

CORTICOSTEROIDS FOR WOMAN AT RISK OF PRETERM BIRTH OR WITH A FETUS AT RISK OF RESPIRATORY DISTRESS - ANTENATAL

This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.

1. AIM

- Appropriate administration of corticosteroids to a pregnant woman to minimise neonatal mortality and morbidity

2. PATIENT

- Woman at risk of preterm delivery between 23-34 weeks where neonatal resuscitation is planned
- Woman who remains at risk of preterm birth <32 weeks gestation, who has received a course of antenatal steroids ≥ 14 days prior
- Woman having an elective caesarean section <37 weeks gestation

3. STAFF

- Medical and midwifery staff

4. EQUIPMENT

- Syringe (3 ml)
- Blunt 18 gauge drawing up needle
- 23-gauge needle

5. CLINICAL PRACTICE

Administration of Initial Course of Antenatal Corticosteroids

- Prescribe an initial course of antenatal corticosteroids to any woman with an imminent risk of early preterm delivery (planned or expected in the next 7 days) who at the time of assessment is ≤ 34 weeks gestation, even if birth is likely within 24 hours
- Prescribe Betamethasone intramuscular injection, either a single dose 11.4 mg, or 2 doses 11.4 mg each, given 24 hours apart
- Consider, where appropriate, estimating the risk of preterm birth by the use of adjunct prediction tests including actum partus and/or cervical length assessment

Repeat Course of Antenatal Corticosteroids

- Consider a single repeat course of antenatal corticosteroids for any woman at continued risk of preterm delivery at ≤ 32 weeks' gestation, if the initial dose of antenatal corticosteroids was given ≥ 14 days prior
- Prescribe Betamethasone 11.4 mg intramuscular injection, either a single dose, or 2 doses given 24 hours apart
- Do not delay the decision for delivery or repeat tocolysis for the administration of a repeat course of corticosteroids

Woman Having a Planned Elective Caesarean Section prior to 37 weeks

- Recommend delaying caesarean section until ≥ 39 weeks if clinically appropriate
- Consider prescribing antenatal corticosteroids 48 hours prior to planned caesarean section to a woman who at the time of birth will be <37 weeks gestation, if she has not received antenatal corticosteroids previously

CLINICAL POLICIES, PROCEDURES & GUIDELINES

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2 June 2016

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- Discuss with woman who will be 34-37 weeks gestation at the time of delivery, on a case by case basis. Prescribing antenatal corticosteroids prior to planned caesarean section at this gestation is considered controversial.
- Prescribe and administer Betamethasone intramuscular injection, two doses of 11.4 mg each given 24 hours apart, commencing 48 prior to planned caesarean section (if the decision has been made to administer)

Administration

- Administer corticosteroid to gluteal region

Woman with diabetes mellitus

- Consult obstetric physician/endocrinologist for potential commencement of insulin, or increase in insulin requirement in the short term
- Consider hospital admission for close glucose monitoring

6. DOCUMENTATION

- Integrated clinical notes
- Medication chart
- ObstetriX
- Antenatal Care Plan

7. EDUCATIONAL NOTES

Effect of an initial course of antenatal corticosteroids

A systematic review and meta-analysis has found that treatment with antenatal corticosteroids is associated with an overall reduction in:

- Perinatal death: Relative risk(RR) = 0.72 (95% Confidence Interval(CI) 0.58-0.89), Number needed to treat(NNT) = 23 (95% CI 15-50)
- Neonatal death: RR = 0.69 (95% CI 0.58-0.80), NNT = 22 (95% CI 16-38)
- Respiratory Distress Syndrome(RDS): RR = 0.66 (95% CI 0.59-0.78), NNT = 13 (95% CI 10-18)
- Intraventricular Haemorrhage(IVH): RR = 0.54 (95% CI 0.43-0.69)
- Severe IVH: RR = 0.28 (95% CI 0.16-0.50)
- Necrotising Enterocolitis(NEC): RR = 0.46 (95% CI 0.29-0.74)
- Need for and duration of respiratory support: RR = 0.73 (95% CI 0.59 – 0.92)
- Systemic infections in the first 48 hours of life: RR= 0.56, (95% CI 0.38-0.86)
- There has been minimal follow-up of long term outcomes. There was a trend to a reduction in developmental delay RR = 0.49 (95% CI 0.24-1.00) and a trend toward improvement in other long term follow-up outcomes, including cerebral palsy
- There were no differences in the risks of maternal infection morbidity outcomes (including chorioamnionitis, puerperal sepsis, pyrexia after trial entry, intrapartum pyrexia or postnatal pyrexia requiring antibiotic treatment), or maternal death between women treated with a single course of antenatal corticosteroids compared with women who had no antenatal corticosteroids.

