Cerebral blood flow velocity changes after rapid administration of surfactant

Sr,-We enjoyed reading the paper by Dr Cowan et al. and note the following problems in relating the findings to the conclusion of the authors. The rationale behind the study appears to be the finding of an increased incidence of severe intraventricular haemorrhage in one study of surfactant replacement.2 The authors do mention two other randomised trials which reported a reduction of intraventricular haemorrhage, to which one might add a further two (this review lists four studies, references 37-40, which demonstrate significant reduction in intraventricular haemorrhage after surfactant treatment). Large intraventricular haemorrhage and IVH have also been shown to be reduced in four studies3 (references 37, 39, 50, 51).

A meta-analysis involving 34 randomised controlled trials shows odds ratios (95% confidence intervals) for the effect of surfactant on intraventricular haemorrhage of 0.89 (0.73-1.07) for prophylaxis and 0.79 (0.64-0.97) for rescue studies.4 The body of scientific evidence points to a modest reduction of intraventricular haemorrhage after surfactant treatment.

The authors go on to say that the collaborative European multicentre study of Curosurf found a surprisingly high incidence (26%) of severe intraventricular haemorrhage, but they omit to say just how ill these infants were, as they required mechanical ventilation in >60% oxygen within the first 15 hours of life.5 Indeed the control infants had a mortality rate in excess of 50%. The incidence of severe intraventricular haemorrhage in this study is less than that reported in at least three other studies6 (references 54, 58, 67) using rescue surfactant.

Many of the babies studied by Cowan et al would not have fulfilled the criteria for the collaborative European multicentre study of Curosurf4 as they were treated up to the age of 72 hours. The authors do not say whether any of their infants suffered from severe asphyxia, although we are told that the infants had pancuronium and pethidine. It seems likely that these babies were extremely ill and in the discussion it is said that seven out of eight had poor or absent cerebral autoregulation.7 The authors correctly point out that there was a modest reduction in mean arterial pressure after giving surfactant and on looking at their results it would seem that in some infants mean arterial pressure and cerebral blood flow velocity (CBFV) actually increased. Levels of mean arterial pressure in the graphs all appear to be above 30 mm Hg which is a level at which the authors had previously noted an increase of cerebral blood flow (CBF). The authors do not state the rate of intraventricular haemorrhage in their babies nor demonstrate any relationship between the reduction in either mean arterial pressure or CBFV and the severity of intraventricular haemorrhage. CBFV may not reliably reflect cerebral blood flow (CBF) when heart rate, blood pressure, carbon dioxide tension, and cerebral vessel diameter may all be changing. CBF measured using 133 xenon clearance (G Greisen and A Bell, personal communication) and near infrared spectrophotometry (FOR Reynolds and AD Edwards, personal communication) shows no consistent change after Curosurf administration and is related to change in carbon dioxide tension (pCO2).

The final paragraph of the discussion again suggests that there is a relationship between surfactant treatment and increase in intraventricular haemorrhage where in fact none exists. The reduction in intraventricular haemorrhage is in keeping with our two year follow up studies with Curosurf which show that 80% of treated survivors have normal development compared with 72% of control infants.8 We report only one study which has looked at a slow continuous infusion of Curosurf and the currently recommended bolus instillation. This pilot study showed that in blood gases was less and the duration of effect greatly shortened. (PW Narayan & C Rudin, personal communication). Perhaps there is a need for larger randomised trials of different methods of surfactant instillation. The haemodynamic changes reported by the authors were due to compromise of their infants before treatment or to their concomitant drug treatment.

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Gastroesophageal perforation in preterm babies treated with dexamethasone for bronchopulmonary dysplasia

Sr,-We read with interest the recent paper by Dr Ng and colleagues1 and would like to add a comment on prostaglandins. The authors did not refer to gastric prostaglandins in patients and preterm infants in maternal breast milk, but these substances may play an important part in the aetiology and treatment of gastroesophageal mucosal lesions and perforation in preterm babies treated with dexamethasone.

Prostaglandins, and PGE2 and PGI, in particular, are known to regulate protective factors in the gastroesophageal mucosa such as mucosal blood flow, mucus production, and bicarbonate secretion. An increase in prostaglandins in the gastroesophageal mucosa will therefore result in the depression of the protective mechanisms, thereby contributing to the development of gastroesophageal mucosal lesions. On the other hand, glucocorticosteroids are known to inhibit prostaglandin biosynthesis through the suppression of phospholipase A2 activity. Nobuhara et al have shown that dexamethasone, PGE2 and 6-keto-PGF1α in the gastric mucosa and have demonstrated a good correlation between this decrease and the development of gastric mucosal lesions.2 We have also demonstrated...
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