

# Selected Abstracts of the 6<sup>th</sup> International Congress of UENPS • Session “Lung and development”

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## ABS 1

### AN OPEN LABEL, DOSE-ESCALATION STUDY OF LUCINACTANT FOR INHALATION DELIVERED VIA NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (nCPAP) FOR TREATING RESPIRATORY DISTRESS SYNDROME (RDS) IN PRETERM NEONATES

J. Mazela, N.N. Finer, S.G. Simonson, P.M. Shore, P. Simmons, R. Segal

*Department of Neonatology, Poznan University of Medical Sciences, Poznań, Poland*

#### INTRODUCTION

Nasal continuous positive airway pressure (nCPAP) supports respiration but limits the ability to deliver early surfactant replacement therapy (SRT) to preterm infants. Aerosolized surfactant via nCPAP could avoid endotracheal intubation (ET) for SRT delivery, but has had limited success. Lucinactant for inhalation is a novel drug-device therapy that delivers an aerosolized SRT using proprietary capillary aerosol-generating technology.

#### METHODS

We conducted a phase 2 dose-escalation study to assess the safety/tolerability of lucinactant for inhalation in preterm infants, 29-34 completed weeks post menstrual age (PMA), with respiratory distress syndrome (RDS). Adverse events (AEs), including common complication of prematurity, CPAP failure, oxygen requirements and physiological parameters were assessed.

#### RESULTS

80 neonates were sequentially enrolled into 5 dosing groups (25, 50, 75, 100 and 150 mg total phospholipids [TPL]/kg; 8 treated and 8 nCPAP-only control subjects/group). The nCPAP interface was well tolerated; peri-dosing events were infrequent. The 3 most common AEs were neonatal jaundice, constipation, and apnea; incidences were comparable between treatment and control groups. Air leak was the most common complication of prematurity in all

treatment groups. FiO<sub>2</sub> decreased from baseline more rapidly with lucinactant for inhalation (30 min) than in controls (3 hours). The dose response for preventing nCPAP failure appeared to be relatively flat above 50 mg TPL/kg. nCPAP failure requiring rescue therapy occurred in 30% of lucinactant for inhalation-treated infants in the 3 highest dose groups (7/23) versus 53% (21/40) in all controls.

#### CONCLUSIONS

Lucinactant for inhalation was well tolerated via nCPAP in preterm infants 29-34 weeks PMA with RDS and may provide an alternative to surfactant administration via an ET tube. The effect of a single dose of lucinactant for inhalation on preventing nCPAP failure may have plateaued above 50 mg TPL/mg. Follow-on studies are evaluating repeat dose regimens in a preterm population 26-32 weeks PMA.

## ABS 2

### PRETERM DELIVERY: PREVENTION AND MANAGEMENT OF RESPIRATORY DISEASES IN THE HOSPITAL OF PERUGIA

L. Fatigoni, L. Minelli, M. Chiavarini

*Department of Experimental Medicine, Public Health Section, University of Perugia, Perugia, Italy*

#### INTRODUCTION

Respiratory distress syndrome (RDS) is the major cause of neonatal respiratory distress. RDS results from lung immaturity in preterm infants and it is associated with increased morbidity and mortality among this population. This study analyzes the outcomes of preterm infants at the Teaching Hospital of Perugia, focusing on the prevention and management of respiratory diseases.

#### METHODS

This is a retrospective study based on data obtained from Vermont Oxford Network (VON) Database. Data were recorded at the Neonatal Intensive Care Unit (NICU) of the Hospital of Perugia, in 2014.

#### RESULTS

In 2014, 44 VLBW infants (501-1,500 grams) were born in Umbria Region (0.6% of all births); of these, 37 were admitted to the NICU of Perugia. Mortality in children of this weight class was 8.1%. Antenatal steroids for the prevention of RDS were administered in the 81.1% of cases,

similar value of the VON (81.7%). In particular, antenatal steroids were administered in 100% of 501-750 grams weight infants, 75% of 1,251-1,500 grams weight infants, 100% of infants with gestational age  $\leq$  26 weeks, and 50% of infants with a gestational age  $>$  32 weeks. The pneumothorax rate was 2.7%; the RDS rate in infants of gestational age  $\leq$  32 weeks was 24.1%, with differences in weight classes and gestational age classes: 7.7% in the 1,251-1,500 grams class, 100% in the 501-750 grams class, 50% in the 24-26 week class, 0% in the 30-32 week class. Considering the support to the respiratory function, in the Hospital of Perugia the use of surfactant was greater than VON data (73.0% vs 58.7%) and the assistance with mechanical ventilation (62.2% vs 58.8%), but the frequency of assistance nCPAP was lower (48.3% versus 57.2%).

### CONCLUSIONS

This study provides useful information for the assistance to the preterm infant. The link of the Hospital of Perugia with VON ensures an essential contribution to the definition of the priorities of the preterm births, in particular with regard to respiratory problems of the preterm infant.

### ABS 3

#### EFFECTS OF HIGH INSUFFLATION PRESSURE ON THE HISTOPATHOLOGICAL AND RADIOLOGICAL FINDINGS IN EXPERIMENTAL ANIMAL LUNGS DURING MECHANICAL VENTILATION

N. Videnović<sup>1</sup>, J. Mladenovic<sup>1</sup>, V. Videnovic<sup>2</sup>, S. Mihajlov<sup>2</sup>, S. Trpkovic<sup>1</sup>, R. Zdravkovic<sup>1</sup>

<sup>1</sup>Department of Anesthesiology and Intensive Care, Faculty of Medicine, University in Kosovska Mitrovica, Serbia

<sup>2</sup>Department of Neonatology, General Hospital, Leskovac, Serbia

### INTRODUCTION

Mechanical lung ventilation has become necessary in general anesthesia and supporting vital procedure in seriously ill patients. While showing beneficial effects, mechanical ventilation also has several potential complications. During the 1990s, ventilator-induced lung injury (VILI) was first identified. The aim of the study is to determine the degree of sensitivity of healthy and previously pathological lungs to the effects of pressure of mechanical lung ventilation with

high values of peak (Ppeak) and medium pressure (Paw) in experimental conditions.

### METHODS

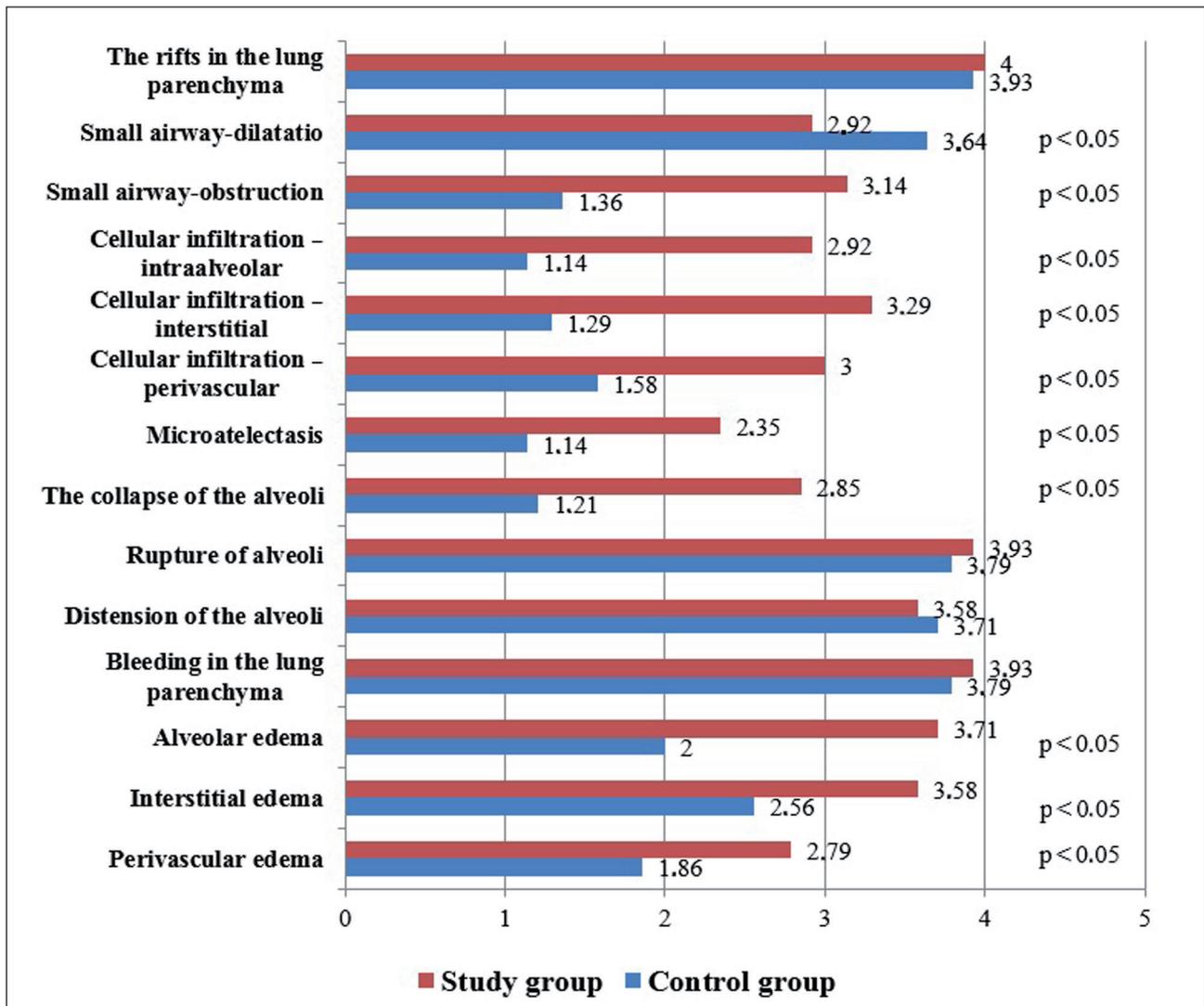
The research was conducted as a prospective experimental study in KBC Pristina based in Gracanica and the Faculty of Medicine in Kosovska Mitrovica. Experimental animals (pigs) were divided into two groups. The control group consisted of experimental animals with healthy lungs. In the intervention group of experimental animals, acute lung injury was previously induced by injecting 2 ml/kg body weight gastric contents through endotracheal tube in pulmonary parenchyma. Pressure controlled ventilation was then applied to all animals. Mechanical ventilation was delivered with high Ppeak (50 mbar), with a respiratory rate of 12 breaths per minute, O<sub>2</sub> Fi 0.4 and PEEP zero. Duration of mechanical lung ventilation was 240 min or 4 hours. Monitoring included, among other parameters, tidal volume (Vt), peak and intermediate pressure in the airway. The second phase entailed taking samples of lung tissue of experimental animals (pigs) at the end of the four-hour duration of mechanical ventilation and send them to histopathological examination. We used the following methods of statistical processing and descriptive statistics to determine the relative numbers and measures of central tendency: arithmetic mean (X), a measure of variability (standard deviation – SD), relative proportions (percentages). Statistically significant difference ( $p < 0.05$ ) in the mean values was tested by t-test of means in the case of two independent samples.

