• ___________________________________________________________________
• ___________________________________________________________________
• ___________________________________________________________________
• ___________________________________________________________________
• ___________________________________________________________________
• ___________________________________________________________________

Antenatal Late Preterm Steroids

How can or did you or your obstetrical service overcome these barriers?

• Identify a “champion” or team of “champions”
• Use the ACOG/SMFM recommendations as a template
• Prepare formal policy
• ? make ALPS a quality measure