Guideline for Corticosteroids administration in the antenatal period to reduce neonatal morbidity

Respiratory distress syndrome (RDS) is an important cause of neonatal morbidity and mortality and occurs mainly because of lung immaturity and insufficient surfactant. Prophylactic corticosteroids accelerate lung maturation which reduces RDS[1].

Indications

- Should be offered:[2]
  - Women between 24^{+0} and 33^{+6} weeks of pregnancy who are in suspected, diagnosed or established preterm labour, are having a planned preterm birth or have P-PROM.

- Should be discussed:
  - Women between 23^{+0} and 23^{+6} weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have P-PROM

- Consider[3]
  - Women between 22^{+0} and 23^{+6} weeks of pregnancy who are in suspected or established preterm labour, are having a planned preterm birth or have P-PROM. There should be discussion between the Obstetric consultant and Neonatal team about the appropriateness of offering this and other interventions, taking into account other risk factors.

- Consider maternal corticosteroids for women between 34^{+0} and 35^{+6} weeks of pregnancy who are in suspected, diagnosed or established preterm labour, are having a planned preterm birth or have P-PROM.
  - Risks may outweight benefits

[1] Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev2006;19:CD004454.pmid:16856047.

[2] NICE guideline [NG25] Preterm labour and birth
https://www.nice.org.uk/guidance/ng25/chapter/Update-information

[3] Framework for Practice on the Perinatal Management of Extreme Preterm Birth Before 27 Weeks of Gestation.

- Fetal fibronectin should be used to reduce the risk of unnecessary courses and hospitalization.

Dosage

- Work best 24hrs < 7 days after a completed course.
- Betamethasone 12mg, second dose at 24 hours
- Dexamethasone 6mg, 4 doses given 12 hours apart
- Repeated doses
  - Do not offer routinely
  - Consider
    - interval since the end of last course
    - gestational age
    - likelihood of birth within 48 hours
  - Cochrane review[4] showed some benefit (less respiratory distress and less neonatal morbidity) where a dose was repeated 7 days or more after the initial course. There was no longer term benefit seen and there was also an association with lower birth weight.
  - WHO recommends that a single rescue course could be considered if preterm birth does not occur within 7 days of initial course[5]
  - If diabetes present consult the Med Obs team/Consultants for advice

Women should be counselled on the expected benefits and potential risks of antenatal steroids.

[4] Crowther CA, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease. *Cochrane Database Syst Rev* 2007;(18):CD003935.

[5] World Health Organization. *WHO Recommendations on Interventions to Improve Preterm Birth Outcomes*. Geneva: WHO; 2015.

Benefits[6]

- Improved survival
- Reduced RDS- 50% reduction in neonatal morbidity[7]
- Reduced IVH
- Reduced NEC
- Extreme prematurity
    - A prospective cohort study showed that the use of antenatal steroid treatment between 23 and 25 weeks gestation was associated with lower death rate and improved neurodevelopmental outcome at 18-22 months. [8]
- Late preterm pregnancies (34+0 – 36+6 weeks)
    - PROSPERO[9] systematic review which included nearly 6000 pregnancies over 6 trials found reduced neonatal respiratory morbidity (reduced RDS, reduced time on a ventilator, reduced need for surfactant therapy and reduced oxygen requirement) where antenatal steroids were used beyond 34 weeks gestation. It also recommended steroids for planned caesarean section between 37 and 38+6 weeks gestation.

[6] Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2017; (3): CD004454.

[7] (2019), Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation. Int J Gynecol Obstet, 144: 352-355. doi:10.1002/ijgo.12746

[8] Carlo WA, McDonald SA, Fanaroff AA, Vohr BR, Stoll BJ, Ehrenkranz RA, et al. Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks gestation. *JAMA* 2011;306:2348–58.

[9] Saccone G, Berghella V. Antenatal corticosteroids for maturity of term or near term fetuses: Systematic review and meta-analysis of randomized controlled trials. *BMJ*. 2016;**355**:i5044.

Risks

- Lower birthweight with repeat courses

- Cerebral demyelination
  - There is very limited long term follow up data of children whose mothers receive antenatal steroids[10] .
  - National Institute of Child Health and Human Development 2000 Consensus Panel [11] noted potential harmful effects on the fetal brain, lungs and function of the hypothalamic-pituitary axis.

- A recent cohort study of 670,000[12] found an association between children whose mothers received antenatal steroids and mental and behavioural disorders (hazard ratio of 1.33). These included ADHD, emotional and sleep disorders. For children who were born at term the risk was more marked (hazard ratio of 1.47). It was also noted that less than 40% of the children who were born preterm had received antenatal steroids and that over 45% were exposed but were born at term.

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[10] Gyamfi-Bannerman C, Thom EA, Blackwell SC, et al.; NICHD Maternal-Fetal Medicine Units Network. Antenatal betamethasone for women at risk for late preterm delivery. *N Engl J Med*. 2016;**374**:1311–1320.

[11] National Institutes of Health Consensus Development Panel. Antenatal corticosteroids revisited: Repeat courses – National Institutes of Health Consensus Development Conference Statement, August 17–18, 2000. *Obstet Gynecol*. 2001;**98**:144–150.

[12] Räikkönen K, Gissler M, Kajantie E. Associations Between Maternal Antenatal Corticosteroid Treatment and Mental and Behavioral Disorders in Children. *JAMA*. 2020;323(19):1924–1933. doi:10.1001/jama.2020.3937