### RESULTS

The research results (**Fig. 1**) indicated significant changes in the histopathological findings of ventilated lung (perivascular, interstitial and alveolar edema, distension and rupture of alveoli, tears in the lung tissue, bleeding, etc.). Radiological findings included the presence of interstitial and alveolar edema, air cyst, expanded intercostal space and pneumothorax in a certain percentage. Histopathological and radiological changes were more pronounced in animals from the test group compared to the control group.

### CONCLUSIONS

Previously pathological lungs showed much greater sensitivity to the violating effect of applied pressure controlled mechanical ventilation compared to healthy and functionally intact lung. Occasional radiological control of ventilated lung may indirectly indicate the emergence of new or



**Figure 1 (ABS 3).** Significant changes in histopathological and radiological findings during mechanical ventilation in experimental animals.

worsening of existing pathological changes in the lung caused by mechanical ventilation.

#### ABS 4

### A CONGENITAL CHYLOTHORAX MIMICKING PNEUMONIA

K.Ş. Tekgunduz, Y. Demirelli, M. Kara, İ. Caner

Ataturk University, Faculty of Medicine, Department of Pediatrics, Erzurum, Turkey

#### INTRODUCTION

Congenital chylothorax is defined as chylous fluid accumulation in the pleural space. It has the potential to cause life-threatening metabolic, nutritional, and immunological complications. Herein, we present a

case of bilateral pleural effusion that presented with severe respiratory failure at birth and improved with conservative treatment alone.

#### CASE REPORT

A baby boy born at 37 weeks with an Apgar score of 4/7 and a birth weight of 2,885 g was admitted to the newborn intensive care unit following intubation due to postnatal severe respiratory distress. The chest x-ray revealed an opaque appearance in the right lung parenchyma. Thoracic ultrasonography revealed pleural effusion. Thoracic surgeons performed bilateral tube thoracostomy. Approximately 250-ml of pleural fluid of milky color was obtained in the tube drainage. Protein and glucose concentrations of the pleural fluid were 686 mg/dL and 85 mg/dL, respectively. On day 3, chest x-ray revealed normal lung parenchyma and the thoracic tube was removed. The patient's overall

condition worsened during intubation. The repeated chest x-ray demonstrated pleural fluid on the right side of the lung. A chest tube was re-inserted. The fluid in the tube drainage was milky. Triglyceride levels were 844 mg/dL in the drainage fluid. The patient was diagnosed with congenital chylothorax. The patient received total parenteral nutrition (TPN) for five days and his chest tube was removed on the third day of enteral feeding, due to the lack of drainage in the chest tube.

#### CONCLUSIONS

Congenital chylothorax, although rare, is the most common cause of pleural effusions in newborns. Its incidence widely varies from 1/5,800 to 1/10,000 in several studies. Conservative and surgical methods can be used in the treatment. In conclusion, congenital chylothorax should be considered in the etiology of respiratory failure in newborn babies. Curative treatment is possible even with a conservative treatment approach alone.

#### ABS 5

##### SINGLE CENTRE USE OF MONTELUKAST

D. Panjwani<sup>1</sup>, R. deBoer<sup>1</sup>, P Satodia<sup>1,2</sup>

<sup>1</sup>Neonatal Department, University Hospital of Coventry and Warwickshire NHS Trust, Coventry, UK

<sup>2</sup>University of Warwick, Coventry, UK

#### INTRODUCTION

Bronchopulmonary dysplasia (BPD) remains a significant problem in extreme preterm (EP) population. Montelukast, a leukotriene inhibitor, appears to be a logical choice for prevention or treatment of evolving or established BPD.

#### AIM

To assess the clinical outcomes in extreme preterm babies treated with montelukast at a tertiary NICU.

#### METHODS

Babies were identified using hospital notes and electronic record system. Thirteen babies were identified as having received montelukast over a period of twenty months (01/08/14 to 31/03/16). Montelukast was used as a last resort in babies with significant oxygen requirement and radiological changes of significant lung disease unresponsive to postnatal steroids. Montelukast was administered at a dose of 2 mg/kg or 2 mg once daily orally.

#### RESULTS

The mean gestation was 25<sup>+3</sup> weeks and mean birth weight was 746 g. 10 babies survived and went home

in oxygen and montelukast. Of 3 babies who died, 2 had an antenatal history of oligohydramnios. All babies received surfactant and postnatal steroids. The mean ventilation days were 41.4 (range 7-69). 12 babies had a patent ductus arteriosus, 5 had ibuprofen and 3 had surgical ligation. 1 baby had necrotising enterocolitis, 6 had culture positive sepsis, 8 had retinopathy of prematurity. No baby had cystic PVL and 2 had intraventricular bleed. No obvious side effects were noted.

#### CONCLUSIONS

Two thirds of patients in our cohort were discharged home. No unusual side effects were noted. Montelukast may be tried in an extreme preterm neonate dependent on significant respiratory support for severe chronic lung disease unresponsive to postnatal steroids. Further phase 3 clinical trials are needed to establish safety and efficacy.

#### ABS 6

##### RESPIRATORY MANAGEMENT AND BRONCHOPULMONARY DYSPLASIA

C. Ramos-Navarro, P. Chimenti-Camacho, N. Gonzalez-Pacheco, S. Villar-Castro, G. Zeballos-Sarrato, Perez-Perez Alba, M. Sanchez-Gomez de Orgaz, M. Sanchez-Luna

*Pediatric Department, Neonatology Division, Gregorio Marañón Hospital, Madrid, Spain*

#### INTRODUCTION

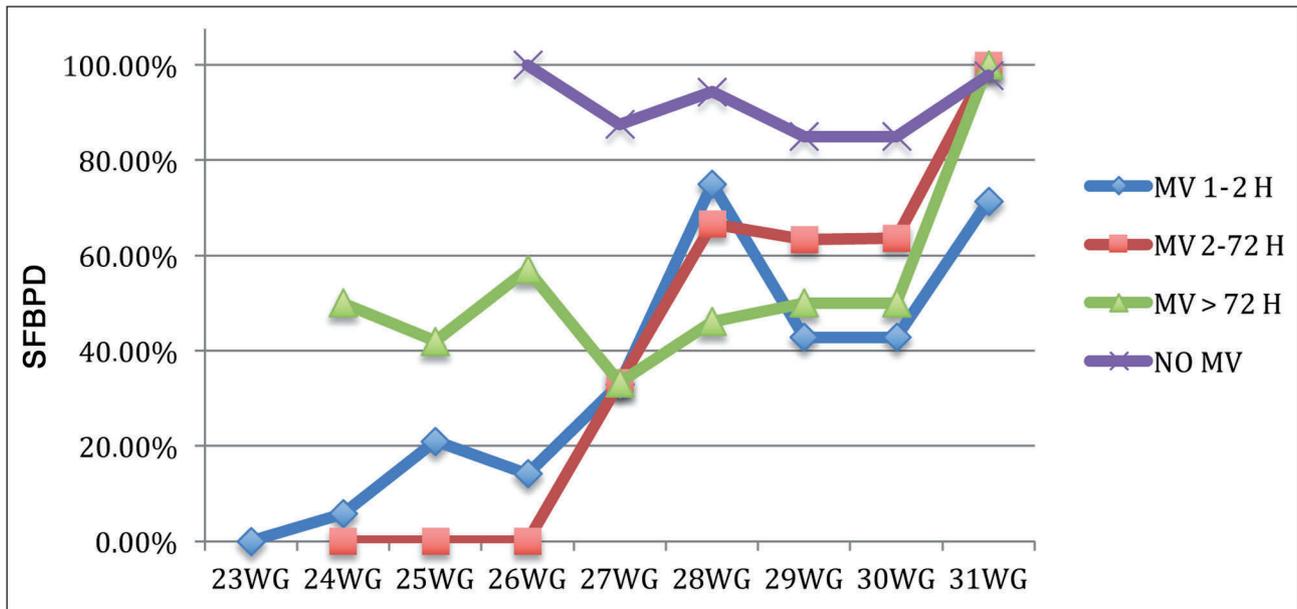
Respiratory approach in preterm infants has been modified in the last three years at our Institution with the implementation of synchronized non-invasive ventilation (SNIPPV), a less invasive technique for surfactant administration and the use of high frequency oscillatory ventilation (HFOV) with low target volume in order to reduce ventilator-induced lung injury.

#### METHODS

Retrospective review of respiratory management of preterm infants born with less than 32 w GA in the last 4 years, evaluating its repercussion in bronchopulmonary dysplasia (BPD) incidence and severity.

