

# Selected Abstracts of the 1<sup>st</sup> Congress of joint European Neonatal Societies (jENS 2015) • Session “Pulmonology”

BUDAPEST (HUNGARY) • SEPTEMBER 16<sup>TH</sup>-20<sup>TH</sup> 2015

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## HOW TO CITE

[Abstract's authors]. [Abstract's title]. In: Selected Abstracts of the 1<sup>st</sup> Congress of joint European Neonatal Societies (jENS 2015); Budapest (Hungary); September 16-20, 2015; Session "Pulmonology". J Pediatr Neonat Individual Med. 2015;4(2):e040213. doi: 10.7363/040213.

## POSTER PRESENTATIONS

## ABS 1

### URINE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A MARKER OF BRONCHOPULMONARY DYSPLASIA AND RETINOPATHY OF PREMATURITY IN PRETERM NEONATES

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## INTRODUCTION

Although improvement in perinatal care over the past few decades has increased the survival of very low birth weight (VLBW) infants, these newborns continue to suffer from significant morbidities such as bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP). There is a need to focus on early biomarkers of the subsequent BPD and ROP, which could facilitate development of preventive strategies. Urine neutrophil gelatinase-associated lipocalin (uNGAL) is a protein produced by the kidney after ischemic or nephrotoxic injury. The purpose of the study is to evaluate risk factors, and the efficacy of uNGAL as predictor for BPD and ROP.

## PATIENTS AND METHODS

Seventy three VLBW infants who were admitted to our tertiary neonatal unit between June 2012 and July 2014 were prospectively evaluated for morbidities of prematurity. Neonates

with any congenital anomaly, renal and heart diseases, those who died within the first week after birth were excluded from the study. Data on demographic-perinatal characteristics and prematurity-associated complications were recorded. Urine samples of the newborn for uNGAL were collected within first 48 hours after birth, and at 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>th</sup>, and 28<sup>th</sup> ( $\pm 1$ ) days.

## RESULTS

Mean gestational age and birth weight were  $28.8 \pm 2.4$  weeks and  $1,099 \pm 273$  g, respectively. The incidence of respiratory distress syndrome, culture (+) sepsis, treated patent ductus arteriosus,  $\geq$  grade II necrotizing enterocolitis, acute kidney injury, perinatal asphyxia, peri-intraventricular hemorrhage, and mortality were found 72.6%, 39.6%, 27.4%, 10.9%, 9.6%, 6.8%, 2.7%, and 10.9%, respectively. The frequencies of BPD and ROP were 38.8% and 10.7% in infants who were discharged (n = 65). Compared to non-BPD and non-ROP infants, uNGAL levels were significantly higher in infants with BPD and ROP in the first 48 hours, at 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>th</sup>, and 28<sup>th</sup> ( $\pm 1$ ) days. Area under the curve, cut-off, sensitivity and specificity values of uNGAL differentiating neonates with BPD and ROP were presented in **Tab. 1**.

**Table 1 (ABS 1).** Area under the curve (AUC), cut-off point, sensitivity and specificity of urine neutrophil gelatinase-associated lipocalin (uNGAL) differentiating neonates with bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP).

Days	Area under the curve (AUC)	p-value	Cut-off point	Sensitivity	Specificity
<b>BPD</b>					
1-2	0.658	0.033	30.21	80%	53%
7	<b>0.734</b>	<b>0.002</b>	<b>31.54</b>	<b>80%</b>	<b>70%</b>
14	0.651	0.042	19.57	80%	53%
21	0.655	0.037	15.91	80%	38%
28	0.660	0.031	13.1	84%	40%
<b>ROP</b>					
1-2	0.803	0.009	47.87	86%	68%
7	<b>0.786</b>	<b>0.014</b>	<b>41.06</b>	<b>86%</b>	<b>69%</b>
14	0.805	0.009	29.91	86%	67%
21	0.839	0.004	24.12	86%	69%
28	0.754	0.029	19.21	86%	63%

**CONCLUSIONS**

We conclude that uNGAL level is elevated from first 48 hrs to 28<sup>th</sup> days in VLBW infants with BPD and ROP. High uNGAL level was significantly associated with the subsequent diagnosis of BPD and ROP in these neonates. It could be speculated that uNGAL may be a useful noninvasive biomarker for BPD and ROP in VLBW infants.

**ABS 2****LUNG COMPLIANCE AND LUNG ULTRASOUND DURING POSTNATAL ADAPTATION IN HEALTHY NEWBORN INFANTS**

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**INTRODUCTION**

The lungs are cleared of perinatal fluid during the first hours of life and the process continues for the first days of life. Lung fluid clearance is motored by active sodium transport through epithelial sodium channel and osmotic pressure. The clearance of lung fluid improves lung function, which can be measured by static lung compliance (LC). Lung fluid content has also been estimated by lung ultrasound (L-U/S). Vertical artefacts in L-U/S, B-lines, correlate with fluid content of the lungs. The purpose of the study was to compare L-U/S and LC for estimation of lung adaptation during the first postnatal day.

**PATIENTS AND METHODS**

We performed LC measurement and L-U/S in 34 healthy term infants born by elective cesarean section. LC was measured with pneumotachometer by double occlusion technique at age < 4 h and 24 h. Separate L-U/S measurements were performed also at age < 4 h and 24 h. The abundance of B-lines were scored on five-step scale by radiologist blinded to the time-point of measurement.

**RESULTS**

There was a significant improvement in LC during the first 24 h postnatally. The mean LC values were 10.9 ml/kPa/kg at age < 4 h and 14.7 ml/kPa/kg at age 24 h ( $p < 0.001$ ). In addition,

a significant decrease in B-lines scores was seen at 24 h (median 1,8) compared to < 4 h of age (median 3.3;  $p < 0.001$ ). The correlation between the results of LC and L-U/S was not significant ( $p = 0.5$  at < 4 h and  $p = 0.95$  at 24 h).

**CONCLUSIONS**

In the early postnatal period lung adaptation is measureable as significant changes in LC and L-U/S. The correlation between the two methods was not statistically significant. Because LC is prone to artefacts, L-U/S may, as an easily implementable technique, be applicable for lung fluid content measurement in newborns.

**ABS 3****PRE-DISCHARGE RESPIRATORY OUTCOMES IN SMALL-FOR-GESTATIONAL-AGE AND APPROPRIATE-FOR-GESTATIONAL-AGE VERY PRETERM INFANTS**

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**INTRODUCTION**

Very preterm infants (born before 32 weeks of gestation) have the greatest risk of respiratory morbidity. Literature data are contradictory regarding differences in respiratory outcomes between small-for-gestational-age (SGA) and appropriate-for-gestational-age (AGA) infants in this gestational group.

**PATIENTS AND METHODS**

We retrospectively collected data of 108 infants who were delivered from single pregnancies before completion of 32 weeks of gestation in regional tertiary-care university hospital. Study period was from January 2011 till September 2012. All newborns with < 10<sup>th</sup> birth weight percentile were considered as SGA. Percentiles were calculated using customized centile calculator software program. We extracted data about respiratory morbidity during primary hospitalization after birth.

**RESULTS**

Out of 108 infants, 47 were SGA and 61 were AGA, with mean gestation of 29.24 and 28.73 weeks, respectively. Mortality during primary hospitalisation was higher in SGA group

(RR 1.83, 95% CI 1.25-2.66). There were no difference in prevalence of RDS (RR 1.029, 95% CI 0.96-1.10). Surfactant was administered more often in SGA infants, although this did not reach statistical significance (RR 1.29, 95% CI 0.97-1.72). Pressure support (n-CPAP and/or mechanical ventilation) was more often applied in SGA infants (RR 1.23, 95% CI 1.02-1.48). Bronchopulmonary dysplasia (BPD – need for supplemental oxygen at the age of > 27 days) and chronic lung disease (CLD – need for supplemental oxygen at 36 weeks corrected age) were calculated only for infants who survived until discharge. BPD was found significantly more often in SGA infants (RR 1.77, 95% CI 1.04-3.00), as well as CLD (RR 2.77, 95% CI 1.11-6.94).

#### CONCLUSIONS

In our survey, SGA infants who were very preterm had more often need for pressure support and surfactant therapy after birth compared with AGA control group. In addition, SGA very preterm infants had a higher risk of developing BPD and CLD.

## Apnea and respiratory control

#### ABS 4

#### THE EFFECT OF CHANGING OXYGEN SATURATION TARGET RANGE ON COMPLIANCE IN OXYGEN SATURATION TARGETING IN THE NEONATAL INTENSIVE CARE UNIT

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#### INTRODUCTION

Recent studies have shown a reduced mortality but increased rate of ROP in preterm infants when higher SpO<sub>2</sub> target range (SpO<sub>2</sub>TR 91-95%) was used compared to lower SpO<sub>2</sub>TR (85-89%). The SpO<sub>2</sub>TR was recently changed in our unit from 85-95% to 90-95%, recognizing

that it could be challenge for the NICU-nurses to comply with this smaller range. To audit the effect of changing the SpO<sub>2</sub>TR we compared before and after the implementation of SpO<sub>2</sub>TR 90-95% the percentage of time SpO<sub>2</sub> within target range (SpO<sub>2</sub>-WTR) as well as the duration and occurrence of hypoxaemia and hyperoxaemia that occur around apneas combined with bradycardia and cyanosis (ABCs).

#### PATIENTS AND METHODS

Retrospectively before and after changing SpO<sub>2</sub>TR from 85-95% to 90-95%, two cohorts of 10 vs. 5 months infants with FiO<sub>2</sub> > 21%, SpO<sub>2</sub> was collected every minute for each infant individually, and aggregated as proportions of recorded time.

In both cohorts, we identified all episodes of ABCs. In ABCs where oxygen supply was required, SpO<sub>2</sub> ≤ 80%, SpO<sub>2</sub> ≥ 95%, baseline oxygen concentration, additional oxygen given and the duration of increased oxygen given was noted.

#### RESULTS

In 68 infants before and 47 infants < 30 weeks GA after changing to SpO<sub>2</sub> TR 90-95% GA (median [IQR] 199 [187-203] vs. 194 [183-203] days; n.s.) and BW (1,005 [883-1,211] vs. 900 [740-1,153]; n.s.) were not different.

Changing to SpO<sub>2</sub>TR 90-95% had no effect on the percentage SpO<sub>2</sub>-WTR (mean [SD] 41.6 [20.8] vs. 41.5 [20.3]%; n.s.), SpO<sub>2</sub> < 85% decreased (7.1 [8.1] vs. 4.5 [2.8]; p < 0.05), but SpO<sub>2</sub> 95-98% increased (22.5 [13.0] vs. 29.0 [11.5]%; p98% (15.7 [26.0] vs. 15.5 [17.8]%; n.s.).

Before and after changing to SpO<sub>2</sub>TR 170 and 201 ABCs needing oxygen were analyzed (**Fig. 1**).

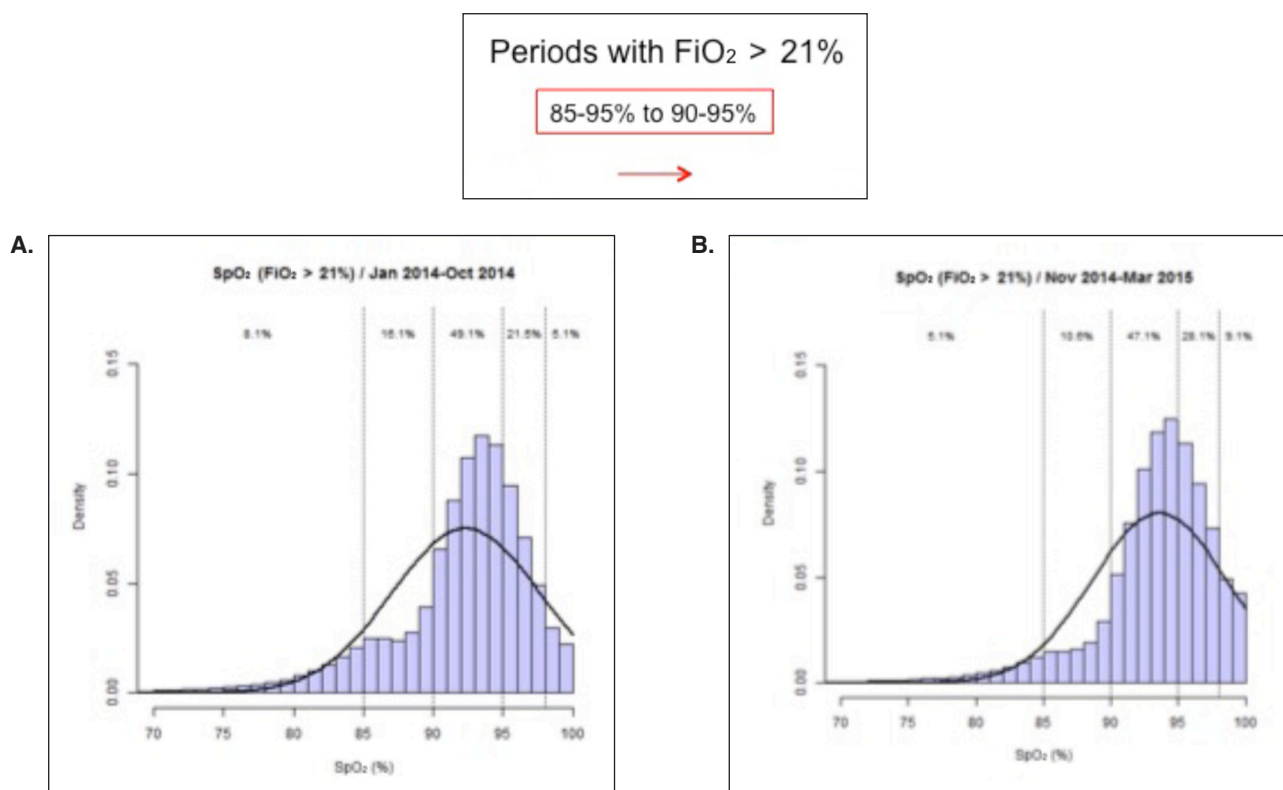
Occurrence of SpO<sub>2</sub> ≥ 95% after ABC increased (63% vs. 71%; p < 0.05), with shorter duration (1 [0-3] min vs. 1 [0-2] min; n.s.).

The depth of hypoxaemia was similar (72 [61-77]% vs. 73 [63-77]%; n.s.), as well as maximum oxygen (43 [36-51]% vs. 41 [31-45]%; n.s.) and duration to return to baseline level FiO<sub>2</sub> (3 [2-6] min vs. 2 [2-6] min; n.s.).

#### CONCLUSIONS

Compliance in SpO<sub>2</sub>TR did not change after changing from 85-95% to 90-95% and had no influence on the occurrence of hypoxaemia and hyperoxaemia during ABCs.

Changing TR to 90-95% reduced occurrence SpO<sub>2</sub> < 85% and 85-90%, the occurrence of SpO<sub>2</sub> 95-98% increased without an increase in > 98%.



**Figure 1 (ABS 4).** Different SpO<sub>2</sub> values in the two cohorts before (A) and after (B) changing SpO<sub>2</sub>TR from 85-95% to 90-95%.

## ABS 5

### BINASAL PRONG VERSUS NASAL MASK FOR APPLYING CPAP TO PRETERM INFANTS: RANDOMIZED CONTROLLED TRIAL

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#### AIM

We aimed to determine whether nasal continuous positive airway pressure (nCPAP) applied with binasal prongs compared with nasal mask reduces the rate of bronchopulmonary dysplasia (BPD) in preterm infants.

#### PATIENTS AND METHODS

Infants between 26-32 weeks' gestation who suffered from respiratory distress syndrome (RDS) and were treated with nCPAP were randomly assigned to receive it via either binasal prongs or nasal mask. Infants were intubated and ventilated if they fulfilled the failure criteria. Relevant secondary outcomes were recorded and data were collected by using the intention-to-treat principle.

## RESULTS

160 infants were screened and 149 infants were randomized. Seventy five infants in binasal prong group (Group 1) and 74 in nasal mask group (Group 2) were analyzed. Mean gestational ages were  $29.3 \pm 1.6$  vs.  $29.1 \pm 2.0$  weeks ( $p = 0.55$ ) and birth weights were  $1,225 \pm 257$  vs.  $1,282 \pm 312$  grams ( $p = 0.22$ ) respectively in Group 1 and Group 2 (**Tab. 1**). The frequency of nCPAP failure within 24 hours of life was higher in Group 1 compared to Group 2 (8% vs. 0%,  $p = 0.09$ ). The median duration of nCPAP was significantly higher in Group 1 (median 4 [1-5] vs. 2 [1-3] h,  $p < 0.01$ ). The rate of moderate and severe BPD was significantly lower in Group 2 ( $n = 2$ , 2.7%) when compared with Group 1 ( $n = 11$ , 14.6%) ( $p < 0.01$ ) (**Tab. 2**). The secondary outcomes are presented in **Tab. 3**.

## CONCLUSIONS

Nasal mask was successfully used for delivering CPAP in preterm infants and no CPAP failure was observed in first 24 h.

This present data shows that applying nCPAP by nasal mask yielded a shorter duration of nCPAP and statistically reduced the rates of moderate and severe BPD.

**Table 1 (ABS 5).** Basic characteristics and prenatal risk factors of the groups.

Characteristics	Binasal prongs (Group 1) (n = 75)	Nasal mask (Group 2) (n = 74)	p-value
Gestational age, mean $\pm$ SD, weeks	29.3 $\pm$ 1.6	29.1 $\pm$ 2.0	0.55
Birth weight, mean $\pm$ SD, g	1,225 $\pm$ 257	1,282 $\pm$ 312	0.22
Caesarean delivery, n (%)	70 (93)	70 (94)	0.78
Male, n (%)	34 (45)	44 (59)	0.08
Antenatal steroids, n (%)	64 (85)	68 (91)	0.06
Premature rupture of membrane > 18 hours, n (%)	14 (18)	13 (17)	1
Apgar score at 1 min, median (min-max)	6 (3-7)	6 (4-8)	0.25
Apgar score at 5 min, median (min-max)	8 (5-9)	8 (5-9)	0.16
Multiple pregnancies, n (%)	26 (34)	22 (29)	0.48
Small for gestational age, n (%)	5 (7)	11 (14)	0.18
Maternal preeclampsia, n (%)	13 (17)	14 (18)	1
Chorioamnionitis, n (%)	-	2 (2.7)	0.72

**Table 2 (ABS 5).** Respiratory outcomes among both groups.

Respiratory outcomes	Binasal prongs (Group 1) (n = 75)	Nasal mask (Group 2) (n = 74)	p-value
MV requirement < 24 h, n (%)	6 (8)	-	0.09
MV requirement < 48 h, n (%)	10 (13.3)	6 (8.1)	0.46
MV requirement < 72 h, n (%)	13 (17.3)	12 (16.2)	0.65
Any MV <sup>a</sup> , n (%)	21 (28)	23 (31.1)	0.72
Surfactant administration, n (%)	45 (60)	35 (47)	0.14
Age at first dose of surfactant, median (IQR), hours	5 (2-8)	2 (0-5)	0.006
Additional doses of surfactant, n (%)	8 (10)	2 (2.7)	0.09
Duration of nCPAP, median (IQR), days	4 (1-5)	2 (1-3)	0.006
Duration of MV, median (IQR), days	3 (2-4)	2 (0-4)	0.88
Duration of supplemental oxygen, median (IQR), days	7 (2-8)	4 (2-8)	0.26
Pneumothorax, n (%)	4 (5.3)	3 (4)	1
BPD, n (%)	15 (20)	11 (14.9)	0.27
Moderate and severe BPD, n (%)	11 (14.6)	2 (2.7)	0.01

MV: mechanical ventilation; IQR: interquartile range; BPD: bronchopulmonary dysplasia.

<sup>a</sup>Any MV: MV requirement in any time during hospitalization.

**Table 3 (ABS 5).** Secondary outcomes among both groups.

Secondary outcomes	Binasal prongs (Group 1) (n = 75)	Nasal mask (Group 2) (n = 74)	p-value
NEC, stage $\geq$ II, n (%)	1 (1.9)	3 (4)	0.61
PDA, n (%)	21 (28)	21 (28)	1
SIP, n (%)	1 (1.3)	-	0.27
IVH, grade > II, n (%)	5 (9.8)	5 (9.6)	0.96
Time to full feeds, median (IQR), days	13 (5-18)	14 (9-19)	0.28
Skin breakdown, n (%)	15 (20)	10 (13.5)	0.35
ROP, n (%)	2 (2.6)	3 (4)	1
Duration of hospitalization, median (IQR), days	18 (10-21)	25 (20-28)	0.36
Mortality, n (%)	4 (5.4)	7 (9.3)	0.53

NEC: necrotizing enterocolitis; PDA: patent ductus arteriosus; SIP: spontaneous intestinal perforation; IVH: intraventricular hemorrhage; IQR: interquartile range; ROP: retinopathy of prematurity.

## ABS 6

### TRAINING AND RAISING AWARENESS IMPROVES COMPLIANCE IN OXYGEN SATURATION TARGETING IN THE NEONATAL INTENSIVE CARE UNIT

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#### INTRODUCTION

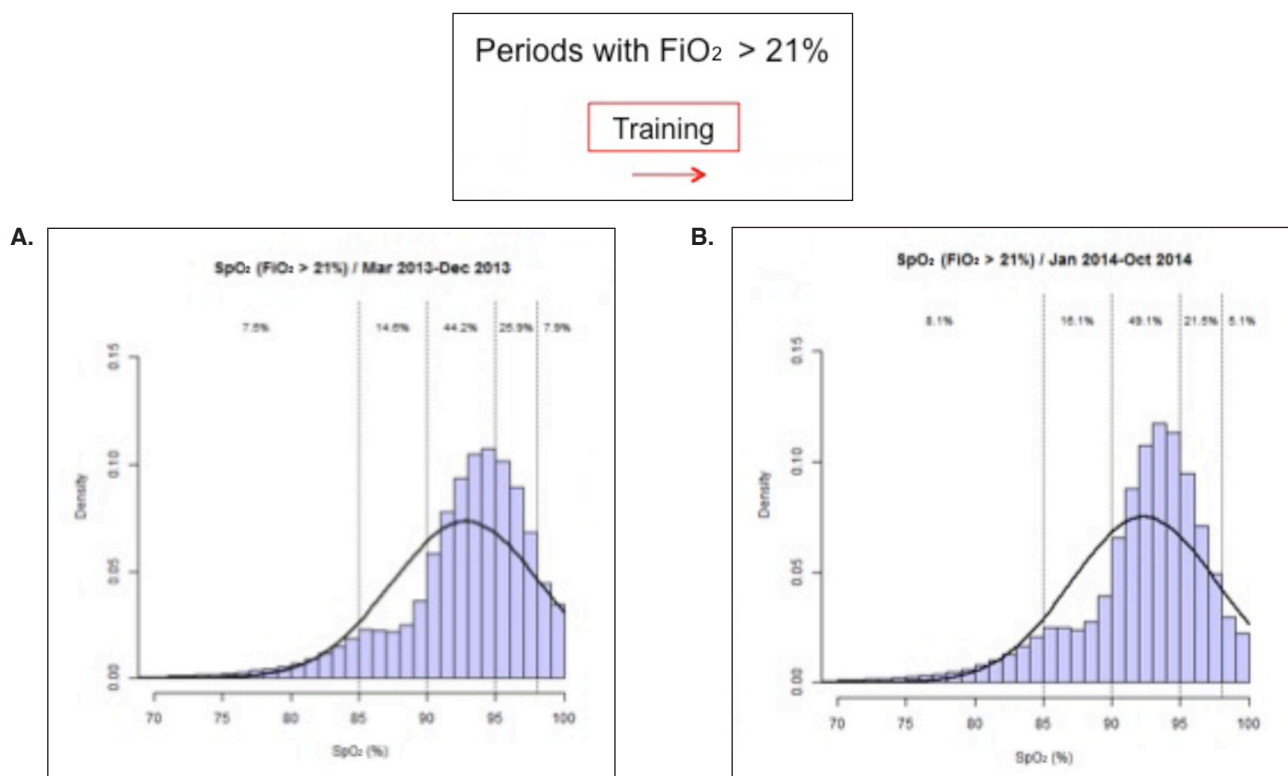
We recently reported compliance in oxygen saturation targeting is low and hyperoxaemia often occurs after apneas combined with bradycardia and cyanosis (ABC). To improve this several trainings were given in a month's period which also included raising awareness in the risk of hypoxaemia and hyperoxaemia. To study the effect we compared before and after the training the percentage of time SpO<sub>2</sub> within target range (SpO<sub>2</sub>-WTR) as well as the duration and occurrence of hypoxaemia and hyperoxaemia with ABCs.

