ABSTRACTS

1

COMPARISON OF TWO SURFACTANTS: IN VITRO SURFACE PROPERTIES AND EARLY EFFECTS IN SURFACTANT DEFICIENT RABBITS.

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In search of the most effective surfactant to use for surfactant replacement therapy, we compared an artificial porcine derived (APS) and neutral sheep surfactant preparation (NSS) with respect to in vitro characteristics and in vivo early effects. In 6 animals APS and 6 others NSS was administered endotracheally. Results: APS had the lowest in vitro minimal surface tension, 7 vs. 21 mN/m (Wilhelmy balance) and nearly zero vs. 22 mN/m (oscillating bubble) and a larger hysteresis compared to NSS. Within 1 min. following endotracheal surfactant instillation, however, PaO_2 increased to significantly higher levels in the NSS group animals: 48.9±16.2 vs. 25.1±12.0 kPa (mean±SD, $p<0.05$). Similarly, static lung compliance was significantly higher in the NSS group: 1.04±0.33 vs. 0.06±0.10 ml/cmH_2O/kg body weight ($p<0.05$). We conclude that early in vivo effects of surfactant preparations do not seem to relate to in vitro properties.

2

IMMEDIATE EFFECTS OF TREATMENT WITH HUMAN SURFACTANT ON VENTILATION, LUNG VOLUME AND MECHANICS IN NEWBORN INFANTS WITH IRDS. Edberg KE,Ekström-Jodal B,Hallman M, Hjalmarson O,Sandberg K,Silberberg A. Dpts of Pediatrics and Anestaesiology, Gothenburg Univ.; Research Lab for Med Electr., Chalmers Univ. of Technology, Gothenburg, Sweden; and Dpt of Pediatr, Univ of Helsinki, Finland.

We have studied lung function in 4 intubated and ventilated newborn infants with IRDS (birth-weights 1.1-1.47 kg, gest. age 26-29 w) immediately before and then repeatedly over 4 hours after instillation of human surfactant (100 mg/kg) into the endotrachealtubes. The infants were ventilated with max. insufflation pressures of 24-33 cmH2O and 4-10 cmH2O PEEP. Ventilatory flow was recorded by body plethysmography and FRC and ventilation efficiency by a N2 wash-out technique. Calculations were made by computer.

In all infants FRC increased 20-120% within 10 min after treatment. Compliance of the respiratory system fell by 20-50%. Resistance was unaffected. Gas mixing improved over the first 30 min in 3/4. The changes in FRC and compliance returned within 45-90 min with a concomitant reduction of oxygenation. However, in 3/4 the need of oxygen or PEEP was persistantly reduced after treatment. We conclude that in these sick, ventilated infants with IRDS, the main effect of human surfactant in given doses was an immediate but transient increase of FRC that paralleled a fall in oxygen needs in 3/4.

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PULMONARY FUNCTION AFTER BOVINE SURFACTANT (SF-RI 1) IN VLBW INFANTS WITH RDS AND CONGENITAL PNEUMONIA

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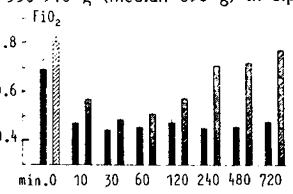
Patients and methods: Since differences in pulmonary function in VLBW infants with RDS and congenital pneumonia (c.p.) after natural surfactant therapy not yet have been described, we analysed the data of 33 infants with RDS and 14 with c.p. C.p. wa s diagnosed from positive bacteriological culture of tracheal aspirate. 30-50 mg/kg birth weight (b.w.) bovine surfactant (SF-RI 1) was given intratracheally, if severe respiratory failure was diagnosed. B.w. ranged from 430-1500 g (median 770 g) in RDS-infants from 530-940 g (median 690 g) in c.p. infants. **Results:** Time response curves for FiO_2 in RDS (solid bars) and c.p. infants (striped bars) after SF-RI 1 are depicted. Peak inspiratory and mean airway pressure showed similar differences. **Conclusion:** Pulmonary effects (decrease in FiO_2, PIP, MAP) after SF-RI 1 are longer stabile in RDS, compared to c.p. infants.