#### RESULTS

423 infants of less than 32 w GA were born in this period of time. When compared with infants born in 2015, infants born in 2012 had lower birth weight and higher CRIB score in the last year. The proportion of infants born before 29 w GA was



**Figure 1 (ABS 6).** Survival free of bronchopulmonary Dysplasia (SFBPD) according to time on which mechanical ventilation (MV) is required by gestational age (WG: weeks of gestation).

higher in 2015. There was an increase in SNIPPV use with a reduction in non-invasive failure rates in the first 3 days of life in 2015. The rate of infants managed with HFOV on day 3 was also higher in the last period. The rate of infants managed without mechanical ventilation (MV) tended to be higher in 2015. There was a reduction in nosocomial sepsis with no significant differences in mortality and pathological cranial ultrasound. Survival free of bronchopulmonary dysplasia (SFBPD) was higher in the 26-29 w group, with also a light reduction in the rate of death or severe BPD. Globally, mechanical ventilation requirement for more than 1 hour increased the risk of death or BPD (OR 10.065; 4.3-23.55;  $p < 0.001$ ) adjusted for GA, prenatal steroids use, and chorioamnionitis. There was also a significant difference in SFBPD according to the time when MV was needed, being lower when it was required in the first hours of life (**Fig. 1**).

#### CONCLUSIONS

There was an upward trend in SFBPD rates and a reduction in death or severe BPD rates since the implementation of non-invasive strategies and lung protective ventilation in our institution. These results are probably attenuated by the increased proportion of extremely preterm infants born in 2015.

#### ABS 7

#### EARLY MANAGEMENT OF NEONATAL RESPIRATORY DISTRESS SYNDROME – A SUR-

#### VEY AMONG UK NEONATAL INTENSIVE CARE UNITS

G. Hendriks, R. Stephenson, K. Yajamanyam

*Neonatal Unit, Liverpool Women's NHS Foundation Trust, Crown St, Liverpool, UK*

#### INTRODUCTION

Emerging new evidence supports the use of very early CPAP (continuous positive airway pressure) to avoid mechanical ventilation (MV) as well as synchronised volume targeted MV (VTV) in the management of neonatal respiratory distress syndrome (RDS). The aim of this study was to evaluate the current practice of early management of RDS in neonatal intensive care units (NICU) across United Kingdom (UK).

#### METHODS

A structured questionnaire was sent to 55 NICUs using Google Survey® and results collected during October and November 2015. Non-responders were followed up by telephone.

#### RESULTS

Responses were obtained from 44 NICUs (80%). Among babies born less than 26 weeks gestation, 35/44 (80%) NICUs practice intubation and ventilation as primary mode of support at birth; in babies greater than 26 weeks gestation, only 9/44 (20%) units use intubation and ventilation at birth whilst 28/44 (80%) units used CPAP as the primary mode of support. Over 80% of NICUs administer

surfactant in the delivery room. When mechanical ventilation is required, 70% units used volume targeted ventilation. Only 10% of NICUs practice intubation, surfactant and extubation (INSURE) technique.

#### CONCLUSIONS

Majority of the UK NICUs still practice routine intubation and ventilation in the extreme preterm babies with limited use of strategies such as INSURE which aim at avoiding MV. Encouragingly, majority of NICUs use synchronised volume targeted mechanical ventilation as recommended by the European consensus guidelines. Our survey highlights the need for implementation of evidence-based recommendations for the early management of RDS in the UK.

#### ABS 8

### DYSREGULATION OF SOLUBLE FMS-LIKE TYROSINE KINASE 1 (SFLT-1) CONTRIBUTES TO PULMONARY HYPERTENSION

C. Chen<sup>1,2</sup>, P. Tsao<sup>3,4</sup>, S. Wei<sup>5</sup>

<sup>1</sup>Department of Pediatrics, National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu, Taiwan

<sup>2</sup>Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University, Taipei, Taiwan

<sup>3</sup>Department of Pediatrics, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan

<sup>4</sup>Research Center for Developmental Biology and Regenerative Medicine, National Taiwan University, Taipei, Taiwan

<sup>5</sup>Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan

#### INTRODUCTION

Vascular endothelial growth factor (VEGF) induces vasodilatation through the regulation of nitric oxide (NO) signaling. Soluble Flt-1 can capture the free form VEGF and attenuates VEGF signaling. Soluble Flt-1 levels have been reported as significantly higher in people with sickle cell anemia who develop pulmonary hypertension. The objective of this study is to test whether excess soluble Flt-1 induces pulmonary hypertension.

#### METHODS

In this study we measured sFlt-1 levels in a mouse hypertension model by chronic hypoxia exposure. The functional effect of sFlt-1 in vivo was determined by intraperitoneal injection with sFlt-1 or vehicle, and then VEGF and NO productions and pulmonary pressure were measured.

#### RESULTS

Both plasma and bronchoalveolar lavage (BAL) levels of sFlt-1 were increased after chronic hypoxia exposure. Soluble Flt-1 treatment not only decreased free form VEGF levels in plasma and BAL, but also inhibited endothelial nitric oxide synthase (eNOS) mRNA expression and NO oxidases production. Finally, chronic sFlt-1 exposure caused pulmonary hypertension and right ventricular hypertrophy.

#### CONCLUSIONS

These results showed that soluble Flt-1 production was regulated by chronic hypertension. Excess of circulating sFlt-1 inhibited NO production and caused pulmonary hypertension. Our study suggests that regulating sFlt-1 production may have therapeutic potential in the treatment of pulmonary hypertension.

#### ABS 9

### SECONDARY RESPIRATORY SUPPORT OF PRETERM INFANTS: NON-INVASIVE VENTILATION VERSUS CONTINUOUS POSITIVE AIRWAY PRESSURE

A. Menshykova<sup>1,2</sup>, D. Dobryansky<sup>2</sup>

<sup>1</sup>Department of Pediatrics, <sup>2</sup>Neonatal Intensive Care Unit, Lviv National Medical University, Lviv, Ukraine

#### INTRODUCTION

Mechanical ventilation (MV) is associated with increased risk of secondary lung injury in preterm infants. It is important to reduce the duration of this intervention by effective application of non-invasive respiratory support. In a randomized study we compared clinical efficacy of nasal non-synchronized intermittent positive pressure ventilation (NNIPPV) and continuous positive airway pressure (CPAP) for prevention of repeated intubation in preterm infants with very low birth weight.

#### METHODS

80 preterm infants with birth weight < 1,500 g on conventional MV were randomized into two groups before extubation within 3 days of life. 40 infants with GA of 28.82 ( $\pm$  1.86) weeks were treated with NNIPPV and 40 infants with GA of 28.9 ( $\pm$  1.64) weeks were extubated to CPAP for at least 48 h. The primary study outcome was the need for repeated MV within 72 h after primary extubation.

#### RESULTS

The frequency of re-intubation within the first 72 h of non-invasive respiratory support was almost

similar in both groups (11 cases [27.5%] in the NNIPPV group compared to 12 cases [30%] in the CPAP group;  $p > 0.05$ ). No difference in total duration of respiratory support was observed between the groups either. No significant difference in BPD incidences according to clinical definition was found between the groups (9 cases [22.5%] in the NNIPPV group compared to 7 cases [17.5%] in the CPAP group;  $p > 0.05$ ). BPD incidence according to physiological definition was similar in both groups (2.5%).

#### CONCLUSIONS

NNIPPV after primary extubation of very preterm infants during the first three days of life has no obvious clinical advantages over the extubation followed by CPAP.

#### ABS 10

#### FATAL NEONATAL RESPIRATORY FAILURE DUE TO NON PREVIOUSLY DESCRIBED ABCA3 MUTATIONS

I. Sanz Fernández<sup>1</sup>, M. Miñambres Rodríguez<sup>1</sup>, J.J. Telleria Orriols<sup>2</sup>, M. Marcos Temprano<sup>3</sup>, M. Pino Velázquez<sup>1</sup>, A. Pino Vázquez<sup>1</sup>

<sup>1</sup>Neonatal and Pediatric Intensive Care Unit, <sup>2</sup>Genetics Department, <sup>3</sup>Pediatric Pneumology Department, Clinic University Hospital, Valladolid, Spain

