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INHALATION OF NITRIC OXIDE: EFFECT ON HEMODYNAMICS, CEREBRAL ACTIVITY AND ANTIOXIDANT STATUS IN THE LAMB. Robbert H. Lopes Cardozo, Arnout Jan de Beaufort, Beerthe J. Geesink, Manon J.N.L. Benders, Ralf M.W. Moison, Margot van de Bor, Howard M. Berger, Frank van Bel. Neonatal Unit, Dept. of Pediatrics, University Hospital Leiden, The Netherlands. Ventilation with NO is increasingly being used to treat pulmonary hypertension in the newborn. In the brain NO is involved in neurotransmission and has vasoactive properties. However, the effect of inhaled NO on cerebral function and blood flow is not known. Furthermore, there is little information on the peroxidative complications by use of this free radical gas.

We investigated the effect of inhaled NO (1-60 ppm) in 6 ventilated newborn lambs before and after group B streptococci (GBS) induced pulmonary hypertension. Blood pressure in the pulmonary artery (P_{ap}) and aorta (P_{ao}), cerebral blood flow (CBF, ultrasonic-determined carotid flow) and cerebral electrical activity (CEA using a cerebral function monitor) were measured. Blood gases, indices of antioxidant status (vitamin C, MDA and glutathione) and methemoglobin were determined in blood samples from the left ventricle. With inhalation of NO before and after GBS induced pulmonary hypertension a decrease of the P_{ap} (16→11 mmHg and 27→12 mmHg resp) and an increase of the pO_2 (13→18 kPa and 10→17 kPa resp) was observed. CBF (65-80 mL/min), CEA (25-45 mV) and indices of antioxidant status were in the normal range and did not change significantly. Methemoglobin was not detected. Inhalation of NO (up to 60 ppm) lowered P_{ap} , without having an effect on CBF, CEA, and antioxidant status in the pulmonary vessels.

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CEREBRAL LACTATE AND N-ACETYLASPARTATE/CHOLINE RATIOS AND DELAYED ENERGY FAILURE FOLLOWING ACUTE HYPOXIA-ISCHAEMIA IN THE NEWBORN PIG. Ann Lorek, Ernest Cady, Juliet Penrice, John Wyatt, Yukito Takei, David Edwards, Marzena Wylezinska, Vincent Kirkbride, Huw Owen-Reece, Guy Brown, Richard Aldridge, Donald Peebles, Christopher Cooper, Simon Roth, David Delpy, Osmund Reynolds. Departments of Paediatrics and Medical Physics, University College London Medical School, London, UK. Falling [phosphocreatine(PCr)]/[inorganic phosphate(Pi)] following perinatal asphyxia indicates a bad prognosis, as may increases in lactate(lac)/choline(cho) peak area ratios. The aim of this study was to define the relation between these ratios in the newborn pig. 11 pigs less than 24h old were studied continuously by magnetic resonance spectroscopy (MRS) at 7T for 48h: 7 were given an acute reversed cerebral hypoxic-ischaemic insult and 4 were sham-operated controls. During the insult [PCr]/[Pi] fell from 1.32(0.21) (mean (SD)) to 0.01(0.01), and lac/cho increased from 0.04(0.01) to 1.62(0.34) ($p<0.001$ for both). These values returned to 1.12(0.31) and 0.31(0.13) after resuscitation. During subsequent delayed ('secondary') energy failure [PCr]/[Pi] decreased to 0.27(0.24), and lac/cho rose gradually to 0.73(0.30) ($p<0.01$ for both). N-acetylaspartate(Naa)/cho fell during the insult from 1.05(0.24) to 0.83(0.16) ($p<0.05$), did not rise on resuscitation, and fell variably over 48 hours to 0.50(0.22) ($p<0.01$). All values in control pigs were unaltered. We conclude that the MRS abnormalities previously seen in the asphyxiated human infant can be reproduced in the piglet, and that increased lac/cho and reduced Naa/cho were related to falling [PCr]/[Pi].

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PRENATAL HORMONAL THERAPY IMPROVES PULMONARY MORPHOLOGY IN RATS WITH NITROFEN-INDUCED CONGENITAL DIAPHRAGMATIC HERNIA
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The high mortality of Congenital Diaphragmatic Hernia (CDH) is due in large part to the pulmonary hypoplasia, which resembles that seen in premature neonates with respiratory distress syndrome (RDS). Using therapies extrapolated from RDS, we applied quantitative stereologic morphometric techniques to evaluate pulmonary development following prenatal hormonal therapy in the nitrofen CDH rat model. Antenatal hormonal therapy was administered on days 18.5 and 19.5 prior to delivery on day 21.5, using dexamethasone (Dex), thyrotropin releasing hormone (TRH), Dex-TRH, or normal saline (NS) as control. Lungs from CDH rats (n=5) in each treatment group were studied, ten morphometric airspace parameters determined by point-counting 18-30 fields/lung/animal, and analysis of variance with post hoc testing was performed.

