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INFANTS WITH NECROTIZING ENTEROCOLITIS: PHARMACOECONOMIC ANALYSIS OF LUCINACTANT (SURFAXIN) VERSUS POOLED ANIMAL-DERIVED SURFACTANTS IN PREVENTING RDS

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Background: Necrotizing enterocolitis (NEC) is a serious complication among pre-term infants. Surfactant replacement therapy can help to prevent respiratory distress syndrome (RDS) among very low birth weight (VLBW) pre-term infants. Currently, there are no pharmacoeconomic analyses that estimate the cost savings in preventing RDS among pre-term infants diagnosed with NEC who receive surfactant therapy.

Objectives: To estimate the economic impact of the synthetic protein-containing surfactant lucinactant (Surfaxin®) and pooled animal-derived surfactants (beractant [Survanta®] and poractant alfa [Curosurf®]) in the prevention of RDS among surviving pre-term infants weighing 600 to 1,250 grams who have been diagnosed with NEC.

Methods: A decision-analytic model was developed using a hospital perspective to estimate the economic impact of initial length of stay in the neonatal intensive care unit (NICU) for pre-term infants with NEC. Clinical outcomes consist of the average initial NICU length of stay from the combined Phase III randomized, controlled clinical trials of surfactant therapy (SELECT and STAR). The cost input was the average cost of treating surviving pre-term infants with medical NEC, U.S. $2,039, the combined level II and level III NICU cost per day (2002).

Results: Pre-term infants with NEC who survived and received lucinactant had 2.27 fewer initial NICU days compared to the pooled animal-derived cohort (73.73 versus 76.00 days, respectively). The estimated average cost of an initial NICU stay per infant was U.S. $150,320 for infants receiving lucinactant compared to U.S. $154,948 for infants receiving animal-derived surfactants. Due to fewer NICU days, lucinactant therapy results in a medical cost savings of U.S. $4,628 per infant.

Conclusion: Among surviving pre-term infants diagnosed with NEC who received surfactant therapy, the synthetic protein-containing surfactant lucinactant reduced total initial NICU hospital costs when compared to pooled animal-derived surfactants.

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INTERMITTENT HYPOXIA IN SUPINE VERSUS SIDE POSITION IN 1–5 D OLD TERM NEONATES

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Introduction: Supine sleeping is recommended to prevent sudden infant death syndrome (SIDS). Anecdotal evidence, however, suggests that cyanotic episodes are more common in neonates sleeping supine. We wanted to determine whether term neonates do indeed have more episodes of intermittent hypoxia in the supine than in the side position.

Methods: We enrolled 1–5 day old term neonates in a controlled 2-phase cross-over study design. They were randomised to sleep, for 6 h each, either in supine followed by side position (right or left) or vice versa. Pulse oximeter saturation (SpO2) values and a signal quality indicator were recorded throughout (VitaGuard VG 300 with Masimo SET, Irvine, CA; 2–4 s averaging). Only recordings lasting at least 3 h in either position were included. Desaturation events to <85% and <80% SpO2 were analysed, excluding events with poor signal quality.

Results: 477 neonates had recordings of sufficient duration. Mean duration of analyzable signal was 4.93 h for supine and 4.89 h for side position. 38% and 75%, respectively, of infants showed no desaturation to <85% or <80%. The average desaturation rate to <85% SpO2 per hour for the entire group was 0.41 in supine and 0.34 in side position, yielding an event ratio of 1.21 (95% confidence interval (95%CI), 1.10–1.33). Corresponding figures for desaturations to <80% SpO2 were 0.11/h vs. 0.05/h (event ratio 2.07; 95%CI: 1.67–2.58).

Conclusion: Side sleeping, compared to supine sleeping, was associated with a 21% increase in desaturation rate to <85% SpO2 and twice as many desaturations to <80% SpO2. Most infants (75%), however, had no desaturation to <80% in either position. Whether this effect of sleep position on intermittent hypoxemia in neonates has any long-term effect remains, at present, unknown.

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MONITORING THE FETAL HEART RATE AND FETAL ELECTROCARDIOGRAM: ABDOMINAL RECORDINGS ARE AS GOOD AS DIRECT ECG MEASUREMENTS

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AIM: The aim of this project is to develop an algorithm to monitor online the fetal heart rate (fHR) and fetal electrocardiogram (fECG) from maternal abdominal recordings.

METHODS: Measurements have been performed using 12 electrodes on the abdomen of the mother. In an initialization phase, the algorithm calculates the fetal signal for each electrode after effectively removing the maternal ECG and suppressing the electromyogram (EMG). Next, the algorithm selects the 4 signals in which the fetal component is most present and uses these signals for further calculations. The reduction of the number of electrodes used in the calculation decreases computation times significantly and enables the algorithm to monitor the fHR online. To increase the signal-to-noise ratio of the calculated fECG complex, 10 consecutive PQRS complexes are averaged. By means of cross correlating the PQRS complexes, PQRS complexes containing artifacts are excluded from the averaging process. The algorithm is validated by comparing the calculated fHR from abdominal recordings to the fHR determined from direct ECG signals measured with a scalp electrode.

RESULTS: A total of 530 paired fECG complexes are analyzed. The fHR obtained from both methods correlates very well (correlation coefficient 0.99, $p<0.001$). The resulting fECG complex clearly shows the fetal P-wave, QRS-complex and T-wave.

