



Antenatal corticosteroids to reduce preterm deaths in low-income settings

Kishwar Azad and Anthony Costello¹ suggest the use of extreme caution in scaling up of antenatal corticosteroid treatment in low-income settings. They raise three important questions with respect to the efficacy, safety, and the appropriate gestational age at which to give corticosteroids to patients in low-income countries.

Firstly, in terms of efficacy, there is high-quality evidence on the benefits of antenatal corticosteroids for lung maturation in utero. A large decrease in neonatal mortality was reported in trials in four middle-income countries, including those in Africa and the Middle East (relative risk [RR] 0.47, 95% CI 0.35–0.64), compared with 14 studies in high-income countries (0.79, 0.65–0.96).^{2,3} Antenatal corticosteroids actually reduced the need for level 2 care, including mechanical ventilation or continuous positive airway pressure in four studies (0.69, 0.53–0.90) and intensive care in two studies (0.80, 0.65–0.99) suggesting that, in regions where mechanical ventilation is not available, substantial benefits could be expected.^{2,3} We agree that more research is needed but in view of the biological basis for the effect of antenatal corticosteroids on infant mortality, it is extremely unlikely, statistically, that antenatal corticosteroids would be shown not to work in African or Asian babies.

Secondly, we agree with Azad and Costello that potential harm to the patient is always a critical issue. However, a one-off course of antenatal corticosteroids (<48 h) poses a very low risk of adverse effects. The Cochrane systematic review² discussed by Azad and Costello shows antenatal corticosteroids are associated with major reductions in, death, severe disability and lower rates of retinopathy

of prematurity so their concerns with respect to perinatal death or disability are hard to justify. Repeat antenatal corticosteroids have been linked to learning disabilities compared with a single dose,⁴ and late-onset metabolic syndrome might also be a risk.⁵ With respect to maternal outcomes there is no robust evidence of increased infections.⁶ Because preterm deaths are now the leading cause of child deaths at 1 million per year, the balance lies in the direction of reducing mortality rather than the unknown risks of less severe outcomes.

Thirdly, although the proven benefit of antenatal corticosteroids is when they are administered to patients at 28–33 weeks' gestation, this gestational age band is partly due to enrolment criteria in the original trials.^{2,3} The gestational-age limit for antenatal corticosteroids in high-income countries has been extended with guidelines supporting use at less than 26 weeks' gestation. More than 85% of preterm infants are born at least 32 weeks' gestation,⁷ and although few have major preterm birth complications, this amounts to a large proportion of infants potentially at risk. The upper gestational-age limit for corticosteroid use is a critical question yet to be answered, especially in health-care settings where mechanical ventilators are not widely available and antenatal corticosteroids are more likely to be life-saving. WHO is presently reviewing the recommended upper and lower gestational-age cutoffs for antenatal corticosteroid treatment. When gestational-age of an infant is unknown or is imprecisely known, the balance of risks needs to be considered and in high mortality settings the balance will be in favour of treatment.

High-income countries have at least 90% coverage of antenatal corticosteroids, with most women in preterm labour being treated, and clinicians would be sued for non-use. Yet countries with the highest rates of preterm births have negligible coverage

of antenatal corticosteroids. We support the call for more research, especially on how to reach the poorest women and how to increase long-term health for both women and their babies. In the meantime, the evidence strongly supports giving a single, short course of corticosteroids to women at risk of preterm birth in hospitals everywhere, not just in high-income countries.

Prof Joy E Lawn is co-lead of ACS Technical Reference Team for UN Commission on Life Saving Commodities and wrote this Correspondence on behalf of the group.

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- 1 Azad K, Costello A. Extreme caution is needed before scale-up of antenatal corticosteroids to reduce preterm deaths in low-income settings. *Lancet Glob Health* 2014; **2**: e191–92.
- 2 Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2006; **4**: CD00004454.
- 3 Mwansa-Kambafwile J, Cousens S, Hansen T, Lawn JE. Antenatal steroids in preterm labour for the prevention of neonatal deaths due to complications of preterm birth. *Int J Epidemiol* 2010; **39**: 1122–33.
- 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; **3**: CD003935.
- 5 Seckl JR1, Cleasby M, Nyirenda MJ. Glucocorticoids, 11beta-hydroxysteroid dehydrogenase, and fetal programming. *Kidney Int* 2000; **57**: 1412–7.
- 6 Crowther C, Brown J. Comment on: extreme caution is needed before scale-up of antenatal corticosteroids to reduce preterm deaths in low-income settings. *Lancet Glob Health* 2014; **2**: e447
- 7 Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet* 2012; **379**: 2162–72.