Figure. Haematoxylin & Eosin sections (x200) a) NS CDH control b) Dex-TRH treated CDH.

Prenatal corticosteroid ± TRH treatment of CDH significantly improved multiple morphometric parameters of lung maturity in the rat model, further supporting the potential use of hormonal therapy for in utero treatment of human CDH.

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THE EFFECT OF EITHER DOPAMINE OR VOLUME-EXPANSION ON BLOOD PRESSURE AND CARDIAC FUNCTION IN MODERATELY HYPOTENSIVE, PRETERM INFANTS
Kaare Lundström. Dept. of Neonatology, Rigshospitalet, Copenhagen, DK. Hypotension is a wellknown risk factor for adverse outcome in preterm infants. This study examines the cardiac function in moderately hypotensive, preterm infants and the effect of either volume expansion or dopamine infusion in these patients.

Design Inclusion criteria: GA<33 weeks, 29mmHg<Mean Arterial blood Pressure(MAP)<40mmHg. The infants (n=26) were randomly assigned to receive an infusion of dopamine; 5 µg/kg/min or a bolus of plasma; 15 mL/kg. Measurements of left ventricular output (LVO) and MAP were taken before treatment (T_0) and two hours later. Data were analysed using ANOVA.

Methods LVO was calculated by measuring the internal aortic diameter using combined B- and M-mode echocardiography, and measuring the blood flow velocity at the same site using Doppler ultrasound. Blood pressure was measured invasively through an indwelling arterial catheter.

Results Patients (median(range)): GA 28(25-32) wks BW 1183(680-2140) gm

T_0 values (mean(range)): LVO 203 (85-368) mL/kg/min. MAP 34 (30-39) mmHg.

At T_0 no differences were found between the groups.

Induced changes, mean values (95% Confidence Intervals) given:

Dopamine (n=13) Volume (n=13) p-value

ΔLVO +15(+3-+28)% +17(0-+33)% 0.88

ΔMAP +20(+11-+28)% +6(0-+12)% 0.009

Conclusions 1. LVO may be low in moderately hypotensive preterm infants and therefore warrant treatment. 2. Dopamine is more effective than volume expansion at increasing blood pressure, though both treatments are equally effective at increasing LVO. Further comparison of the two treatment regimes require assessment of organ perfusion.

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INCREASED PLASMA cGMP IN HYPOTENSIVE PRETERM INFANTS

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Arterial hypotension is a common problem among preterm infants. EDRF/nitric oxide is a potent vasodilator which affects through a generation of cGMP. We studied whether EDRS/nitric oxide system is involved in hypotensive events in preterm infants by measuring the plasma levels of cGMP in 25 infants with a mean birthweight of 1390g (range 870-2910). Arterial blood samples were obtained at days 2 and 9 of life. cGMP was measured with radioimmunoassay after acetylation. Blood pressure was recorded with Dinamap® sphygmomanometer at 15 to 60 min intervals for the first 48 hours. The infants were divided in two groups according to the frequency of the occurrence of mean arterial blood pressure (MAP) <30 mmHg: group 1 (N=10) in whom the frequency was >10% and group 2 (N=15) in whom that was <10%. At day 2 cGMP was significantly higher in group 1 than in group 2 (0.919 pmol/ml vs. 0.675 pmol/ml, $p=0.015$). By day 9 it decreased in both groups, but the difference remained (0.763 pmol/ml vs. 0.516 pmol/ml, $p=0.014$). cGMP concentration had a positive correlation with the frequency of low MAP values, and a negative correlation with gestational age and birth weight.

In conclusion, in preterm infants hypotension was associated with increased plasma concentration of cGMP. This may indicate adverse hemodynamic effect of EDRF/nitric oxide system.

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DEVELOPMENT OF BEHAVIORAL STATES IN PRETERM INFANTS

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We have examined the development of behavioral states in preterm infants born at a postmenstrual age < 30 weeks. The infants were longitudinally recorded up until 40 weeks of postmenstrual age.

The data of the first 16 babies recorded four times or more have been analysed. The behavioral states were assessed by 120 minutes of continuous observation and polygraphic recordings. Using the three-minute moving window, five different behavioral 'states' were scored according to Precht. The remainder of each recording session was assigned as 'no-state'. In a two-hour recording the total amount of no-state showed a significant systematic decrease from an average of 70 to 20 minutes as a function of development (fig). These results suggest that assessment of behavioral states is a good indicator for estimating the degree of brain maturation in preterm infants.