CONCLUSIONS: The proposed algorithm provides a valuable tool for obtaining noninvasively and online information of the fHR and fECG in stages of pregnancy earlier than labor. Future research is aimed at the uterine EMG, morphology of the fetal PQRS complexes and fHR variability analysis in order to obtain more detailed information of the fetal condition.

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NEURONAL DAMAGE AFTER MODERATE HYPOXIA AND ERYTHROPOIETIN

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Both mild hypoxia and exogenonus erythropoietin may protect the brain against subsequent severe hypoxia, and the conditioning effect of transient hypoxia is partly mediated by hypoxia-induced endogenous erythropoietin. We now observed in several experimental models that combining transient hypoxia and exogenous erythropoietin may cause neuronal damage. High-dose erythropoietin (40 IU/mL) profoundly impeded synaptic transmission of rat hippocampal slice cultures when used in conjunction with moderate hypoxia (10% O2 for two 8-h periods). Addition of erythropoietin increased viability of cultured rat embryonic cortical neurons at 21% O2 but decreased viability under hypoxic conditions (2% O2) in a dose-dependent fashion. Death of human neuronal precursor cells challenged by oxygen and glucose deprivation was increased by erythropoietin when cells were cultured under hypoxic but not under normoxic conditions. In neonatal rats exposed to moderate hypoxia plus erythropoietin, numbers of degenerating cerebral neurons were increased, as compared to controls or rats subjected to either hypoxia or erythropoietin alone. Thus, erythropoietin may aggravate rather than ameliorate neuronal damage when administered during transient hypoxia. This work was supported in parts by grants from the Bundesministerium für Bildung und Forschung, Bonn (01ZZ0101), the Wilhelm Sander Stiftung, Munich (2000.091.1), the Sonnenfeld-Stiftung, Berlin, and the Förderverein für Frühgeborene im Virchow-Klinikum, Berlin, Germany.

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DIFFERENT OUTCOME AFTER AIR EMBOLISM IN TWO PRETERM INFANTS

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Background: Systemic air embolism is a rare but fatal complication in the course of neonatal intensive care patients. Risk factors are ventilatory support or central venous lines. We herein report two cases without a direct link to risk factors and with diverse outcome.

Case reports: The first patient was a male preterm triplet of 28 weeks gestational age, weighing 1180 g, treated with nasal CPAP and supplemental oxygen in the first hours of life. Parenteral fluid supply was administered by a peripheral intravenous catheter. At day 12 of life an aggravation of the patients general condition accompanied by livid discoloration of the upper leg and abdomen occurred. Ultrasonography demonstrated presence of intracerebral, intrarenal, intraintestinal and intracardiac air. 12 hours after the initial event the patient developed necrotizing enterocolitis, warranting abdominal surgery. The further clinical course was complicated by extensive periventricular leukomalacia with cerebral seizures. 9 weeks after the air embolism the patient died from decompensated congestive cardiomyopathy. Post-mortem examination revealed an infarction of the left ventricle. The other patient, a female preterm infant of 27 weeks gestational age with a birth weight of 735 g, was ventilated for 24 hours and then managed on CPAP at room air. On the third day of life a sudden deterioration with acute bradycardia required cardiopulmonary resuscitation which resulted in a small pneumothorax that resolved spontaneously. Air embolism was the suspected trigger of this episode. Ultrasound examination revealed air in heart, liver and brain. The patient was stabilized and showed no residual findings during the further clinical course.

Conclusion: In both cases a direct cause of the air embolism could not be revealed since common risk factors did not apply for both patients. Although the precise nature of this complication is not well understood the contrasting outcomes of the reported neonatal cases is striking.

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MICROCIRCULATORY PARAMETERS AS EARLY MARKERS FOR INFECTION IN PRETERM INFANTS

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Background We have previously shown that orthogonal spectral imaging (OPS imaging) can be used to measure microcirculatory parameters such as Red Blood Cell Velocity (RBC Vel) and Functional Capillary Density (FCD). As neonatal infections often manifest unspecificly in e. g. paleness and prolonged capillary refill time we examined if a decrease in FCD can predict neonatal infection.

Methods In 25 preterm infants (gestational age of 28 (26,18 - 27,58) wks; birth weight 900 (807,9 - 992,8) g) RBC Vel and FCD was determined from d 3 till d 30 of life. OPS imaging was applied to the upper arm near the axilla, images were stored on videotape and analyzed off-line with the CapiScope Program.

Results There were 17 episodes of proven infections (PosInf) with either increased C-reactive Protein or increased interleukine-6. The day when antibiotic treatment was started was defined as d 0 of infection and the evaluation was concentrated on five days before (d -5 until d -1) and five days after (d +1 until d +5). In nine cases the suspected infection was not confirmed biochemically (NegInf). Four infants had no episode of infection for entire time. In PosInf we found a statistical significant decrease in FCD from d -5 to d -1 (mean (95% CI) 231 (187 - 236) cm/cm2 versus 234 (190 - 257) cm/cm2 ; $p = 0{,}0127$), but not for NegInf ($p = 0{,}58$). RBC Vel did not change from d -5 to d -1 nor during infection.

Conclusion A decreasing FCD correctly identified episodes of infections already one day earlier than changes in laboratory parameters. OPS-Imaging could be used for early diagnosis of secondary infection in preterm infants. However, these changes in FCD during infection are not represented by absolute values, but must be identified by daily intra-individually.