#### INTRODUCTION

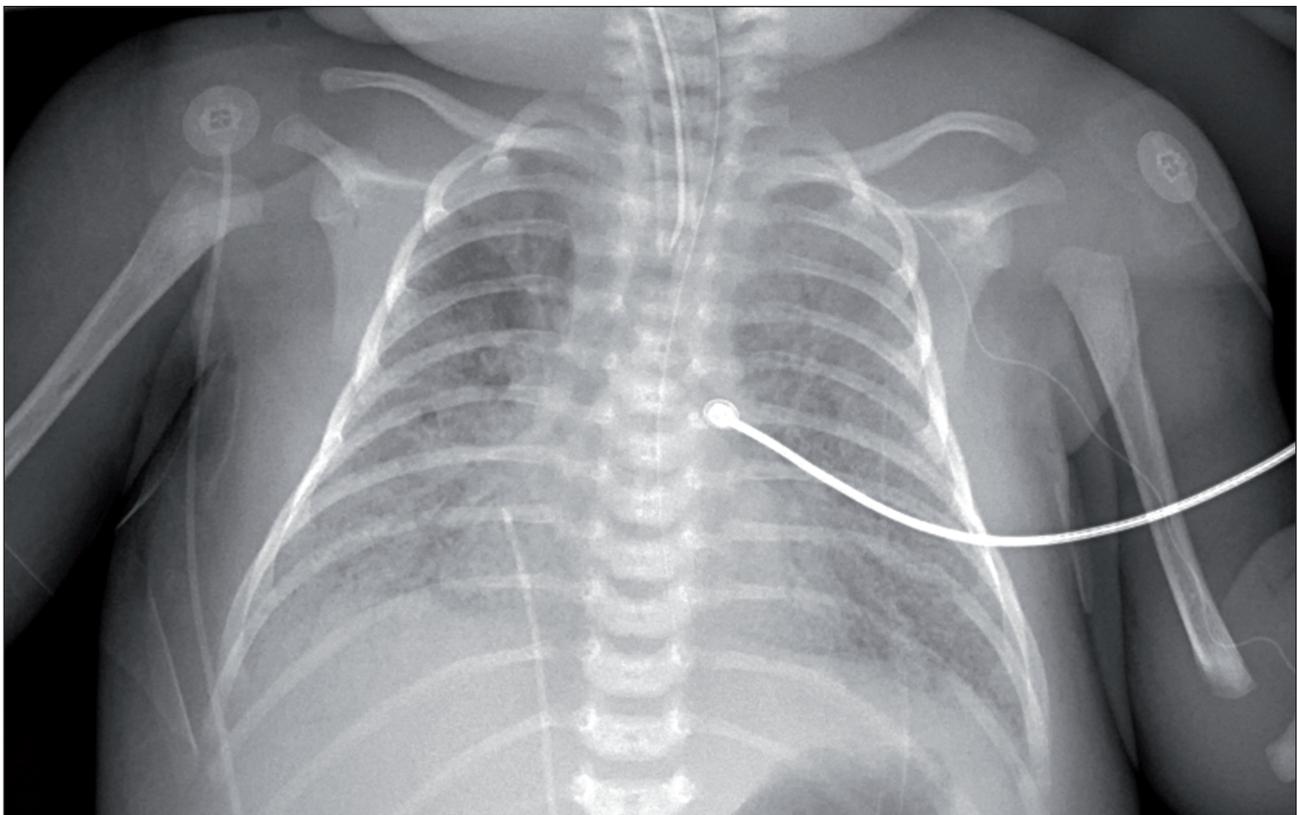
Diffuse parenchymal lung disease caused by surfactant deficiency is a rare cause of respiratory failure in the term newborn, which must be considered after excluding more common etiologies. Mutations in ABCA3 result in pulmonary surfactant deficiency and can lead to fatal neonatal respiratory failure.

#### METHODS

Case report and literature review.

#### CASE REPORT

A female term newborn was admitted to the neonatal unit 5 hours after birth due to respiratory distress. She was the first child of non-consanguineous parents, delivered by cesarean section due to cardiotocographic alterations at 41 weeks after a normal pregnancy. Apgar score was 9/10. On admission, high flow oxygen therapy was started, then changed to non-invasive ventilation after 12 hours due to increased work of breathing and hypoxemia. Chest X-ray after admission showed bilateral fine granular pattern. On day 3 she suffered an acute deterioration, so she was intubated and ventilated (**Fig. 1**); a dose of intratracheal surfactant was



**Figure 1 (ABS 10).** Chest X-ray after acute clinical deterioration.

given. Within the next hours she developed high respiratory support requirements on high frequency oscillatory ventilation (FiO<sub>2</sub> 0.7-1) and inhaled nitric oxide was started, with no improvement. She presented repeated air leaks requiring multiple chest drains. Clinical condition of the patient remained unchanged over the next weeks. Transient mild improvement after repeated surfactant doses was found, with no response to systemic corticosteroids. Repeated chest X-rays showed severe bilateral interstitial infiltrates and chest CT scan revealed alveolar-interstitial pattern with marked ground-glass appearance, cystic areas and bronchiectasis. She was studied for heart diseases, infections, cystic fibrosis and immunodeficiencies with normal results. In view of the poor prognosis, resuscitation care was terminated on day 32 in agreement with the family, and she died. Postmortem pulmonary biopsy showed multiple changes suggestive of congenital surfactant disorders. Genetic study did not find mutations in genes related to congenital surfactant disorders but identified compound heterozygosity for two new mutations c.C557T and c.T1262C in ABCA3.

#### CONCLUSIONS

ABCA3 mutations can lead to fatal neonatal respiratory failure. Different treatments have been tried with no success and the prognosis is poor.

#### ABS 11

##### CONGENITAL STRIDOR DUE TO BILATERAL VOCAL CORD PARALYSIS

I. Sanz Fernández, M. Miñambres Rodríguez, A. Pino Vázquez, M. Brezmes Raposo, C. Fernández García-Abril, C. Villa Francisco

*Neonatal and Pediatric Intensive Care Unit. Clinic University Hospital, Valladolid, Spain*

#### INTRODUCTION

Vocal cord paralysis represents up to 10% of laryngeal congenital anomalies. Most cases present within the first weeks of life with symptoms such as stridor, weak cry, increased work of breathing, recurrent aspirations or feeding problems. We present a case of a neonate with marked stridor since birth.

#### METHODS

Case report and literature review.

#### CASE REPORT

A 10-day-old male neonate was transferred to our centre from another hospital for further

investigation due to congenital stridor. He was the second child of non-consanguineous healthy parents, born at 41 weeks after a normal pregnancy. Apgar score was 7/9. Immediately after birth he presented with stridor and increased work of breathing, being admitted in the neonatal unit with non-invasive respiratory support (nCPAP). The chest X-ray, chest CT scan and echocardiography were normal. CPAP was stopped, but he continued with stridor and increased work of breathing. On the day of admission to our unit, physical examination showed continuous stridor (severe when he was agitated or crying) with mild-moderate subcostal retractions, with no feeding problems. Different supportive therapies were tried (high flow oxygen therapy with and without Heliox and non-invasive ventilation) without improvement. Repeated direct laryngoscopy showed absence of vocal fold movement and the diagnosis of bilateral vocal cord paralysis was established. A brain MRI was performed (normal), a 24-hour esophageal pH monitoring excluded significant gastroesophageal reflux and a fibrobronchoscopy revealed mild laryngomalacia (incomplete examination due to the inability to progress through the glottis). On day 40 of life he was transferred to a pediatric reference hospital for a second opinion. He suffered deterioration on day 43, for which he was intubated and mechanically ventilated. A tracheostomy was performed on day 47 with no complications. Two weeks after surgery he was discharged home. He has not presented any complications since then.

#### CONCLUSIONS

Although rare, bilateral vocal cord paralysis is a life-threatening condition and needs to be promptly recognized. Up to 65% present a spontaneous recovery, so non-invasive management can be attempted. However, most severe cases frequently require a tracheostomy.

#### ABS 12

##### THE GESTATIONAL EFFECT OF ANTENATAL CORTICOSTEROIDS ON RESPIRATORY DISTRESS SYNDROME IN VERY LOW BIRTH WEIGHT INFANTS: A POPULATION BASED STUDY

S.Y. Liu<sup>1</sup>, H.I. Yang<sup>2</sup>, H.C. Chou<sup>1</sup>, C.Y. Chen<sup>1</sup>, W.S. Hsieh<sup>1</sup>, K.I. Tsou<sup>3</sup>, P.N. Tsao<sup>1,4</sup>

<sup>1</sup>Department of Pediatrics, National Taiwan University Hospital, National Taiwan University, Medical College, Taipei, Taiwan

<sup>2</sup>Genomics Research Center, Academia Sinica, Taipei, Taiwan

<sup>3</sup>Department of Pediatrics, Cardinal Tien Hospital and College of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan

<sup>4</sup>The Research Center of Developmental Biology and Regenerative Medicine, National Taiwan University, Taipei, Taiwan

## INTRODUCTION

Neonatal respiratory distress syndrome (RDS) is a major problem that causes neonatal mortality and morbidity. According to current guidelines, antenatal corticosteroids are used for all infants delivered between 24-34 weeks of gestation. However, the protective effect of antenatal corticosteroids at different gestational age is still unclear. We aimed to analyze the efficacy of antenatal corticosteroids in infants at different gestational ages.

## METHODS

We retrospectively analyzed the very low birth weight (VLBW) preterm infants registered at the Premature Baby Foundation of Taiwan from 2007 to 2014. A total of 8,150 VLBW infants were registered in the database. We included VLBW infants who received antenatal corticosteroids at 20-34 weeks of gestation. Infants with congenital anomaly, chromosomal anomaly, and congenital infection were excluded. Data on antenatal corticosteroids course were collected along with the use of Survanta® as an indicator of severe RDS. The beneficial effect of antenatal corticosteroids to prevent the use of Survanta® was evaluated.

## RESULTS

A total of 8,060 VLBW infants were included. Antenatal corticosteroids were administered in 5,448 infants. Multivariate analysis revealed that gestational age, birth body weight, gender, the presence of small for gestational age, preeclampsia, and antenatal corticosteroids use were all independent risk factors of severe RDS required Survanta® use. In VLBW infants with gestational age less than 28 weeks, completion of a total of two doses of antenatal corticosteroids had a protective effect against severe RDS and decreased the need of Survanta® use (odds ratio [95% CI]: 0.55 [0.46-0.67]). For VLBW infants over 31 weeks of gestation, the use of antenatal corticosteroids had no obvious beneficial effects (0.78 [0.52-1.16]).

## CONCLUSIONS

Completion of 2-dose-course of antenatal corticosteroids is of great importance in VLBW infants under 28 week of gestation in the prevention of severe RDS and in decreasing Survanta® use.

## ABS 13

### PREECLAMPSIA AND THE RISK OF RESPIRATORY DISTRESS SYNDROME IN VLBW INFANTS: A POPULATION BASED STUDY

Y.H. Wen<sup>1</sup>, H.I. Yang<sup>2</sup>, W.S. Hsieh<sup>1</sup>, H.C. Chou<sup>1</sup>, C.Y. Chen<sup>1</sup>, K.I. Tsou<sup>3</sup>, P.N. Tsao<sup>2</sup>

<sup>1</sup>Department of Pediatrics, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan

<sup>2</sup>Genomics Research Center, Academia Sinica, Taipei, Taiwan

<sup>3</sup>Department of Pediatrics, Cardinal Tien Hospital and College of Medicine, Fu Jen Catholic University, New Taipei City, Taiwan

<sup>4</sup>The Research Center of Developmental Biology and Regenerative Medicine, National Taiwan University, Taipei, Taiwan

## BACKGROUND

Preeclampsia is a leading cause of maternal and neonatal morbidity and mortality. In women who develop preeclampsia, the excess of sFlt-1 results in decreasing free circulating levels of vascular endothelial growth factor (VEGF). Low VEGF concentration was reported to be associated with the severity of respiratory distress syndrome (RDS) in preterm infants. However, the relationship between preeclampsia and RDS remains unclear. This study aims to test whether or not preeclampsia is associated with RDS in premature infants.

