Is it the magnesium or is it the sulphate? Neuroprotective benefit of antenatal magnesium sulphate therapy for preterm infants

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Preterm birth places more than 4000 Australian infants born each year at an increased risk of life-long health outcomes, including cerebral palsy and cognitive dysfunction. Administration of magnesium sulphate to women in preterm labour is an established neuroprotective therapy for preterm infants (Doyle *et al.*, 2009). The neuroprotective benefit is currently attributed to the magnesium content, whereas sulphate has not been considered.

Sulphate is an obligate nutrient for fetal development (Dawson, 2011). The fetus has no mechanism for producing sulphate and is reliant on sulphate from the maternal circulation (Dawson, 2013). This is relevant to preterm babies that are born at a gestational age when they lack the capacity to generate sulfate. In addition, external provision of sulphate to the preterm infant is minimal as TPN, HMF, breast milk and colostrum have negligible sulphate content. Hence, it would seem highly likely that the preterm infant will rapidly become sulphate deficient. Our recent data has confirmed that this is the case.

Within the first 24 hours after birth, supra-physiological plasma sulphate levels were measured in infants whose mothers received magnesium sulphate (mean±SD 709±411 µmol/L, n=26, 95%CI 543-875), whereas sulphate levels in the group without magnesium sulphate (257±162, n=10, 141-373) were similar to that found in term cord blood. At 1 and 4 weeks of age, babies without antenatal magnesium sulphate were hyposulphataemic (1week: 85±32, n=5, 45-125; 4 weeks 125±79, n=6, 41-208) whereas the group with antenatal therapy maintained normal levels (1 week: 222±150, n=21, 154-290; 4 weeks 235±102, n=15, 178-292). These data are the first to positively correlate antenatal magnesium sulphate administration with neonatal plasma sulphate levels.

Since sulphate is important for modulating brain development, we propose that sulphate deficiency in preterm babies is detrimental to normal neurodevelopment. Our research into neonatal sulphate biochemistry has the potential to develop more cost-effective and universally applicable neuroprotective therapies for preterm infants.

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