#### PATIENTS AND METHODS

Retrospectively before and after the training, two cohorts of ten months infants with FiO<sub>2</sub> > 21%, SpO<sub>2</sub> was collected every minute for each infant individually, and aggregated as proportions of recorded time. In both cohorts, we identified all episodes of ABCs. In ABCs where oxygen supply was required, SpO<sub>2</sub> ≤ 80%, SpO<sub>2</sub> ≥ 95%, baseline oxygen concentration, additional oxygen given and the duration of increased oxygen given was noted.

#### RESULTS

In 171 infants before and 201 infants after training median (IQR) GA (188 [184-199] vs. 185 [177-197] days; n.s.) and BW (960 [684-997] vs. 770 [680-995]; n.s.) were not different. When compared to before training, after training the %SpO<sub>2</sub>-WTR increased (mean [SD] 44.2 [24.5]% vs. 54.7 [25]%; p < 0.01), while SpO<sub>2</sub> 95-98% (29.4 [13.2]% vs. 22.5 [13.0]%; p 98% (19.3 [21.7]% vs. 15.7 [26.0]%; p < 0.05) decreased, but no effect on SpO<sub>2</sub> < 85% (7.1 [10.0]% vs. 7.1 [8.1]%; n.s.). Before and after training 224 and 171 ABCs needing oxygen were analyzed. Occurrence of SpO<sub>2</sub> ≥ 95% after ABC decreased after training (78% vs. 63%; p < 0.05) as well as duration (6 [1-23] min vs. 1 [0-3] min; p < 0.001) (**Fig. 1**). The depth of hypoxaemia was less (68 [62-73]% vs. 72 [61-77]%; p < 0.05), maximum



**Figure 1 (ABS 6).** Different SpO<sub>2</sub> values in the two cohorts before (A) and after (B) training.

oxygen given increased (38 [30-67]% vs. 43 [36-51]%;  $p < 0.05$ ) and duration decreased (13 [3-49] min vs. 3 [2-7] min;  $p < 0.001$ ).

#### CONCLUSIONS

Training and raising awareness improved the compliance to stay within SpO<sub>2</sub> target range with a reduction in hyperoxaemia but not hypoxaemia. Oxygen was better titrated after ABCs and the occurrence and duration of hyperoxaemia reduced.

#### ABS 7

### CORRELATION AND INTERCHANGEABILITY OF VENOUS AND CAPILLARY BLOOD GASES FOR MONITORING GAS EXCHANGE IN THE NEONATAL INTENSIVE CARE UNIT

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#### INTRODUCTION

For monitoring gas exchange arterial blood gas is the gold standard and capillary blood gas (CBG) is considered a good alternative. Venous blood gas (VBG) for monitoring gas exchange is not recommended, but in a recent survey most neonatologists considered VBG as a good alternative for CBG. Studies comparing VBG with CBG are small and showed conflicting results in correlation. It is not clear whether a VBG and CBG measurement are interchangeable. We aimed to investigate the correlation and interchangeability of the components of VBG and CBG.

#### PATIENTS AND METHODS

In a prospective study in the neonatal unit in Leiden University Medical Center (the Netherlands) simultaneously VBG and CBG were withdrawn in infants where venipuncture or intravenous access and blood gas monitoring was indicated. VBG and CBG were taken sequentially as soon as possible within 5 minutes and with a maximum of 3 paired samples per patient. The Bland-Altman analysis is based on the 95% limits of agreement, estimated by mean difference (bias)  $\pm$  2 SD of the differences, that provides a 95% confidence interval of the differences between VBG and CBG are expected to lie. Clinically acceptable difference for each blood gas value was defined up-front by means of an absolute difference (pH  $\pm$  0.03], pCO<sub>2</sub> [ $\pm$  0.3 kpa], pO<sub>2</sub> [ $\pm$  0.3 kpa], BE [ $\pm$  3 mmol/l] and BIC [ $\pm$  3 mmol/l]).

#### RESULTS

In 93 patients (median gestational age 31 weeks [IQR 29-34]), 193 paired samples of VBG and CBG were taken. The correlation between VBG and CBG was very strong for pH ( $r = 0.79$ ;  $p < 0.001$ ), BE (0.90;  $p < 0.001$ ) and BIC ( $r = 0.87$ ;  $p < 0.001$ ), strong for pCO<sub>2</sub> ( $r = 0.68$ ;  $p < 0.001$ ), moderate for pO<sub>2</sub> ( $r = 0.31$ ;  $p < 0.001$ ) and weak for oxygen saturation ( $r = 0.45$ ;  $p < 0.001$ ). The mean difference and 95% limits of agreement between the two blood gases ranged for pH (-0.01 [-0.09, 0.07]), pCO<sub>2</sub> (0.17 kPa [-1.7, 2.0]), pO<sub>2</sub> (-0.4 kPa [-4.1, 3.3]), BE (0.0 mmol/l [-3.5 and 3.5]) and for BIC (0.2 mmol/l [-3.9 and 4.3]). Given our data, for the blood gasses pH, pCO<sub>2</sub> and PO<sub>2</sub>, there was a systematic difference (fixed bias) between VBG and CBG as indicated by significant paired t-tests. There was no evidence that the differences between VBG and CBG varied across the range of blood gas value (no proportional bias).

#### CONCLUSIONS

The use of correlation to decide on interchangeability of VBG and CBG can be misleading; as this study showed, a strong correlation between certain components of VBG and CBG, and not an agreement between VBG and CBG being dependent on the range of blood gas values.

Therefore a VBG should not be used as a substitute for CBG for monitoring gas exchange.

#### ABS 8

### ALTERATION OF TONIC GABAERGIC INHIBITION ON CONTROL OF BREATHING IN 12 DAYS OLD RATS CHRONICALLY TREATED WITH CAFFEINE

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#### INTRODUCTION

Caffeine (CAF) is used worldwide for apnea treatment in newborn infants. However, apnea may persist despite of adequate CAF therapy. GABA is the main inhibitory transmitter in the central nervous system. Since perinatal exposure to CAF increases GABA<sub>A</sub> receptor expression in the brain stem respiratory nuclei of newborn rats, we tested the hypothesis that chronic CAF modulates GABA<sub>A</sub> receptor function on control of breathing. Recently, we showed that progesterone, a respiratory stimulant, failed to enhance ventilation in newborn rats chronically treated with CAF, which may be related



to allopregnanolone a major progesterone metabolite that acts as allosteric modulator of GABA<sub>A</sub> receptors.

#### PATIENTS AND METHODS

To evaluate the GABA<sub>A</sub> receptor function on respiration we used rats that were randomly assigned to receive a daily gavage with water (control group) or CAF (CAF group, 15 mg/kg) between the postnatal (P) days 3-12. At P12 (n = 92), using the whole body plethysmography, respiration was recorded while rat was freely behaving and unrestrained following an intraperitoneal injection of bicuculline (a specific GABA<sub>A</sub> receptor antagonist, 2 mg/kg based on dose response study); or allopregnanolone (10 mg/kg); or vehicle. Minute ventilation (respiratory frequency X tidal volume: ml/min/100 g) and metabolism (O<sub>2</sub> consumption and CO<sub>2</sub> production) were assessed under normoxia (21% O<sub>2</sub>). Spontaneous and post-sigh apnea frequency (n/10 min) and duration (sec) were also studied. Data are mean ± SEM.

#### RESULTS

In CAF rats, bicuculline increased normoxic minute ventilation (control: 131 ± 7.2; CAF: 166 ± 8.6 ml/min/100 g; p < 0.0001 vs. control) and decreased apnea frequency – spontaneous (control: 5 ± 0.30; CAF: 3 ± 0.26/10 min; p < 0.0001 vs. control) and had no significant effect on post-sigh apnea. On the other side, allopregnanolone decreased normoxic ventilation in treated rats (control: 158 ± 1.5; CAF: 111 ± 4.8 ml/min/100 g; p < 0.0001 vs. control) and significantly increased apnea frequency – spontaneous (control: 5 ± 0.45; CAF: 8 ± 0.36/10 min; p < 0.0001 vs. control) and post-sigh (control: 3 ± 0.32; CAF: 5 ± 0.26/10 min; p = 0.01 vs. control) with no effect on apnea duration in normoxia. Neither bicuculline nor allopregnanolone had any effect on metabolism in normoxia.

#### CONCLUSIONS

We conclude that newborn rats chronically treated with CAF showed an enhancement of the inhibitory GABA<sub>A</sub> receptor function suggesting an increase in tonic GABA effects inhibiting respiration (bicuculline results). This might have masked the progesterone stimulating breathing (allopregnanolone results). The overall modulation in GABA<sub>A</sub> receptor function observed here would participate in persisting apnea despite adequate CAF therapy.

#### ABS 9

#### DIAPHRAGMATIC FUNCTION BEFORE AND AFTER APPLICATION OF EXTERNAL INSPIRATORY LOADING IN PRETERM AND TERM INFANTS

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#### INTRODUCTION

Newborns, especially those born prematurely, may present limited ability to adapt to additional respiratory loads. The diaphragmatic pressure-time product (PTP<sub>di</sub>) reflects the diaphragmatic energy expenditure and has been used as a measure of work of breathing. The diaphragmatic pressure-time index (PTI<sub>di</sub>) describes the pressure-generating activity of the diaphragm and assesses the balance between the diaphragmatic capacity and the imposed load. In adults, a PTI<sub>di</sub> > 0.15-0.18 may indicate impending diaphragm fatigue. The aim of our study was to compare the diaphragmatic function before and after application of inspiratory flow-resistive loading in preterm and term infants.

#### PATIENTS AND METHODS

Fifteen preterm infants (median GA 32.5 weeks, range 30-34) and 15 term infants (median GA 38 weeks, range 37-40) were studied before discharge. None of the preterm infants had chronic lung disease and all infants were breathing on room air when studied. PTP<sub>di</sub> was calculated as the integral of transdiaphragmatic pressure over time. PTI<sub>di</sub> was calculated as the product of the mean to the maximum transdiaphragmatic pressure (P<sub>di</sub>mean/P<sub>di</sub>max) and the inspiratory duty cycle (T<sub>i</sub>/T<sub>tot</sub>). Mean (over 10 breaths) PTP<sub>di</sub> and PTI<sub>di</sub> were computed before and during application of an inspiratory flow resistance of 200 cmH<sub>2</sub>O.

#### RESULTS

Compared to term-born infants, preterm newborns had higher PTI<sub>di</sub> at baseline (median [range] 0.068 [0.045-0.097] vs. 0.054 [0.032-0.071], p = 0.033), and after application of inspiratory resistance (0.102 [0.077-0.189] vs. 0.074 [0.044-0.098], p < 0.001). Resistive loading resulted in higher PTP<sub>di</sub> and PTI<sub>di</sub> increase in preterm compared to term infants (PTP<sub>di</sub> 58% [32-138] vs. 37% [25-51], p < 0.001 and PTI<sub>di</sub> 68% [31-142] vs. 35% [15-42], p < 0.001). Three preterm infants (20%) had post-resistance PTI<sub>di</sub> higher than the adult diaphragm fatigability threshold of 0.15. Multivariable regression analysis revealed that PTI<sub>di</sub> increase was inversely related to GA (regression coefficient β -1.17; p = 0.020), independently to gender (β 0.147; p = 0.312), birthweight (β 0.432; p = 0.120), days of mechanical ventilation (β 0.026; p = 0.847) and postmenstrual age on the day of measurement (β 0.017; p = 0.961).

**CONCLUSIONS**

Under conditions that increase the inspiratory load, prematurity is associated with increased work of breathing and higher risk of diaphragmatic muscle fatigue.

**ABS 10****PROGESTERONE DECREASES VENTILATION AND ENHANCES APNEA IN DEVELOPING RATS CHRONICALLY TREATED WITH CAFFEINE**

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**INTRODUCTION**

Caffeine as a respiratory stimulant is currently used in the treatment of apnea in newborn infants. Recently, progesterone (prog) has been proposed as an alternative or a complement to caffeine for the persistent apnea to adequate caffeine treatment. Prog is a potent respiratory stimulant in adult mammals. Our previous data in newborn rats indicate that prog enhances the ventilatory response to hypoxia and reduces apnea frequency. Here, we tested the hypothesis that in newborn rats addition of prog to daily caffeine administration, as used in clinic, enhances respiration and decreases apnea frequency than caffeine alone.

**PATIENTS AND METHODS**

We used rats that were daily gavaged with water (control group) or caffeine (treated group, 15 mg/kg) between postnatal (P) days 3-12. At P4 (n = 64) and P12 (n = 60), we used whole body plethysmography to measure minute ventilation and metabolism ( $O_2$  consumption and  $CO_2$  production) following intraperitoneal injection of prog (4 mg/kg) or saline. These measures were performed under normoxia and following exposure to moderate hypoxia (HVR, 12%  $O_2$ , 20 min). We also determined the total apnea frequency (n/10 min) and duration (sec) under normoxic and hypoxic conditions. Two apnea types were assessed, spontaneous (absence of flow for at least two normal respiratory cycles) and post-sigh (apneas preceded by a breath with amplitude at least twice the resting tidal volume). Data are mean  $\pm$  SEM.

**RESULTS**

At P4 control and caffeine treated rats, prog had no effect on normoxic ventilation but it increased total apnea frequency in treated rats (saline:  $3 \pm 0.4$ ; prog:

$6 \pm 0.4/10$  min;  $p < 0.01$  vs. saline). There were no significant changes in HVR. At P12 control rats, prog also had no effects on ventilation and apnea under normoxia but it enhanced the early phase of hypoxia (at 3 min, saline:  $135 \pm 6.2$ ; prog:  $153 \pm 5.5$  ml/min/100 g;  $p < 0.01$  vs. saline). In caffeine treated P12 rats, prog decreased ventilation (saline:  $112 \pm 6.4$ ; prog:  $103 \pm 5.0$  ml/min/100 g;  $p < 0.0001$  vs. saline), increased apnea frequency (saline:  $3 \pm 0.5$ ; prog:  $7 \pm 1.3/10$  min;  $p < 0.0001$  vs. saline) in normoxia. Prog depressed the early and late phase of HVR ( $p < 0.001$  vs. saline) and increased apnea frequency (saline:  $6 \pm 0.4$ ; prog:  $9 \pm 0.8/10$  min;  $p < 0.001$  vs. saline). Prog did not alter metabolism in all groups and conditions studied.

**CONCLUSIONS**

Our results showed that chronic caffeine administration to newborn rats may induce changes in neurotransmitters milieu that consequently affected the role of prog as a respiratory stimulant. Contrasting with our initial hypothesis, these results suggest that the addition of prog to chronic caffeine therapy may not be an option for the treatment of newborn apnea persistent to caffeine.

**ACKNOWLEDGMENT**

Funded by CIHR (MOP 119272).

## Delivery room management

**ABS 11****A RANDOMISED FEASIBILITY TRIAL AND *IN-VITRO* PERFORMANCE OF A NEW SYSTEM FOR RESPIRATORY SUPPORT DURING INITIAL STABILISATION OF PRETERM INFANTS**

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**INTRODUCTION**

Resuscitation of newborn infants with prongs and CPAP with low imposed work of breathing could offer advantages to a standard T-piece resuscitator. We have developed a new resuscitation system that can be used with either prongs or face mask. The

system is handled in a similar way to a T-piece resuscitator with positive pressure ventilation (PPV) provided by occlusion. CPAP is provided during PPV or spontaneous breathing. The aim of the study was: 1) to describe the *in-vitro* performance of the New System and 2) to perform a randomised feasibility trial for initial stabilisation of preterm infants.

#### PATIENTS AND METHODS

Imposed work of breathing was determined in a mechanical lung model (sinusoidal flow, I:E 1:1, 16 ml TV and RR 60). The New System and the T-piece resuscitators were tested at increasing levels of CPAP at a fresh gas flow 10 l/min.

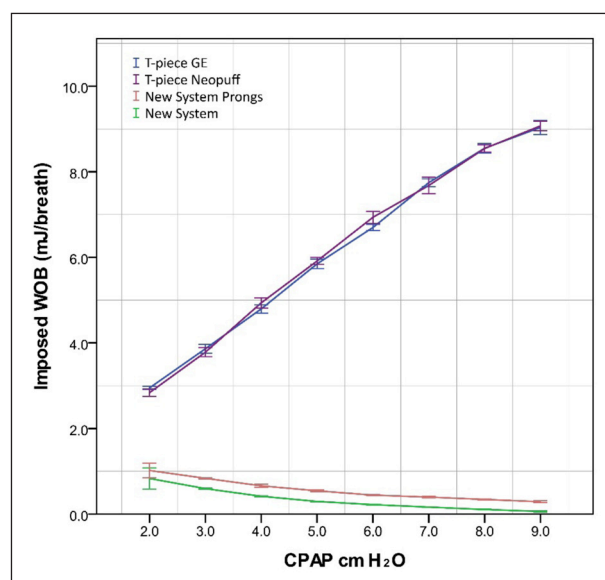
The feasibility trial included 36 infants (27-34 weeks gestational age). Exclusion criteria included: no need for respiratory support and known malformations. After consent the subjects were randomised into three groups (12 in each arm, CPAP 4 cm and minimum of 10 min): 1) T-piece (Neopuff™ or GE) 2) New System – face mask or 3) New System – prongs. Collected variables included problems with usage and safety. The response to respiratory support included time to stable breathing, need for PPV and intubation. The study had institutional ethics committee approval.

#### RESULTS

Simulations: imposed work of breathing for the New System was reduced compared to the T-piece systems (Fig. 1). At 4 cm H<sub>2</sub>O the reduction was

93% (mask) and 84% (medium prongs) compared to Neopuff™ ( $p < 0.05$ ).

Feasibility trial: informed consent was obtained from 45 patients, 39 were randomised and 36 needed support. Randomisation resulted in imbalance: the New System infants ( $n = 24$ ) had lower GA and birth weight compared to the T-piece



**Figure 1 (ABS 11).** Imposed Work of Breathing (WOB) at different CPAP levels. Simulations with 16 ml TV and RR 60.

Bars represent 95% CI.

**Table 1 (ABS 11).** Summary of the three treatment groups.

	Neopuff™ face mask	New System		Total
		Face mask	Prongs	
n	12	12	12	36
Gestational age (w)	33 <sup>+0</sup>	32 <sup>+4</sup>	30 <sup>+5</sup>	32 <sup>+1</sup>
Weight (g)	2,109	1,581	1,663	1,784
F/M	6/6	6/6	5/7	17/19
Vaginal delivery	5	4	2	11
PPV	5	6	2	13
Intubated DR	0	1	1	2
Intubated NICU	0	0	2	2
INSURE	2	0	2	4
Surfactant	2	0	5	7
APGAR 1 min	8.3	7.5	8.2	8.0
APGAR 5 min	8.2	8.3	8.9	8.5
APGAR 10 min	9.3	9.7	9.9	9.6
Time regular breathing	2.6	2.5	1.0	2.0
Time SpO <sub>2</sub> 90%	7.8	7.9 <sup>a</sup>	6.4	7.3
Pneumothorax	0	0	2	2

<sup>a</sup>Two missing (n = 10).

resuscitator group (n = 12) (p < 0.05). Two infants supported with the New System needed delivery room intubation. Overall, the time for establishing spontaneous breathing was 2.0 min and SpO<sub>2</sub> 90% 7.3 min. Two pneumothoraces were diagnosed in the NICU (prong group, no PPV, 4 cm CPAP). There were no problems with the equipment or safety. The clinical feedback was that stabilisation with prongs was easier than with a face mask. The results are presented in **Tab. 1**.

#### CONCLUSIONS

Compared to the T-piece system the New System had a marked reduction in the imposed work of breathing during bench tests. The feasibility trial did not reveal problems with usability or safety. The possible effect on intubation rates by using systems with prongs and low imposed work of breathing needs to be investigated in a large randomised trial.

#### ABS 12

### USE OF A RESUSCITATION TRAINING APP SIGNIFICANTLY IMPROVES HEART RATE ASSESSMENT DURING NEWBORN SIMULATION

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#### INTRODUCTION

About 5-10% of newborn babies require resuscitation at birth with 1% needing cardiopulmonary resuscitation (CPR) (Perlman, 1995). Heart rate (HR) is used to guide the need for, and efficacy of, resuscitation after birth. However, assessment of HR is incorrect in ~1/3 of cases potentially resulting in inappropriate management (Voogdt, 2010). Our previous study demonstrated marked improvements in HR accuracy using a 6 second visual timer. This study aimed to establish whether the use of a newborn resuscitation training app (NeoRate), incorporating a 6 second visual timer, improves accuracy and speed of HR assessment during simulated neonatal resuscitation.

#### PATIENTS AND METHODS

Newborn resuscitation trained staff used an in-house designed training app 'NeoRate' to practise HR estimation. Following their period of training they were assessed during a newborn resuscitation

simulation. Participants assessed 5 HRs using a 6 second interval timer (Timer) and 5 with their usual estimation method (Own) in a randomised crossover design. To allow standardisation, all HRs were played through an electronic stethoscope (Thinklabs® ANR2) at the same volume. Accuracy ( $\pm$  10 bpm) and HR assessment time were compared. Fischer's exact test was used to compare groups. Ethical approval was given.

#### RESULTS

A total of 27 neonatal healthcare professionals performed 270 HR assessments (14 clinicians, 13 nurses). HR accuracy using Own methods resulted in 27 of 135 incorrect assessments (20%) compared with only 8 of 135 (6%) using the Timer method (p = 0.0009, OR 3.97, 95% CI 1.7-9.1). When assuming each of the 5 HR assessments by an individual occurred during a single resuscitation, only 11 (41%) Own method participants made no errors compared to 22 (81%) Timer method participants (p = 0.005, OR 0.16, 95% CI 0.05-0.54). Median time taken to assess each HR was not different at 10 s but the variance was markedly reduced using the Timer method (IQR, Own 7-16 s vs. Timer 9-11 s). Compared to our previous data (6 s timer without training app) the error rates have fallen from 16% to 6% and assessment time from 15 s to 10 s.

#### CONCLUSIONS

This is the first study to demonstrate the use of a resuscitation training app, incorporating a 6-s interval timer, improves accuracy and time taken to assess HR during newborn resuscitation simulations. This simple intervention could result in improved newborn resuscitation, especially during the first few minutes of life when technological approaches are unreliable, or unavailable such as in low-middle income countries.

#### ABS 13

### DOES THE BAG-VALVE-MASK VENTILATION TECHNIQUE (2-FINGER VS. 5-FINGER-TECHNIQUE) OR THE GLOVE SIZE OF HEALTH CARE PROVIDERS AFFECT TIDAL VOLUME DURING SIMULATED NEONATAL RESUSCITATION?

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## INTRODUCTION

International guidelines emphasize the importance of effective bag-valve-mask ventilation during neonatal resuscitation. The sufficiency of bag-valve-mask ventilation may be evaluated by assessing chest excursions, monitoring heart rate and oxygen saturation, and lung auscultation. Recent guidelines do not provide recommendations which bag-valve-mask ventilation technique (2-finger vs. 5-finger-technique) should be preferred. Moreover, the potential effect of the glove size of health care providers on applied tidal volumes during neonatal resuscitation has not yet been investigated.

## PATIENTS AND METHODS

40 health care providers (20 neonatal intensive care nurses, 20 emergency medical technicians) were included. They were asked to perform an adequate bag-valve-mask ventilation on an modified, leak-free neonatal mannequin (CPR Resusci® Baby, Laerdal; Norway) by using an Ambu® Baby-R bag (Ambu®; Denmark) and a silicone mask (Laerdal; Norway) unaware of the study aim. Each participant was recorded for 90 seconds in two simulated resuscitations in random order: one by using 2-finger technique (thumb and index finger), one by using 5-finger-technique (the whole hand). Between both recordings, participants had a 2 minute break to reduce potential bias due to fatigue. Tidal volume, mask leak and ventilation rate were measured by using a Florian respiratory function monitor (Acutronic; Switzerland).

## RESULTS

There were no significant difference in mean tidal volume comparing 2-finger and 5-finger-technique ( $p = .22$ ). The mean mask leak was significantly higher during 5-finger bag-valve-mask ventilation compared to the 2-finger-technique ( $p = .02$ ).

The medical glove size of health care providers did not correlate with the applied tidal volume ( $p = .70$ ). Comparing professional groups (neonatal intensive care nurses vs. emergency medical technicians) we did not observe significant differences in mean tidal volume ( $p = .55$ ) and mask leak ( $p = .32$ ). Emergency medical technicians used a significantly higher ventilation rate compared to neonatal intensive care nurses ( $p < .001$ ).

## CONCLUSIONS

Sufficient bag-valve-mask ventilation with adequate tidal volumes during simulated neonatal simulation might be performed by health care provider by using both, 2-finger and 5-finger-technique. Nevertheless, there was less mask leak with the 2-finger technique. The medical glove size of the health care provider

who was performing bag-valve-mask ventilation seems to have no effect on applied tidal volume.

