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PROLONGED OXIDATIVE STRESS AND INCREASED INCIDENCE OF NEONATAL MORBIDITIES AFTER EARLY POSTNATAL EXPOSURE TO OXIDANTS IN INFANTS LESS THAN 29 WEEKS GESTATIONAL AGE

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Background The antioxidant defenses are poorly developed in preterm infants. Oxygen and parenteral nutrition (PN) which is contaminated with peroxides are two major sources of oxidants. **Objective** To assess the effect of early oxygen (on day 7 and 28) and the PN duration on oxidative stress markers at 36 weeks post menstrual age (PMA) and on the incidence of neonatal morbidities.

Design/methods A prospective observational study including 120 infants less than 29 weeks gestational age without major congenital anomalies. Consent for blood sample at 36 weeks PMA was obtained for 51 infants. GSH and GSSG (nmol/mg protein) were measured by capillary electrophoresis and were used for redox potential (mV) calculation using Nernst equation, and expressed as mean (\pm sem). BPD was defined as the need of O₂ supplement at 36 weeks PMA. ROP that required either laser or anti-VGF treatment and NEC grade 2 or higher according to Bell's criteria were included. Student's t test or Chi squared were used as appropriate, * = $p < 0.05$, ** = $p < 0.01$.

Results FiO₂ $\geq 25\%$ on day 7 and 28 of life and PN duration > 14 days resulted in higher GSSG concentration, more oxidised redox potential at 36 weeks PMA and increased the incidence of BPD, ROP and NEC

Conclusions Early life exposure to oxidants is associated with prolonged oxidative stress and higher incidence of neonatal morbidities. These results suggest that strategies targeting judicious O₂ use and either decreasing the duration or using safer formulation PN will help decreasing the incidence of BPD, ROP and NEC.

Abstract PS-279 Table 1

	GSH	GSSG	Redox potential	BPD or Death	ROP	NEC
FiO ₂ $< 25\%$ on day 7	7.6 (0.5)	0.18 (0.02)	-198 (2)	26/54	2/56	7/56
FiO ₂ $\geq 25\%$ on day 7	7.4 (0.6)	0.29 (0.04)	-191 (2)	46/50	6/50	17/50
P	NS	*	*	**	NS	**
FiO ₂ $< 25\%$ on day 28	8.3 (0.8)	0.17 (0.02)	-201 (4)	9/36	0/37	4/37
FiO ₂ $\geq 25\%$ on day 28	7.3 (0.5)	0.26 (0.03)	-193 (2)	55/60	8/60	17/60
P	NS	NS	*	**	*	*
PN ≤ 14 days	7.5 (1.2)	0.13 (0.02)	-203 (5)	16/42	0/44	2/44
PN > 14 days	7.5 (0.4)	0.26 (0.03)	-193 (2)	58/64	8/65	22/65
P	NS	*	*	**	*	**

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SURFACE FILM FROMATION *IN VITRO* BY INFANT AND THERAPEUTIC SURFACTANTS: ROLE OF SURFACTANT PROTEIN B

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Background Essential surfactant properties include transfer to gas-liquid interface, reduction of surface tension and film replenishment during respiratory cycles.

Objective To compare component-specific film formation properties of infant and therapeutic surfactants.

Design/methods Using a multiwell fluorescence assay, we compared maximal fluorescence (Max), time to reach Max (tMax) and phospholipid concentration for $\frac{1}{2}$ maximal signal ($\frac{1}{2}$ Max) for calfactant (CAL), poractant (POR), beractant (BER), colfosceryl palmitate (COL), with surfactant from immature infants with RDS. Dose-response studies were performed for addition of SP-B, albumin and budesonide.

Results Max and $\frac{1}{2}$ Max values for CAL were higher/similar to those of rat surfactant. There were significant differences between CAL and other therapeutic surfactants for Max (CAL $>$ COL $>$ POR $>$ BER) whereas $\frac{1}{2}$ Max were similar except for COL.

In surfactant from 39 infant tracheal aspirates, $\frac{1}{2}$ Max was inversely correlated with SP-B content ($p = 0.001$). Addition of SP-B to samples with low endogenous content ($< 0.1\%$) decreased $\frac{1}{2}$ Max in a dose-dependent way. Addition of 1.25% SP-B to BER (SP-B content 0.04%) increased Max by 324%. Addition of albumin to CAL (0.75 μ g/ μ g PL) increased $\frac{1}{2}$ Max by 110% and reduced Max by 13%. By contrast, addition of budesonide to CAL at 2% and 10% increased Max by $51 \pm 26\%$ and $93 \pm 19\%$, with no effect on $\frac{1}{2}$ Max.

Conclusions This assay reveals differences in film formation efficiency for therapeutic surfactants reflecting differences in SP-B content and lipid composition. Film formation by infant surfactant is strongly influenced by SP-B content. The findings support the key physiological role of SP-B and the safety of surfactant as anti-inflammatory drug vehicle.

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LUNG ULTRASOUND SCORE TO EVALUATE OXYGENATION AND SURFACTANT NEED IN CRITICALLY ILL NEONATES

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Background and aims Lung ultrasound (LUS) has been recently proposed to obtain fast and reproducible informations in critical care and to diagnose respiratory distress syndrome, wet lung or air leaks. Nevertheless, no data are available about its use for monitoring lung function and eventually guide respiratory support. We investigate the use of LUS score to estimate oxygenation status and surfactant need in neonates.

Methods 55 consecutive neonates under CPAP underwent LUS with a 7.5 MHz microconvex probe both on transversal and longitudinal scan. Three lung areas (upper, lower, lateral) were examined according to a score previously published in critically ill adults and modified for neonates.[1] Such score is based on prevalence of A-lines, < 3 B-lines, > 3 crowded B-lines or consolidation (0–3 points, respectively). Transcutaneous PaO₂ and PaCO₂, FiO₂, airway pressure were recorded during LUS. PaO₂/FiO₂, oxygenation index and A-a gradient were calculated.

