Antenatal Steroids in Late Preterms

Abstract:

Antenatal steroid therapy has been one of the major breakthroughs in terms of improving perinatal outcome for preterm infants. A single course of antenatal steroid for babies born before 34 weeks gestation reduces the rate of Respiratory Distress Syndrome (RDS) and mortality by 50% and also decreases the rate of intraventricular haemorrhage (IVH). Babies born between 32-36 weeks gestation i.e. moderate and late preterms represent 6-7% of all births in the UK and 75% of all preterm births. It is now established that late preterm infants are also at a higher risk of mortality and morbidity when compared with term infants. Respiratory disorders including transient tachypnea of new born (TTN), RDS, pneumonia and pulmonary hypertension are more often associated with late preterms than full term infants (29% vs. 4%). There is no doubt that antenatal administration of steroids accelerates the fetal lung maturation and reduces the production of surfactant, thus helping babies born before 34 weeks gestation in whom RDS is more common. However RDS is much less common in late preterms in whom the principal respiratory disorder is TTN, thus raising the question of the relative benefits and risks of antenatal steroids in this population.

The incidence of respiratory disorders is reduced in late preterms who are exposed to antenatal steroids before 34 weeks gestation. A Cochrane review in 2006 using evidence from 2 studies concluded that there was a significant reduction in RDS in babies born between 33-34+6 weeks gestation who received antenatal steroids, but no significant benefit in babies born between 35-36+6 wk gestation (RR 0.61, 95% CI 0.11 to 3.26). A more recent a single centre retrospective study of 1078 babies born between 34-36 weeks gestation showed that antenatal steroids between 24-34 weeks reduce RDS from 81% to 21%.[2] However it is not yet clear whether administering antenatal steroids after 34 weeks gestation would be associated with a similar beneficial effect.

Porto and colleagues have recently tried to address this issue in a study of 273 babies born between 34-36+6 wks in a centre in Brazil who were randomised to antenatal betamethasone or placebo. They found that the rate of RDS was low in both corticosteroid and placebo group, while the rate of TTN was high in both groups. The incidence of RDS was 1.4% as compared to TTN (94%) in the corticosteroid group and 8.9% and 22% respectively in the placebo group. (p-value 0.54, 0.77 respectively). There was no reduction in risk of morbidity with corticosteroids use even after adjustment for subgroup of gestational age (34-36 wk, 35-36 wk and a 36 wks). There was no difference in neonatal morbidity (82% vs.72%) or in duration of hospital stay (5.1 vs. 5.2 days; p=0.87). They reported that the babies born to mothers who had received corticosteroids required less phototherapy (risk ratio 0.63, 0.44 to 0.91) though the rate of jaundice (53% vs. 57%) was similar in the two groups.

Antenatal steroids are not without risk. Lawson has summarised the growing number of reports of adverse long term effects associated with antenatal steroid therapy. He shows that maternal corticosteroid administration delays myelination in the fetal brain (which normally continues up to the age of two years) and reduces the growth of all fetal brain areas, particularly the hippocampus.[3] Other studies suggest that the repeated use of antenatal steroids reduce neonate head circumference and birth weight. A Cochrane systematic review in 2007 supports this issue, suggesting that although repeated doses of antenatal steroids do reduce the occurrence and severity of neonatal lung disease, at the same time they are associated with decrease in birth weight and head circumference. Multivariate analyses of behaviour of children in a Western Australian preterm infant follow up cohort study have demonstrated that increasing number of antenatal steroid courses is associated with reduced birth weight and an increase in behavioural disorders at age 3.

So far no substantial benefit has been shown for the use of antenatal steroids after 34weeks gestation, except in the setting of term elective caesarean section, where antenatal steroids appear to reduce the risk of admission for respiratory distress. More data should soon be available. A population based prospective study of late and moderate preterm infants (LAMBS study) currently being conducted in UK will examine perinatal and neonatal outcomes for babies born before 36 weeks gestation in relation to antenatal interventions including steroids. More specifically the ALPS trial (Antenatal Late Preterm Steroids) is designed to explore this issue. This study will attempt to answer the following primary research question: Do steroids, compared to no steroids, decrease babies need for oxygen support when given to pregnant women at least 12 to 24 hours before they deliver at 34 weeks to 36 weeks gestation?[2] The study will also collect information on whether steroids improve the chances that the baby will not go on to develop other morbidities. This study is due to complete in 2013. Until data from these studies become available, current evidence does not justify the routine use of antenatal corticosteroids in late preterm infants.

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References:
8. Multivariate analyses of behaviour of children in a Western Australian preterm infant follow up cohort study have demonstrated that increasing number of antenatal steroid courses is associated with reduced birth weight and an increase in behavioural disorders at age 3.
9. Animal studies
10. Lawson has summarised the growing number of reports of adverse long term effects associated with antenatal steroid therapy. He shows that maternal corticosteroid administration delays myelination in the fetal brain (which normally continues up to the age of two years) and reduces the growth of all fetal brain areas, particularly the hippocampus.
11. Other studies suggest that the repeated use of antenatal steroids reduce neonate head circumference and birth weight.
12. Multivariate analyses of behaviour of children in a Western Australian preterm infant follow up cohort study have demonstrated that increasing number of antenatal steroid courses is associated with reduced birth weight and an increase in behavioural disorders at age 3.
13. So far no substantial benefit has been shown for the use of antenatal steroids after 34weeks gestation, except in the setting of term elective caesarean section, where antenatal steroids appear to reduce the risk of admission for respiratory distress.

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