## ABS 14

### ACCURACY OF CURRENT AVAILABLE NEONATAL RESPIRATORY FUNCTION MONITORS DURING NEONATAL RESUSCITATION

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## INTRODUCTION

Adequate mask ventilation is the cornerstone of neonatal resuscitation at birth. Lungs of preterm infants at birth are prone to lung injury and volume trauma could easily occur, especially when we are not aware of the volumes being given during pressure controlled ventilation. A respiratory function monitor (RFM) measures pressures given and gas flow from which volume is calculated.

## OBJECTIVE

To test the accuracy of current available RFMs for neonatal resuscitation and to test the effect of changing gas conditions on the volume measurements.

## METHODS

Three RFMs, the Florian, the New Life Box Neo-RSD (NLB) and the NICO RFM, were tested *in vitro* on both accuracy with known volumes of 10 and 20 mL using a glass syringe, deviations larger than 10% were considered clinically relevant. Changes in volume measurements under changing gas conditions (increase oxygen level from 21-100%) and from cold dry air ( $24 \pm 2^\circ\text{C}$ ) to heated humidified air ( $37^\circ\text{C}$ ) were monitored.

## RESULTS

In all three devices the mean (SD) deviation was clinically acceptable when 10 ml and 20 mL volumes were given, except for the NICO with 20 mL (Florian 8.4% [1.2%], 8.4% [0.5%]; NLB 5.8% [1.1%], 4.3% [1.4%]; NICO -8.2% [0.9%], -12.0% [1.5%]). Changes in volume measurements during changes in oxygen occurred in all devices, but only the Florian showed clinically relevant changes (cold

air, heated air) (FiO<sub>2</sub> 0.21, FiO<sub>2</sub> 1.0: Florian 5.2% [1.2%], 12.2% [0.9%]; NLB 2.0% [1.6%], 3.4% [2.8%], NICO -2.3% [0.8%]; 0.1% [0.6%]), similar when changing for cold dry to heated humidified air (FiO<sub>2</sub> 0.21, FiO<sub>2</sub> 1.0: Florian 12.2% [1.0%], 19.8% [1.1%]; NLB 0.2% [1.9%], 1.1% [2.8%], NICO -5.6% [0.9%]; -3.7% [0.9%]). When both gas conditions were changed a large deviation was observed with the Florian (Florian 25.7% [1.7%]; NLB 3.8% [2.4%]; NICO -5.7% [1.4%]).

#### CONCLUSIONS

The NLB and NICO are suitable as a direct feedback device during neonatal resuscitation, while, when the Florian is used, a correction factor should be incorporated.

#### ABS 15

### OROPHARYNGEAL AIRWAY TO ASSIST VENTILATION OF PRETERM INFANTS IN THE DELIVERY ROOM

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#### INTRODUCTION

Positive Pressure Ventilation (PPV) is recommended for compromised newly born infants in the delivery room (DR). Mask ventilation in the DR is

associated with airway obstruction and leak, which may contribute to failure of resuscitation. Using an airway adjunct may improve efficacy of mask PPV but has not been tested in a randomised controlled trial (RCT) in the DR. We aimed to determine if using a Geudel™ oropharyngeal airway (OPA) with mask PPV during the stabilisation of infants < 34 weeks' gestation reduces airway obstruction and improves clinical outcomes.

#### PATIENTS AND METHODS

An RCT (ACTRN: 12612000392864) was performed at two sites. Infants were stratified by GA (24-27 and 28-33 weeks), centre and randomised after birth if assessed to need PPV by the clinical team. Resuscitation guidelines were standardised and respiratory support was provided by a T piece ventilator with a soft round face mask alone or mask + OPA. Physiological recordings of PPV were made and reported for the first five minutes after birth. The primary outcome was the incidence of (i) complete and (ii) relative airway obstruction defined as (i) no gas flow or (ii) minimal gas flows resulting in expired tidal volumes < physiological deadspace (2 mL/kg) during PPV; 132 infants would be sufficient to detect a 50% reduction of relative obstruction from 46% with an  $\alpha$  error of 0.05 and 80% power.

#### RESULTS

One hundred and thirty seven infants (53 & 84 by 24-27 and 28-33 subgroup) were randomized. Baseline variables and clinical outcomes were similar between groups. Relative obstruction was more common in infants stabilized with an OPA (**Tab. 1**).

**Table 1 (ABS 15).** Baseline characteristics, physiological and clinical outcomes in the two groups.

	Control (n = 70)	OPA (n = 67)	OR (95% CI) or p-value
<b>Baseline</b>			
GA (weeks)	28.1 (2.5)	28.0 (2.3)	-
Birth weight (g)	1,102 (418)	1,088 (405)	-
Male	29 (41%)	42 (63%)	-
Antenatal steroids (complete)	64 (91%)	58 (87%)	-
<b>Physiological outcomes</b>			
Complete obstruction	21 (30%)	15 (22%)	0.30 (0.65-1.40)
Relative obstruction	37 (53%)	47 (70%)	2.09 (1.04-4.23)
Relative obstruction in 28-33 wk subgroup	21/45 (47%)	28/39 (72%)	2.9 (1.17-7.23)
<b>Clinical outcomes</b>			
5-minute Apgar	7 (6-8)	7 (6-8)	0.47
Intubation in DR	28 (40%)	22 (33%)	0.66 (0.33-1.32)
Air leak	10 (14%)	4 (6%)	0.40 (0.12-1.32)
Death	4 (6%)	3 (4.5%)	0.81 (0.18-3.76)

Data are numbers (%), mean (SD) or median (IQR).

OPA: oropharyngeal airway; DR: delivery room.

**CONCLUSIONS**

Face mask obstruction is common during PPV of preterm infants in the DR. Oropharyngeal airways do not reduce the rate of complete airway obstruction during mask PPV and is associated with significantly higher rates of partial obstruction more notably in moderate preterm infants. No differences in hospital based clinical outcomes were observed using an OPA.

## Long-term lung function

**ABS 16**

### RESPIRATORY MORBIDITY OF PRETERM INFANTS WITH AND WITHOUT BRONCHOPULMONARY DYSPLASIA, AFTER DISCHARGE, IN THE FIRST 2 YEARS OF LIFE

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**INTRODUCTION**

Although the pathophysiology of bronchopulmonary dysplasia (BPD) in preterm infants has changed over the years, little data is available whether this also led to a change in respiratory morbidity after discharge. We aimed to compare the respiratory morbidity in the first 2 years of age of infants with moderate/severe BPD in three cohorts over time and also compared this with the respiratory morbidity of infants with no/mild BPD.

**PATIENTS AND METHODS**

Three cohorts of infants < 30 weeks gestational age, born at the Leiden University Medical Center (LUMC) in 1996-1997 (cohort '96), 2003-2004 (cohort '03) and 2008-2009 (cohort '08), were retrospectively compared. BPD was defined according to the National Institute of Child Health and Human Development. We noted the following parameters until 2 years of age: grade of BPD, mortality during admission, duration of extra oxygen (O<sub>2</sub>) need; after discharge: supplemental oxygen at home, readmission, frequency of readmission and if supplemental O<sub>2</sub> was needed, and the use of inhalation medication.

**RESULTS**

In cohort '96, '03, '08 respectively 106, 120, 156 infants were analyzed (mean [SD] GA 27.6 [1.2] vs. 27.5 [1.2] vs. 27.6 [1.3] weeks; n.s.; BW 1,088 [239] vs. 1,063 [276] vs. 1,083 [268] grams; n.s.). Mortality was similar (12 vs. 16 vs. 12%; n.s.), the incidence of mod/sev BPD, decreased over time (30 vs. 22 vs. 18%; p < 0.05), duration of extra O<sub>2</sub> was n.s.

Readmission rate was similar (62% vs. 55% vs. 53%; n.s.), as well as supplemental O<sub>2</sub> (33% vs. 33% vs. 36%; n.s.), intensive care admission (7% vs. 16% vs. 7%; n.s.) and use of inhaled corticosteroids (48% vs. 35% vs. 47%; n.s.). After discharge, mod/sev-BPD infants needed less frequent home O<sub>2</sub> therapy (24% vs. 14% vs. 4.5%; p < 0.05). Readmission rate was similar with mod/sev BPD infants in cohort '96 (58% vs. 73%; n.s.), '03 (53% vs. 60%; n.s.), but lower in '08 (48% vs. 78%; p < 0.05). The use of inhaled corticosteroids was similar in cohort '96 (39% vs. 48%; n.s.), '03 (31% vs. 35%; n.s.), but lower in '08 (17% vs. 47%; p < 0.05).

**CONCLUSIONS**

The respiratory morbidity of infants with moderate/severe BPD did not decrease over time, except for the need of oxygen at home. The respiratory morbidity in mod/sev BPD infants was higher as compared to no/mild BPD infant and this did not change in the last decade.

**ABS 17**

### 10 YEAR OUTCOMES OF CONGENITAL DIAPHRAGMATIC HERNIA IN A TERTIARY NEONATAL UNIT

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**INTRODUCTION**

Congenital diaphragmatic hernia (CDH) has an incidence of 1 in 2,000 to 1 in 4,000. Despite the emergence of new therapies such as high frequency oscillatory ventilation (HFOV), nitric oxide (iNO), Extra Corporeal Membrane Oxygenation (ECMO) and planned delivery of antenatally diagnosed cases, the overall mortality of babies born with CDH remains high.

**PATIENTS AND METHODS**

A 10 year retrospective review of case notes from January 2005 to January 2015 inclusive of all babies diagnosed with CDH in Norfolk and Norwich

University Hospital was completed. Patients were divided into groups according to year of presentation (2005 to 2010 and 2010 to 2015). Demographic data, associated anomalies, laterality of CDH, resuscitation, operative and medical management were collected.

## RESULTS

30 patients between 2005 and 2015 were identified (M:F 13:17). Demographic data was comparable in both groups (**Tab. 1**). 47% (14) patients had associated anomalies and 50% of these were cardiac. There were 22 left CDHs, 7 right CDHs and 1 bilateral CDH. All CDH repairs in our centre underwent open repair of CDH (2005 to 2010 83% suture repair, 17% patch versus 2010 to 2015 65% suture 9% patch). Length of stay ranged from 0-97 days (median 16 days). 40% patients had HFOV and 40% required iNO.

**Table 1 (ABS 17).** Comparative results of congenital diaphragmatic hernia (CDH) over 10-year period.

Year	2005-2010	2010-2015
Live born babies (n = 30)	7	23
Antenatal diagnosis, n (%)	2 (28.5)	17 (74)
Postnatal diagnosis, n (%)	5 (71.5)	6 (26)
Transferred for ECMO, n	1 (14.2)	4 (17.4)
Withdrawal of care, n (%)	1 (14.2)	5 (22)
Mortality, n (%)	1 (14.2)	8 (35)
Post mortem, n	Unknown	4 declined, 1 unknown
Overall survival to discharge, n (%)	6 (86)	15 (65)

## CONCLUSIONS

Despite an increase in antenatal detection of CDH (74%) and emergence of new medical therapies, mortality remains high. Lack of post mortem examination impeded accurate estimation of lung volumes and ventilator-induced damage due to hypoplastic lungs contributing to mortality. The use of antenatal MRI and foetal pulmonary artery doppler may help in accurately assessing the lung volume. This may help in improving the prediction of outcomes.

## ABS 18

### RESPIRATORY MORBIDITY AFTER NICU DISCHARGE OF PRETERM BABIES WITH CHRONIC LUNG DISEASE

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## INTRODUCTION

The study aims to investigate respiratory morbidity of preterm babies with chronic lung disease (CLD).

## PATIENTS AND METHODS

All preterm babies born between 2008 and 2010 (inclusive) at less than 32 weeks gestation treated at, and local to, Luton and Dunstable university hospital NHS Foundation trust, LDH, were enrolled retrospectively. Data on morbidity and readmission was obtained from electronic hospital records.

## RESULTS

32 of 38 eligible babies with CLD represented to hospital at least once during the observational period, on a total of 182 occasions. 84 of 182 (46%) presentations were with respiratory illness by 25 babies; 10 of whom required high dependency care (high dependency unit [HDU] admission) at least once for a total of 20 HDU admissions, and 2 required transfer to paediatric intensive care unit (PICU) on a total of 3 occasions. Respiratory admissions' cumulative length of stay (LOS) was 368 days, 73 of which required HDU care, equating to almost one-fifth of all days.

## CONCLUSIONS

Pre-term babies born before 32 weeks who develop CLD have frequent re-presentations to hospital with predominantly respiratory illnesses. With increasing numbers of extremely pre-term babies surviving, (Costeloe et al., 2012), paediatric in-patient services need to ensure adequate facilities and availability of HDU care.

## ABS 19

### A RANDOMISED CLINICAL TRIAL: ORAL VITAMIN A SUPPLEMENTATION FOR PREVENTING BRONCHOPULMONARY DYSPLASIA IN VERY LOW BIRTH WEIGHT INFANTS

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**AIM**

To assess whether early high dose oral vitamin A supplementation reduces the rate of bronchopulmonary dysplasia (BPD) in very low birth weight infants (VLBW).

**PATIENTS AND METHODS**

We conducted a prospective randomized control study in VLBW infants (birth weight 1,250 g or less, gestational age 32 week or less). The infants who were born and admitted to our neonatal intensive care unit between March 2012 to March 2013 were included in this study. Infants were divided into two groups randomly according to birth weight, gestational age and sex in seven day of life. Vitamin A was administered orally 30,000 IU/kg/week for 6 weeks.

Primary outcomes were BPD and mortality rates. Secondary outcomes were prematurity related problems.

**RESULTS**

A total of 209 patients were enrolled (control group: 110, prophylactic vitamin A group: 99). The mean birth weight, gestational age, and sex distribution were similar between the groups. There was no difference between the groups in terms of demographic and clinical characteristics of infants. Both groups had similar duration of hospital stay and respiratory support. There was no difference in the incidence of death (18.2%, 20.2%) or BPD (22%, 22%) in the control groups and prophylactic vitamin A group ( $p > 0.05$ ).

**CONCLUSIONS**

We found that the incidence or severity of BPD does not decrease with early high dose oral vitamin A supplementation.

Vitamin A efficacy has not been achieved in the prevention of BPD.

**ABS 20**

**CLINICAL COURSE AND PROGNOSIS AT ONE YEAR OF CORRECTED AGE OF A 6,135 COLOMBIAN LOW BIRTH WEIGHT (LBW) INFANTS COHORT DISCHARGED HOME IN KANGAROO POSITION WITH AMBULATORY OXYGEN: A 15 YEARS EXPERIENCE**

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**OBJECTIVE**

To evaluate clinical course and prognosis at one year of corrected age of a cohort of 6,235 oxygen dependent preterm and/or LBW infants cared in our ambulatory Kangaroo Mother Care (KMC) program between 2001 and 2015.

**PATIENTS AND METHODS***Patients and Design*

Prospective cohort of 6,235 oxygen dependent (OD) infants < 37 weeks GA and/or weight  $\leq$  2,500 at birth, discharged home in kangaroo position (KP) with periodical follow-up until 12 months of corrected age to determine survival, growth, development and morbidity.

*Intervention*

1) Continuous KP (skin-to-skin contact 24 hours),  
2) Exclusive breastfeeding whenever possible and  
3) Early discharge in KP with close monitoring and follow-up (dynamic oxymetry each day until reaching a daily weight gain of 15 g/kg/day, then each week up the weaning).

**RESULTS**

Of 20,835 eligible infants, 30% were discharged home with oxygen. 27.5% were < 30 weeks GA, 38% were 37 weeks GA. 70% were NICU graduates, 57% of them had ventilatory support. Median length of hospital stay was 20 days. 40.2% was diagnosed with BPD at entry and 11.5% had intraventricular hemorrhage. 14.3% had history of nosocomial infection. Lost of follow up was 11%. Up to one year, overall mortality was 1.5%; 72% of deaths occurring the first 3 months. At 3 months, 16% of infants has been readmitted for acute respiratory infection and at 12 months 25% has been readmitted at least one. Oxygen was discontinued at a median of 72 days with mean of 4,135 g. 45% of infants received exclusive breastfeeding up to term. 9.7% had retinopathy, 2.3% laser surgery and 0.2% blindness. At one year risk of cerebral palsy was 3.6% and mean developmental coefficient was 98.6.

**CONCLUSIONS**

Weight, over age, is a major indicator of oxygen discontinuation.

Early discharge in kangaroo position (median of 20 days) allows less intrahospital infections, higher rate of breast-feeding with better somatic growth, and probably better and earlier bonding with the mother and family without considering economic impact.

More studies are needed to compare these results with other practices like discharge after oxygen weaning.

## ABS 21

**BRONCHODILATOR RESPONSE TO SALBUTAMOL MODIFIES LUNG VENTILATION PATTERN IN PRESCHOOL CHILDREN WITH BPD, BUT NOT IN PRESCHOOL EX-PREMATURELY BORN CHILDREN WITHOUT BPD**

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## INTRODUCTION

Long-term effect of bronchopulmonary dysplasia (BPD) on regional properties of lung function has not been precisely determined. Aim of this study was to assess the impact of bronchodilator response (BDR) to salbutamol on the pattern of lung ventilation in a group of spontaneously breathing preschool VLBW children using electrical impedance segmentography (EIS) monitoring.

## PATIENTS AND METHODS

Regional lung electrical impedance was measured in a group of VLBW preschool children at the age of four (n = 30; gestational age = 28.2 ± 2.4 weeks; 60% boys) with history of BPD (n = 18, gestational age = 26.9 ± 2.2 weeks; 72% boys) and without BPD (n = 12, gestational age = 30 ± 1.5 weeks; 42% boys) before and after salbutamol (400 µg with pressurized metered-dose inhaler [pMDI] and spacer). BPD was defined as oxygen demand at 28 days after birth. Monitoring was performed during spontaneous tidal breathing in upright position for five minutes, using Angelie EIS System (EMS Biomedical, Austria, sampling frequency = 1,000 Hz). Data was expressed as mean segmental impedance amplitude difference and segmental ventilation inhomogeneity index (II – **Fig. 1**) in four lung segments (upper left [UL], upper right [UR], lower left [LL], lower right [LR]).

$$II_{UL} = \frac{\sigma_{I_{UL}}}{\frac{\sum_{i=1}^n I_{UL_i} + I_{UR_i} + I_{LL_i} + I_{LR_i}}{n}}$$

**Figure 1 (ABS 21).** Inhomogeneity index calculation.

$II_{UL}$ : inhomogeneity index of the upper left segment;  $\sigma_{I_{UL}}$ : standard deviation of the segmental percentage impedance values.

## RESULTS

We observed a significant increase in inhalation-exhalation mean impedance amplitude in both upper segments of the lungs in children with BPD after salbutamol inhalation (UL: 649 ± 236 vs. 853 ± 368; +31%; p = 0.007; UR: 738 ± 348 vs. 986 ± 536; +33%; p = 0.02). Similar trend, however without statistical significance was observed in lower segments of the lungs. There were no similar differences in children without BPD. Inhomogeneity index was increasing after salbutamol in all four segments in children with BPD (II-UL: 8.3% vs. 12.3%, p = 0.004; II-UR: 8.5% vs. 17.7%, p = 0.007; II-LL: 6.7% vs. 9.3% p = 0.04; II-LR: 7.6% vs. 10.9%, p = 0.02). No significant differences in inhomogeneity of ventilation were observed in children without BPD. There was no association between observed parameters and history of wheezing, or lower respiratory tract infections and length of oxygen support after birth in children with BPD.

## CONCLUSIONS

Bronchodilator response to salbutamol increases breath amplitude in gravity non-dependent regions of the lungs during spontaneous tidal breathing in upright position in preschool VLBW children with BPD, but not in children without BPD. Bronchodilation increases regional inhomogeneity of lung ventilation in both gravity dependent and non-dependent lung regions in children with BPD.

## ACKNOWLEDGMENT

Study supported by National Science Center, Poland; grant number: 2011/03/B/NZ5/05678.

## Lung injury

## ABS 22

**OBSERVATIONAL STUDY IN PREMATURE INFANTS EVALUATING THE ROLE OF *U. UREALYTICUM* ON CHRONIC LUNG DISEASE**

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## INTRODUCTION

Controversy exists over whether or not *U. urealyticum* colonization or infection of the respiratory tract contributes to the severity of chronic lung disease (CLD), a major cause of morbidity and mortality in preterm infants.

*Ureaplasma spp.* is a common commensal of the maternal genital tract, as up to 80% of women have been reported to be colonised. Mother to child transmission may occur *in utero*, during delivery, or even postnatally through nosocomial transmission. Numerous studies and reviews have discussed the potential role of *Ureaplasma spp.* in the development of CLD.

We aim to evaluate the effect of treating *Ureaplasma spp.* colonisation/infection with erythromycin on development of CLD.

#### PATIENTS AND METHODS

Retrospective observational study of 4 years (from Feb 2011 to Jan 2015) in a busy tertiary neonatal intensive care unit of all the positive and negative *Ureaplasma spp.* cases in preterm infants. Test for *Ureaplasma spp.* is done by PCR technique on the endotracheal/nasopharyngeal aspirate.

#### RESULTS

Total number of preterms (< 36 weeks) admission to NICU during study period: 1,524.

Incidence of CLD (Oxygen requirement at 36 weeks) during study period: 94 (61/1,000 preterms < 36 weeks admissions).

Total number of *Ureaplasma spp.* tests done during study period: 82.

Number of *Ureaplasma*-positive cases: 27, and *Ureaplasma*-negative cases: 55.

Comparing *Ureaplasma*-positive and *Ureaplasma*-negative groups, median gestational age: 25<sup>+5</sup> weeks in *Ureaplasma*-positive vs. 25 weeks in *Ureaplasma*-negative.

Median birth weights: 750 grams in *Ureaplasma*-positive group vs. 710 grams in *Ureaplasma*-negative group.

Both groups were demographically similar.

Erythromycin treatment was given in 81% (22/27) of cases in *Ureaplasma*-positive cases.

One infant died in both the groups.

CLD rate is 92% (24/26) in *Ureaplasma*-positive group vs. 83% (44/53) in *Ureaplasma*-negative group.

Relative risk: 1.1 (Tab. 1)

**Table 1 (ABS 22).** Correlation between presence/absence of *Ureaplasma spp.* and chronic lung disease (CLD).

	CLD present	CLD absent
<i>Ureaplasma</i> -positive	24	2
<i>Ureaplasma</i> -negative	44	9

Relative risk: 1.1.

#### CONCLUSIONS

The incidence of CLD is marginally higher in *Ureaplasma*-positive group than in *Ureaplasma*-negative group in spite of treating with erythromycin. Treating *Ureaplasma spp.* infection/colonisation in extreme preterm infants does not reduce incidence of CLD.

#### ABS 23

#### THE ANTIOXIDANT DEFENSE OF PRETERM NEWBORNS WITH RESPIRATORY DISTRESS

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#### INTRODUCTION

The intra- and extracellular antioxidant defense of preterm newborns is poor, according to their gestational age.

The most important extracellular enzymatic antioxidant are caeruloplasmin and transferrin. The most common non-enzymatic antioxidants are: cysteine, glutathione, ascorbic acid, tocopherol, polyphenols, aromatic amines, and proteic sulphhydryl groups (SH). Proton donors evaluate non-enzymatic antioxidative defense capacity. The aim of our study was to evaluate the antioxidant defense capacity. We evaluated caeruloplasmin as extracellular, enzymatic antioxidant and also we measured the proton donors as non-enzymatic antioxidants.

#### PATIENTS AND METHODS

We conducted a prospective non-randomised study. In the study group we included 52 preterm neonates. We measured caeruloplasmin in the first and third day of life. In 20 preterm newborns out of the study group we measured the proton donor capacity as well. The preterms of the study group had associated different pathologies. The control group consisted of 13 healthy term newborns. In the control group we did only one measurement (on the first day of life). We used the spectrophotometric Ravin method for caeruloplasmin determination and Hatano method for proton donors evaluation. Statistical analysis was performed using statistical program SPSS®. The patients were enrolled in the study after obtaining the parents' informed consent. The study has obtained the approval of the Ethics Board of the unit.

## RESULTS

In the study group all preterm newborns presented different severity of respiratory distress. Asphyxia was present in 23 neonates of the study group. An intraventricular hemorrhage was present in 8 cases. All these associated pathologies were oxidative stress generating. The caeruloplasmin value in the study group was higher on the third day of life than on the first day. The proton donor capacity had the same behavior. In the control group the proton donor capacity level was higher than in the study group on the first and third day of life. The antioxidant defense improves with the postnatal age of the preterm newborns. Due to preterm birth, both enzymatic and non-enzymatic antioxidant defenses are underdeveloped. Our study showed the same results. In term newborns from the control group, without oxidative stress factors associated, the antioxidant defense was in better condition.

