Where Are We Now with the Prenatal Steroids and Postnatal Surfactant

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A number of hormones are known to affect lung development but only corticosteroids and thyrotropin-releasing hormone (TRH) have undergone suitable clinical trials for the prevention of respiratory distress syndrome (RDS). About 25 trials of prenatal steroids have been performed since Liggins and Howie first reported their benefits in 1972. Twelve of these trials have been included in a meta-analysis involving more than 3,000 women at high risk of preterm delivery. Infants whose mothers had received steroids for at least 24 h before delivery and were born less than 7 days after the first dose showed a reduced incidence of RDS (OR 0.31, 95% CI 0.23-0.42), of early neonatal death (OR 0.59, 95% CI 0.47-0.75) and other complications such as intraventricular haemorrhage, necrotising enterocolitis, patent ductus arteriosus and bronchopulmonary dysplasia. Six trials have studied prenatal TRH treatment with somewhat conflicting results. Although TRH may

reduce the risk of bronchopulmonary dysplasia there is no clear evidence that it reduces the rate of RDS or neonatal mortality. Further trials of TRH are currently being performed.

Postnatal surfactant treatment is an effective therapy and meta-analyses involving more than 30 trials and over 3,500 babies show that the odds of neonatal mortality are reduced by about 40-50% and of pulmonary air leaks by about 30-70%. This is true whether the surfactant is natural or synthetic and whether it is given as prophylaxis or rescue treatment of established RDS.

Recent studies would suggest that prophylaxis or early treatment is better than delayed treatment and multiple doses up to a cumulative total of about 300 mg phospholipid/kg are better than single doses.

Eleven randomised clinical trials have compared different surfactant preparations. Seven trials which involved, 2,488 babies compared Surfactant and Exosurf. Babies treated with Surfactant had lower oxygen requirements for at least 3 days than those treated with Exosurf. They also had reduced risks of neonatal mortality (OR 0.81, 95% CI 0.65-1.01), retinopathy of prematurity (OR 0.81, 95% CI 0.66-0.99) and death or

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bronchopulmonary dysplasia (OR 0.86, 95% CI 0.75-0.99). Infasurf has also been compared with Exosurf and similar although nonsignificant benefits were found for the natural surfactant.

When results from these trials are combined, the meta-analysis of 3,554 babies shows a

significant reduction in the odds of pulmonary air leaks (OR 0.53, 95% CI 0.41-0.64) and death (OR 0.80, 95% CI 0.66-0.95) with natural compared to synthetic surfactants.

Two further trials compared different natural surfactant preparations. Reduced oxygen needs for 24 h after treatment were found for Infasurf and Curosurf when each was compared to Survanta. The apparent longer term benefits from these surfactants were not statistically significant.

In conclusion, prevention of preterm birth and maternal treatment to enhance fetal lung maturity are more important and probably cheaper options than postnatal surfactant treatment. The need for surfactant treatment should be looked upon as a failure to prevent RDS by other means.

There is also recent evidence that the effects of steroids and surfactant on the lungs are synergistic. If surfactant treatment becomes a necessity then it should be given early rather than late, in a dose of at least 100 mg/kg, repeated twice if needed, and if the clinician chooses a natural surfactant rather than a synthetic one he or she can expect an additional survivor for every 40-45 babies treated. Further comparative studies will be needed to ascertain the indications for using the newer genetically engineered surfactants.

Extended Abstracts

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