

MAGNESIUM SULPHATE (Comment)**Intrapartum use to reduce the risk of cerebral palsy in the preterm baby**

The results of the NICHD funded trial in America designed to see if the short-term intrapartum use of IV magnesium sulphate is 'neuroprotective' were finally published in the *New England Journal of Medicine* on 28 August 2008. They confirm, and greatly strengthen, the findings of the four earlier trials, as summarised in the recent Cochrane Review (Doyle *et al.*, 2007) and, in particular the findings from the Australian trial published five years ago (Crowther *et al.*, 2003). Use did nothing to reduce perinatal mortality in either trial, but it did have some effect on the number of babies with cerebral palsy two years later. Intrapartum treatment for just 12-24 hours did little to reduce the number of babies with relatively mild cerebral palsy, but it almost halved the number with severe cerebral palsy in the two largest trials. A French trial seems to be in the process of coming up with very similar findings (Marret *et al.*, 2007; 2008).

It does seem reasonably clear that any reduction in the risk of cerebral palsy is not at the expense of a rise in the number of perinatal deaths. Only one trial found such a trend (Mittendorf *et al.*, 2002). However, it is not yet clear which women are really likely to benefit. The Australian trial recruited mothers where delivery seemed imminent before 30 weeks, the American trial before 32 weeks, and the French trial before 33 weeks gestation. No overview of the individual patient data from the women recruited into the five trials is yet available and, as Stanley and Crowther say in the editorial that accompanies the report of the outcome of the Australian trial, this needs to be done before use becomes widespread. The reduction in the incidence of moderate or severe cerebral palsy was only seen in pregnancies that had lasted less than 28 weeks in the American trial, and comparable information is not, at the moment, available for the other four trials. Cerebral palsy is rare in babies born at term (0.1% to 0.2% of all such births), but *some* degree of cerebral palsy currently affects 1% of babies born at 33 weeks gestation, 5% of babies born at 30 weeks gestation, and about 8% of babies born at 28 weeks gestation (Drummond and Colver, 2002).

Readers are urged to look at the updated Commentary and to take note of the changes that have been made to the monograph on this drug.

Drummond PM, Colver AF. Analysis by gestational age of cerebral palsy in preterm births in north-east England 1970-94. *Paediatr Perinat Epidemiol* 2002;**16**:172-80.

Mittendorf R, Dambrosia J, Pryde PG, *et al.* Association between the use of antenatal magnesium sulfate in preterm labour and adverse health outcomes in infants. *Am J Obstet Gynecol* 2002;**186**:1111-8. [RCT]

Crowther CA, Hiller JE, Doyle LW, *et al.* Effect of magnesium sulfate given for neuroprotection before preterm birth. A randomized controlled trial. *JAMA* 2003;**290**:2669-76. [RCT] (See also 2730-2.)

Marret S, Marpeau L, Zupan-Simunek V, *et al.* Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial. *BJOG* 2007;**114**:310-8. [RCT]

Doyle LW, Crowther CA, Middleton P, *et al.* Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database of Systematic Reviews*. 2007, Issue 3. Art. No.:CD004661. [SR]

Marret S, Marpeau L, Follet-Bouhamed C, *et al.* Effet du sulfate de magnésium sur la mortalité et la morbidité neurologique chez le prématuré de moins de 33 semaines, avec recul à deux ans: résultats de l'essai prospectif multicentrique contre placebo PREMAG. *Gynecol Obstet Fertil* 2008;**36**:27888. [RCT]

Rouse DJ, Hirtz DG, Thom E, *et al.* A randomized controlled trial of magnesium sulfate for the prevention of cerebral palsy. *N Engl J Med* 2008;**359**:895-905. [RCT]

Stanley FJ, Crowther C. Antenatal magnesium sulfate for neuroprotection before preterm birth? [Editorial] *N Engl J Med* 2008;**359**:962-4.