## CONCLUSIONS

The antioxidant defense in preterm newborns with different pathologies generating oxidative stress is poorer than in term newborns. The study of antioxidant defenses in different neonatal circumstances could help to implement antioxidant treatment and avoid as much as possible the oxidative stress in preterm neonates.

## ABS 24

### URINARY N-TERMINAL PRO-B TYPE NATRIURETIC PEPTIDE PREDICTS MODERATE OR SEVERE BRONCHOPULMONARY DYSPLASIA IN PRETERM INFANTS

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## INTRODUCTION

In preterm infants, postnatal adaptation may be complicated by bronchopulmonary dysplasia (BPD). The N-terminal pro-B type natriuretic peptide levels (NT-proBNP) have been shown to be increased in preterm infants with hemodynamically significant patent ductus arteriosus. Only few studies have investigated the relationship between NT-proBNP and patients who developed BPD. We aimed to analyze urinary NT-proBNP concentrations to predict moderate or severe BPD in preterm infants.

## PATIENTS AND METHODS

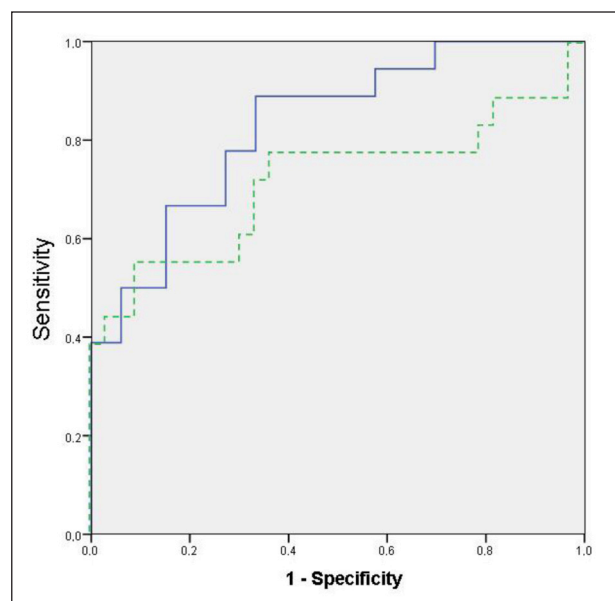
NT-proBNP were determined in urine collected on day of life (DOL) 14 and 28 in 163 preterm infants < 1,500 g birth weight, 39 of whom developed BPD (oxygen supplementation at 36 weeks gestational age). Of these, 17 infants developed a moderate and 22 infants a severe BPD. BPD severity was defined according to National Institutes of Health (NIH) criteria. Non-BPD and BPD infants differed significantly in the median (IQR) gestational age (27 [26-29] weeks vs. 26 [25-27] weeks;  $p < 0.001$ ) and birth weight (979 [823-1,114] g vs. 636 [525-925] g;  $p < 0.001$ ).

## RESULTS

Urinary NT-proBNP on DOL 14 and 28 were elevated in infants who developed moderate or severe BPD, as compared to controls (median 8,190 [2,848-25,446]  $\mu\text{g/l}$  vs. 727 [251-3,422]  $\mu\text{g/l}$  and 1,786 [502-5,538]  $\mu\text{g/l}$  vs. 418 [222-1,140]  $\mu\text{g/l}$ ;  $p < 0.001$  on day 14 had a sensitivity of 89% and a specificity of 67% for predicting moderate or severe BPD with a high negative predictive value of 94.1% (**Fig. 1**). Urinary NT-proBNP concentrations correlate with clinical severity of BPD.

## CONCLUSIONS

Elevated urinary NT-proBNP concentrations were significantly associated with moderate or severe BPD. Estimation of urinary NT-proBNP may be useful in risk-stratification in very low birth weight infants who develop BPD.



**Figure 1 (ABS 24).** Receiver operating characteristic curves describing the ability of urinary NT-proBNP levels on day of life (DOL) 14 (solid line) and 28 (dotted line) to predict the development of bronchopulmonary dysplasia (BPD).

## ABS 25

### LOW CONCENTRATIONS OF CLUB CELL SECRETORY PROTEIN (CC16) IN GASTRIC FLUID AT BIRTH IS ASSOCIATED WITH LUNG INFLAMMATION AND MORE SEVERE LUNG DISEASE IN VERY PRETERM INFANTS

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#### INTRODUCTION

CC16 is an anti-inflammatory protein secreted by club cells in the distal airways of the lung, diffusing into the circulation along a concentration gradient. Concentrations of CC16 in amniotic fluid increase dramatically during gestation. After birth, a postnatal surge of CC16 occurs in the lungs as well as in the circulation, less pronounced in preterm infants. Maternal chorioamnionitis is associated with lower concentrations of CC16 in the trachea, and persistent low plasma concentrations have been reported in infants who develop BPD.

#### PATIENTS AND METHODS

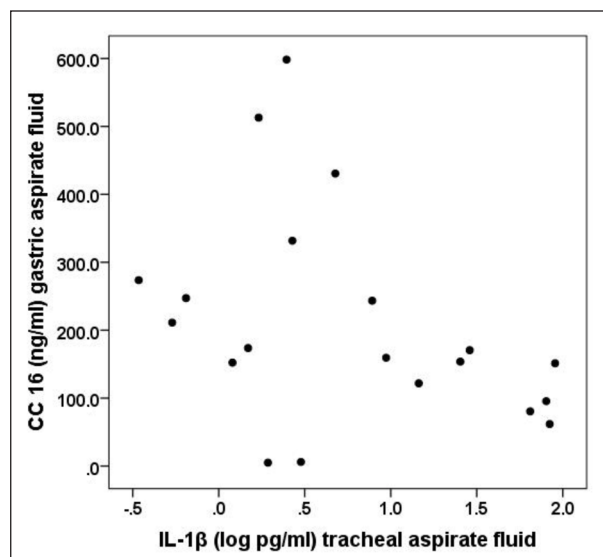
A descriptive study in 61 very preterm infants with a mean (SD) gestational age (GA) at birth of 25.8 (1.9) weeks and BW of 850 (275) g. CC16 was measured by ELISA in plasma at birth (n = 47) and at 24 h of age (n = 61), in gastric aspirate fluid (GAF) at birth (n = 32) and in tracheal aspirate fluid (TAF) at 24 h of age in ventilated infants (n = 35). Concentrations in TAF were adjusted for total protein content. IL-1 $\beta$ , TNF- $\alpha$ , and MMP-9 were analyzed by a multiplex assay (Luminex®).

#### RESULTS

Concentrations of CC16 in GAF and in TAF were median (range) 230 (5-671) and 97 (1.6-834) ng/ml. Median plasma CC16 at birth were 4.3 (1.1-13.1) ng/ml and increased significantly to 9.9 (1.7-41.4) at 24 h of age, p < 0.001.

CC16 concentrations in TAF and GAF correlated positively with CC16 concentrations in cord blood and in blood at 24 h of age, r = 0.61, r = 0.54, and r = 0.46, r = 0.43, all p < 0.05.

CC16 concentrations in GAF showed an inverse correlation with IL-1 $\beta$  (Fig. 1), TNF- $\alpha$  and MMP-9, r = -0.49, p = 0.028; r = -0.48, p = 0.034 and r = -0.53, p = .015 in TAF. Concentrations of CC16 in



**Figure 1 (ABS 25).** Correlation between CC16 in gastric aspirate fluid (GAF) and IL-1 $\beta$  in tracheal aspirate fluid (TAF).

GAF correlated inversely with FiO<sub>2</sub> (%) at 6 h of age r = -0.45, p = 0.009, with arterial PCO<sub>2</sub> levels at 24 h of age r = -0.4, p = 0.03 and with number of ventilator days r = -0.44, p = 0.012. Concentrations of CC16 in TAF correlated inversely with mean airway pressure at 24 h, r = -0.52, p = 0.012.

#### CONCLUSIONS

Low levels of CC16 in gastric fluid and in trachea were associated with more inflammation in the lungs and with an increased need for respiratory support in the early neonatal period. An imbalance between pulmonary anti-inflammatory and pro-inflammatory proteins may be of importance for injury in the immature lung.

#### ABS 26

### LOCAL INFLAMMATORY REACTIONS AND DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN VERY PRETERM INFANTS WHO REQUIRED MECHANICAL VENTILATION SHORTLY AFTER BIRTH

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#### INTRODUCTION

Pulmonary inflammation plays an important role in pathophysiology of bronchopulmonary dysplasia (BPD). Excessive pro-inflammatory stimulation of immature lungs often begins *in*

*utero* and continues after preterm birth. The lack of anti-inflammatory suppression may perpetuate the inflammatory response and contribute to BPD development. In a prospective cohort study we studied the association between features of local inflammatory reactions and development of moderate or severe BPD in very preterm infants who required mechanical ventilation (MV) shortly after birth.

#### PATIENTS AND METHODS

89 very low birth weight newborns (gestational age < 32 wks) on MV who survived to corrected age of 36 wks were under observation. 13 infants developed BPD (the BPD group), which was defined as oxygen dependency at the corrected age of 36 wks. 75 babies without BPD were included into the control group. Tracheal aspirate (TA) was taken at the age of about 11 and 66 hrs after birth to determine pro- and anti-inflammatory cytokine concentrations (IL-8 and IL-10 respectively) with enzyme-linked immunosorbent assay.

#### RESULTS

Initial values of interleukins and total numbers of leukocytes were similar in the both groups. At the mean age of approximately 66 hrs we found significantly lower levels of IL-10 in the BPD group compared to the control one (0 [0; 0.18] pg/mL vs. 0.14 [0.12; 0.47] pg/mL accordingly;  $p < 0.05$ ). The IL-8/IL-10 ratio was also increased (146.27 [60.06; 185.03]) in comparison with infants without BPD (62.94 [53.24; 197.10];  $p < 0.05$ ). There was the reliable negative correlation between the BPD formation and the IL-10 level in TA ( $r = -0.21$ ;  $p < 0.05$ ) before extubation. The results of logistic regression analysis showed that higher concentrations of IL-10 in TA after about 72 hrs of ventilation were associated with lower risk of BPD development (OR-0.99; 95% CI: 0.99-1.0).

#### CONCLUSIONS

Our data suggest that decreased concentrations of TA IL-10 in very preterm infants after about 72 hrs of ventilation may reflect an inability to regulate inflammation, increasing the risk of BPD development.

#### ABS 27

#### ANIMAL MODEL FOR THE BETTER UNDERSTANDING OF BRONCHOPULMONARY DYSPLASIA

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#### INTRODUCTION

The chronic lung disease of preterm infants is called bronchopulmonary dysplasia (BPD). In the Hungarian NICUs more than 50% of preterms born with less than 1,000 grams are affected by BPD. The pathophysiology of the disease is complex, the exact mechanism(s) and the mediators are still not known, there is no proper therapy either. There is an urgent need for an adequate animal model to reveal the underlying pathomechanisms.

The aim of our study was to create a relevant rat model with good reproducibility to investigate the formation and course of BPD.

#### PATIENTS AND METHODS

Our study is based on the known clinical fact, that the intrauterine infections, inflammations have an important role in the development of the disease. On gestational day 20, Wistar rats were anesthetized and, following abdominal section, 0.75 µg or 1.00 µg LPS were injected into the amniotic sacs. Control animals were injected with saline. The respiratory function and the carbachol-induced bronchial resistance of the pups ( $n = 6/\text{group}$ ) were measured by whole-body pletysmography on the 2<sup>nd</sup> and 4<sup>th</sup> weeks. The structural alterations of the lung were analyzed by micro computer tomography (CT) and routine histological methods. Bronchoalveolar lavage was done in each pup and the inflammatory cells were counted by flow cytometry. Furthermore, cytokine profile of the lungs was examined.

#### RESULTS

The offspring of the mothers treated with 1.00 µg LPS developed inflammatory hyperreactivity on the 4<sup>th</sup> postnatal week. The bronchial resistance induced by muscarine-receptor agonist carbachol was significantly higher than that of the control group. Between the 0.75 µg LPS-treated and the control group there was no significant difference. The CT examination revealed decreased air content of the airways on the 2<sup>nd</sup> week which further decreased by the 4<sup>th</sup> week. The observed alterations were more characteristic in animals treated with higher dose of LPS. The routine histological examination showed elevated number of granulocytes and lymphocytes. The lung structure of control pups was normal. We observed significant differences between the cytokine profiles of the control and the treated groups.

**CONCLUSIONS**

We created a reproducible animal model with the characteristic functional and morphological changes of BPD. This model could be useful to identify the mediators, target molecules and even to test new therapeutic modalities.

## Mechanical ventilation

**ABS 28****OPTIMISING ENDOTRACHEAL TUBE (ETT) LENGTH IN NEONATES: PRE-CUT STRATEGY OR UNCUT STRATEGY?**

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**INTRODUCTION**

Endotracheal tube (ETT) length is very important to successful ventilation in neonates. Neonatal services opt for either a pre-cut strategy or a post-intubation adjustment strategy, using various 'adjustable' fixation devices. Incorrect ETT length is associated with accidental extubations, sub-optimal ventilation, right upper lobe collapse, physiological instability and the need for repeat intubations and radiation exposure. Extremely premature neonates may not tolerate repeated intubations well.

**PATIENTS AND METHODS**

Over a 3 month period, we prospectively surveyed the procedure of endotracheal intubation, its placement and fixation across the two neonatal networks covering the East Midlands in the UK. This included 14 hospitals (four level 3, four level 2 and six level 1 units). Network 1 uses ETTs pre-cut to a defined standard length based on gestational age and weight, whereas network 2 uses uncut ETTs placed using the similar length guidance. Pre-cut ETT length cannot be adjusted but uncut ETT length can be adjusted with the device used to secure the tube. We collected data on all elective and emergency intubations including gestational age, birth weight, ETT length strategy, ETT fixation device, ETT position on Chest X-ray and details on ETT length adjustments and re-intubations.

**RESULTS**

There were 231 intubations in total, 100 in network 1 and 131 in network 2; 82 and 110 preterm infants respectively. Overall 8% of ETT's in network 1

(precut ETT) were changed for inappropriate length and none in network 2 (uncut ETT). With the pre-cut strategy; ETTs were changed in 15% of 23-27 weeks gestation (500-1,000 g birth weight) infants, 7% in 28-32 weeks (1,001-2,000 g), 4-5% in > 32 weeks (> 2,000 g). 18% were short, 45% of those short tubes were changed, 20% were long, 85% of those were adjusted with dental rolls. With uncut ETT, 1 was short and 30% were long; all of which were altered via the fixation device. Accidental extubations were 9% with pre-cut compared to 3% with uncut ETT.

**CONCLUSIONS**

We conclude that the pre-cut strategy is associated with a need to re-intubate in 15% of neonates < 28 weeks gestation. This group will benefit most from a more precise ETT position. The uncut strategy is associated with an increased risk of the placement of ETTs in the lower trachea (30%), but these can be safely adjusted without the need for re-intubation. The fixation device (ETT clamp) used appeared effective and we plan to extend its use.

**ABS 29****ACCURACY OF TRANSCUTANEOUS MEASUREMENT OF CO<sub>2</sub> IN NEONATES**

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**INTRODUCTION**

Blood gas analysis and acid-base is one of the basic laboratory parameters in assessment of newborns with respiratory failure. Late recognition of hyper-/hypocapnia or fluctuation of CO<sub>2</sub> levels can increase the risk of intraventricular haemorrhage in preterm. Therefore not only the oxygenation deserves continual monitoring but carbon dioxide levels too. The continual transcutaneous monitoring of CO<sub>2</sub> brings benefits in the treatment of ventilation disorders and prevention of their complications.

**AIMS**

This study tends to find the possibilities and limitations of transcutaneous CO<sub>2</sub> measurement in neonates and its correlation to the values obtained from blood samples.

**PATIENTS AND METHODS**

Twenty nine severely ill newborns were included in the study, 207 paired values of CO<sub>2</sub> were analyzed. We compared the values of CO<sub>2</sub> levels from blood

samples and those obtained by transcutaneous measurements. The correlation, the impact of risk factors and the standard deviation were evaluated.

## RESULTS

The values of CO<sub>2</sub> obtained from blood samples correlated with those from transcutaneous measurements in our patient cohort (25<sup>th</sup>-41<sup>st</sup> postconceptional week; actual weight of 610-4,230 g) The standard deviation of measurement was  $-0.3 \pm 1.492$  kPa; covariance 3.09 and correlation coefficient  $-r$  is 0.923. From selected risk factors, neither actual weight, nor PaCO<sub>2</sub> levels appeared to have an influence to accuracy of measurement and correlation. Correlation coefficients according to postconceptional weeks  $\leq 28$ , 29-32, 33-36,  $\geq 37$  were 0.819, 0.943, 0.967 and 0.942, respectively.

## CONCLUSIONS

Transcutaneous monitoring is a continuous method that can be used in all postconceptional age and weight groups of neonates with stated differences compared to the blood samples.

# Non-invasive ventilation

## ABS 30

### NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION VERSUS BI-LEVEL NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOLLOWING EXTUBATION IN INFANTS < 1,250 G BIRTHWEIGHT: PRELIMINARY REPORT

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## INTRODUCTION

To compare the effectiveness of nasal intermittent positive pressure ventilation (nIPPV) and bi-level nasal CPAP (BiPAP) following extubation in preterm infants < 1,250 g birthweight.

## PATIENTS AND METHODS

In this prospective randomized study, preterm infants with birthweight between 500 to 1,250 g and 25-31 weeks gestational age were screened for eligibility following parental consent. Enrolled infants were randomized into two groups: nIPPV group and BiPAP group. Noninvasive respiratory

support was delivered using the device of SLE 5000 (Specialised Laboratory Equipment, South Croydon, UK) in nIPPV group and infant flow-deriver device (VIASYS®, CareFusion, CA, USA) in BiPAP group. Poractant alfa was administered using a noninvasive technique if necessary. The primary end-point, rate of extubation failure within 96 hours following first extubation, was compared between the groups. Other short and long term neonatal outcomes were also evaluated.

## RESULTS

A total of 43 infants were enrolled in the study. There were no significant differences between nIPPV and BiPAP group in terms of demographic and clinical characteristics. Median duration of mechanical respiratory support and noninvasive respiratory support did not differ between two groups ( $p > 0.05$ ). Rate of extubation failure within 96 hours following first extubation was not significantly different between nIPPV and BiPAP groups ( $p > 0.05$ ). There were no significant differences in the incidence of BPD, BPD or death, IVH, ROP, PDA, NEC and sepsis between the groups ( $p > 0.05$ ).

## CONCLUSIONS

Preliminary results showed that rate of extubation failure within 96 hours following first extubation was similar between nIPPV and BiPAP groups. However short and long term outcomes will be more clearly defined after completion of the study.

## ABS 31

### TRENDS IN NEONATAL RESPIRATORY SUPPORT IN THE AUSTRALIAN & NEW ZEALAND NEONATAL NETWORK (ANZNN) 2009-2012

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## INTRODUCTION

Neonatal clinicians aim to avoid intermittent positive pressure ventilation (IPPV) due to its association with adverse outcomes. "Non-invasive" support modes, continuous positive airway pressure (CPAP) and high flow (HF) are of increasing interest. The ANZNN is a network of 29 tertiary and 27 non-tertiary neonatal units in Australia and New Zealand. Infants are registered in the ANZNN



dataset if they: are born at < 32 weeks' gestation or < 1,500 grams, receive assisted ventilation for  $\geq 4$  hours, or receive major surgery or therapeutic hypothermia. We aimed to assess trends in the overall and primary use of neonatal respiratory support within the ANZNN as well important neonatal outcomes.

#### PATIENTS AND METHODS

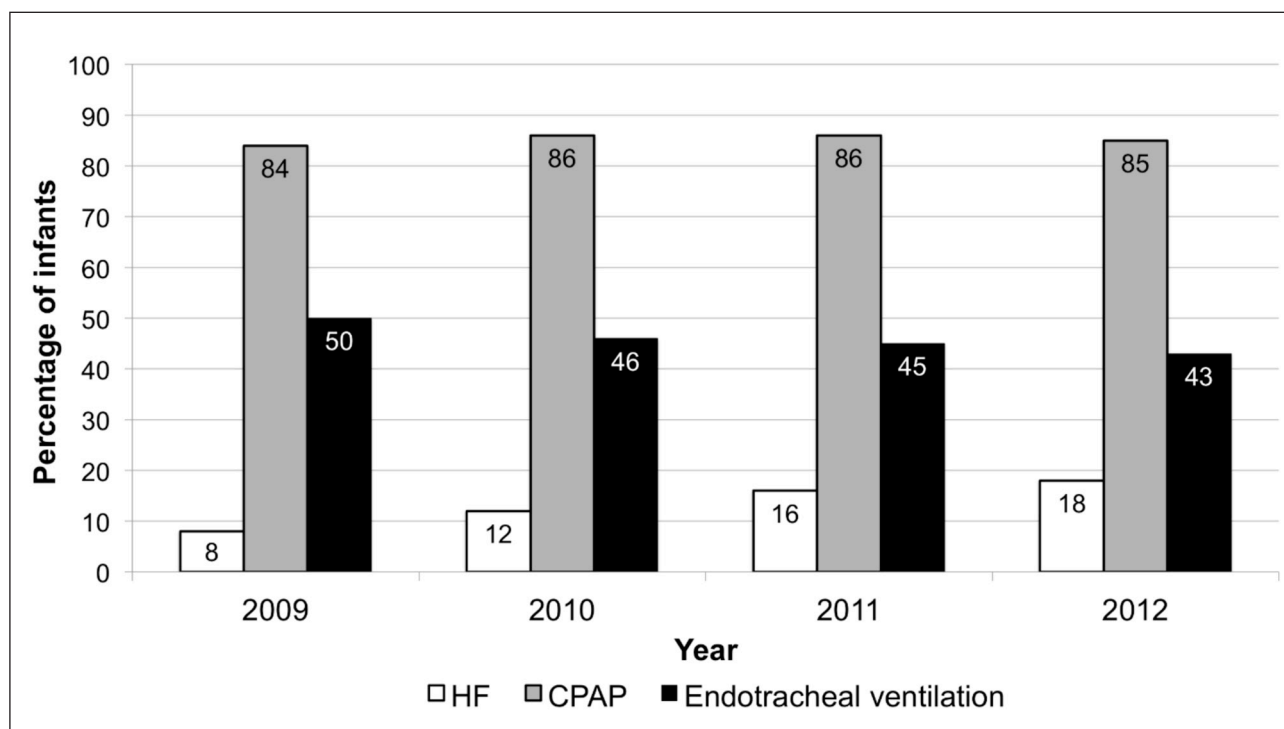
We conducted a population-based study of all infants receiving respiratory support at any time during their hospital admission, within the ANZNN dataset from 2009 to 2012. Use of HF was first recorded in 2009, and 2012 is the most recent available data. Primary respiratory support was defined as the first mode of support commenced at < 24 hours of age. Chronic lung disease was defined as receiving oxygen and/or respiratory support (endotracheal ventilation, CPAP or HF) at 36 weeks' corrected gestation.

Significant linear trends over time were assessed using a Chi square test.

#### RESULTS

36,606 infants were included. Mean gestation was 33.4 weeks (70% were preterm < 37 weeks) and median birth weight 2,100 grams. Respiratory support received is shown in **Fig. 1**. From 2009-2012 there was a significant increase in HF use, no change in CPAP use, and a significant decrease in endotracheal ventilation ( $p < 0.01$ ).

32,072 infants commenced initial respiratory support < 24 hours of age; CPAP was most commonly used (**Tab. 1**). During the study period, there was a significant decrease ( $p < 0.05$ ) in rates of intubation at resuscitation (25.1% in 2009 to 22.1% in 2012), air leak requiring drainage (5.2% in 2009 to 3.8% in 2012), and death (5.9% in 2009 to 4.2% in 2012). In very preterm infants < 32 weeks' gestation, there was a significant reduction in mortality (8.3% to 6.8%,  $p$



**Figure 1 (ABS 31).** Respiratory support received by calendar year.

**Table 1 (ABS 31).** Percentage of infants who received primary respiratory support in the first 24 hours of life.

Primary respiratory support	Percentage of infants by birth year				p-value
	2009	2010	2011	2012	
HF	0.7	0.9	1.4	1.8	< 0.01
CPAP	65.1	66.1	66.7	70.3	< 0.01
Endotracheal ventilation	34.2	33.0	31.9	27.9	< 0.01

< 0.01), and a significant increase in the diagnosis of chronic lung disease (19.0% to 24.0%,  $p < 0.01$ ).

#### CONCLUSIONS

Overall, CPAP remained the most commonly used respiratory support, the use of endotracheal ventilation declined, and HF use increased. There was a significant decrease in primary endotracheal ventilation from 2009-2012, with a corresponding increase in primary CPAP and HF, although primary HF use was rare. During the four-year period a reduction in mortality was seen, but also increased chronic lung disease in infants < 32 weeks' gestation.