Results Mean GA and BW were 33 (SD 3.2) wks and 2310 (SD 893) g, respectively. LUS score is highly correlated with PaO₂/FiO₂ ($\rho = -0.77$; $p < 0.001$), oxygenation index ($\rho = 0.79$; $p < 0.001$) and A-a gradient ($\rho = 0.78$; $p < 0.001$). These correlations remained significant after adjustment for birth weight,

gestational and postnatal age. LUS score shows high reliability for surfactant need (AUC = 0.82; $p = 0.005$; best cut off 11.5 [sensitivity 75%, specificity 90%]).

Conclusions LUS score is well correlated with oxygenation status and shows enough reliability to predict surfactant need. LUS can be used to monitor serially the course of respiratory conditions in critically ill neonates.

REFERENCE

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PS-282

RESTRICTED USE OF REPEAT DOSES OF SURFACTANT AFTER THE PROPHYLACTIC DOSE DOES NOT INCREASE THE RISK OF BPD OR DEATH IN PRETERM INFANTS

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Repeat doses of surfactant after the prophylactic dose for treatment of RDS are currently recommended by the manufacturers to be administered at minimal levels of respiratory support. Reducing the number of unnecessary repeat doses will represent a significant cost-saving.

We determined if restricting repeat doses of Surfactant by using high-threshold criteria for respiratory support increased the risk of the composite primary outcome of BPD or death before hospital discharge.

Methods A total of 140 infants of ≤ 28 weeks gestation who received prophylactic Surfactant soon after birth were reassessed 12 h after the initial dose for retreatment if the infant remained intubated and required at least 40% inspired oxygen with a MAP > 10 cm H₂O, and compliance of < 0.5 ml/cm H₂O.

Multivariate analysis identified which risk factors from a set of a priori predictors including the need for Surfactant retreatment could predict the primary outcome.

Results Eighty-eight (59%) of 140 infants reached the retreatment criteria and received repeat doses of Surfactant. Sixty-eight (49%) infants developed BPD or died. Infants who developed BPD or died were younger and smaller; were more likely to have PDA, NEC or sepsis, longer (> 28 days) stay on mechanical ventilation, and receive retreatment with Surfactant. On forward stepwise logistic regression analysis of a priori risk factors only the need of ventilation > 28 d ($p < 0.001$, OR 7.3, 95% CI 2.7–19.5) was independently associated with increased risk of primary outcome.

Conclusion Restricting repeat doses of Surfactant did not increase the risk of BPD or death in preterm infants with RDS.

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INSURENCPAP APPROACH VERSUS SURFACTANTMECHANICAL VENTILATION IN EXTREMELY LOW BIRTH WEIGHT INFANTS

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Background and aims We evaluated the efficacy of nasal continuous positive airway pressure (nCPAP) treatment following the administration of surfactant using the INSURE (INTubation SURfactant Extubation) approach. We aimed to compare the efficacy of INSURE during nasal CPAP application and post-surfactant mechanical ventilation in extremely low birth weight (ELBW) infants.

Methods A total of 182 ELBW infants with a diagnosis of respiratory distress syndrome admitted to the neonatal intensive care unit during January 2012 and 2014 were retrospectively screened. Of these 74 received INSURE during nasal CPAP application (INSURE-nCPAP group) and 108 received mechanical ventilation following endotracheal surfactant application (MV group). The rate of mortality, intraventricular haemorrhage (IVH), repeat doses of surfactant, pneumothorax, pulmonary haemorrhage, necrotizing enterocolitis (NEC), sepsis, broncho pulmonary dysplasia (BPD) the duration of hospitalisation were compared between the two groups.

Results Infants in the INSURE-nCPAP group had significantly lower rates of IVH and pulmonary haemorrhage ($p = 0.02$ and 0.01 ; respectively). The need for mechanical ventilation, BPD and the rate of mortality was lower in infants in the INSURE-nCPAP group. While there was no significant difference in the rates of bloodstream infection and ROP between the groups; the duration of hospitalisation was shorter in infants in the INSURE-nCPAP group.

Conclusions In the current study we found that the INSURE-nCPAP approach in preterm infants with respiratory distress syndrome was effective. Additionally, we found that the rate of mortality, IVH, pulmonary haemorrhage and BPD was lower in infants treated with INSURE approach.

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EARLY INTUBATE-SURFACTANT-EXTUBATE (INSURE) VERSUS NON-INVASIVE CONTINUOUS POSITIVE AIRWAY PRESSURE (NCPAP) TO PREVENT BRONCHOPULMONARY DYSPLASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and aims In preterm infants, early non-invasive continuous positive airway pressure (NCPAP) use decreases “bronchopulmonary dysplasia (BPD) or death” compared with early intubation. However, it was not yet clear whether early Intubation-for-SURfactant-followed-by-Extubation to NCPAP (INSURE) is more effective to prevent BPD or Death or “BPD or death” or either than keeping infants on NCPAP. This systematic review aimed to investigate this question.

Methods This systematic review included randomised control trials comparing the INSURE and NCPAP for preterm infants with or at high risk of respiratory distress syndrome who had never been intubated before the study entry. Primary outcomes included BPD at 36 weeks postmenstrual age, Death, and “BPD or Death”. A systematic literature search was conducted of MEDLINE, EMBASE, CENTRAL, and CINAHL as well as conference proceedings and trial registrations. Two reviewers independently selected studies and extracted data. Meta-analyses were conducted with a random-effect method using Review