Antenatal corticosteroids in preterm small-for-gestational-age infants: what is the evidence?

Dr Clare Thiele
clare.thiele@health.qld.gov.au
Department of Obstetrics and Gynaecology, Logan Hospital QLD Australia

Introduction
While the benefits of antenatal corticosteroids (ACS) in preterm delivery have been well established for decades, the role of ACS for small-for-gestational-age (SGA) infants is less clear. SGA babies are a heterogeneous group of infants that may not have reached their growth potential due to a variety of maternal, placental or fetal factors. In fetal growth restriction (FGR), variations in the timing, intensity and duration of placental restriction results in different cardiovascular, neuroendocrine and metabolic responses. The current literature is inconsistent regarding the benefits or harms of ACS in preterm SGA. This poster reviews recently published literature and guidelines on the use of ACS in preterm SGA.

Key adaptations in fetal growth restriction
• Cardiovascular, e.g. redistribution of cardiac output
• Neuroendocrine, e.g. increased adrenaline and noradrenaline
• Hypothalamic pituitary axis, e.g. high cortisol levels
• Decreased size of fetal brain and reduced neuronal growth
• Decreased bone and muscle growth

Methods
Current Australian and New Zealand as well as Royal College of Obstetrics and Gynaecology (RCOG) guidelines are reviewed. Relevant articles were identified on Pubmed and Cochrane Database of Systematic Reviews, including sheep models, case-control studies, retrospective cohort studies and meta-analyses.

Results
There are a variety of studies investigating the role of ACS to improve outcomes in small-for-gestational age fetuses delivering preterm. Below is a table summarising recent studies. Several studies found significant benefit from ACS in SGA infants delivered preterm with lower rates of neonatal mortality as well as improved respiratory and neurological outcomes. Conversely, other studies found no significant benefit or potential harm such as increased risk of respiratory distress syndrome (RDS), increased risk neonatal hypoglycaemia and reduced physical growth.

Studies investigating use of ACS in SGA fetus

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>No. of infants</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schaap 2001</td>
<td>Case-control</td>
<td>124</td>
<td>ACS in SGA at 26-32 weeks</td>
<td>Increased survival without disability at 2 yrs.</td>
</tr>
<tr>
<td>Miller 2007</td>
<td>Sheep model</td>
<td>10</td>
<td>Betamethasone in IUGR sheep</td>
<td>ACS may induce brain injury in IUGR fetus</td>
</tr>
<tr>
<td>Ishikawa 2015</td>
<td>Retrospective cohort</td>
<td>1931</td>
<td>ACS at 22-33+6 weeks in SGA fetuses with BW &lt; 1.5kg</td>
<td>No effect on short- or long-term outcomes</td>
</tr>
<tr>
<td>Melamed 2016</td>
<td>Retrospective cohort</td>
<td>918</td>
<td>ACS in SGA from 24+0-33+6</td>
<td>Reduced neonatal death</td>
</tr>
<tr>
<td>Riskin-Mashiah 2016</td>
<td>Retrospective cohort</td>
<td>1171</td>
<td>ACS from 24-31 weeks</td>
<td>Reduced risk neonatal mortality</td>
</tr>
<tr>
<td>Kim 2018</td>
<td>Retrospective cohort</td>
<td>82</td>
<td>ACS from 29-34 weeks</td>
<td>Increased risk RDS in those who received ACS</td>
</tr>
<tr>
<td>Amiya 2016</td>
<td>Systematic review and meta-analysis</td>
<td>8 studies with total 1126 infants</td>
<td>ACS in SGA at risk of preterm birth</td>
<td>No significant reduction in RDS</td>
</tr>
</tbody>
</table>

Conclusions
Research investigating the role of ACS to improve outcomes in SGA is conflicting which warrants caution in clinical practice and further studies including randomised controlled trials.

AUS and NZ guideline 2015 section on IUGR
For women with an IUGR fetus at risk of preterm birth
• Use a single course of ACS if ≥34+6 or less
• Use repeat ACS if ≥32+6 or less
• Where appropriate, monitor women for signs of puerperal sepsis

NB: largely based on Cochrane reviews which included small actual number of IUGR infants (see table below for actual number of IUGR infants informing recommendation for single course ACS in IUGR)

RCOG Green-top guideline 2010 section on use of ACS in fetal growth restriction (FGR)
• Pregnancies affected by FGR between 24+0 to 35+6 at risk of delivery should receive single course ACS
• Evidence to suggest ACS may have different effect on cerebral blood flow in growth-restricted fetuses and acknowledges speculation about use in SGA
• Refers to Schaap 2001 showing improved survival without disability at 2 yrs if given ACS