#### ABS 32

##### WEANING OF NASAL CPAP IN SCANDINAVIA

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#### INTRODUCTION

In Scandinavia early CPAP treatment has been practiced since the 1970s, but there are only a few studies on weaning from CPAP and there is no clear consensus as to the optimal duration of CPAP treatment, criteria for weaning or weaning method. In this study we wanted to see how CPAP weaning is practiced in different Scandinavian neonatal intensive care units (NICUs).

#### PATIENTS AND METHODS

The study consists of a web-based survey and a retrospective study from one single unit. The web-based survey was sent by email to neonatal intensive care units (NICUs) in Scandinavia November 2013. The retrospective study from St. Olavs University Hospital is based on medical records and the Norwegian Neonatal Medical Quality Registry. Infants with GA < 34 weeks admitted to the NICU between January 1<sup>st</sup> 2009 and December 31<sup>st</sup> 2011 and who received non-invasive ventilation (NIV) for more than 7 days, were included in the study. Initiation of weaning was defined as the first day with pauses lasting at least one hour or a flow reduction of at least 1 L/min and below 8.0 L/min. Total duration of NIV treatment was defined as days on CPAP before and after any ventilator treatment.

#### RESULTS

19 of 41 units (46%) responded to the survey. Criteria for weaning were oxygen below 30% in six

units, breathing room air in five, while six units had no specified criteria for weaning from CPAP. Seven units reported that they use a combination of time off CPAP and reduction in flow/CPAP pressure for weaning. Four units use reduction of flow, three increasing time off CPAP and two discontinue CPAP with no prior weaning. Criteria for cessation of CPAP were similar to the criteria for initiation of weaning. Seventeen units (41%) use High Flow Nasal Cannula (HFNC) in connection with weaning. In the single unit study the infants were weaned through a combination of flow reduction and increasing time off CPAP in 90% of cases. In infants with GA 28-31 weeks median time on NIV was 27 days while median duration of weaning was 21 days.

#### CONCLUSIONS

The survey of the Scandinavian units showed no correlation between nationality, size of unit and routines for non-invasive ventilation.

The retrospective study from St. Olavs University Hospital showed that weaning constituted a large part of total time on NIV. It seems that the clinicians have been aiming for a reduction of level of NIV soon after initiation of treatment.

#### ABS 33

##### A PROSPECTIVE RANDOMIZED, CONTROLLED TRIAL COMPARING HUMIDIFIED HIGH FLOW NASAL CANNULA VERSUS NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE AS RESPIRATORY SUPPORTS AFTER EXTUBATION IN PRETERM INFANTS

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#### INTRODUCTION

Humidified high flow nasal cannula (HHFNC) is considered relatively easy and comfortable as a form of respiratory support. But, it is not proved the effectiveness and safety of HHFNC in preterm infants yet. After new type of HHFNC (RT329 Infant Oxygen Delivery System, Fisher & Paykel) was introduced, there are few studies using this system. The aim of this study is to evaluate the effectiveness and safety of HHFNC as a form of respiratory support after extubation in preterm infants comparing with nasal continuous positive airway pressure (nCPAP).

## PATIENTS AND METHODS

This is a prospective randomized controlled study in 84 preterm infants (gestational age < 37 weeks) with respiratory distress syndrome who were about to be extubated from mechanical ventilation. They were randomized to either HHFNC or nCPAP after extubation. The primary outcome was extubation failure rate defined as the change to other mode from the study support mode within 72 hours after extubation. The rate of successful weaning from the devices, complications with the device and outcomes during hospitalization were also analyzed. In infants with extubation success, time from extubation to full bottle feeding was checked to investigate the effect of the device on feeding process.

## RESULTS

HHFNC group (n = 42) and nCPAP group (n = 42) had similar gestational age and birth weight. The extubation failure rate was 16.7% (7/42) in HHFNC group and 2.4% (1/42) in nCPAP group (p = 0.026). The rate of successful weaning from the device within 72 hours was 57.1% (24/42) in HHFNC group and 45.2% (19/42) in nCPAP group (p = 0.275). There were no statistically significant differences in complications with the device and outcomes during hospitalization between both groups. Days from extubation to full bottle feeding were 19.0 ± 15.1 days in HHFNC group and 25.9 ± 19.1 days in nCPAP group (p = 0.091).

## CONCLUSIONS

HHFNC is not effective to prevent extubation failure in preterm infants comparing with nCPAP. However, HHFNC application after extubation can be effective on feeding process than nCPAP in case of extubation success. Further randomized investigations on wider populations are needed to define the utility of HHFNC as a form of respiratory support after extubation in preterm infants.

## ABS 34

### LEAKAGE DURING NONINVASIVE HIGH FREQUENCY OSCILLATORY VENTILATION IMPROVES CARBON DIOXIDE CLEARANCE IN A NEONATAL LUNG MODEL

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## INTRODUCTION

Nasal high frequency oscillatory ventilation (nHFOV) is a new mode of noninvasive neonatal respiratory support. An oscillatory pressure waveform is applied over a constant gas flow using a nasal or nasopharyngeal interface thus combining effects of nasal continuous positive airway pressure (nCPAP) and high frequency oscillatory ventilation. nHFOV has been described in bench studies and case series to be superior to nCPAP in terms of CO<sub>2</sub> elimination and is utilized in a number of European neonatal units. Influence of leakage on CO<sub>2</sub> elimination has not been investigated in nHFOV before. We explored the effect of a nasopharyngeal leak on CO<sub>2</sub> elimination during nHFOV in a neonatal airway model.

## PATIENTS AND METHODS

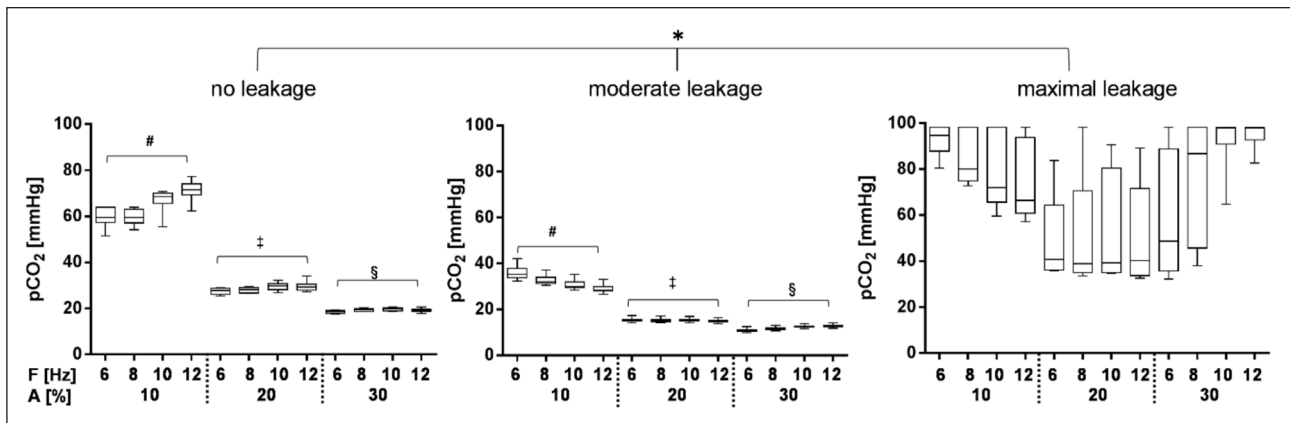
A neonatal ventilator was connected to an airway- and lung model using regular prongs as nasal interface. Alveolar CO<sub>2</sub> was maintained by constant circulatory CO<sub>2</sub>-flow into the artificial lung and CO<sub>2</sub> partial pressure was determined using a midstream CO<sub>2</sub> analyzer. Gas flow and pressure respectively were measured simultaneously at the prongs, pharynx, lung and leakage. Effects of combined nasopharyngeal air leak (0 l/min, 5.3 l/min, 10.4 l/min) on CO<sub>2</sub> elimination, gas flow and pressure were determined at various settings to frequency (6, 8, 10, 12 Hz) and amplitudes (10%, 20%, 30% of maximum ventilator performance) at a median airway pressure of 10 mbar. Median and range of 8 measurements are given. Data were analyzed using t-test, one-way ANOVA and Šídák post hoc correction test, p < 0.05.

## RESULTS

Without airleak higher amplitudes or lower frequencies enhanced CO<sub>2</sub> clearance. At medium leak flow CO<sub>2</sub> elimination was more effective as compared to nHFOV without leak (p < 0.001). This effect was true for all amplitudes and frequencies tested. Maximum air leak allowed no effective or a highly variable CO<sub>2</sub> elimination (**Fig. 1**).

## CONCLUSIONS

To our knowledge this is the first bench model study exploring the effect of air leaks on CO<sub>2</sub> elimination in noninvasive neonatal ventilation. We demonstrated that a moderate nasopharyngeal leak improves CO<sub>2</sub> elimination. Various means are applied to reduce nasopharyngeal leaks during noninvasive ventilation to achieve a desired positive end expiratory airway pressure. However, according to our study a moderate mouth leak may rather improve gas exchange during noninvasive ventilatory support.



**Figure 1 (ABS 34).** Partial pressure of alveolar  $pCO_2$  [mmHg] at various frequencies (6, 8, 10, 12 Hz), amplitudes (10%, 20%, 30%) and leakage (0, 5.3, 10.4 l/min).

Shown are median and interquartile range. T-bars represent min, max.

\* $p < 0.001$ . Post hoc comparison: # $p < 0.001$ , † $p < 0.001$ , § $p < 0.01$ .

## ABS 35

### HIGH FLOW SUPPORT IN VERY PRETERM INFANTS WITHIN THE AUSTRALIAN & NEW ZEALAND NEONATAL NETWORK (ANZNN) 2009-2012

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## INTRODUCTION

Randomised controlled trials suggest that high flow (HF) is comparable to continuous positive airway pressure (CPAP) for post-extubation respiratory support in neonates. Trials investigating HF have typically recruited very preterm infants (< 32 weeks' gestation) after extubation. The ANZNN is a network of 29 tertiary and 27 non-tertiary neonatal units in Australia and New Zealand. Infants are registered in the ANZNN dataset if they: are born at < 32 weeks' gestation age (GA) or < 1,500 grams, receive assisted ventilation for  $\geq 4$  hours, or receive major surgery or therapeutic hypothermia. We aimed to assess trends in HF use in very preterm infants within the ANZNN.

## PATIENTS AND METHODS

We conducted a population-based study of all very preterm infants within the ANZNN dataset who received respiratory support between 2009-2012. Use of HF was first recorded in 2009, and 2012 is

the most recent available data. Chronic lung disease (CLD) was defined as receiving oxygen and/or respiratory support (endotracheal ventilation, CPAP or HF) at 36 weeks' corrected gestation. Subgroup analysis by GA (< 28 weeks;  $\geq 28$  weeks) was performed, and statistical significance determined using a Chi square test for linear trend over time.

## RESULTS

13,298 very preterm infants (mean GA 28.4 weeks, median weight 1,203 g) received respiratory support from 2009-2012; 3,372 (mean GA 27.6 weeks, median weight 1,031 g) were treated with HF during admission (**Fig. 1**). Initiation of HF was at median 17 days of life, and median time on HF was 12 days; 17 days for infants < 28 weeks' and 8 days for those 28-31<sup>+6</sup> weeks' GA. In 99.5% of infants HF was initiated after endotracheal ventilation or CPAP treatment. Most infants received HF gas flows consistent with those in published trials ( $\leq 8$  litres/minute): mean minimum flow was 3.3 litres/minute, and mean maximum flow 5.8 litres/minute. HF use increased significantly over time in the subgroups and in very preterm infants overall ( $p < 0.01$ ). Rates of air leak requiring drainage (4% of infants) and death (2% of infants) were low in infants receiving HF. CLD was present in 43% of HF treated infants.

## CONCLUSIONS

HF use in very preterm infants has rapidly increased within the ANZNN, particularly for those infants < 28 weeks' GA. The majority of HF use was after extubation, and was initiated after more than two weeks of life. Most gas flows were  $\leq 8$  litres/minute, in keeping with published randomised trials.

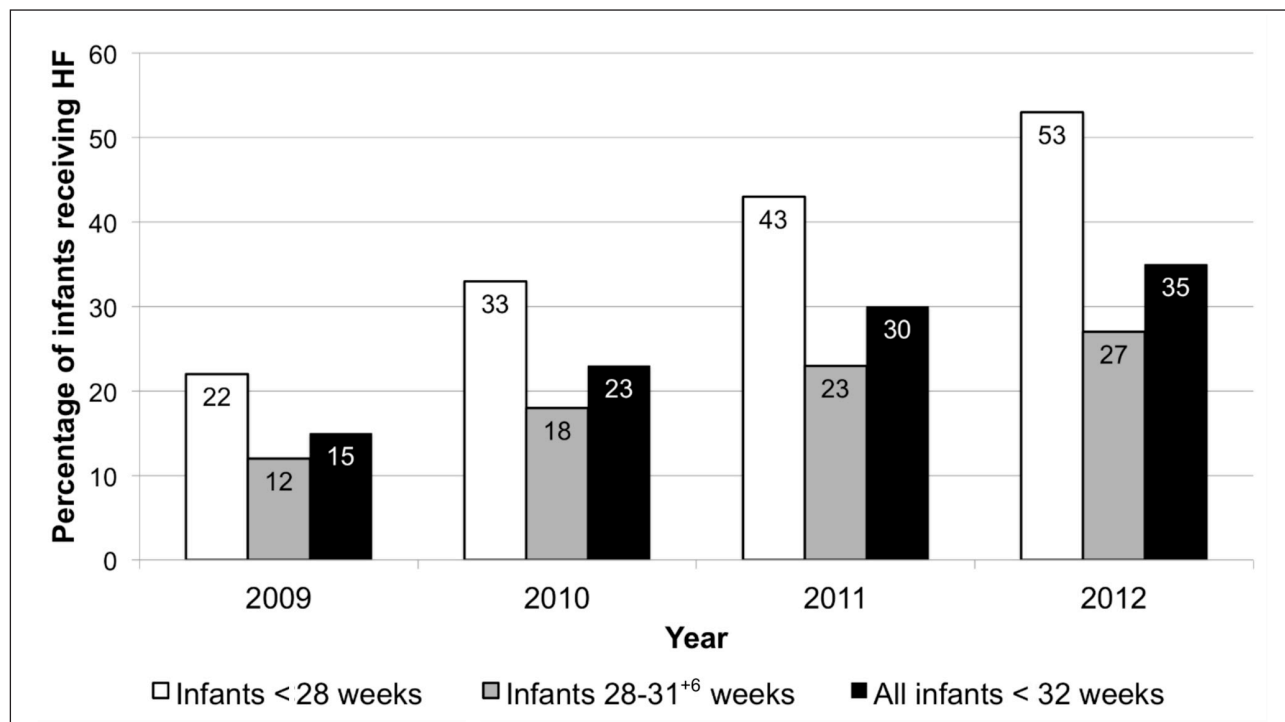


Figure 1 (ABS 35). Very preterm infants receiving high flow (HF) by calendar year.

#### ABS 36

### IMPACT OF NASAL PRONG RESISTANCE ON PRESSURE DELIVERY DURING NON-INVASIVE VENTILATION WITH FIXED AND VARIABLE FLOW USING A PNEUMATIC LUNG MODEL

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#### INTRODUCTION

Nasal continuous positive airway pressure (nCPAP) has probably become the most frequent ventilatory strategy for preterm infants. Different nasal prongs are currently available for administering nCPAP but *in vivo* studies have been inconsistent on how resistance and leak can affect pressure delivery. One study has suggested that using devices that provide variable circuit flow for compensating for pressure loss due to leak, could reduce work of breathing but the mechanism remains unclear. The aim of the current study is to evaluate the impact of prong resistance and circuit flow (fixed and variable) on pressure delivery using a pneumatic lung model.

#### PATIENTS AND METHODS

Two commercially available nasal prongs (xs Argyle® and premie RAM cannula®) were tested using a custom made pneumatic lung model in variable and constant flow mechanical ventilators delivering nCPAP (AVEA® – CareFusion, Babylog® 8000Plus, Dräger). Each ventilator was calibrated using a new disposable ventilator circuit leaving the humidifier dry to standardise all measurements. A leak orifice in the lung model remained constant for every experiment. Circuit flow and pressure, leak, simulated alveolar and pleural pressures using an active breathing lung model (Fig. 1) were measured

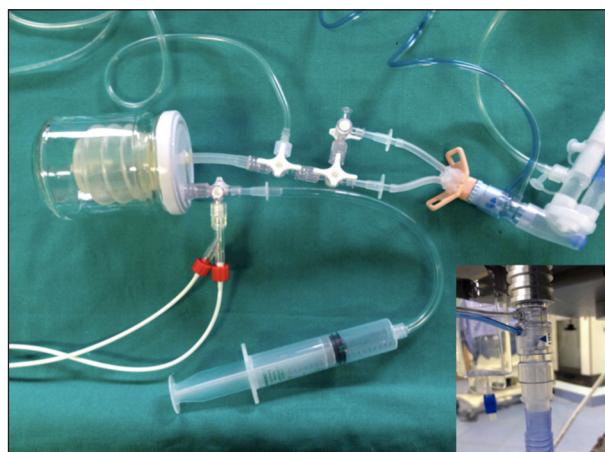


Figure 1 (ABS 36). Instruments used for measurements.

**Table 1 (ABS 36).** Pressure delivery at different set pressures using a variable flow ventilator.

Prongs/pressure	True flow <sup>a</sup> (L/min)	Circuit pressure <sup>a</sup> (mbar)	Distal pressure <sup>a</sup> (mbar)	Pressure drop (%)	Leak (%)
Argyle/4 mbar	8.1 (7.9-8.6)	2.3 (2.2-2.5)	1.0 (0.9-1.1)	66.6	34.2
Argyle/6 mbar	9.1 (8.8-9.4)	4.2 (4.1-4.3)	1.8 (1.7-1.9)	57.2	45.5
Argyle/8 mbar	9.9 (9.6-10.2)	6.0 (5.9-6.1)	2.7 (2.6-2.8)	55.0	52.9
RAM/4 mbar	6.8 (7.6-8.1)	2.2 (2.2-2.3)	0.5 (0.5-0.6)	77.3	29.8
RAM/6 mbar	7.8 (7.6-8.1)	4.2 (4.1-4.3)	1.1 (1.0-1.1)	73.9	40.5
RAM/8 mbar	9.0 (8.6-9.6)	6.2 (6.0-6.3)	1.6 (1.5-1.6)	74.2	46.4

<sup>a</sup>Values are shown as mean and range.

**Table 2 (ABS 36).** Pressure delivery at different set pressures using a fixed flow ventilator.

Prongs/pressure	True flow <sup>a</sup> (L/min)	Circuit pressure <sup>a</sup> (mbar)	Distal pressure <sup>a</sup> (mbar)	Pressure drop (%)	Leak (%)
Argyle/4 mbar	8.5 (8.3-8.8)	3.4 (3.2-3.8)	1.5 (1.3-1.6)	55.9	42.3
Argyle/6 mbar	8.6 (8.3-8.8)	7.4 (7.2-7.6)	4.1 (4.0-4.3)	44.6	56.2
Argyle/8 mbar	8.5 (7.2-8.7)	8.6 (8.3-8.8)	4.0 (3.9-4.2)	53.5	76.7
RAM/4 mbar	8.9 (8.7-9.1)	3.6 (3.4-3.9)	0.9 (0.8-1.0)	75.0	32.0
RAM/6 mbar	8.4 (8.0-8.7)	5.3 (4.9-5.7)	1.4 (1.3-1.5)	73.6	43.8
RAM/8 mbar	8.8 (8.6-9.1)	9.9 (8.7-11.5)	3.1 (2.6-3.6)	68.7	64.4

<sup>a</sup>Values are shown as mean and range.

with two synchronised Bicare-II (CareFusion) instruments. The data was recorded and analysed using data managing software (Pulmochart®).

## RESULTS

Delivered pressure was reduced significantly in all experiments (**Tab. 1** and **Tab. 2**). Leak increased with pressure difference and circuit flow and leak varied between 29 and 76% in different experiments in spite that the orifice in the lung model remained constant. A greater pressure drop was observed using the higher resistance RAM cannula®. There were significant differences between set and measured circuit pressure in both tested ventilators. Circuit pressure was lower than set pressure but remained more stable in the variable flow ventilator (AVEA® – CareFusion).

## CONCLUSIONS

We chose a high and a low resistance nasal prong for testing as extremes of the spectrum of currently available devices. Variable flow maintained a more constant pressure in the circuit but did not reduce pressure drop. Leak compensation with flow does not seem to improve pressure delivery to the airway. Clinicians should consider leak and nasal prong resistance as contributing factors for less efficacy of nCPAP in the clinical setting.

## ABS 37

### COMPARISON OF EXTUBATION FAILURE IN NIV-NAVA AND nCPAP FOR PRETERM INFANTS

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## INTRODUCTION

Prolongation of mechanical ventilation hospital stay and increase morbidity of bronchopulmonary dysplasia and mortality in preterm infants. To shorten duration of invasive mechanical ventilation, early extubation and weaning with non-invasive ventilation is very important. NIV-NAVA (Non-Invasive Neurally Adjusted Ventilator Assist) is a new mode of Non-Invasive ventilation during weaning from mechanical ventilation. Although some studies have demonstrated that NIV-NAVA is effective in adults, there are few studies in preterm infants. We aimed at comparing safety and usefulness of NIV-NAVA with nCPAP (nasal Continuous

Positive Airway Pressure) in weaning of mechanical ventilation in preterm infants.

#### PATIENTS AND METHODS

This is a retrospectively historical review using case-control approach. 20 infants with gestational age of less than 32 weeks in period I (from July 2013 to June 2014) were weaned from mechanical ventilation by NIV-NAVA and 18 infants weeks in period II (from July 2013 to June 2012) were weaned by nCPAP. Planned extubation was meant as intentional extraction of endotracheal tube on setting less than MAP 9 cmH<sub>2</sub>O, FiO<sub>2</sub> 40%, and PEEP 7 cmH<sub>2</sub>O. Extubation failure was defined as reintubation within 72 hours of planned extubation. Prior and after extubation, the peak inspiratory pressure, peak expiratory end pressure and inspired oxygen concentration were recorded and capillary blood gas exam was performed. Morbidities of prematurity were compared between both groups.

#### RESULTS

Important demographics of study population were not different between the two groups (median gestational age 26.2 weeks vs. 25.7 weeks,  $p = 0.31$ ), except that the proportion of histologic chorioamnionitis was higher in the nCPAP group (25% vs. 61%,  $p = 0.04$ ). Baseline characteristics and settings of mechanical ventilation at extubation had no significant difference in both groups. Rate of extubation failure was lower in NIV-NAVA groups than in nCPAP groups (5% versus 39%,  $p < 0.05$ ). morbidities of bronchopulmonary dysplasia, ROP (retinopathy of prematurity), NEC (necrotizing enterocolitis), IVH (intraventricular hemorrhage) in both groups did not differ.

#### CONCLUSIONS

NIV-NAVA seems to be more effective mode than nCPAP for weaning from invasive mechanical ventilation in preterm infants. And morbidities of preterm infants did not differ significantly after weaning with NIV-NAVA as compared with nCPAP.

#### ABS 38

#### A RANDOMIZED TRIAL OF LOW FLOW OXYGEN VERSUS NASAL CPAP IN PRETERM INFANTS

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#### INTRODUCTION

Nasal Continuous Positive Airway Pressure (nCPAP) stabilizes the residual volume and may decrease the risk of “atelectotrauma” potentially promoting lung development in neonates. Our objective was to assess if replacing nCPAP by low flow O<sub>2</sub> by nasal cannula affects lung function expressed as the arterial/alveolar oxygen tension ratio (a/A pO<sub>2</sub>-ratio) on postnatal day 28.

#### PATIENTS AND METHODS

Preterms (birth weight < 1,500 grams and GA > 26<sup>+0</sup> weeks), stable on nCPAP between postnatal days 4 to day 7 were randomized to nCPAP or low flow O<sub>2</sub> by nasal cannula (< 0.2 L/min). Study-criteria defined how to wean/restart respiratory support or change from low flow O<sub>2</sub> to nCPAP and vice versa. Transcutaneous monitoring was used for assessment of a/A pO<sub>2</sub>-ratio on day 28 using a head-box for all infants for accurate measurement and to eliminate possible effects from nCPAP or low flow O<sub>2</sub> on oxygen requirement.

