

1.0 g/kg(5). Given the possible side-effects it is important to identify the lowest possible efficacious dose. In this issue of the journal, Girish and colleagues(6) have compared the outcome of Rh isoimmunized infants (>31 weeks of gestational age) given 0.5 g/kg or 1.0 g/kg HDIVIG. They conclude that the two regimes of HDIVIG had comparable effects on the duration of phototherapy, duration of hospital stay and need for exchange transfusion. The study, however, was powered only to detect a difference in the duration of phototherapy between the two groups of 24 hours and not to confidently assess differences in other outcomes reported. The authors found the mean duration of phototherapy was 77.3 hours in the low dose group and 55.4 hours in the high dose group (mean difference 21.9, 95% CI-13.1 to 56.9), even though the high dose group was disadvantaged by containing more infants who were hydropic at birth (1/19 versus 6/19) and had required intrauterine transfusions (2/19 versus 8/19, $P=0.06$). The results of this study(6), should encourage further randomized trials to identify the optimum dose of HDIVIG, but such trials should have sample size sufficiently large enough to detect clinically important long term outcomes.

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Single versus Multiple Courses of Antenatal Corticosteroids

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Antenatal steroids for preterm labor, a revolutionary low cost intervention in perinatology, is responsible for improving the neonatal survival and reducing severity of respiratory distress syndrome (RDS) in preterm babies(1). The current recommendations originate from the 1994 National Institute of Health (NIH) Consensus Conference and reinforced by a second NIH Consensus Conference in 2000(2). One

of the key points from the guidelines mention repeated courses of corticosteroids may not be safe and should not be administered outside of clinical trials.

After one course (total of 24 mg of Betamethasone or Dexamethasone, given over 24 or 48 hours respectively) of antenatal steroid, the

maximum benefits are seen if the fetus is delivered 24 hours after and within 7 days of the last dose(1). Because the beneficial effects wanes off after 7 days, it is conjectured, there might be benefit from repeated courses of antenatal steroids. However, concerns have been raised about the safety of multiple courses of antenatal steroids. The study by Mazumder, *et al.* again cautions about the use of multiple courses(3). The authors did not find any beneficial effect on the immediate neonatal morbidity including severe RDS. Though not adequately powered to detect the major difference, the findings are in accordance with the recent National Institute of Child Health (NICHD) trial which failed to show an effect on the primary composite outcome of severe respiratory distress syndrome, grade III or IV intraventricular hemorrhage, chronic lung disease or periventricular leukomalacia. However, repeat doses did result in better lung function as compared to single course in infants delivered below 32 weeks of gestation(4). Another trial performed in Australia and New Zealand, Australian Collaborative Trial of Repeat Doses of Steroids (ACTORDS) demonstrated significant reduction in the rates of respiratory distress syndrome or severe lung disease(5). Even the Cochrane review concluded that there is a short term beneficial effect of multiple courses of antenatal corticosteroids on respiratory distress syndrome as compared with those given a single course (26 % vs 32 %, RR 0.82; 95 CI 0.72-0.93; four trials, 2155 women)(6).

Another significant finding of the study were the effect on anthropometric parameters at 6 months of age. Other studies have found detrimental effects on the head circumference and weight at birth but not at 40 weeks of corrected age(5). Though there are some methodological issues in the current study (unacceptably high lost to follow up rates and some babies still to be accessed at six months), the effect on anthropometry highlights another potential harm of such an intervention. The study, though underpowered, is yet to report the results of neurodevelopmental outcome at 18 months of age. It has to be noted that ACTORDS study did not find any change in either survival free major neurosensory disability or body size at 2 years of age(7). On the contrary, the NICHD study reported trends

towards higher rate of cerebral palsy among children at 2-3 years of age who have been exposed to repeat courses of corticosteroids(8). Even animal studies have shown delayed myelination and decreased growth of all areas of the fetal brain, especially the hippocampus, following repeated antenatal steroid use(9,10).

To conclude, though repeat dosing of antenatal corticosteroids could improve the immediate outcomes after preterm birth, given the evidence of potential adverse effects it is recommended that only a single course be used in clinical practice until results of more robust randomized controlled trials with neuromotor outcomes are available. The current data argue against the weekly administration of antenatal corticosteroids.

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