## METHODS

We conducted a retrospective cohort study in very-low-birth-weight (VLBW) infants registered at the Premature Baby Foundation of Taiwan from 2007 to 2014. All 21 neonatal departments in Taiwan participated in the data collection. A total of 8,150 VLBW infants were registered. The exclusion criteria included congenital and chromosome anomalies, maternal chronic hypertension, and those whose RDS status was unavailable. Severe RDS was defined by clinical diagnosis and as requiring surfactant therapy. The association between maternal preeclampsia and RDS was assessed using a multivariate-adjusted logistic regression model.

## RESULTS

A total of 6,852 cases were enrolled in this study. The incidence of preeclampsia was 17.3% (n = 1,187) in this population and the overall incidence of severe RDS was 45.5% (n = 3,115). In the univariate analysis, infants with maternal preeclampsia had a higher gestational age (GA), higher incidence of being small for their gestational age (SGA), but lower incidence of severe RDS. In the multivariate logistic regression analysis which included pre-

eclampsia, GA, sex of baby, birth weight, and SGA as risk predictors, preeclampsia was positively associated with the risk of developing severe RDS, showing a multivariate-adjusted odds ratio (95% CI) of 1.28 (1.10-1.05).

#### CONCLUSIONS

This data supports the association between maternal preeclampsia and severe RDS in the VLBW infants who required surfactant therapy.

#### ABS 14

### EFFECTIVENESS OF SINGLE DOSE SALBUTAMOL NEBULIZATION IN THE TREATMENT OF TRANSIENT TACHYPNEA OF THE NEWBORN: A DOUBLE BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL

M.L.B. Cruz<sup>1</sup>, M.J.C. Racoma<sup>1</sup>, V.O.M. Cloma-Rosales<sup>2</sup>, M.V.J. Cabahug<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Makati Medical Center, Makati City, Philippines

<sup>2</sup>101 Health Research, Makati City, Philippines

#### INTRODUCTION

Transient tachypnea of the newborn (TTN) is a self-limiting disease, but may lead to multiple diagnostic studies, prolonged hospitalization with NICU admission and parental anxiety. Salbutamol increases lung liquid clearance through its action on sodium ion transport in alveolar type II epithelial cells, and decreases duration of tachypnea. We aimed to compare TTN duration and severity among term neonates who received salbutamol compared to placebo.

#### METHODS

We conducted a parallel, superiority RCT among term neonates with transient tachypnea of the newborn. They were randomized to receive single dose nebulization with salbutamol or saline. Outcomes of interest were time to resolution of tachypnea, TTN scores, heart rate and respiratory rates, admission to NICU, duration of oxygen support, and adverse events.

#### RESULTS

We analyzed a total of 14 term neonates with tachypnea. Baseline clinical characteristics such as the median onset of tachypnea, respiratory rate, O<sub>2</sub> saturation, TTN scores, X-ray, and complete blood count were similar between groups. There was insufficient evidence to determine a difference in respiratory rate, heart rate, and TTN scores over four hours of treatment between the two groups. The salbutamol group had a longer median duration of

TTN (20 versus 15 hours,  $p = 0.947$ ), and resolution was observed later compared to placebo (24 versus 17 hours of life,  $p = 0.894$ ). However, the salbutamol group had a shorter duration of requirement for oxygen support (12 versus 47 hours,  $p = 0.077$ ). One out of five salbutamol patients, and 3 out of 9 placebo patients were transferred to NICU. No adverse events were observed.

#### CONCLUSIONS

We had insufficient evidence to demonstrate a difference in duration and severity of tachypnea between neonates who received single dose salbutamol versus placebo. Further investigations with larger sample are needed before recommending this as part of standard therapy.

#### ABS 15

### COMPARING THERAPEUTIC IMPACT OF BUBBLE CPAP WITH VARIABLE CPAP IN PREMATURE INFANT WITH RESPIRATORY DISTRESS

M. Noorishadkam<sup>1</sup>, M.H. Lokzade<sup>1</sup>, M. Eslami-Abrandabadi<sup>2</sup>, E. Abbasi Shavazi<sup>1</sup>

<sup>1</sup>Premature Neonates Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Yazd, Iran

<sup>2</sup>Shahid Sadoughi University of Medical Sciences, Yazd, Yazd, Iran

#### INTRODUCTION

Respiratory distress syndrome (RDS), due to surfactant deficiency, occurs mainly in preterm infants. Continuous Positive Airway Pressure (CPAP) is a non-invasive method of treatment which to prevent to collapse of alveoli and distal airways, especially during expiration. Today CPAP is applied in two ways: continuous flow and variable flow. Continuous flow CPAP is applied by the ventilator or Bubble. This study was designed to investigate the efficacy of Bubble CPAP and Variable CPAP in preterm infants with RDS.

#### METHODS

This was a randomized clinical trial with the sample size of 112 preterm infants with moderate RDS and gestational age of 28 to 34 weeks and birth weight 1,000 to 2,400 g, who were born from January 2013 to March 2014 and admitted to NICU. These infants required FiO<sub>2</sub> > 21% and their respiratory score based on Silverman Anderson table was 5-7. They were randomized to one of the bubble CPAP or variable CPAP groups. Data were analyzed using SPSS® version 17.

**RESULTS**

Treatment duration with CPAP and mechanical ventilation in variable CPAP was significantly less than bubble CPAP ( $p = 0.044$  and  $p = 0.043$  respectively). Duration of oxygen therapy in bubble CPAP and variable CPAP were  $5.38 \pm 4.31$  and  $5.37 \pm 4.55$  days respectively but there was no significant difference between them ( $p = 0.772$ ). The rate of complications was not different between the two groups significantly. Median of hospitalization was not significantly different 19 days in bubble CPAP and 18 days in variable CPAP. The mean weight at discharge in bubble CPAP was  $1,720 \pm 259$  g and in variable CPAP  $1,755 \pm 261$  g. In the bubble CPAP group, 30 cases (55.6%) and in the variable CPAP group 22 cases (43.1%) received surfactant and there was no significant difference between two groups ( $p = 0.243$ ).

**CONCLUSIONS**

This study showed that the duration of CPAP and mechanical ventilation was shorter in the variable CPAP method group than in the bubble CPAP group.

**ABS 16****THE INCIDENCE OF RESPIRATORY MORBIDITY IN LATE PRETERM INFANT**

G. Olariu, S. Olariu, M. Tunescu

*Municipal Emergency Hospital Timisoara, Maternity Odobescu; Timisoara, Romania*

**INTRODUCTION**

The incidence of preterm births has increased in the last years, as demonstrated by the growing number of late preterm (LPT) births. The incidence represents 74% of all preterm infants and 8-9% of all births, with high respiratory morbidity.

**OBJECTIVE**

The objective of the study was to elucidate the role of gestational age in the incidence of increased neonatal respiratory morbidity in late preterms (34-36 weeks) compared with term newborns (39-41 weeks).

**METHODS**

A retrospective study, conducted on a period of 3 years and 6 months (from January 2012 until 30 June 2015) in a third level maternity, compared respiratory morbidity and respiratory therapy in late preterm infants and term newborns.

**RESULTS**

We analyzed a total of 10661 preterm births with a mean gestational age between 34-41 weeks, who were divided into two study groups (late preterm and term newborns). RDS incidence was 34.2% at 34 weeks and 0.7% in term newborns. 53% of LPT newborns compared to 31.2% term infants were born by cesarean delivery. The incidence of transient tachypnea was 7.9% in late preterm compared with 0.5% in term newborns. Odd ratio (OR) of RDS decreased with the increase of GA up to 38 weeks compared with the 39-40 weeks group. OR at 34 weeks was 39.1; 95% confidence interval (CI), 31.0-47.3; at 38 weeks, OR 1.15; 95% CI, 0.9-1.4. At 37 weeks, RDS incidence increased compared to the 39-40 weeks group (adjusted OR, 3.1; 95% CI, 2.5-3.7), but at 38 weeks incidence was less different from that of the 39-40 weeks group. Similarly, the incidence of TTN was greatly increased at 34 weeks (14.7; 95% CI, 11.7-18.4) compared with 38 weeks (1.0; 95% CI, 0.8-1.2), neonatal pneumonia incidence was 5.4% (95% CI 6.9-16.1) at 34 weeks and 0.4% (95% CI, 0.6-1.2). The need for ventilator support was 7.5% at 34 weeks 0.2% after 38 weeks.

**CONCLUSIONS**

Respiratory distress syndrome remains a common disease of the late preterm infant, with severity increasing with the decrease in gestational age. Respiratory morbidity for this age includes neonatal transient tachypnea, deficit/inactivation of surfactant and pulmonary hypertension. Caesarean section without labor increases the risk for this disease with decrease in gestational age, and the need for ventilatory support is higher in LPT infants.

**ABS 17****HYDROCORTISONE IN PRETERM INFANTS**

C. Ramos-Navarro, M. Tomé-Perez, M. R. Ruiz-Gutierrez, S. Zeballos-Sarrato, N. Navarro-Patiño, I. Pescador-Chamorro, A. Rodriguez-De la Blanca, I. Marsinyach-Ross, M. Arriaga-Redondo, M. Sánchez-Luna

*Pediatric Department, Gregorio Marañón Hospital; - Madrid, Spain*

**INTRODUCTION**

Postnatal steroids use in preterm infants is actually restricted to mechanical ventilation (MV) dependent infants with high respiratory assistance due the association between dexamethasone treatment and neurodevelopment impairment. Hydrocortisone

therapy has not been associated with significant neurological sequelae in RCTs, but there is still not enough evidence to recommend a systematic use in preterm infants. In our institution, hydrocortisone treatment is indicated since 2014 in preterm infants with severe respiratory distress, requiring sustained ventilator and oxygen support. The aim of this study was to analyze short and long-term respiratory and neurodevelopmental outcomes in preterm infants treated with hydrocortisone.

