Biophysical Aspects of the Surfactant System in Relation to Neonatal Lung Function

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The pool size of surfactant in a full-term neonatal lung, expressed per unit body weight, is about 10 times larger than that of a normal adult lung [1], and more than 30 times larger than the amount required to coat the inside of the lung with a monolayer of surfactant phospholipids. It is not quite clear why this is so. To some extent it may reflect a safety margin to ensure rapid establishment of a stabilizing surface film in the air spaces at birth and increase resistance to inactivation by vascular-to-alveolar protein leakage and other possible pathophysiological mechanisms. Recent biophysical studies by Schürch et al. [2] indicate that natural surfactant is capable of generating a multilayer of phospholipids at the air-liquid interface, corresponding to a surface film plus a 'surface-associated reservoir', from which new sheets of surfactant material can slide into the surface film when the surface area is expanded. Under in vitro conditions, the surface-associated reservoir may amount to the equivalent of at least five monolayers. The possible re-

quirement of multilayers of surfactant during neonatal adaptation, especially in a sick neonatal lung with increased alveolar permeability, may be one reason why so much surfactant (at least 100mg/kg) is needed to obtain a satisfactory clinical response in a baby with respiratory distress syndrome. The role of the surfactant proteins in the interaction between the surface film and the surface-associated reservoir deserves further investigation. The therapeutic response to exogenous surfactant depends not only on dosage but also on the timing of treatment and on the ventilator strategies applied before and after administration of surfactant. The issue of treatment timing was addressed in recent experiments in which surfactant dysfunction was induced in near-term newborn rabbits by tracheal instillation of lysophosphatidylcholine (lyso-PC) [3]; the animals were then kept in body plethysmographs and subjected to mechanical ventilation for 120 min under standardized conditions, allowing repeated measurements of lung-thorax compliance. Lung protein leak-

Supported by the Swedish Medical Research Council (project 3351) and the Oscar II:s Minnesfond.

age during the period of ventilation was assessed by intravenous injection of human albumin at birth and quantification of the marker in lung lavage fluid by immuno-diffusion. One group of animals exposed to lyso-PC at birth and treated simultaneously with modified natural surfactant (Curosurf, 200 mg/kg) showed a satisfactory therapeutic response, reflected by a significant increase in compliance. Another group, not receiving surfactant until 30 min after the lyso-PC insult, failed to respond; these animals also had a much larger leak of albumin into the air spaces, associated with elevated minimum surface tension of the lavage fluid in a pulsating bubble surfactometer. One possible interpretation of these findings is that the effect of 'late' surfactant treatment was compromised by alveolar protein leakage, and that even a comparatively large dose of surfactant was unable to overcome the combined inhibitory effects of the leaking proteins and high levels of lyso-PC in the air spaces.

Ventilation of the surfactant-deficient lung results in epithelial disruption [4], which may aggravate vascular-to-alveolar leakage of protein in an immature neonate. A recent study by Björklund et al. [5] was designed to clarify whether vigorous resuscitation with manual ventilation at birth might have a negative impact on the response to subsequent administration of surfactant. Immediately after delivery, immature lambs with a gestational age of 127-128 days received six manual insufflations with tidal volumes of 35-40 ml/kg ('bagging'). Twin controls were not subjected to the bagging maneuver. All lambs were ventilated for 3 h and surfactant (Curosurf, 200 mg/kg) was administered via the airways after 30 min. Animals not undergoing manual ventilation at birth showed the expected response to surfactant treatment, with improved inspi-ratory capacity and compliance, and mostly uniform alveolar expansion in histological sections. In contrast, animals subjected to the bagging maneuver showed a poor response with little or no improvement in physiological parameters and large areas of alveolar collapse and lung injury including epithelial necrosis, hyaline membranes, and recruitment of granulocytes to the air spaces. Thus, in a surfactant-deficient lung the effect of surfactant therapy can be seriously compromised by just a few large inflations at birth. These findings challenge the resuscitation practice of rapidly establishing normal lung gas volume by vigorous manual ventilation.

References

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Extended Abstracts

Biol Neonate 1996;69:165-212