#### RESULTS

We enrolled  $n = 52$ , ( $n = 30$ /nCPAP-group and  $n = 22$  /low flow O<sub>2</sub>-group) (Tables 1, 2 and 3). The

**Table 1 (ABS 38).** Characteristics of enrolled infants at time of randomisation.

	nCPAP group (n = 30)	Low flow O <sub>2</sub> group (n = 22)	p-value
Gestational age (weeks)	28.0 ± 1.2	28.4 ± 1.4	
Birth weight (grams)	1,107 ± 185	1,086 ± 234	
Preeclampsia	27%	23%	
Corticosteroid	61%	77%	
PPROM	10%	9%	
Caesarean section	70%	68%	
Apgar 1 min	7.7 ± 2.3	8.4 ± 2.6	
Apgar 5 min	9.6 ± 1.3	9.6 ± 1.3	
Surfactant	67%	36%	0.05
Mechanical ventilation	12 (40%)	1 (5%)	0.008
Days of mechanical ventilation <sup>a</sup>	2.2 ± 1.5	2 ± 0	
Postnatal age at randomization (days)	6.4 ± 0.9	5.4 ± 1.7	0.002

Data are means (± SD) or numbers (%). Only p-values < 0.05 are shown.

<sup>a</sup>Mean duration of mechanical ventilation in ventilated patients only (12 in CPAP group, 1 in O<sub>2</sub> group).

**Table 2 (ABS 38).** Outcomes at postnatal day 28.

	nCPAP group (n = 24)	Low flow O <sub>2</sub> group (n = 20)	p-value
In nCPAP at day 28	17 (74%) <sup>a</sup>	3 (15%)	< 0.0005
a/A pO <sub>2</sub> -ratio	0.43 ± 0.17	0.48 ± 0.18	0.36
Age (days)	29.7 ± 2.2	29.5 ± 3.0	
FiO <sub>2</sub> (%)	0.29 ± 0.1	0.31 ± 0.17	
Transcutaneous pO <sub>2</sub> (kPa)	7.9 ± 1.6	8.6 ± 1.3	
Transcutaneous pCO <sub>2</sub> (kPa)	6.9 ± 1.1	7.0 ± 1.3	
SpO <sub>2</sub>	93.8 ± 2.2	94.9 ± 2.1	
Weight (grams)	1,572 ± 346	1,585 ± 316	

Data are means (± SD) or numbers (%). Only p-values < 0.05 are shown except for primary outcome of a/A pO<sub>2</sub>-ratio.

1 patient died at postnatal day 8 in the nCPAP group, 5 patients in the nCPAP group had missing data, 2 patients had missing data in the low flow O<sub>2</sub> group.

<sup>a</sup>One patient had data for a/A pO<sub>2</sub>-ratio but missing data for nCPAP status at day 28.

**Table 3 (ABS 38).** Outcomes at 36 weeks PMA.

	nCPAP (n = 29)	Low flow O <sub>2</sub> (n = 22)	p-value
In oxygen at 36 weeks	2 (7.1%)	6 (27.3%)	0.12
In nCPAP at 36 weeks	4 (14.0%)	1 (4.5%)	0.38
Any resp. support at 36 weeks	4 (14.3%)	6 (27.3%)	0.30

Data are numbers (%).

1 patient died in the nCPAP group at day 8 due to *Klebsiella spp.* sepsis. Data on the need for oxygen at 36 weeks is missing for 1 patient in the nCPAP group.

a/A pO<sub>2</sub>-ratio at 28 days was 0.43 ± 0.17 (nCPAP group) versus 0.48 ± 0.18 (p = 0.36). Duration of nCPAP was 16.4 (low flow group) versus 41.1 days (nCPAP group), p < 0.001. There was no difference between groups in the fraction needing any respiratory support at 36 weeks corrected age, length of stay, weight at discharge and the relative weight gain (**Tab. 4**).

#### CONCLUSIONS

Replacing nCPAP by low flow O<sub>2</sub> in preterm infants at the end of the first week of life did not affect pulmonary function or weight gain negatively and may be associated with a reduction in cost, equipment use and increased ease of nursing.

**Table 4 (ABS 38).** Outcomes at discharge.

	nCPAP group (n = 30)	Low flow O <sub>2</sub> group (n = 22)	p-value
Length of total hospital stay (days)	75.1 ± 21.4	69.0 ± 13.1	
Total days in nCPAP	41.1 ± 24.7	16.4 ± 18.2	0.000
Total days in oxygen	34.6 ± 25.5	39.2 ± 20.7	
Mechanical ventilation, overall (%)	15 (50%)	2 (9.1%)	0.002
Total days mechanical ventilation <sup>a</sup>	2.4 ± 1.45	4 ± 2.83	
Death	1	0	
Weight at discharge (grams)	2,913 ± 528	2,710 ± 291	
Delta-SDS	0.16 ± 0.84	0.33 ± 0.87	
NEC	0%	5%	
ROP	12%	5%	
PVL	7.4%	5%	

Data are means (± SD) or numbers (%). Only p-values < 0.05 are shown.

<sup>a</sup>Mean duration of mechanical ventilation in ventilated patients only.

## Placenta and prenatal factors

### ABS 39

#### SHEDDING LIGHT ON PRETERM IMMUNITY

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#### INTRODUCTION

There is little knowledge on the immune system of extremely premature infants (born 24-29 weeks



of gestation). This paucity of evidence impedes advances in the fight against bronchopulmonary dysplasia (BPD), a common, severe chronic lung disease that entails significant morbidity and mortality. No safe and effective treatment exists.

#### PATIENTS AND METHODS

In order to improve our understanding on preterm immunity and to characterize the immunological hallmarks of BPD so that high-risk infants can be identified for early intervention, an observational study was set up to shed light on this topic by aiming to recruit a cohort of 75 extremely premature infants. Blood was collected from 20 extremely preterm infants at 5 timepoints (birth, days 1, 7 and 14 and 36 weeks corrected gestational age [WCGA]) till date. Following overnight *in vitro* stimulation with PMA/ionomycin, LPS or vehicle, flow cytometry was used to explore T cells and their polarisation, macrophages, dendritic cells (DC) and neutrophils and their activation status as well as endothelial progenitor cells (EPC).

#### RESULTS

From the analysis of seven preterm babies, the ability of neonatal CD4<sup>+</sup> T cells to produce IFN-gamma in response to cell stimulation increases over time, leading to a clearly positive but still attenuated response at 36 WCGA. Comparing the three infants that developed BPD with the four that did not at 36 WCGA, we observed a marked increase in macrophage (6-fold), DC (2-fold) and neutrophil activation (9-fold), but fewer circulating EPC (0.3% vs. 1.4% of viable cells).

#### CONCLUSIONS

These early data from preterm infants reveal that this first-of-its-kind study will revolutionise the understanding of preterm immunity. BPD appears associated with markedly increased cellular activation – a promising finding that may provide a basis for therapeutic innovations.

#### ABS 40

### PRENATAL THERAPY IMPROVES THE SURVIVAL OF PREMATURE INFANTS WITH CONGENITAL CHYLOTHORAX

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#### INTRODUCTION

Chylothorax is a rare condition among neonates, although it is considered clinically significant, as it is difficult to manage in these patients. In addition, the course of chylothorax varies widely. Prolonged severe fetal pleural effusion can compromise normal lung maturation and progress to fetal hydrops, ultimately resulting in premature birth and pulmonary hypoplasia, with a high rate of intrauterine death and perinatal mortality. No consensus has been reached regarding the management of congenital chylothorax. Therefore, we aimed to elucidate the clinical features and effect of prenatal therapy on the prognosis of congenital chylothorax in neonates.

#### PATIENTS AND METHODS

We retrospectively reviewed the medical records of all infants with congenital chylothorax who were admitted to National Taiwan University Hospital, a tertiary perinatal and neonatal unit in northern Taiwan, between January 2000 and December 2012. Congenital pleural effusion was defined as pleural effusion that was diagnosed antenatally or at birth. Their demographic characteristics, as well as their antenatal, perinatal, and postnatal information, were collected for our analysis of the mortality rate.

#### RESULTS

We found 29 infants who were diagnosed with congenital chylothorax during the study period. The median gestational age at birth was 34 weeks (range, 28-41 weeks), and 71% of the infants presented with hydrops fetalis. Most cases of congenital chylothorax involved bilateral presentation (bilateral: 86.21%, unilateral: 13.79%), and the overall survival rate was 59.62%. Among the cases with a prenatal diagnosis that was made at < 34 weeks of gestation (n = 22), infants who received prenatal therapy had a significantly higher survival rate, compared to infants who did not receive prenatal therapy (76.92% vs. 11%, respectively; p = 0.008) (**Tab. 1**). After logistic regression analysis, fetal therapy could independently improve the perinatal outcome of chylothorax that was diagnosed before 34 weeks of gestation (odds ratio: 0.004, 95% confidence interval: 0.000-0.33, p = 0.014).

#### CONCLUSIONS

If chylothorax is diagnosed at < 34 weeks of gestation, we recommend transabdominal thoracentesis, *in-utero* pleurodesis, or the placement of a thoracoamniotic shunt as prenatal therapy to improve the perinatal outcome, due to the risk of pulmonary hypoplasia.

**Table 1 (ABS 40).** Prenatal and postnatal characteristics of infants with and without prenatal therapy after a prenatal diagnosis at < 34 weeks of gestation.

Characteristics	Prenatal therapy		p-value
	With (Yes) (n = 13)	Without (No) (n = 9)	
<b>Perinatal factors</b>			
Gestational age at diagnosis (mean, weeks)	25	29	0.963
Hydrops fetalis (%)	76.92	88.89	0.616
Bilateral pleural effusion (%)	84.62	100	0.24
<b>Postnatal factors</b>			
Gestational age at delivery (mean, weeks)	32	33	0.638
Birth body weight (grams)	2,448.46	2,798.89	0.404
Male sex (%)	23.08	66.67	0.387
1-min Apgar score (mean)	4	1	0.007 <sup>a</sup>
5-min Apgar score (mean)	6	2	0.005 <sup>a</sup>
Thoracocentesis after birth (%)	85	100	0.494
Chest tube insertion after birth (%)	69	56	0.662
Pneumothorax (%)	8	78	0.007 <sup>a</sup>
<b>Ventilator parameters</b>			
Ventilator use (%)	23	89	0.616
OI at admission	28	75	0.017 <sup>a</sup>
AaDO <sub>2</sub> at admission	375	557	0.329
OI at second arterial blood gas test	23	69	0.009 <sup>a</sup>
AaDO <sub>2</sub> at second arterial blood gas test	339	575	0.009 <sup>a</sup>
OI at 24 h	16	51	0.245
AaDO <sub>2</sub> at 24 h	208	646	0.121
Survival to discharge (%)	76.92	11	0.008 <sup>a</sup>

OI: oxygen index; AaDO<sub>2</sub>: alveolar arterial oxygen partial pressure gradient.

<sup>a</sup>p < 0.05.

## Surfactant

### ABS 41

#### REFERENCE RANGES OF LAMELLAR BODY COUNTS ON GASTRIC ASPIRATE IN HEALTHY TERM NEWBORNS

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### AIM

The aim of this study was to determine the reference ranges of lamellar body counts on gastric aspirate in healthy term newborns.

### PATIENTS AND METHODS

Term newborns with gestational age  $\geq$  37 weeks were included in this prospective study. Gastric aspirates were collected within 30 minutes of birth by using a feeding tube and 5-ml syringe. The samples were diluted with dithiothreitol (DTT, 10 mg/ml) (1 part gastric aspirate, 6 parts DTT), and mixed for 10 seconds with a vortex mixer. Lamellar body counts were performed by using the platelet channel of the automated cell counter.

### RESULTS

A total of 262 samples of gastric aspirates were evaluated. Median gestational age was 39 weeks (37-42), mean birth weight was  $3,360 \pm 420$  g. Median lamellar body counts were 441,000 (56,000-2,695,674). There were no significant differences between the lamellar body counts when evaluated according to gender and type of delivery. Lamellar body counts at different gestational ages were similar. Reference intervals according to weeks and percentile values of lamellar body count were determined.

### CONCLUSIONS

This is the first study evaluating the reference ranges of lamellar body counts on gastric aspirate in healthy term newborns. These data can be used as a guide to evaluate lung maturation and with the purpose of diagnosis in newborns with respiratory distress.

## ORAL COMMUNICATIONS

### ABS 42

#### CORD BLOOD PENTRAXIN-3 LEVELS IN RESPIRATORY DISORDERS OF THE NEWBORN

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## INTRODUCTION

Respiratory distress is one of the most common causes of neonatal intensive care unit (NICU) admissions. Respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), and congenital pneumonia (CP) are the main respiratory diseases in the newborn. Pentraxin-3 (PTX-3) a member of the pentraxin superfamily behaves as an acute phase protein and increases rapidly in response to inflammatory signals. We aimed to investigate the role of PTX-3 in differential diagnosis of respiratory distress in term and preterm neonates.

## PATIENTS AND METHODS

Umbilical cord blood was collected from all live newborns between March 2010 and July 2011 in Eskişehir Osmangazi University Hospital. Among those, infants diagnosed with RDS (n = 23), TTN (n = 36) and CP (n = 12) and randomly selected 27 healthy infants were included in the study. Infants with congenital heart disease, multiple congenital anomalies and genetic disease were excluded. IL-6, CRP and PTX-3 levels were measured in umbilical cord blood samples.

## RESULTS

Antenatal and demographical characteristics of the study groups were similar. Pentraxin-3 levels in RDS, TTN, CP and control groups were 13.7 ng/ml, 2.77 ng/ml, 15.7 ng/ml, and 2.41 ng/ml respectively. Umbilical cord PTX-3 levels were significantly higher in infants with RDS and CP compared to those with TTN and controls (p < 0.001). Infants with RDS and CP have similar cord blood PTX-3 levels. Pentraxin-3 levels were negatively correlated with gestational age. Umbilical cord IL-6 levels were higher in patients with RDS and CP (p < 0.05).

## CONCLUSIONS

Umbilical cord PTX-3 levels were increased in RDS and CP. Umbilical cord PTX-3 measurement can differentiate TTN from RDS and CP.

# Apnea and respiratory control

ABS 43

## EVALUATION OF PHYSIOLOGICAL ADAPTATION OF THE LUNG TO POSTNATAL LIFE BY LUNG ULTRASOUND

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## INTRODUCTION

It is well known that spontaneous delivery (SD) predisposes to a better adaptation of the lung to extra uterine life. In spontaneously delivered infants, compared to infants delivered by caesarean section (CS), lung fluid is supposed to be more rapidly cleared to allow gas exchange. Lung ultrasound (LUS) is a reproducible and not harmful method that easily analyze the persistence of liquid in the lung, discriminating between liquid and air content. Our aim was to update LUS profiles on physiologic lung adaptation to postnatal life in relationship to different modes of delivery in normal term neonates.

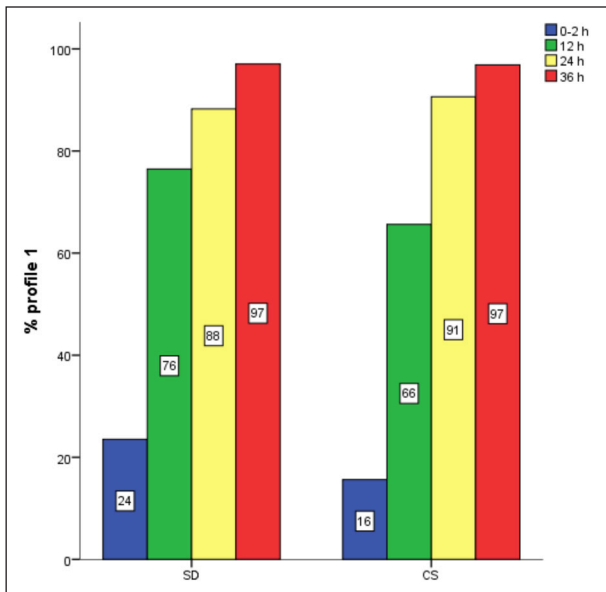
## PATIENTS AND METHODS

Term infants with GA ≥ 37 wks consecutively delivered by SD or CS. Upon parental consent, enrolled infants underwent LUS to examine adaptation profiles within the first 2 h of life and scans were repeated at 12, 24 and 36 h post delivery. A longitudinal and trasversal scan of the anterior and lateral chest walls were obtained for each lung in each patient. Each scan was classified according to the following profiles: type 1 (prevalence A lines), type 2 (prevalence of B-lines), type 3 (white lung) and type 4 (white lung with small subpleural consolidations areas). Chi-square test was applied to assess the differences of the distribution between SD and CS. Generalized linear model allowed to evaluate the eventual differences of the echographic evolutions between the two groups.

## RESULTS

Ninety-nine term infants (mean GA 38.9 ± 1.2 weeks, mean BW 3,285 ± 534 g) were enrolled, 46 delivered spontaneously and 53 by CS. At first LUS the distribution in SD group was: 9 (20%) profile 1, 19 (42%) profile 2, 12 (27%) profile 3, 5 (11%) profile 4, while in CS group was: 8 (15%) profile 1, 25 (47%) profile 2, 18 (34%) profile 3, 3 (4%) profile 4. These distributions were not significantly different (p = 0.436). The time-related behaviour of percentage of profile 1 is presented in **Fig. 1**.

In both groups the percentages of profile 2-4 decreased rapidly (time effect: p < 0.001) without any significant differences between SD and CS in



**Figure 1 (ABS 43).** Time-related behaviour of percentage of profile 1 in term newborns born with spontaneous delivery (SD) and caesarean section (CS).

their evolution ( $p = 0.400$ ). As shown the percentage raised from 24 to 97% in SD group and from 16 to 97% in CS group.

#### CONCLUSIONS

In healthy term newborns mode of delivery seems not to influence timing of clearance of pulmonary liquid. LUS profiles at birth, 12, 24 and 36 h of life show a similar significant improvement in both groups.

## Long-term lung function

#### ABS 44

#### NON-INVASIVE MONITORING OF OXYGEN IN THE LUNGS OF NEWBORN INFANTS BY DIODE LASER

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#### INTRODUCTION

Infants born preterm have high risk for pulmonary disorders with abnormal gas distribution, e.g. respiratory distress syndrome with both atelectatic and hyperexpanded lung areas. X-ray radiography is routinely used for diagnosing this condition. The main purpose of this study was to investigate a new, non-invasive, rapid, bed-side optical technique for detecting free oxygen gas in the lungs of full-term newborn infants. The long term intent is to evaluate its potential use on improving diagnosis for preterm infants and the possibility of reducing the usage of X-ray radiography.

#### PATIENTS AND METHODS

The measurement technique GASMAS (GAs in Scattering Media Absorption Spectroscopy) is quantifying gas constituents in cavities surrounded by solid materials, and is based on detecting gas absorption imprints in light transmitted through the cavity. Diode laser spectroscopy prototype was developed and used to measure gas content (oxygen at 760 nm and water vapor at 935 nm) in the lungs of 29 newborn healthy infants. The skin area above the lungs was illuminated using two low-power diode lasers, and diffusively emerging light was detected a few centimeters away.

#### RESULTS

In total 390 lung measurements on infants weighing between 2,900 and 3,900 g were conducted. A clear detection of oxygen was observed in 60%, defined as yielding a signal-to-noise ratio  $> 3$ . The optimal geometry for gas detection in the lungs was most likely found. No difference in signal quality due to gender, side or weight was noted.

#### CONCLUSIONS

The results indicate that this novel non-invasive technique could be developed into a valuable tool for monitoring infants with lung disease and abnormal gas distribution in neonatal intensive care units.

#### ABS 45

#### CELLULAR AGING, MEASURED AS TELOMERE ATTRITION RATE, IS NOT ACCELERATED IN PRETERM INFANTS DURING THE FIRST 18 MONTHS OF LIFE

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## INTRODUCTION

Preterm born infants are at high risk for oxidative stress due to hyperoxia, infections and low antioxidant capacity. Oxidative stress may contribute to the development of bronchopulmonary dysplasia (BPD) and accelerate cellular aging. Today we lack reliable biomarkers to predict long-term lung morbidity in preterm infants. Telomere length, a marker of oxidative stress, shortens faster in children compared to adults. At birth, infants born preterm were previously reported to have longer telomeres than those born at term, but at school-age telomere length was similar. We aimed to longitudinally follow telomere length over the first 18 months of life, related to prematurity and lung function.

## PATIENTS AND METHODS

Children born without major malformations at Karolinska University Hospital Danderyd during 2009-2011 were eligible to this longitudinal case-control study. Relative telomere length (RTL) was determined at two time-points by quantitative real-time PCR after extracting DNA from whole blood; at birth from puncture of the umbilical cord and at 18 months of age by venous puncture. During the first two years of life, spirometry for evaluation of lung function was performed and all episodes of infections of the child were monitored and evaluated. Perinatal data was obtained from chart reviews.

## RESULTS

We included 105 preterm born infants with a mean gestational age of 31<sup>+2</sup> weeks (mean birth weight 1,642 ± 422 grams) and 92 term born infants as controls (39<sup>+6</sup> weeks, 3,551 ± 452 grams). Cord blood was available from 30 (29%) preterm infants and 85 (92%) term controls. At 18 months of age blood samples were obtained from 92 (88%) preterm and 51 (55%) control infants. RTL did not differ on a group level at birth (preterm 1.69 ± 0.23 vs. term 1.65 ± 0.31, *p* = 0.52) or at 18 months of age (1.60 ± 0.28 vs. 1.53 ± 0.30, *p* = 0.20). Telomere shortening over time, i.e. telomere attrition rate was evaluated

in 17 preterm infants and in 44 controls. RTL show both shortening and elongation over time, but on a group level the term group showed significant RTL shortening during the first 18 months of life (1.64 ± 0.19 vs. 1.51 ± 0.30, *p* = 0.005) in contrast to preterms that did not (1.75 ± 0.12 vs. 1.74 ± 0.24, *p* = 0.81).

## CONCLUSIONS

This is the first study to measure telomere length over time in early life. Contrary to our hypothesis, we were not able to detect a faster telomere attrition rate following preterm birth compared to term. The results are reassuring and suggest that preterm infants, despite susceptibility to oxidative stress damage, do not exhibit an accelerated cellular aging. However, extremely preterm infants were not included and will need further studies.

## ABS 46

### INHALED NITRIC OXIDE DECREASES MORTALITY IN INFANTS LESS THAN 28 WEEKS GESTATION FOLLOWING PRETERM PRE-LABOUR RUPTURE OF MEMBRANES

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## INTRODUCTION

Preterm pre-labour rupture of membranes (PPROM) continues to be associated with significant morbidity and mortality, predominantly as a result of respiratory failure due to pulmonary hypoplasia and/or pulmonary hypertension. Treatment with inhaled nitric oxide (iNO) is not advocated for treatment of respiratory failure in the preterm infant although its efficacy has been reported in small studies of infants following PPRM. Our aim was to assess effectiveness of iNO for treatment of severe respiratory failure secondary to PPRM in a larger cohort of preterm infants.

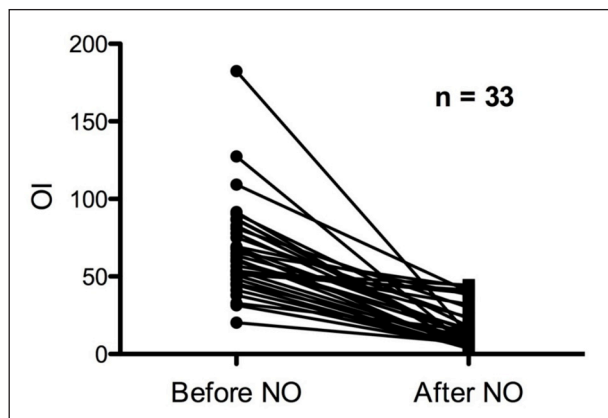
## PATIENTS AND METHODS

Retrospective chart review of neonates with PPRM of latency 14 days or more at gestation < 35 weeks at birth from June 2008-March 2015 at three tertiary Neonatal Intensive Care Units. Mechanical ventilation for > 12 hours and an oxygenation index (OI) of > 20 was deemed respiratory failure. A clinically significant response to iNO was defined

as an absolute reduction of 20 in OI. Mortality rates were compared in the extreme preterm group (< 28 weeks gestation) and the overall group.

## RESULTS

96 infants had PPROM of whom 51/96 (53%) had OI > 20. 33 infants received iNO. There was no significant difference between gestation and birth weight between the group that received iNO vs. those who did not. 28/33 (85%) infants receiving iNO had a predefined clinically significant change in OI ( $p < 0.0001$ , Wilcoxon signed-rank test) (**Fig. 1**). In infants < 28 weeks gestation there was significantly lower mortality (3/12 vs. 8/10,  $p = 0.03$  Fishers exact test) in those who received iNO compared to those who did not.



**Figure 1 (ABS 46).** Oxygen indices before and after NO.

## CONCLUSIONS

Treatment with inhaled nitric oxide improved oxygenation in all babies with respiratory failure and achieved an absolute reduction in OI of 20 in 85% with a significant reduction in mortality in a high risk group < 28 weeks gestation. Reversal of pulmonary hypertension and secondary hypoxia in this cohort is rapid and effective using inhaled nitric oxide.