#### METHODS

Retrospective review of preterm infants treated with hydrocortisone (total dose 72 mg/kg) since 2014 for respiratory insufficiency comparing their outcomes with a historical cohort of ventilator dependent (more than 7 days of MV) preterm infants (< 28 weeks GA) not exposed to postnatal steroids.

#### RESULTS

Hydrocortisone was administered between 2014-2015 in 15 of 78 less than 28 weeks GA infants (19.2%) (characteristics are depicted in **Tab. 1**). Infants treated with hydrocortisone had significantly higher risk score (CRIB) and number of days on MV compared with the cohort not receiving hydrocortisone (**Tab. 2**). There were no significant differences in the outcomes analyzed between the two groups (oxygen duration,

BPD severity, re-admissions for respiratory disease, respiratory treatment at 6-12 months, pathological cranial ultrasound, ROP, hearing loss and abnormal neurologic examination at 6-12 months) except for a lower head circumference percentile at birth ( $p = 0.013$ ) and at discharge ( $p < 0.01$ ) in hydrocortisone treated group.

#### CONCLUSIONS

Hydrocortisone treatment was not associated to neurodevelopmental impairment in this study. The main limitations of the study were the low number of patients included and the limited follow up to 6-12 months of PMA in hydrocortisone group. Actually, in our institutional protocol, hydrocortisone total dose has been reduced to 17 mg/kg.

#### ABS 18

#### THE VALUE OF ULTRASOUND EXAMINATION IN PREDICTING CHRONIC LUNG DISEASE IN VLBW INFANTS UNDERGOING RESPIRATORY SUPPORT: PRELIMINARY RESULTS

S. Aversa, C. Zambelloni, R. Marzollo, V. Materia, F. Matina, G. Chirico

Neonatal Intensive Care Unit, Children Hospital, "Spedali Civili" of Brescia, Brescia, Italy

#### INTRODUCTION

Chronic lung disease (CLD) is one of the most relevant complications of neonatal ventilation. Early diagnosis may influence treatment strategies, such as early steroid administration. The study assesses the role of ultrasound (US) of the lungs in predicting the development of CLD in infants with hyaline membrane disease (HMD) and to determine the earliest possible age to predict CLD.

**Table 1 (ABS 17).** Characteristics of the 15 infants treated with hydrocortisone.

	Hydrocortisone
Days of life	22 (15-31)
Postmenstrual age (weeks)	28.3 (27-30)
Mean airway pressure (mmH <sub>2</sub> O)	15 (13-17)
FiO <sub>2</sub>	75% (50-100)
Time to extubation (days)	22 (9.5-25.7)

Data are expressed as median (IQR).

**Table 2 (ABS 17).** Basal characteristics.

	Hydrocortisone (n = 15)	Control (n = 29)	p
Gestational age (weeks)	25.1 (24.4-26)	25.7 (25.1-26.9)	0.07
Weight percentile	33 (13-47.5)	47 (28.5-66)	0.137
Intubation at birth, rate (n)	86.60% (13)	55.10% (16)	0.06
Prenatal steroids	46.60% (7)	55.1% (16)	0.19
CRIB score	9 (6-11)	5 (2.5-8)	<b>0.001</b>
HFOV on day 3, rate (n)	86.6% (13)	44.8% (13)	0.059
MV (days)	49 (35-58)	27 (20-35)	<b>0.002</b>
Chorioamnionitis, rate (n)	20% (3)	36% (10)	0.285

Data are expressed as median (IQR).  
MV: mechanical ventilation.

**METHODS**

65 preterm infants with gestational age lower than 32 weeks who were admitted because of HMD requiring respiratory support were studied prospectively during 2015. The first US of the lungs was performed within 3 days of birth, and the following were performed at 7, 10, 14 days of life and once a week thereafter until discharge from the neonatal intensive care unit. Each patient was clinically evaluated for the presence or absence of CLD at 28 days of life. Babies with CLD were also evaluated for the severity of disease at 36 weeks of post-conceptual age. Lung US scans were correlated with the development of CLD and its severity. A new scoring model has been created in order to study their predictive value for CLD.

**RESULTS**

“White lung” pattern was initially observed in 82.4% of the newborns who developed CLD and in 32.6% of disease-free infants, who later showed a progressive resolution of the abnormal US finding. In 77.8% of the infants who developed CLD, “white lung” pattern persisted at day 10, which was the earliest day where the new scoring model score showed the highest predictive values for CLD.

**CONCLUSIONS**

Lung US seems to be a valuable diagnostic test for predicting the development of CLD. Further studies with larger sample size are needed to confirm this promising results and support the use of lung ultrasound in order to optimize lung protection strategies.

**ABS 19**

**RESPIRATORY DISTRESS OUTCOME AFTER SURFACTANT TREATMENT IN PREMATURE NEONATES OF LESS THAN 28 WEEKS OF GESTATION**

M. Matyas<sup>1</sup>, L. Blaga<sup>1</sup>, M. Hășmășanu<sup>1</sup>, V. Obada<sup>2</sup>, G. Zaharie<sup>1</sup>

<sup>1</sup>Neonatology Department, University of Medicine and Pharmacy, Iuliu Hatieganu Cluj Napoca, Cluj Napoca, Romania

<sup>2</sup>Neonatology Unit I, County Emergency Hospital Cluj Napoca, Cluj Napoca, Romania

**INTRODUCTION**

Surfactant treatment indication is clearly established by guidelines for preterm neonates. The INSURE technique is recommended as it is followed by fewer long term complications.

**AIM**

In the current paper we analysed mortality and morbidity of preterm neonates of less than 28 weeks of gestation who received single or multiple dose of surfactant for the respiratory distress treatment at different postnatal ages.

**METHODS**

We performed a retrospective study at the 1st Neonatology Department of County Emergency Hospital Cluj, Romania, between January 2014-December 2015. Preterm neonates of less than 28 weeks of gestation (inborns and outborns) were included. We analyzed the age at surfactant treatment, number of doses, length of mechanical ventilation after the surfactant, CPAP duration, associated pathologies and death.

**RESULTS**

In the study group 36 preterm neonates with an average gestational age of 26.13 weeks and weight 868 g were included. 19 patients were inborns and 17 were outborns. The age at surfactant administration was 1.57 hour in inborns and 19.66 hours in outborns. Mechanical ventilation was used after surfactant in 24 patients (67%), and 6 (16.6%) patients needed HFV. Five patients received a second dose of surfactant. The INSURE technique was successfully applied in patients with gestational age of 27-28 weeks. At lower gestational age the INSURE technique was not applied due to poor outcome. Patent ductus arteriosus (PDA) was observed in 14 patients and 7 received IV treatment for its closure. One case did not respond to IV treatment, therefore surgical treatment was performed.

**CONCLUSIONS**

Surfactant treatment was given significantly earlier in inborns than in outborns. The INSURE technique was applied successfully at 27-28 weeks of gestation in our study group.

**ABS 20**

**METABOLOMICS ANALYSIS ON THE BALF OF PRETERM INFANTS WITH A GESTATIONAL AGE LESS THAN 30 WEEKS TO IDENTIFY NEW BIOMARKERS OF BPD**

F. Piersigilli<sup>1</sup>, M. Syed<sup>2</sup>, A. Dotta<sup>1</sup>, C. Auriti<sup>1</sup>, G. Salvatori<sup>1</sup>, P. Vernocchi<sup>1</sup>, E. Voss<sup>3</sup>, T. Lam<sup>3</sup>, V. Bhandari<sup>2</sup>

<sup>1</sup>Division of Neonatology, Bambino Gesù Children's Hospital, Rome, Italy

<sup>2</sup>Department of Pediatrics and Yale Child Health Research Center, Yale University School of Medicine, New Haven, CT, USA

<sup>3</sup>Yale Keck MS & Proteomics Resource, Yale University, New Haven, CT, USA

## INTRODUCTION

Metabolomics is a promising “omic” approach that can help in elucidating the signaling pathways involved in the pathogenesis of pulmonary bronchodysplasia (BPD). Metabolomics consists of the quantitative analysis of a large number of metabolites to identify changes in the composition of metabolites caused by the interaction between specific pathophysiological states, gene expression, and environment.

## METHODS

The aim of the study was to use an “omic” approach to identify some new signaling pathways involved in BPD. We performed a study on tracheal aspirate samples collected in the first 7 days of life in preterm infants with a GA less than 30 weeks. We performed a profile of 188 metabolites (40 acylcarnitines, 21 amino acids, 21 biogenic amines, 90 glycerophospholipids, 15 sphingolipids and glucose) on the supernatant of the tracheal aspirate samples. Extraction was carried out using a Waters Oasis HLB 1mL cartridge; 500 µl of bronchoalveolar lavage fluid (BALF) were eluted in methanol. The assay was performed with the AbsoluteIDQ® p180 Kit (Biocrates Life Sciences) using a 4000 QTRAP® LC-MS/MS system (SCIEX™) coupled to a PerkinElmer® Flexar Ultra High Pressure Liquid Chromatography.