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IMMUNOLOGICAL REACTIONS TO BOVINE SURFACTANT IN PRETERM INFANTS

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The respiratory distress syndrome of preterm infants can be effectively treated by endotracheal administration of the bovine surfactant preparation SF-RI 1. Though the protein content of SF-RI 1 is less than 1 %, immunological reactions of the human infant against the bovine protein antigens have to be considered. Antigenicity of SF-RI 1 was demonstrated by antibody production in rats and rabbits.

Methods: An ELISA with a lowest detection limit of 1 ng/ml specific antibody against bovine surfactant was set up. Sera of 52 preterm infants were tested before as well as 2, 4 and 6 weeks after the administration of SF-RI 1. T-cell proliferation was quantitated by measuring 3H-thymidine uptake.

Results: Anti-SF-RI 1 antibodies of the IgA, IgE, IgG or IgM isotype were undetectable in all serum probes. SF-RI 1 did not stimulate T-cell proliferation in vitro. T-cells of patients treated with SF-RI 1 in vivo did not proliferate on incubation with SF-RI 1 in vitro.

Conclusion: The lack of demonstratable immunological reactions of preterm infants to bovine surfactant encourages the further clinical application of SF-RI 1.

5

RESPONSES IN FETAL SHEEP TO CHANGES PRODUCED BY AN EXTRACORPOREAL MEMBRANE OXYGENATION SYSTEM (ECMO).

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Breathing during fetal life is periodic, it is inhibited by maternal/fetal hypoxia and it is stimulated by maternal/fetal hypercapnia.

We use ECMO to study the influence of direct changes in blood gases or temperature on the fetus in 8 sheep at 125-130 days of gestation. For ECMO a 12 F silastic catheter (drainage, external jugular) and a 9.6 F catheter (return, carotid artery) were placed. Total blood flow varied between 60-80 ml/kg/min. After connection the fetuses were maintained normocapnic and hyperoxic (PaO2 63 ± 8 mmHg in carotid or axillary artery) for 8 to 19 hours to observe changes in breathing incidence or sleep cycling. Fetal PaCO2 was varied in 3 fetuses during fetal hyperoxia or normoxia. Fetal temperature was varied by decreasing blood temperature of the system (2 fetuses). 2 Fetuses were kept hyperoxic during maternal hypoxia.

Preliminary observations: a) During fetal hyperoxia the fetuses continued to cycle between high and low voltage and fetal breathing showed in some cases a decrease in incidence, but overall it did not change significantly. b) During fetal hypercapnia (4-8 mmHg), fetal breathing was stimulated and it seemed to bear a relationship with oxygenation. c) During fetal hypothermia fetal breathing was stimulated. d) Fetal breathing was stopped when the ewe was made hypoxic and the fetus was kept hyperoxic, this suggests that during maternal/placental hypoxia a substance is produced which has a direct action on fetal breathing. ECMO proved to be a possible technique to study fetal physiology.

6

LIMITING FACTORS IN PROLONGED ECMO TREATMENT BY IMMUNOLOGICAL INTERFERENCE.

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In association with impaired tissue perfusion or sepsis factors affecting blood pressure, vascular permeability and cell lysis are released. Several observations indicate that they are some of the factors leading to ARDS and hemolysis, responsible for the anemia in these diseases.

Material and Methods: CPD blood was perfused within the ECMO equipment in six different experiments. Blood samples were analysed before start of ECMO, 5 minutes, 12, 24 and 48 hours after start. C3a and C5a were determined by a RIA method. Membrane attacking complexes were measured by an Eliza technique.

Results: During ECMO perfusion as well C3a and C5a as plasma hemoglobin, as the concentration of membrane attacking complexes, rose with time ($p < 0.05$).

Conclusion: The results indicate accumulation of anaphylatoxins as well as products resulting from cell injury as membrane attacking complexes. They can influence blood pressure and anemia during the ECMO procedure. When occuring in a situation without calcium blockade, as in vivo., an even more profound formation of these substances will appear in a time dependent fashion.