### ABS 47

#### PLASMA PRO-ENDOTHELIN-1 AND PRO-ATRIAL NATRIURETIC PEPTIDE AS EARLY BIOMARKERS FOR DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN VERY PRETERM INFANTS

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## INTRODUCTION

In very preterm infants early detection of incipient bronchopulmonary dysplasia (BPD) might influence clinical management. Circulating natriuretic and endothelial pro-peptides have been shown to be associated with respiratory distress. They might serve as potential biomarkers for prediction of BPD development. We aimed to assess the value of plasma CT-pro-Endothelin-1 (CT-proET1) and mid-regional atrial natriuretic peptide (MR-proANP) for prediction of BPD development in very preterm infants.

## PATIENTS AND METHODS

In an ongoing two-center prospective cohort study including very preterm (gestational age 23-32 weeks) (Clinical Trials Identifier: NCT02083562) plasma levels of CT-proET1 and MR-proANP were measured on day 7 of life (B.R.A.H.M.S. Biomarkers, Thermo Fisher Scientific, Henningsdorf, Germany). Bronchopulmonary dysplasia was defined as supplemental oxygen for > 28 days (BPD28) and supplemental oxygen requirement at 36 weeks corrected gestational age (BPD36).

## RESULTS

Blood samples of 63 preterm infants with a gestational age of 28.8 ( $\pm 2.49$ ) weeks, and a birth weight of 1,122 ( $\pm 382$ ) g were analysed. Levels of CT-proET1 were significantly higher in infants with BPD28 (243.5 vs. 173.9 pmol/L,  $p < 0.01$ ) and also elevated in infants with BPD36 (237.7 vs. 195.5 pmol/L,  $p = 0.06$ ). MR-proANP levels were significantly higher in infants with BPD28 (737.4 vs. 364.6 pmol/L,  $p < 0.025$ ) but not significantly different at 36 weeks corrected gestational age (BPD36): (609.1 vs. 505.1 pmol/L,  $p < 0.56$ ).

## CONCLUSIONS

CT-proET-1 and MR-proANP measured on day 7 of life are associated with BPD28. The association for BPD36 is borderline significant for CT-proET1 but not significant for MR-proANP. The biomarkers might be useful for the prediction of BPD in very preterm neonates.

### ABS 48

#### TIMELY IN-HOSPITAL VACCINATION OF VLBW INFANTS REDUCES THE RATE OF BRONCHITIS AFTER DISCHARGE OF VLBW INFANTS

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## INTRODUCTION

Obstructive bronchitis is a frequent cause of hospital re-admission in very low birth weight infants (VLBW). In Germany, early vaccination at two months of age is recommended for VLBW infants. The German Neonatal Network (GNN) cooperation is a prospective multicenter collaboration of 50 NICUs providing a platform for benchmarking practice, interventional trials and investigation of genetic and clinical risk profiles of VLBW infants. We aimed to analyse risk factors for bronchitis during the first year after discharge and the effect of early in-hospital standard vaccination.

## PATIENTS AND METHODS

An established standardized questionnaire requested the number of episodes of non asthmatic bronchitis of VLBW infants during the past 7 month after discharge at home. Furthermore, the parents were asked about smoking during pregnancy, breast feeding, or at home. Responses were allocated to the database containing clinical recordings during primary hospital stay. Episodes of bronchitis were statistically correlated to the items gender, multiples, small for gestational age, mechanical ventilation, bronchopulmonary dysplasia, sepsis, presence of older siblings and environmental tobacco smoking. Additionally, subgroups with a length of hospital stay of > 60 and > 90 days, suitable for recommended vaccination, were analysed in order to analyze the effect of in-hospital vaccination.

## RESULTS

We analyzed 1,967 responses of VLBW infants born in the period 2009-2011. Male gender and presence of older siblings were significant risk factors for bronchitis during the first 7 month at home. In total, 24 percent of the population reported episodes of bronchitis. The subgroup analysis showed an increased rate of bronchitis (31%) in infants discharged after day 60. This rate was significantly less (17%;  $p = 0.003$ ) in infants receiving standard vaccination (hexavalent vaccine plus pneumococci ± palivizumab). In hospital vaccination with hexavalent vaccine and pneumococci vaccine and without RSV immunoprophylaxis was protective, too.

## CONCLUSIONS

Male gender, presence of older siblings and non-timely vaccination are risk factors for bronchitis

in VLBW infants. The rate of timely vaccination should be increased. The protective mechanisms of timely vaccination are yet unknown and should be a topic for further research.

# Lung injury

## ABS 49

### A MURINE MODEL OF BRONCHOPULMONARY DYSPLASIA – PRELIMINARY RESULTS FROM WHOLE-GENOME mRNA EXPRESSION STUDY IN BLOOD

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## INTRODUCTION

Bronchopulmonary dysplasia (BPD) affects an increasing number of newborns due to improved neonatology care worldwide. BPD often results in reduced physical and cognitive effects; however, the pathomechanisms of the condition is still not completely understood and requires further investigation. We have applied a murine BPD-model to investigate gene expression changes in blood and lung tissue.

Cardinal genes will be compared to those identified in clinical studies with human children.

## PATIENTS AND METHODS

Litters of two mouse dams (C57Bl/6Tac) were randomized to hyperoxia (85% O<sub>2</sub>) or normoxia (21% O<sub>2</sub>) group for 14 days. They were further randomized to dexamethasone (DXM) or placebo (0.9% NaCl) injections on day 4, 5, and 6. CO<sub>2</sub> levels were kept at < 2,000 ppm. After 14 days the pups with mothers were kept under standardized conditions in air. All animals were sacrificed on day 28 and blood and lung tissue was harvested. Gene expression was analysed by SurePrint G3 Mouse Gene Expression 8x60K Microarray (Agilent).

## RESULTS

100 C57Bl/6Tac mice pups were included into the study; hyperoxia/NaCl n = 25, normoxia/NaCl n

= 26, normoxia/DXM n = 23 and hyperoxia/DXM n = 26.

No differences in birth weight or weight at day 28 were seen between the groups. DXM alone lead to a significantly lesser weight gain during the first week after injection regardless of oxygen treatment.

Preliminary results of whole-genome mRNA expression studies of the blood samples taken at 28 applying principal component analysis revealed no obvious differences between groups. Histological examination exhibited a significant reduction of alveolar septa in lungs treated with hyperoxia.

#### CONCLUSIONS

Preliminary results hint that the significant differences identified in the histological structure of the lungs treated with hyperoxia are not reflected in the whole-genome gene expression of blood at day 28. It will be interesting to see, if the gene expression pattern of the lungs will reflect the significant differences in histological structure or the blood expression pattern.

#### ACKNOWLEDGMENT

Study supported by EEA grants; grant number: PL12-0036.

#### ABS 50

### TARGETED NEXT GENERATION SEQUENCING FOR MUTATION DETECTION IN NEONATAL AND PEDIATRIC DIFFUSE LUNG DISEASES

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#### INTRODUCTION

Next-Generation Sequencing (NGS) techniques allow fast, high-throughput mutation detection in cohorts of patients with heterogeneous genetic disorders. Genetic diffuse lung disease in newborns and children are a heterogeneous group of rare diseases, still underrecognized and poorly understood. Our objectives were to identify disease-causing genetic variants in genes related to surfactant or vascular development in a retrospective cohort of 127 children with a median age of 1 year (0-18) with variable respiratory phenotypes ranging from neonatal hypoxic respiratory failure to chronic pulmonary hypertension or interstitial pneumonitis, and to validate a targeted NGS panel as diagnostic tool.

#### PATIENTS AND METHODS

84 infants were initially studied by Sanger exon sequencing of genes encoding SP-B, SP-C, ABCA3, TTF-1 or FOXF-1 based on age of onset and clinical presentation, a time-consuming process limited to coding sequences. A custom-designed NGS panel broadly covering coding and non-coding regions of 9 surfactant-related genes (ABCA3, SFTPA1, SFTPA2, SFTPB, SFTPC, SFTPD, NKX2.1, CSF2Ra, CSF2Rb) and 15 developmental vascular genes (FOXF1, BMP2, TBX4, MEOX2, TXNDC3, SMAD9, SMAD1, SMAD5, THBS1, ACVRL1, ENG, CBLN2, CRHBP, CRHR1, PPARg), selected either by published data review or candidate gene approach, was applied in a subset of 17. Newly detected deleterious variants were confirmed by Sanger sequencing. Copy number variations (CNV) were assessed by array comprehensive genomic hybridization (aCGH).

#### RESULTS

Disease-causing mutations were identified in 26/84 cases (31%) analyzed by direct sequencing: ABCA3 (11 cases), SFTPC (9), NKX2.1 (3), FOXF1 (2) and TBX4 (1). In addition, single heterozygous mutations were present in ABCA3 (5 cases) and SFTPB (2 cases), of uncertain clinical significance since the related diseases are autosomal recessive. In the subset studied by NGS, 100% of the previously identified coding variants were confirmed; in addition, combinations of heterozygous deleterious coding variants were identified in other genes including TBX4 (1 case), CSF2Rb, NKX2.1, CRHR1 and SMAD9. Numerous benign coding and non-coding variants of unknown significance were also present in all cases. aCGH, performed for microdeletion detection in 8 infants with no variant otherwise identified, revealed potentially disease-causing CNVs in 4 cases, including TBX4 (1 case) and MEOX2 (1 case).

#### CONCLUSIONS

The wide clinical heterogeneity of these disorders can be explained by the number of different genes involved and the variety of mechanisms involved, including homozygosity, compound heterozygosity or, as suggested by these data, trans-heterozygosity. Targeted panel NGS appears a reliable method for mutation screening and complex genotype identification, and should be integrated in combined gene and genome strategies for comprehensive diagnosis and characterization of these rare diseases.



## ABS 51

**GENETIC INACTIVATION OF *Pdgfra* LEADS TO ALVEOLAR MYOFIBROBLAST APOPTOSIS, BLOCKS ALVEOGENESIS AND CAUSES BPD IN NEONATAL MICE**

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## INTRODUCTION

Mechanisms in pathogenesis of Bronchopulmonary Dysplasia (BPD), a failure in alveogenesis are only poorly understood. Alveogenesis is the most clinically relevant and least understood phase of lung development. While disruption of alveogenesis is associated with BPD in neonates, destruction of alveoli is hallmark of COPD and IPF in adults. Platelet-derived growth factor receptor- $\alpha$  (PDGFR $\alpha$ ) is expressed throughout lung development, with dynamic changes in expression pattern and cell type specificity. Recent studies indicate that PDGFR $\alpha$  is reduced in BPD lungs. Little is known about the precise role, timing and cell-type specificity of PDGFR $\alpha$  in alveogenesis.

## PATIENTS AND METHODS

We used the *Pdgfra* (floxed) mice in two genetic models to target *Pdgfra* in lung mesodermal cells during lung development.

## RESULTS

Inactivation of *Pdgfra* in mesoderm progenitors via Dermo1-cre caused neonatal death during alveogenesis. *Pdgfra* dermo1 lungs showed disrupted septation, decreased cell proliferation and increased apoptosis. Realtime PCR revealed altered multiple alveolar cell-type markers including *Acta2*, *Adrp*, *Wisp2*, *Fabp4*, *Flk1* & *Aqp5*. Therefore *Pdgfra* is essential for multiple mesenchymal progenitors. For cell type-specific function for PDGFR $\alpha$ , we targeted *Pdgfra* specifically in secondary crest myofibroblast progenitors by using the regulable Gli1creER that targets secondary crest myofibroblast progenitors (Stem Cell, 2015). Deletion of *Pdgfra* by Gli1creER in neonatal mice disrupted alveogenesis and phenocopied BPD. The mutant lungs showed enlarged alveoli with reduced number of secondary crest. Importantly, lack of PDGFR $\alpha$  on secondary crest myofibroblasts reduced their number by increased apoptosis.

## CONCLUSIONS

As PDGFR $\alpha$  is reduced in human BPD lungs, our data indicate that apoptosis of secondary crest myofibroblasts may be the critical mechanism involved in pathogenesis of BPD.

## ABS 52

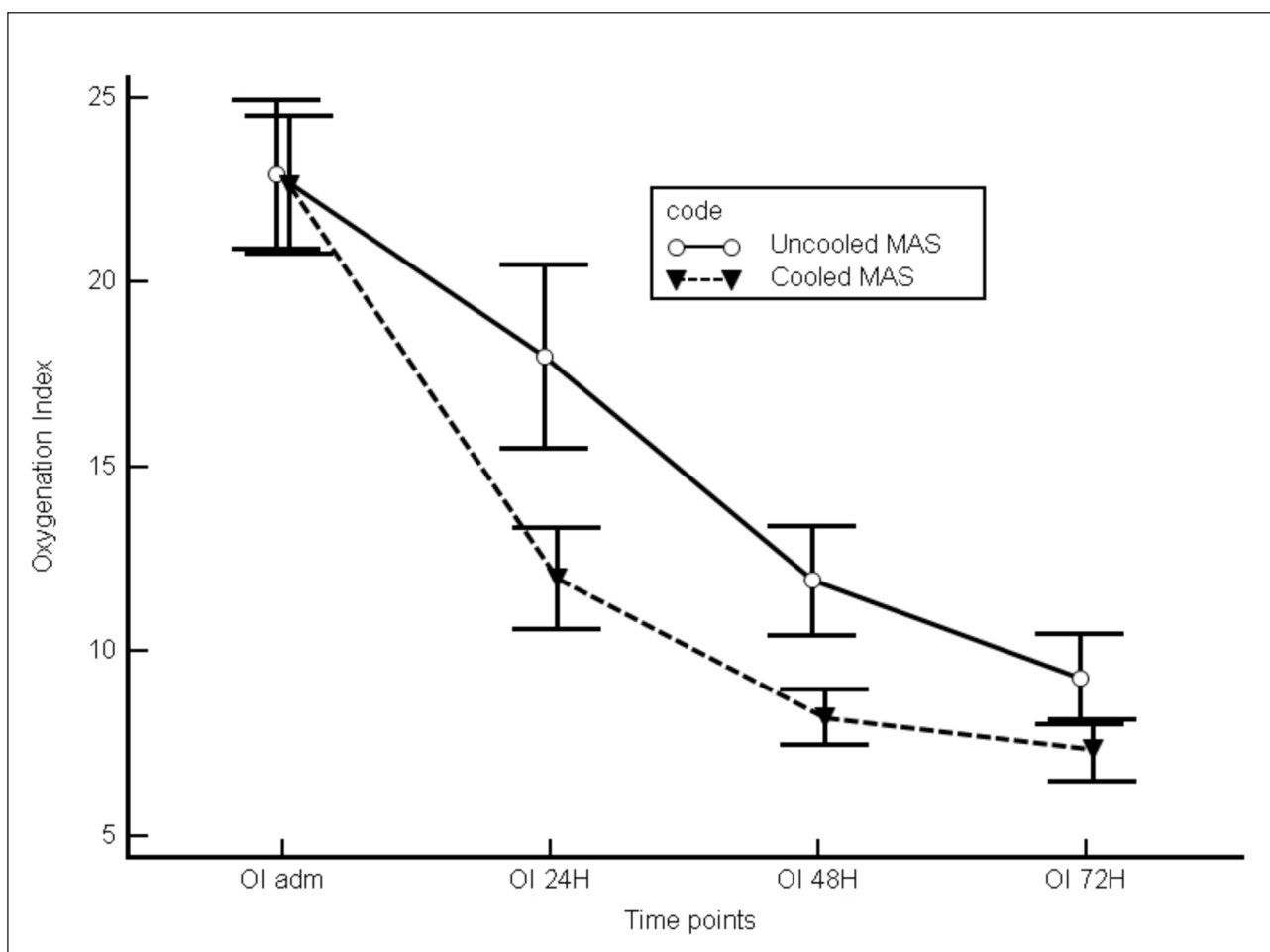
**IMPACT OF WHOLE BODY COOLING ON RESPIRATORY OUTCOMES IN MECONIUM ASPIRATION SYNDROME: INTERNATIONAL MULTICENTRE RETROSPECTIVE STUDY**D. De Luca<sup>1</sup>, D. Tingay<sup>2</sup>, L. Perkins<sup>2</sup>, A. van Kaam<sup>3</sup>, A. Debray<sup>1</sup>, C. Boussard<sup>1</sup>, E. Valverde<sup>4</sup>, S. Ares-Segura<sup>4</sup>, MP. De Carolis<sup>5</sup>, CC. Roehr<sup>6</sup>, R. Jeenakeri<sup>6</sup>, EM. de Albuquerque-Diniz<sup>7</sup>, CE. Valdo-Carlomagno<sup>7</sup>, W. Brunow de Carvalho<sup>7</sup>, O. Danhaive<sup>8</sup><sup>1</sup>*Division of Pediatrics and Neonatal Critical Care, South Paris University Hospitals, Medical Center "A. Beclere", Paris, France*<sup>2</sup>*Royal Children Hospital & Murdoch Research Institute, University of Melbourne, Melbourne, VIC, Australia*<sup>3</sup>*NICU, Amsterdam Medical Center-AMC, University of Amsterdam, Amsterdam, the Netherlands*<sup>4</sup>*NICU Hospital "La Paz", Universidad Autonoma de Madrid, Madrid, Spain*<sup>5</sup>*NICU, Department of Pediatrics, University Hospital "A. Gemelli", Catholic University of the Sacred Heart, Rome, Italy*<sup>6</sup>*Newborn Services, John Radcliff Hospital, Oxford University Hospitals NHS Trust, Oxford, UK*<sup>7</sup>*PICU/NICU Children Institute, University of Sao Paulo, Sao Paulo, Brasil*<sup>8</sup>*Infant Care Center, San Francisco General Hospital, UCSF University of California, San Francisco, CA, USA*

## INTRODUCTION

Whole body hypothermia (WBH) is the standard of care for hypoxic-ischaemic encephalopathy (HIE). In preliminary human and animal studies, hypothermia decreases lung inflammation and influence surfactant function in cooled babies without lung disease. HIE is often associated with meconium aspiration syndrome (MAS). We designed a multicentre retrospective cohort study in 11 NICUs in Europe, Australia, South and North America to clarify the effect of WBH on oxygenation and respiratory outcomes in MAS.

## PATIENTS AND METHODS

Electronic databases of the last 5 years were searched for infants with MAS: cases consisted of cooled MAS babies with oxygenation index at the admission ( $OI_{adm}$ ) > 10, born in the last 5 years. Cooling was applied according to TOBY trial protocol for HIE. In the same database we identified uncooled MAS babies matched for 1)  $OI_{adm}$  ( $\pm$



**Figure 1 (ABS 52).** Oxygenation trend in meconium aspiration syndrome (MAS) babies.

5 points); 2) SNAPPE-II score ( $\pm 5$  points); 3) gestational age ( $\pm 1$  week).

#### RESULTS

We enrolled 86 MAS neonates: 43 receiving WBH and 43 matched controls. Cases and controls were not different for basic clinical variables, iNO administration, surfactant bolus and BAL. There was a trend towards an improved oxygenation in those neonates that were cooled (**Fig. 1**;  $p = 0.05$  RM-ANOVA). Respiratory outcomes were not significantly different between uncooled and cooled MAS (duration of ventilation:  $173 \pm 122$  vs.  $152 \pm 96$  hrs,  $p = 0.393$ ; NICU stay:  $13 \pm 12$  vs.  $11 \pm 9$  d,  $p = 0.601$ ; hospital stay:  $19 \pm 12$  vs.  $17 \pm 10$  d,  $p = 0.560$ ; total duration of respiratory support:  $279 \pm 227$  vs.  $262 \pm 239$  hrs,  $p = 0.755$ ; Ventilator free days:  $2.6 \pm 10$  vs.  $4.7 \pm 8.2$ ,  $p = 0.314$ , respectively; all data mean  $\pm$  SD).

#### CONCLUSIONS

Besides a trend towards improved oxygenation, WBH did not impact on respiratory outcomes in MAS in this population.

## Mechanical ventilation

### ABS 53

#### LUNG ULTRASOUND AS A PREDICTOR OF MECHANICAL VENTILATION IN NEONATES OLDER THAN 32 WEEKS

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#### INTRODUCTION

Neonatal respiratory distress prognosis may be difficult to estimate at admission. Lung ultrasound is a useful diagnostic tool that is quick, requires little training and is radiation free. This study analyzes

whether early lung ultrasound can predict respiratory failure.

#### PATIENTS AND METHODS

From January to December 2014, a lung ultrasound was performed to neonates admitted with breathing difficulties, if they were older than 32 weeks and were not intubated. A neonatologist, not aware of the patients' clinical condition, analyzed the stored ultrasound images. Findings were classified into two groups according to their potential risk of bad respiratory outcome.

- Low risk: normal, transient tachypnea of the newborn.
- High risk: respiratory distress syndrome, meconium aspiration syndrome, pneumothorax, pneumonia.

A second investigator made the same classification after reading chest x-ray pictures. Respiratory failure was defined as the need for invasive mechanical ventilation during the first day of life.

#### RESULTS

105 neonates were recruited, 64.8% in the low risk group sonography and 35.2% in the high risk one. 20% needed intubation, more frequent in the high-risk group (RR, 17.5; 95% CI, 4.3-70.9,  $p < 0.01$ ). As predictors of respiratory failure, lung ultrasound and chest x-ray showed a high index of agreement (kappa coefficient, 0.91; 95% CI, 0.83-1,  $p < 0.01$ ) and good accuracy (for ultrasound: sensitivity 95%, specificity 82.5%, and negative predictive value 98.5%).

#### CONCLUSIONS

Early lung ultrasound is a useful tool to discriminate which neonates admitted with respiratory distress will require mechanical ventilation. It may help the clinician in carrying out appropriate transferring.

#### ABS 54

### VOLUME GUARANTEE ON HIGH FREQUENCY OSCILLATORY VENTILATION IN PRETERM INFANTS: IS IT A NEW LUNG PROTECTIVE STRATEGY?

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#### INTRODUCTION

High frequency oscillatory ventilation (HFOV) theoretically limits baro/volutrauma using subdeadspace volumes but lack of direct control

over tidal volume resulting in fluctuating  $PCO_2$  level. A new concept of volume targeting ventilation (VTV) during HFOV has been introduced in some new generation neonatal HFOV devices. This important new development allows the user to set tidal volume during HFOV like with conventional volume targeted ventilation. We hypothesized that HFOV with a volume guarantee (VG) option may result in constant tidal volume delivery and less fluctuant  $CO_2$  levels compared to HFOV ventilation in premature infants with respiratory distress syndrome (RDS).

#### PATIENTS AND METHODS

Inborn infants at less than 32 weeks of gestation with respiratory distress syndrome (RDS) were enrolled in the study if they required invasive mechanical ventilation. Patients were randomized to receive either HFOV plus VG or HFOV as the initial ventilator mode and then crossed over to the other mode of ventilation. The ventilator strategy was performed with "optimal lung volume strategy" similarly in both groups.

#### RESULTS

During the study period twenty-four infants ventilated for RDS were included in the study. The mean high frequency tidal volume ( $V_{Thf}$ ), minute ventilation ( $MV_e$ ) and carbon dioxide diffusion coefficient ( $DCO_2$ ) values were significantly higher in the HFOV plus VG mode than HFOV alone (1.82 ml/kg vs. 1.59 ml/kg  $p: 0.019$ , 1.1 ml/kg/min vs. 0.9 ml/kg/min  $p: 0.023$ , 40.5 ml<sup>2</sup>/s vs. 35.6 ml<sup>2</sup>/s  $p: 0.038$ , respectively) (**Tab. 1, Fig. 1**). HFOV plus VG maintain  $V_{Thf}$  within target range more consistently than HFOV alone ( $p = 0.004$ ). The proportion of  $PCO_2$  values outside the target range was significantly lower during HFOV plus VG period, when compared to HFOV alone ( $p = 0.01$ ). All of the newborns achieved target blood gas by the end of HFOV plus VG epoch, whereas four infants did not achieve it at the end of HFOV epoch ( $p = 0.034$ ).