## RESULTS

91 neonates were recruited, 26 neonates were excluded due to the low quantity of the samples. 68 neonates (GA  $25.9 \pm 1.5$  w; BW  $820 \pm 189$  g) were included, of whom 44 developed BPD (GA  $25.6 \pm 1.4$  w; BW  $772 \pm 178$  g) and 24 not (GA  $26.6 \pm 1.7$  w; BW  $909 \pm 178$  g). 160 BALF samples were examined (48 collected on day 1, 42 on day 3, 39 on day 5 and 31 on day 7). We performed a statistical PLS-DA analysis with 4 latent variables on all metabolites, pretreatment was done with autoscaling. We found 53 significant metabolites. We then performed a PLS-DA analysis only on the 53 significant metabolites with 5 latent variables. Results were significant for 18 metabolites.

## CONCLUSIONS

Specific metabolite profiles can be discerned in tracheal aspirate samples of infants with BPD, compared to controls. Based on these results a cluster of metabolites can be proposed as a biomarker for the early identification of those neonates who will develop BPD. Furthermore

these results lay the basis for further analysis of these metabolic pathways to better understand the pathogenesis of this complex and multifactorial disease.

## ABS 21

### VENTILATOR-ASSOCIATED PNEUMONIA IN A NEONATAL INTENSIVE CARE UNIT: A POTENTIALLY SERIOUS COMPLICATION ASSOCIATED WITH MECHANICAL VENTILATION

R.C. Negrillo, M. González, M. Rodríguez, L. Núñez, C. Gómez, E. Salguero

Department of Neonatology, Hospital Materno-Infantil of Malaga, Malaga, Spain

## INTRODUCTION

Advances in perinatal care, particularly the use of mechanical ventilation (MV), have increased the survival of the most immature newborns. However, MV carries complications including ventilator-associated pneumonia (VAP). VAP data referring to the neonatal population are very limited.

## METHODS

A retrospective observational study with neonates who required MV for > 48 h was conducted to determine the incidence, risk factors, microbiology, treatment and outcomes of VAP in the Neonatal Intensive Care Units (NICU) of a third level hospital from January 2013 to December 2015. VAP was diagnosed using the following criteria: worsening of respiratory conditions, progressive radiological infiltrates or consolidation in 2 sequential radiographs and counts > 103 CFU/ml of pathogenic bacteria obtained by bronchoscopic bronchoalveolar lavage (B-BAL) or > 105 CFU/ml by tracheal aspirates (TA).

## RESULTS

In 338 neonates intubated for > 48 h, a total of 21 episodes of VAP occurred in 20 patients (incidence of VAP: 6.2%). The pooled mean VAP rate was 6.4/1,000 ventilator days. Epidemiologic, clinical, laboratory and radiological results are shown in **Tab. 1**. Gram-negative bacteria were isolated in 100% episodes. The most common pathogens isolated were *P. aeruginosa* (57.1%). 38% episodes were polymicrobial cultures. The mean duration of antibiotic treatment in VAP was  $16 \pm 6$  days. 66.7% episodes received combination antibiotic therapy. The mean hospital length of stay in NICU and duration of MV were longer

**Table 1 (ABS 21).** Epidemiologic, clinical, laboratory and radiological findings in neonates and ventilator-associated pneumonia (VAP) episodes.

Variables	Results
<b>Patient characteristics (n = 20 patients)</b>	
• Median gestational age (weeks)	28 (24-40)
• Median birth weight (g)	920 (440-3,800)
• Gender (%)	
Male	11/20 (55%)
Female	9/20 (45%)
• Underlying disorders	
Hyaline membrane disease	2/20 (10%)
Chronic lung disease	10/20 (50%)
Congenital malformations	6/20 (30%)
Other	2/20 (10%)
• Mean age at diagnosis of VAP	27.9 ± 16
• Mean duration of MV (days) before VAP	21.5 ± 15
<b>Risk factors (n = 21 VAP episodes)</b>	
• Reintubation	16/21 (76.2%)
• Transfusions	18/21 (85.7%)
• Bloodstream infection	5/21 (23.8%)
• Surgical treatment	13/21 (61.9%)
• Full enteral feeding	5/21 (23.8%)
<b>Clinical and radiological findings (n = 21 VAP episodes)</b>	
• Worsening of the respiratory conditions	21/21 (100%)
• Thermal instability	3/21 (14.3%)
• Radiological consolidation	11/21 (52.4%)
• Radiological infiltrate	3/21 (14.3%)
• Radiological consolidation + infiltrate	7/21 (33.3%)
• Median PCR (mg/l)	69.5 (14.3-291)
• Median PCT (ng/ml)	1.7 (0.2-53)

MV: mechanical ventilation; VAP: ventilator-associated pneumonia.

for VAP patients: 66 days in NICU and 40 days of MV in neonates with VAP, 43 days in NICU and 8 days of MV in neonates intubated without VAP. In our series, 3 patients with VAP died (14% episodes).

## CONCLUSIONS

VAP is a serious nosocomial infection with potential mortality and morbidity in neonates on MV. In our series, patients with VAP had higher hospital length of stay and duration of MV than non-VAP patients. We should promote different strategies as rapid extubation to prevent VAP in NICU patients.

## ABS 22

### USE OF HIGH FLOW NASAL CANNULAE IN MODERATE AND LATE PRETERMS, EXPERIENCE IN ONE SINGLE CENTER

M. Ramon, E. Capdevila, R. Porta

*Pediatric Department, Hospital Universitari Dexeus, Barcelona, Spain*

## INTRODUCTION

High flow nasal cannulae (HFNC) are widely used in NICU. HFNC seem to be more comfortable for babies and are well accepted for use among nurses. During the past years many authors have published their experience with HFNC, so now its use is accepted in term babies. For preterm babies there is a limited experience, but promising studies.

## METHODS

We present a descriptive analysis conducted over one year (2015) in a population of moderate and late preterm babies at our center, a IIIB center which is reference for *in-vitro* fecundation techniques. We classified early respiratory distress into mild, moderate and severe categories and ventilatory support into initial non-invasive (HFNC or nCPAP) or mechanical ventilatory support. We also recorded any complications of every technique and the evolution during the stay in hospital. We excluded from analyses 6 patients: 3 patients with congenital heart disease, 1 patient with apneas at 3<sup>rd</sup> day of live who needed respiratory support, 1 patient with duodenal atresia and 1 patient who had severe anti-D isoimmunization.

## RESULTS

No severe distress was reported during the first hours of life. Only one patient presented failure in non-invasive ventilatory support and needed mechanical ventilation and surfactant, and was initially supported with nCPAP. The comparison between late preterms with no support or with any support is reported in **Tab. 1**. The comparison between the use of HFNC and nCPAP was stratified for 32.0-36.6, 32.0-34.6 and 35.0-36.6 weeks. Two patients were excluded because they received support with conventional oxygen cannulae for persistent pulmonary hypertension.

## CONCLUSIONS

Despite the limited evidence of this study, HFNC are secure with no important differences with nCPAP in evolution of patients. However neonatologists at our institution still reserve

**Table 1 (ABS 22).** Comparison of characteristics without or with any support.

	No support n = 84 Median/Percentage	IR	Support n = 39 Median/Percentage	IR	p
GA (32.0-36.6)	35.0	34.1-35.4	34.3	33.2-35.3	0.149
Weight <sup>a</sup>	2,204	1,815-2,593	2,144	1,704-2,536	0.443
Cesarean	54.7%		69.2%		0.053
Twins	48.8%		53.8%		0.46
Immature	44%		43.5%		1
Staying (days)	9	7-14.25	16	7-24	0.007
Total feeding (days)	1	< 1-1	1	< 1-3	0.001

<sup>a</sup>Average and standard deviation for weight.

nCPAP for patients with more severe conditions, so we are unable to draw any firm conclusion from the present study.

### ABS 23

#### **SURFACTANT ABC3A TRANSPORTER POLYMORPHISM IDENTIFIED IN A TERM NEONATE WITH RDS USING NAVA MODALITY OF MECHANICAL VENTILATION**

M. Abuauf, F. Sabbagh, M. Abou-Alsoud

*Neonatology Division King Fahad Armed Hospital, Jeddah, Saudi Arabia*

#### CASE REPORT

G.S., a female newborn, was born at term in our hospital following an uneventful pregnancy and delivery (birth weight 3.5 kg) and was transferred to the post-natal ward. At the age of 3 hours she was admitted to NICU with grunting, and desaturation (saturation was 80% on room air). The baby was started on NCPAP; initial blood gas showed respiratory acidosis. She was screened for sepsis and antibiotic therapy was started. FiO<sub>2</sub> requirement was 80% thus she was intubated with patient-triggered ventilation (PTV) mode of mechanical ventilation. With respiratory support, her FiO<sub>2</sub> requirement decreased to 40%, with a respiratory rate of 70/min. By 60 hours her respiratory rate increased to 100/min, FiO<sub>2</sub> of 80%, CXR showing no atelectasis and blood gas analysis acceptable. She was then started on Neurally Adjusted Ventilatory Assist (NAVA), with initial settings of PEEP 6, and NAVA level of 2 was then increased to 3 based on the electrical activity of the diaphragm (Edi) measurement. On NAVA her RR was 60-70/min, and FiO<sub>2</sub> 40% with

acceptable blood gas analysis results. We noted that Edi minimal was frequently > 5 uV with periodic increase of Edi max > 20 uV, and increasing NAVA level to 3.5 resulted in respiratory alkalosis but did not affect the Edi minimum frequent elevation. The impression was that the patient was trying to prevent alveolar atelectasis/recruit alveoli to maintain the lung functional residual capacity by sustaining a high diaphragmatic resting potential. The same phenomenon was noted on noninvasive NAVA (NIV-NAVA).

#### RESULTS

Based on the clinical history and the findings on NAVA, the possibility of cystic fibrosis, surfactant B and C and *ABCA3* mutation were considered. Patient gene studies were negative for cystic fibrosis and surfactant B&C gene mutations, but 5 different *ABCA3* gene polymorphisms were detected, two of which have been linked with respiratory distress in neonates were found (rs13332514 and rs323043).

#### CONCLUSIONS

NAVA is an emerging modality of mechanical ventilation and the respiratory support provided by NAVA is proportionate to the patient requirements. NAVA may help in differential diagnosis.

