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

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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.

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)

Roberts Cochrane review - trials that included IUGR

Primary outcome	Trials contributing	Number of infants	Risk ratio (95% CI)	Actual no. of IUGR infants
Perinatal death	Garite 1992	77	1.14 (0.59-2.21)	**5**
Fetal death	Garite 1992	77	3.42 (0.37-31.41)	**5**
Neonatal death	Garite 1992 Porto 2011 Silver 1996	489	0.77 (0.43-1.35)	**16**
RDS	Garite 1992 Porto 2011 Silver 1996	489	0.97 (0.81-1.16)	**16**
Puerperal sepsis	Garite 1992 Silver 1996	146	2.16 (1.09-4.26)	**11**

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 fetus and acknowledges speculation about use in SGA
- Refers to Schaap 2001 showing improved survival without disability at 2 yrs if given ACS

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

Study	Study design	No. of infants	Intervention	Outcomes
Schaap 2001	Case-control	124	ACS in SGA at 26-32 weeks	• Increased survival without disability at 2 yrs • Negative impact on physical growth
Miller 2007	Sheep model	10	Betamethasone in IUGR sheep	• ACS may induce brain injury in IUGR fetus
Ishikawa 2015	Retrospective cohort	1931	ACS at 22-33+6 weeks in SGA fetus with BW < 1.5kg	• No effect on short- or long-term outcomes
Melamed 2016	Retrospective cohort	918	ACS in SGA from 24+0-33+6	• Reduced neonatal death • Reduced mechanical ventilation • Reduced severe brain injury
Riskin-Mashiah 2016	Retrospective cohort	1171	ACS from 24-31 weeks	• Reduced risk neonatal mortality • Reduced composite outcome of severe neonatal morbidity
Kim 2018	Retrospective cohort	82	ACS from 29-34 weeks	• Increased risk RDS in those who received ACS • Increased risk hypoglycaemia over 32/40
Amiya 2016	Systematic review and meta-analysis	8 studies with total 1126 infants	ACS in SGA at risk of preterm birth	• No significant reduction in RDS • Insufficient evidence to conclude on benefits or harms of ACS in SGA

Conclusion

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.

1. *Roberts et. al. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. 2017. Cochrane database.*
2. *Antenatal corticosteroids given to women prior to birth to improve fetal, infant, child and adult health. NZ and Aus practice guidelines 2015.*
3. *RCOG Greentop guideline No 7 - Antenatal corticosteroids to reduce neonatal morbidity and mortality. Oct 2010.*
4. *Schaap et al. Effects of ACS administration on mortality and long-term morbidity in early preterm, growth-restricted infants. O&G. 2001.*
5. *Miller et al. Effects of Maternal Betamethasone Administration on the Intrauterine Growth-Restricted Fetus. Endocrinology, 2007*
6. *Ishikawa et. al. The effects of antenatal corticosteroids on short- and long-term outcomes in SGA infants. Int J of Med Sciences. 2015.*
7. *Melamed et. al. Antenatal corticosteroids and outcomes of SGA neonates. Obstetrics and gynecology. 2016.*
8. *Kim et. al. Antenatal corticosteroids and outcomes of preterm SGA neonates in a single medical center. O&G Science 2018.*
9. *Amiya et. al. ACS for reducing adverse maternal and child outcomes in special populations at risk of preterm birth. PLoS One. 2016.*
10. *Riskin-Mashiah et. al. ACS treatment in singleton, small-for-gestational-age infants born at 24–31 weeks' gestation: a population-based study. BJOG. 2016.*