#### CONCLUSIONS

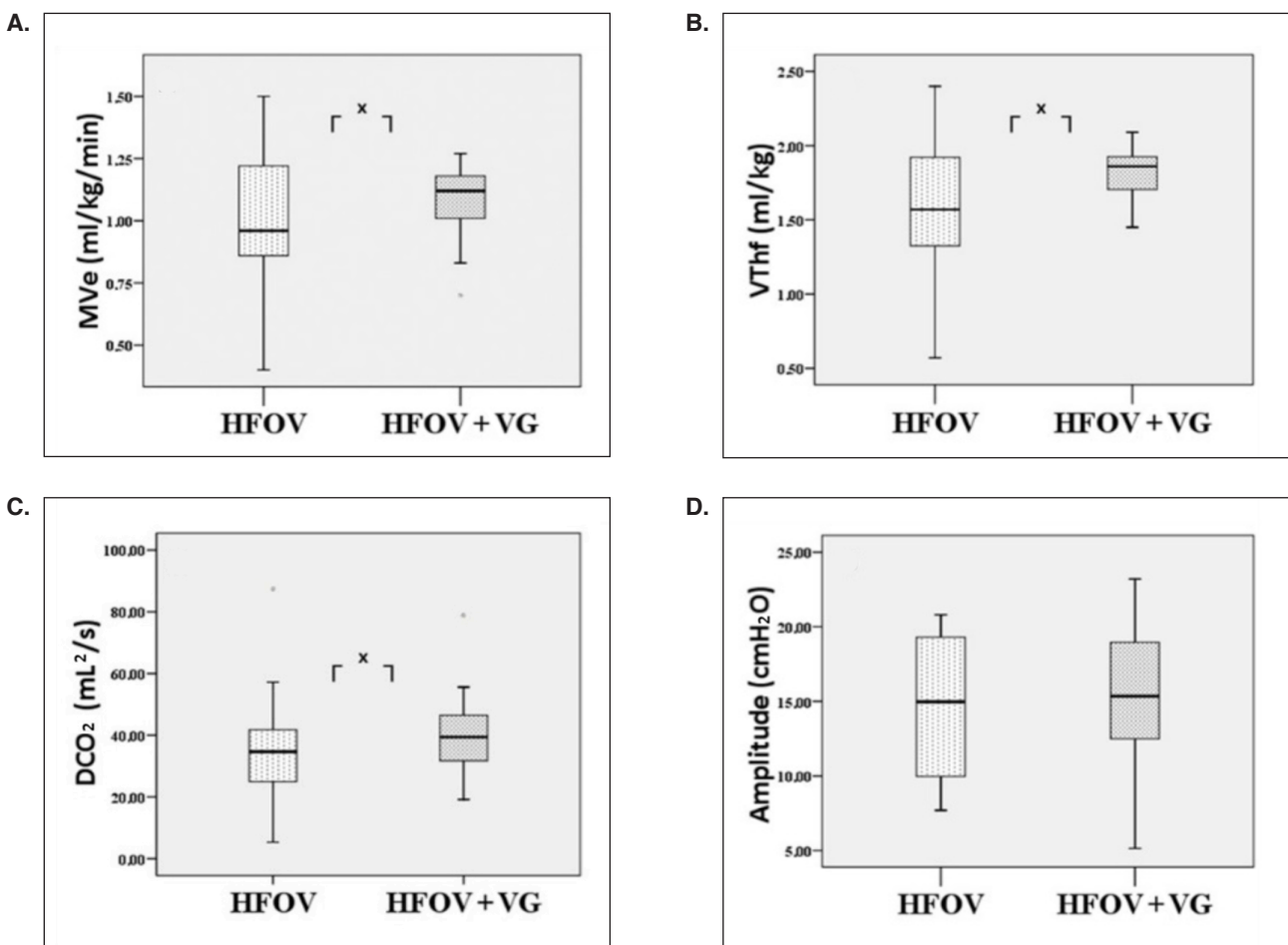
This is the first prospective, randomized, crossover clinical study that compared HFOV with and without VG in infants with acute RDS. Our results suggest that HFOV combined with VG strategy provides better ventilation and can achieve optimal gas exchange compared to HFOV alone using equal airway pressure. Because of the lower  $V_{Thf}$  variability and lower incidences of out of target  $PCO_2$  levels, HFOV combined with VG seems to be effective and feasible for preterm infants.

**Table 1 (ABS 54).** Ventilation characteristics and blood gas analysis results during each trial period.

Measurements	HFOV (n = 20) Mean ± SD	HFOV + VG (n = 20) Mean ± SD	Paired t-test p-values	Difference score		
				Mean (SD)	(95% CI)	
					Lower	Upper
Frequency (Hz)	10	10	-	-	-	-
Amplitude (cmH <sub>2</sub> O)	14.04 ± 4.72	15.47 ± 4.55	0.218	-1.43 (5)	-3.77	0.91
Paw (cmH <sub>2</sub> O)	10.05 ± 1.85	9.99 ± 1.86	0.195	0.06 (0.22)	-0.03	0.17
FiO <sub>2</sub> (%)	23.45 ± 3.72	22.35 ± 3.15	0.217	1.1 (3.85)	-0.7	2.9
VThf (ml/kg)	1.59 ± 0.45	1.82 ± 0.18	0.019 <sup>a</sup>	-0.22 (0.39)	-0.41	-0.04
DCO <sub>2</sub> (ml <sup>2</sup> /s)	35.6 ± 19.1	40.5 ± 13.4	0.038 <sup>a</sup>	-4.88 (7.2)	-13.4	-3.6
MVe (ml/kg/min)	0.9 ± 0.3	1.1 ± 0.15	0.023 <sup>a</sup>	-0.2 (0.23)	-0.21	-0.02
CDyn (ml/cmH <sub>2</sub> O/kg)	1.01 ± 0.87	0.86 ± 0.63	0.437	0.15 (0.88)	-0.25	0.56
R (cmH <sub>2</sub> O/l/s)	96.8 ± 30	87.6 ± 33.6	0.075	9.2 (21.8)	-1	19.4
pH	7.29 ± 0.75	7.33 ± 0.54	0.014 <sup>a</sup>	-0.4 (0.3)	-0.04	-0.01
PCO <sub>2</sub> (mmHg)	49.1 ± 10.7	43.9 ± 7.5	0.013 <sup>a</sup>	5.2 (2.4)	3.5	5.1
HCO <sub>3</sub> (mEq/l)	21.1 ± 1.6	21.8 ± 1.6	0.07	-0.69 (2)	-1.2	0.07

Paw: mean airway pressure; FiO<sub>2</sub>: fraction of inspired oxygen; VThf: expiratory high frequency tidal volume; DCO<sub>2</sub>: carbon dioxide diffusion coefficient; MVe: expiratory minute volume; CDyn: dynamic compliance; R: airway resistance.

<sup>a</sup>p < 0.05.



**Figure 1 (ABS 54).** **A.** Minute ventilation (MVe) in the two groups: high frequency oscillatory ventilation (HFOV) without and with a volume guarantee (VG). **B.** High frequency tidal volume (VThf) in the two groups. **C.** Carbon dioxide diffusion coefficient (DCO<sub>2</sub>) in the two groups. **D.** Amplitude in the two groups.

## ABS 55

**INTERVENTIONS TO IMPROVE RATES OF EXTUBATION SUCCESS IN PRETERM INFANTS: A SYSTEMATIC REVIEW OF THE EVIDENCE**K. Ferguson<sup>1,4</sup>, C. Roberts<sup>1,2</sup>, B. Manley<sup>1,2</sup>, P. Davis<sup>1-3</sup><sup>1</sup>The Royal Women's Hospital, Melbourne, VIC, Australia<sup>2</sup>The University of Melbourne, Melbourne, VIC, Australia<sup>3</sup>Murdoch Children's Research Institute, Melbourne, VIC, Australia<sup>4</sup>Deakin University, Melbourne, VIC, Australia

## INTRODUCTION

The introduction of mechanical ventilation for the treatment of respiratory failure in preterm infants has significantly reduced mortality. However, prolonged mechanical ventilation increases the risk of developing bronchopulmonary dysplasia, sepsis, neurological injury and retinopathy of prematurity. Therefore, clinicians attempt to extubate as early as possible. Extubation may be unsuccessful due to apnoea, atelectasis, or intercurrent illness. Infants in whom extubation fails may have cardiorespiratory instability and suffer airway trauma from repeated intubation. A systematic review of interventions aimed at improving rates of successful extubation in preterm infants was conducted.

## PATIENTS AND METHODS

Relevant studies were identified through a search of PubMed and The Cochrane Library. The primary outcome was extubation failure, defined as (1) treatment failure (however defined) within 7 days, or (2) reintubation within 7 days. Studies were required to meet the following inclusion criteria: (1) participants were preterm infants born at < 37 weeks'

gestational age (GA), and (2) extubation success or failure was a reported outcome. Included studies were grouped by intervention and the relevant Cochrane Library reviews (2014) were identified. When no Cochrane Review existed for an intervention, or the Cochrane Review did not include all identified studies, a new pooled-analysis was conducted and reported in keeping with PRISMA guidelines. All included studies were assessed for risk of bias.

## RESULTS

1,334 trials were identified in the literature search, with 48 eligible for inclusion. The main findings are summarised below (**Tab. 1**).

## CONCLUSIONS

nCPAP and nIPPV improved extubation success, with nIPPV the superior intervention. HFNC and nCPAP had similar efficacy. Methylxanthines reduced extubation failure. Corticosteroids and chest physiotherapy improved extubation rates, but carry significant side effects and warrant cautious use. The evidence for chest physiotherapy may have limited applicability to current practice. Doxapram did not aid successful extubation.

## Non-invasive ventilation

## ABS 56

**EXTUBATE: A RANDOMISED CONTROLLED TRIAL OF NASAL BIPHASIC POSITIVE AIRWAY PRESSURE VS. NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOLLOWING EXTUBATION IN INFANTS LESS THAN 30 WEEKS' GESTATION**

**Table 1 (ABS 55).** Treatment effects for extubation failure, presented as risk ratio (RR), risk difference (RD) and number needed to treat (NNT) with 95% confidence intervals.

Treatment	Number of trials	Number of subjects	Pooled RR	Pooled RD	NNT
nCPAP vs. headbox oxygen	9	726	0.62 (0.51 to 0.76)	-0.17 (-0.23 to -0.10)	6 (4 to 10)
nIPPV vs. nCPAP	8	1,301	0.71 (0.61 to 0.82)	-0.12 (-0.17 to -0.07)	8 (6 to 14)
HFNC vs. nCPAP	3	661	1.12 (0.85 to 1.47)	0.02 (-0.04 to 0.09)	N/A
Methylxanthines vs. placebo	6	197	0.48 (0.32 to 0.71)	-0.27 (-0.39 to -0.15)	4 (3 to 7)
Corticosteroids vs. placebo	3	160	0.18 (0.04 to 0.97)	-0.09 (-0.16 to -0.01)	11 (6 to 100)
Doxapram vs. placebo	1	29	0.80 (0.22 to 2.97)	-0.05 (-0.36 to 0.26)	N/A
Chest physiotherapy vs. standard treatment	4	315	0.32 (0.13 to 0.82)	-0.07 (-0.13 to -0.02)	14 (8 to 50)

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## INTRODUCTION

Non-invasive respiratory support has been demonstrated to be less injurious to the premature lung. Standard clinical practice is to use nasal continuous positive airway pressure (n-CPAP) for support in preterm infants following extubation. Many clinicians also use nasal biphasic positive airway pressure (n-BiPAP) in efforts to improve rates of successful extubation. However, there is currently no clear evidence that this confers any advantage over conventional n-CPAP. Our hypothesis was that preterm infants born before 30 weeks' gestation and less than two weeks old when extubated on to n-BiPAP will have a lower risk of extubation failure than infants extubated onto conventional n-CPAP.

## PATIENTS AND METHODS

We conducted an unblinded multi-centre randomised trial comparing n-CPAP with n-BiPAP in babies born before 30 weeks' gestation and less than 2 weeks old. Babies with congenital abnormalities and severe intra-ventricular haemorrhage were excluded. The primary outcome variable was the rate of extubation failure within 48 hours after the first attempt at extubation. Web based block randomisation stratified by centre and gestation (< 28 weeks or ≥ 28 weeks) was used. To minimise bias 'Criteria for extubation' and 'Criteria for failure of extubation' were defined. Following extubation, n-CPAP was commenced at 6 cm water and n-BiPAP was commenced giving a mean airway pressure (MAP) of 6 cm water. A standardized weaning regime was prescribed for 6 days maintaining equivalent MAP in both arms.

## RESULTS

544 babies were randomised following informed parental consent. 540 babies (270 in each group) were eligible to be included in the statistical analysis as four babies who did not satisfy our inclusion and exclusion criteria were enrolled into the study.

No significant differences were found in the pre-randomisation characteristics between the two groups. 57 (21%) of n-BiPAP group and 55 (20%) of n-CPAP group failed extubation at 48 hours post-extubation (adjusted odds ratio: 1.01; 95% CI: 0.65-1.56; p = 0.97). Sub-group analysis of babies born before and after 28 weeks' gestation showed no significant differences between the two groups. 35 babies died on follow-up. There were no significant differences in death; oxygen requirement at 28 days; oxygen requirement at 36 weeks' corrected gestation; intraventricular haemorrhage, necrotising enterocolitis requiring surgery and pneumothorax.

## CONCLUSIONS

This was the first randomised trial that aimed to exclusively compare the effectiveness of n-BiPAP vs. n-CPAP at equivalent mean airway pressures in preventing extubation failures in premature babies born before 30 weeks' gestation. Our trial shows that there is no added benefit to using n-BiPAP over n-CPAP at equivalent mean airway pressures in preventing extubation failures in babies born before 30 weeks' gestation and less than two weeks old.

# Placenta and prenatal factors

## ABS 57

### LUNG ULTRASOUND DIAGNOSTIC ACCURACY FOR PNEUMOTHORAX IN THE SUDDENLY DECOMPENSATING NEONATE: AN INTERNATIONAL, PROSPECTIVE STUDY

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## INTRODUCTION

Pneumothorax is a common and potentially lethal emergency in the NICU. Adult emergency medicine data show that pneumothorax can be reliably diagnosed by ultrasound. Neonatal data are currently lacking.

The aim of the study was to evaluate the accuracy of lung ultrasound for the differential diagnosis of pneumothorax in the suddenly decompensating newborn infant keeping the chest radiograph as a reference standard.

#### PATIENTS AND METHODS

Sudden deterioration was defined as a prolonged significant desaturation (Sat O<sub>2</sub> < 65% for over 40 seconds) and bradycardia (HR < 100) OR sudden increment of oxygen requirement to meet a 50% increase in less than 10 minutes with a final FiO<sub>2</sub> ≥ 0.7 to keep stable saturations. The attending neonatologist declared her/his clinical suspicion for pneumothorax after examining the patient clinically and with cold light chest transillumination, if possible. A lung ultrasound scan was then rapidly performed by a skilled ultrasonographer.

Clinical and ultrasound evaluations were compared to chest film interpretation by a certified radiologist unaware of the purpose of the study.

#### RESULTS

Thirty eight consecutive infants (BW = 1,671 ± 907 grams; GA = 31 ± 4.1 weeks) fitting the inclusion criteria were enrolled in 6 centers; pneumothorax was detected in 23 of them. Lung ultrasound accuracy in diagnosing pneumothorax: sensitivity, specificity, PPV and NPV were all 100%. Clinical evaluation of pneumothorax showed sensitivity 84%, specificity 46%, VPP 72%, VPN 66%. After clinical crashing, lung ultrasound was performed in an average time of 6 minutes versus a mean time of 21 minutes required for CXR. Emergency drainage was performed after lung ultrasound but before CXR in 10 cases. Chest transillumination was used only in 6 cases.

#### CONCLUSIONS

Lung ultrasound is very accurate in detecting pneumothorax in the crashing infant, outperforming clinical evaluation and reducing time to imaging diagnosis and often to drainage.

## Surfactant

### ABS 58

#### BRIEF ANTENATAL INHIBITION OF NOTCH SIGNALING ATTENUATES FETAL RESPIRATORY DISTRESS IN PRETERM MICE

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#### INTRODUCTION

Respiratory distress syndrome (RDS) is a common cause of morbidity and mortality in premature infants. Antenatal corticosteroids showed remarkable efficacy in reducing the severity of RDS, however there are still several concerns about their side-effects. Developmental changes in lung Hes1 and Hey1 mRNAs, two Notch target genes, in two mouse strains with different length of gestation and Notch activation inhibited expression of several maturation-associated lung mRNAs *in vitro* suggesting a potential repressive role for Notch signaling in lung maturation. Thus, we hypothesize that inhibition of Notch signaling in late gestation may improve fetal lung maturation.

#### PATIENTS AND METHODS

*In vitro*, embryonic day 15 (E15) lung explants were cultured with Notch inhibitor (DAPT) or vehicle for 72 hours. *In vivo*, the anti-Dll4 antibody was intrauterine injected antenatally at gestational 17.5 and pups were prematurely delivered by cesarean section one day before gestation (E18.5). To avoid bias in different pregnant mice, in each pregnant mouse, the fetus on right side of uterus received saline injection, and the fetus on left side of uterus received anti-Dll4 antibody. Pups are prematurely delivered by cesarean section one day before gestation (E18.5). Apgar-like score and survival are recorded and analyzed. In addition, the RNA and lung tissue blocks were collected for QPCR and IHC staining analysis.

#### RESULTS

Blocking Notch signaling in E15 lung explants not only induced the expressions of SP-A (2.5-fold), SP-B (1.5-fold), SP-C (2.6-fold), but also enhanced expression of genes known to be associated with surfactant lipid synthesis and transportation, such as Lpcat1 (1.6-fold), Napsa (1.5-fold) and Abca3 (1.6-fold) in embryonic lung explants. Antenatal anti-Dll4 injection significantly inhibited expression of Notch target genes, but the surfactant proteins were not significantly increased as *in vitro*. However, when the mouse pups was delivered prematurely, the Apgar-like scores were significantly improved in anti-Dll4 antibody treated group at postnatal 10 minutes (4 vs. 2), 20 minutes (6 vs. 2), and 30

minutes (10 vs. 2). Furthermore, the survival rate was also significantly improved after antenatal anti-DII4 antibody treatment at postnatal 1 hour (81.2% vs. 11.2%) and 2 hours (62.5% vs. 2.6%).

## CONCLUSIONS

Antenatal anti-DII4 antibody treatment significantly increased surfactant proteins expression *in vitro* and improved Apgar-like score and survival rate in a premature mouse model. This data suggest that brief antenatal Notch inhibition maybe a potential treatment to prevent RDS in preterm infants in the future. Further studies about the safety issue and the detail mechanism will be performed.

## ABS 59

### A FIRST-IN-HUMAN CLINICAL STUDY ON THE SAFETY AND EFFICACY OF A NEW SYNTHETIC SURFACTANT (CHF5633) IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME

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## INTRODUCTION

Respiratory distress syndrome (RDS) is the commonest respiratory disease in preterm infants. Treatment with animal-derived and synthetic surfactants has been studied extensively. CHF5633

(Chiesi Farmaceutici S.p.A., Parma, Italy) is the first fully synthetic surfactant in which the phospholipid portion is enriched by peptide analogues of both surfactant proteins B (SP-B) and C (SP-C). The main objective of this first-in-human, multinational, multicentre, per-cohort study was to assess the safety and tolerability of 2 different single CHF5633 doses (100 and 200 mg/kg) in preterm infants from 27<sup>+0</sup> to 33<sup>+6</sup> weeks GA with RDS.

## PATIENTS AND METHODS

Forty infants with clinical and radiological findings of RDS and fraction of inspired oxygen (FiO<sub>2</sub>) > 0.35 to maintain SpO<sub>2</sub> between 90-95% in the first 48 hours after birth were treated with endotracheal CHF5633 (20 in each dose cohort) (Tab. 1). Safety was assessed by monitoring adverse events (AEs) and adverse drug reactions (ADRs). Complications of prematurity were considered AEs if they occurred or worsened after CHF5633 administration. Moreover, systemic absorption of SP-C analogue and development of antibodies to both peptide analogues contained in CHF5633 were measured. Preliminary efficacy was assessed by monitoring FiO<sub>2</sub> over 1 week. The need for Poractant Alfa (Curosurf®) as rescue treatment for persisting RDS was also monitored.

## RESULTS

A total of 79 AEs were experienced by 19 (95%) infants in 100 mg/kg cohort and 53 by 20 (100%) infants in the 200 mg/kg cohort. Most AEs were expected complications of prematurity. Two serious AEs occurred in the 200 mg/kg cohort. One infant died of necrotizing enterocolitis and another one developed RSV bronchiolitis after discharge from hospital. The single reported ADR was an episode of endotracheal tube obstruction after administration of the 200 mg/kg dose. No quantifiable amounts of

**Table 1 (ABS 59).** Baseline patient characteristics.

	100 mg/kg (n = 20)	200 mg/kg (n = 20)
<b>Gestational age, weeks (mean, SD)</b>	29.6 (2.1)	29.6 (1.9)
<b>Birth weight, g (mean, SD)</b>	1,274 (398)	1,364 (416)
<b>Apgar score at 5 min (median, min-max)</b>	8.5 (7-10)	8 (7-10)
<b>Gender, n (%): male</b>	11 ( 55.0%)	10 (50.0%)
<b>Antenatal corticosteroids, n (%)</b>	18 (90%)	19 (95%)
<b>Antenatal antibiotics, n (%)</b>	11 (55%)	9 (45%)
<b>FiO<sub>2</sub> pre-dose (mean, SD)</b>	0.47 (0.16)	0.52 (0.13)
<b>Time to treatment, h (median, min-max)</b>	7.0 (1-41)	5.0 (2-33)



SP-C analogue were detected in any blood sample at any time point and no detectable antibody response to either the SP-C or the SP-B analogue was observed. Rapid decrease of  $\text{FiO}_2$  was observed 30 min after administration of both CHF5633 doses and maintained until day 7 (Fig. 1). One infant did not respond to CHF5633 100 mg/kg dose, with no response to two rescue Poractant Alfa doses.

## CONCLUSIONS

Both 100 and 200 mg/kg CHF5633 doses were safe and well tolerated, with no absorption of the SP-C analogue and no immune response to either protein analogue. Preliminary efficacy data on the oxygenation status and respiratory support are promising and provide a basis for further randomized controlled trials.

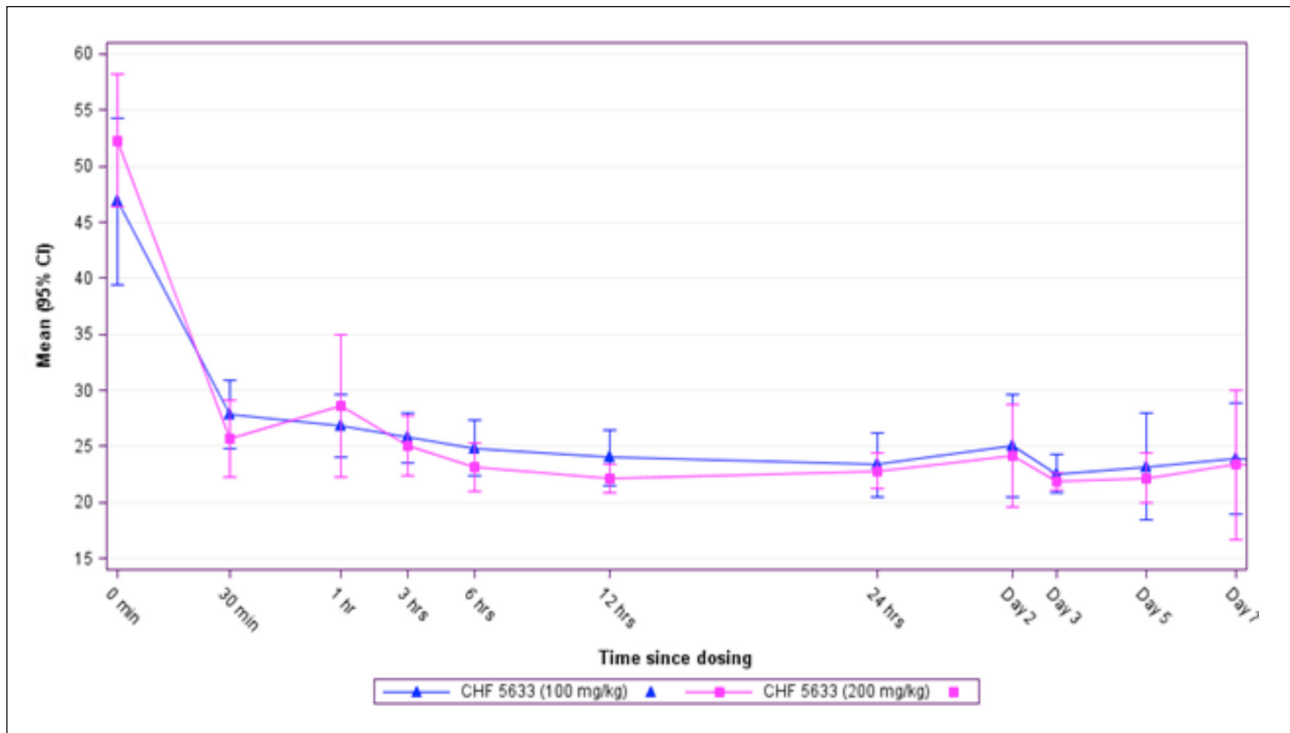


Figure 1 (ABS 59).  $\text{FiO}_2$  (%) profile by cohort (100 and 200 mg/kg) (n = 40) in the first week of life.