### ABS 24

#### **PREDICTION OF MORTALITY IN NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA**

J. Clotet<sup>1</sup>, À. Pertierra<sup>1</sup>, M. Camprubí<sup>1</sup>, M. Castañón<sup>2</sup>, J. Moreno<sup>1</sup>

<sup>1</sup>Neonatology Department, BCNatal Hospital Sant Joan de Déu-Clínic, University of Barcelona, Barcelona, Spain

<sup>2</sup>Pediatric Surgery Department, Hospital Sant Joan de Déu, University of Barcelona, Barcelona, Spain

## INTRODUCTION

Congenital diaphragmatic hernia (CDH) is associated with significant mortality and morbidity. The ability to predict survival outcomes in these infants is essential to evaluate individual cases, direct intervention and treatment plans. Some clinical variables have been described to be predictive of mortality in several series. The aim of this study is to identify prenatal and immediate postnatal factors associated with increased mortality.

## METHODS

This is a single-center retrospective review of all CDH infants admitted to our level IIIC NICU between 2005 and 2015. Main prenatal variables and the most relevant postnatal parameters have been collected and analysed. Severity score was based on observed/expected lung to head ratio (O/E LHR) and liver herniation. Multivariable logistic regression analysis was used to assess mortality risk for each neonate. Patient survival rate was defined as survival to discharge from hospital.

## RESULTS

During this period, 175 CDH patients were admitted and 29 (17.14%) of them were treated with ECMO. Global survival rate was 70.85%. The main perinatal characteristics of our population are shown in **Tab. 1**. The resultant logistic regression equation was then used to obtain a predictive mortality risk (Pmr) for each neonate:  $Pmr = 1 - [1 + e^X]^{-1}$  where  $X = 1.02 + (1.12 \cdot \text{severity score}) + (0.06 \cdot \text{OI}_{\text{max}}) - (0.02 \cdot \text{pCO}_{2,\text{max}}) - (0.53 \cdot \text{Apgar 5min})$ . The AUC was 0.94,

with a sensitivity of 77.8% and a specificity of 94.3%. It is difficult to assess the implication of ECMO as a predictor factor, because those patients who needed ECMO presented a higher severity score ( $p = 0.03$ ).

## CONCLUSIONS

Within our population, the main variables related to mortality were prenatal severity score, 5-minute Apgar, Oxygenation Index and maximum  $\text{pCO}_2$  determination. With the present data we cannot identify any parameter to be a good indicator of mortality in this subpopulation among ECMO patients.

## ABS 25

### THE ROLE OF LUNG ULTRASOUNDS IN DETECTING PNEUMOTHORAX IN NEONATES: REVIEW OF 4 CASES

I. Koltunov<sup>1</sup>, M. Degtyareva<sup>2</sup>, A. Mazaev<sup>1</sup>, A. Gorbunov<sup>1,2</sup>, A. Erokhina<sup>1,2</sup>, A. Demina<sup>1</sup>

<sup>1</sup>Morozovsky Children Municipal Clinical Hospital, Moscow, Russia

<sup>2</sup>Pirogov Russian National Research Medical University, Moscow, Russia

## INTRODUCTION

Pneumothorax (Ptx) is a common life-threatening condition of the respiratory tract. Lung ultrasound (LUS) is a well-established method to detect pneumothorax in adults but there are few studies assessing the efficacy of LUS examination to detect

**Table 1 (ABS 24).** Demographic and clinical information on 175 patients with congenital diaphragmatic hernia.

Characteristic	Total (n = 175)	Survivors (n = 124)	Non-survivors (n = 51)	p-value
FETO	40.24%	32.74%	56.86%	0.0034
Prenatal diagnosis	87.05%	83.19%	96.07%	0.0218
O/E-LHR at diagnosis	40.60%	46.23%	30.40%	< 0.0001
PROM	36.97%	33.33%	46.87%	0.177
5-minute Apgar	7.7 ± 0.16	8.2 ± 0.15	6.4 ± 0.33	< 0.0001
Gestational age (w)	37.38 ± 0.21	37.63 ± 0.24	36.79 ± 0.41	0.0729
Birth weight (g)	2,727 ± 47	2,820 ± 54	2,500 ± 86	0.0024
Age of repair (h)	44.12 ± 3.8	40.31 ± 31	70.58 ± 18.37	0.0002
iNO	49.01%	33.05%	87.77%	< 0.0001
PaO <sub>2</sub> minimum	47.2 ± 2.2	54.67 ± 2.6	34.08 ± 3.15	< 0.0001
PaCO <sub>2</sub> maximum	59.94 ± 1.3	57.42 ± 13.6	65.75 ± 2.8	0.0034
OI maximum	29.23 ± 2.4	16.17 ± 1.77	51.66 ± 4.1	< 0.0001
Age of start ECMO (days)	1.5 ± 0.29	0.74 ± 0.24	3.4 ± 0.74	< 0.0001

Data are expressed as mean ± SEM and proportions.

FETO: fetoscopic endoluminal tracheal occlusion; O/E-LHR: observed/expected lung-to-head ratio; PROM: premature rupture of membranes; iNO: inhaled nitric oxide; OI: oxygenation index; ECMO: extracorporeal membrane oxygenation.

pneumothorax in neonates. The purpose of our study is to assess the accuracy of LUS in detecting tension and non-tension Ptx in neonates.

#### METHODS

This was a prospective, single-centre, observational study conducted at the Morozovsky Children Hospital (Moscow, Russia). 98 neonates underwent LUS and chest radiography in 0.2-4 hours after LUS. 4 of them had Ptx, one baby had tension Ptx and 2 examinations (before and after drainage); each of other 3 neonates had non-tension Ptx and 1 LUS examination. LUS was made by liner 6-15 MHz transducer via Logiq™ S8 ultrasound machine, anterior, lateral and posterior areas of the chest were scanned. The mean gestation age of the patients was  $33 \pm 5.9$  (26-39 w), mean body weight  $2,218.0 \pm 1,389.5$  g (750-3,670 g). LUS was made before X-ray examination in all cases, and results were compared.

#### RESULTS

In all 5 cases the lung point was visualized. In non-tension Ptx of minimal volume (2 cases) lung point was located in anterior subdiaphragmatic area at the level of midclavicular line, in larger non-tension pneumothorax (2 cases) lung point was located at the level of anterior axillary line. In tension pneumothorax lung point was located at the level of scapular line. A-lines and absence of B-lines and lung sliding were detected in all cases. On radiograms Ptx was diagnosed in all cases, the decision about its volume was made according to radiographic data. The sensitivity of LUS was 100%, specificity was 100%.

#### CONCLUSIONS

Lung ultrasound is a feasible diagnostic tool in the detection or ruling out of Ptx in neonates. The location of lung point can help to assess the volume of Ptx. Randomized controlled trials involving nonqualified operators (neonatologists) are required to implement LUS into routine clinical practice.

#### ABS 26

### OUTCOMES IN VERY PRETERM NEONATES WITH SEVERE HYPOXEMIC RESPIRATORY FAILURE (HRF) RESCUED WITH HIGH FREQUENCY OSCILLATORY VENTILATION (HFOV) AND INHALED NITRIC OXIDE (iNO)

A. Golfar<sup>1</sup>, J. Bhogal<sup>2,3</sup>, B. Kamstra<sup>3</sup>, A. Hudson-mason<sup>3</sup>, G.M. Schmölzer<sup>2,3</sup>, P.-Y. Cheung<sup>2,3</sup>

<sup>1</sup>Faculty of Medicine & Dentistry, University of Alberta, Canada

<sup>2</sup>Centre for the Studies of Asphyxia and Resuscitation, Royal Alexandra Hospital Edmonton, Alberta, Canada

<sup>3</sup>Neonatal Research Unit, Northern Alberta Neonatal Program, Edmonton, Alberta, Canada

#### INTRODUCTION

Despite being an experimental therapy in preterm neonates, iNO has increasingly been used to improve oxygenation in those neonates who are unresponsive to conventional therapies including rescue HFOV. We aimed to report the outcome of very preterm neonates with life-threatening HRF unresponsive to rescue HFOV and treated with iNO.

#### METHODS

We present an experience on 47 very preterm neonates (< 33 weeks of gestation) treated with HFOV and iNO (retrospective study) (**Tab. 1**). Twelve of 47 (26%) received a second course of iNO (10-20 ppm).

#### RESULTS

The mortality was 49% (n = 23): withdrawal of treatment for persistent HRF (8) or complications (6), multi-organ failure (7) and other reasons (2). Of 24 infants who survived to discharge, 23 (96%) developed complications including intraventricular hemorrhage (n = 10, 42%), necrotizing enterocolitis (n = 6, 25%), sepsis (n = 11, 46%), chronic lung disease (n = 20, 83%) and retinopathy of prematurity (n = 12, 50%).

#### CONCLUSIONS

In this study of very preterm neonates who had severe HRF despite HFOV treatment and were rescued with iNO, many survived but the survivors frequently had major and multiple short-term complications. Further research is necessary to understand the clinical course and risk factors of adverse outcomes and to improve the management care of these critically ill neonates.

**Table 1 (ABS 26).** Clinical characteristics of 47 neonates treated with HFOV and iNO.

Gestational age (weeks)	26.8 [23 <sup>+4</sup> -32 <sup>+4</sup> ]
Birth weight (g)	888 [520-1,490]
Male	26 (55%)
Cesarean section	33 (70%)
Antenatal steroids	41 (87%)
Prolonged premature rupture of membranes for > 24 h	26 (55%)
Oligohydramnios	24 (51%)
Chorioamnionitis	13 (28%)
Apgar score at 1 minute	3 [0-7]
Apgar score at 5 minutes	5 [2-9]
Required medications for cardiovascular support	42 (89%)
> 1 dose of surfactant given	25 (53%)

Data are presented as mean [range] or n (%).