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- Only two of the 26 trials have provided follow-up of infants of mothers recruited into the original trials of a single course of antenatal corticosteroids. Reassuringly, no overall difference was seen in sensory impairment, body size, systolic blood pressure, respiratory outcomes, cardiovascular or hypothalamic pituitary adrenal axis function between in utero exposure to antenatal corticosteroids and no exposure. The authors of one of the follow-up studies suggested that the results could indicate an increased risk of diabetes and cardiovascular disease later in life

Repeat course of antenatal corticosteroids for women at continued risk of preterm birth

- Repeat doses of antenatal corticosteroids reduce the incidence and severity of neonatal respiratory distress, and possibly the risk of serious infant morbidity in the first few weeks after birth. The short term benefits for babies support the use of repeat dose corticosteroids for women at risk of preterm birth
- An updated meta-analysis of eight clinical trials and 5224 infants found treatment with repeat dose(s) of corticosteroid was/were associated with a reduction in:
 - RDS RR = 0.83 (95% CI 0.75-0.91), number needed to treat to benefit (NNTB) 17 (95% CI 11-32)
 - Serious infant outcome RR = 0.84 (95% CI 0.75-0.94), NNTB 30 (95% CI 19-79). (Variously defined by the trials that included fetal, neonatal or later death, severe respiratory distress, severe intraventricular haemorrhage (Grades 3 or 4), chronic lung disease, necrotising enterocolitis, retinopathy of prematurity, cystic periventricular leukomalacia, patent ductus arteriosus, neonatal encephalopathy)
 - use of mechanical ventilation, oxygen supplementation, surfactant and inotropic support
 - patent ductus arteriosus.
- All trials used repeat courses of betamethasone, some trials used weekly courses of corticosteroids until maximum of 34 weeks gestation, while some others used a single repeat course
- A further meta-analysis of ten trials and 5650 babies in 2011 showed that at early childhood follow-up, no statistically significant differences were seen for infants exposed to repeat prenatal corticosteroids compared with unexposed infants for the primary outcomes (total deaths, survival free of any disability or major disability, disability or serious outcome) or in the secondary outcome growth assessments
- Treatment with repeat dose(s) of corticosteroid was associated with a reduction in mean birthweight [mean difference (MD) -75.79 g, (95% CI -117.63- -33.96), nine trials, 5626 infants].
- More follow-up data is emerging about the ideal dosing regimen. Accepted current practice if a full course of corticosteroids is given as a repeat course, is to not give any further courses. If a single dose is given, a repeat dose could be given in a week's time (to a maximum of three single doses) if the patient remains at risk of preterm birth

Elective Caesarean Section at term (≥37-39 weeks gestation)

- A course of antenatal corticosteroids may also be considered for any woman undergoing elective caesarean section up to 39 weeks gestation. There is evidence of reduced respiratory distress, less need for respiratory support and fewer admissions with shorter duration of stay in neonatal intensive care when corticosteroids were given at term in two studies. However, respiratory distress was not the reported primary outcome of these.

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- There remain concerns regarding long term neurodevelopmental outcomes and educational attainment in children who have been exposed to antenatal corticosteroids at term gestation (≥ 37 weeks' gestational age). The balance between benefits and harm is unclear based on the current evidence
- A course of antenatal corticosteroids may also be considered for any woman if there are other risk factors for respiratory morbidity such as diaphragmatic hernia

Alternatives to Betamethasone (e.g. if not available)

- An alternative regimen to Betamethasone is Dexamethasone 24mg in divided doses completed between 24 and 40 hours prior to birth (administer Dexamethasone IM in 4 doses of 6mg 12 hours apart)
- Diabetes mellitus is not a contraindication to antenatal corticosteroid treatment for fetal lung maturation

8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP

- Preterm Labour – Diagnoses and Management
- Preterm Premature Rupture of Membrane (PPROM): Assessment and Management Guideline
- Nifedipine for Tocolysis
- Estimating due date
- Pre-eclampsia – Intrapartum Care
- Placenta Praevia
- Transfers – In Utero at 23 – 25 Weeks Gestation
- Progesterone Prevention of Preterm Labour
- Diabetes Mellitus (GDM) Management – Gestational
- Diabetes in Pregnancy Policy – Management of Pre-Gestational

9. RISK RATING

- High

10. NATIONAL STANDARD

- CC – Comprehensive Care

11. REFERENCES

- 1 Antenatal Corticosteroid Clinical Practice Guidelines Panel. Antenatal corticosteroids given to women prior to birth to improve fetal, infant, child and adult health: Clinical Practice Guidelines. 2015. Liggins Institute, The University of Auckland, Auckland. New Zealand.
- 2 Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews. 2006;3:CD004454.
- 3 Crowther CA, McKinlay CJD, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD003935. DOI: 10.1002/14651858.CD003935.pub4

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- 4 Garite TJ, Kurtzman J, Maurel K, Clark R, Network. OCR. Impact of a 'rescue course' of antenatal corticosteroids: a multicenter randomized placebo-controlled trial. American Journal of Obstetrics & Gynecology. 2009;200:e1-9.
- 5 Antenatal Corticosteroids to Reduce Neonatal Morbidity and Mortality. RCOG Greentop guideline number 7. 2010.
- 6 Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis JPA. Corticosteroids for preventing neonatal respiratory morbidity after elective caesarean section at term. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD006614.
- 7 Behavioural, educational and respiratory outcomes of antenatal betamethasone for term caesarean section (ASTECS trial). Stutchfield PR, Whitaker R, Gliddon AE, Hobson L, Kotecha S, Doull IJM, Arch Dis Child Fetal Neonatal Ed 2013;98, F195-F200
- 8 Brownfoot FC, Gagliardi DI, Bain E, Middleton P, Crowther CA. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD006764.

REVISION & APPROVAL HISTORY

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