

Dublin
May 25th - 28th 2017



SPiN 2017

Sharing Progress in Neonatology

including
32nd International Workshop on Surfactant Replacement

SCIENTIFIC PROGRAM

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Dublin

May 25th - 28th 2017

Dear Friends and colleagues,

Welcome to the "SPIN (Sharing Progress in Neonatology)" including the 32nd International Workshop on Surfactant Replacement. This Congress will highlight research progress in Neonatology including brain injury and development and lung diseases.

We are grateful to the eminent international speakers, very fortunate to have well - known speakers from all over of the world who will discuss cutting edge issues in the field of the vulnerable newborn brain, neuroimaging, stem cell treatment, pulmonary circulation, retinopathy of prematurity, new non-invasive ventilation strategies, new guidelines on RDS, bronco-pulmonary dysplasia, the appropriate level of oxygen etc.

It is also very important to obtain abstracts from the participants in order to sustain a highly qualitative program, which also includes free papers and posters. Experienced chairmen will undoubtedly catalyze lively discussions in every session.

The opening ceremony will be held on May 26th and will include the 9th Bengt Robertson Memorial Lecture held by Prof. Dominique Haumont (Bruxelles, Belgium). We expect over 400 delegates from numerous countries and different continents attending the meeting. In spite of the changes in the title of the Congress, we assure to keep the traditional workshop style in a very friendly atmosphere.

This meeting is characterized by friendly interactions between speakers and delegates to allow an active debate on basic and clinical issues aimed at improving the quality of care of sick newborns and preterm babies. Returning home armed with better approaches to everyday clinical problems probably constitutes one of the most important achievements of this meeting.

Both the Organizing Committee and I as President of this Workshop look very much forward to meeting you all in Dublin, and we hope you enjoy a very interactive scientific meeting.

Prof. Eleanor Molloy
President of SPIN 2017



FRIDAY, 26TH MAY 2017

08.30 – 08.40

WELCOME ADDRESS

Eleanor Molloy (Ireland)

Chairpersons: Tore Curstedt & Henry Halliday

08.40 – 08.50

INTRODUCTION

Tore Curstedt (Sweden)

08.50 – 09.20

9th BENGT ROBERTSON MEMORIAL LECTURE

Dominique Haumont (Belgium)

09.20 – 09.35

Discussion

Chairpersons: Nikki Robertson & Luca Ramenghi

Invited Lecture

09.35 – 10.05

NEONATAL SEIZURES IN THE 21ST CENTURY

Geraldine Boylan (Ireland)

10.05 – 10.20

Discussion

10.20 – 10.50

Coffee Break

Chairpersons: Mikko Hallman & Jan Johansson

Invited Lecture

10.50 – 11.20

OVERVIEW OF LUNG DEVELOPMENT

David Warburton (USA)

11.20 – 11.35

Discussion

Oral Presentations

11.35 – 11.50

Commensal or true pathogen? Ureaplasma species induce and differentially modulate immune responses in human monocytes
Kirsten Glaser (Germany)

11.50 – 12.05

IGF1 signaling & downstream targets are required for alveolar formation
Parviz Minoo (United States)

12.05 – 12.20

Exploring the mRNA transcriptome of bronchopulmonary dysplasia
Cecilie Revhaug (Norway)

12.20 – 12.35

Effects of maternal folic acid supplementation on airway remodelling and allergic airway disease risk
Funda Tuzun (Turkey)

12.35 – 14.00

Lunch and Poster Viewing

Poster Presentations 1

Chairpersons: David Sweet & Virgilio Carnielli

- 13.10 – 13.15 **Identification of a regulatory alveogenesis genes cluster using a novel genetic approach**
Parviz Minoo (USA)
- 13.15 – 13.20 **Setting-up and validation of a lung-lavaged spontaneously-breathing rabbit managed in nCPAP as a model for respiratory distress syndrome**
Francesca Ricci (Italy)
- 13.20 – 13.25 **Bronchoscopic surfactant administration in newborn infants with respiratory distress syndrome: a retrospective study**
Paolo Biban (Italy)
- 13.25 – 13.30 **Surfactant reduces growth of e.coli in neonatal rabbit pneumonia**
Guido Stichtenoth (Germany)
- 13.30 – 13.35 **The effect of continuous PEEP administration during surfactant treatment on cerebral haemodynamics in intubated preterm infants: a NIRS study**
Nilufer Okur (Turkey)
- 13.35 – 13.40 **Accuracy of lung ultrasonography in the diagnosis of respiratory distress syndrome in newborns**
Ahmet Oktem (Turkey)
- 13.40 – 13.45 **Comparison of synchronized nasal intermittent positive pressure ventilation vs nasal CPAP vs high flow nasal canula in preterm infants with respiratory distress syndrome: prospective randomized study**
Merih Cetinkaya (Turkey)
- 13.45 – 13.50 **NIPPV versus Bi-level CPAP For Early Rescue Treatment of Respiratory Distress Syndrome In Preterm Infants: Preliminary Report**
Mehmet Buyuktiryaki (Turkey)
- 13.50 – 13.55 **Intubation-surfactant-extubation on continuous positive pressure ventilation (insure) strategy - five years experience in preterm infants ≤ 32 weeks gestation**
Maria Livia Ognean (Romania)
- 13.55 – 14.00 **Rescue high frequency oscillatory ventilation in newborns who fail conventional ventilation: preliminary data**
Omer Erdeve (Turkey)

Chairpersons: Afif El-Khuffash & Samir Gupta

Invited Lecture

- 14.00 - 14.30 **WHAT SHOULD WE DO ABOUT BLOOD PRESSURE IN PRETERM INFANTS?**
Eugene Dempsey (Ireland)
- 14.30 - 14.45 **Discussion**

Oral Presentations

- 14.45 - 15.00** **Intravenous paracetamol effects on closure of ductus arteriosus in extremely preterm infants**
Outi Aikio (Finland)
- 15.00 - 15.15** **Inhaled Nitric Oxide (iNO) as an adjunct gas to Neonatal Resuscitation in Premature Infants: A Pilot double blind randomized controlled safety trial**
Kris Sekar (United States)
- 15.15 - 15.30** **Oxygen load influences DNA methylation in preterm infants upon delivery room stabilization**
Maximo Vento (Spain)

15.30 - 16.00

Coffee Break

Chairpersons: Jatinder Bhatia & Rangasamy Ramanathan

Invited Lecture

- 16.00 - 16.30** **TECHNICAL ADVANCES IN SURFACTANT RESEARCH**
Boris Kramer (The Netherlands)
- 16.30 - 16.45** **Discussion**

Oral Presentations

- 16.45 - 17.00** **Analyses of synthetic surfactant protein B analogues**
Jan Johansson (Sweden)
- 17.00 - 17.15** **The effect of surfactant/polymyxin B in double-hit model of neonatal lung injury**
Andrea Calkovska (Slovakia)
- 17.15 - 17.30** **Less invasive surfactant administration (LISA) – long term pulmonary function data**
Egbert Herling (Germany)

SATURDAY, 27TH MAY 2017

Chairpersons: Eric Shinwell & Maximo Vento

Invited Lecture

08.15 – 08.45 **UPDATE ON POSTNATAL STEROIDS**
Henry Halliday (United Kingdom)

08.45 – 09.00 **Discussion**

Oral Presentations

09.00 – 09.15 **Caffeine reduces glucocorticoid-induced expression of CTGF in lung epithelial cells and fibroblasts**
Markus Fehrholz (Germany)

09.15 – 09.30 **Notch signaling in lung innate immunity cells of extremely premature infants: implications for pathogenesis of BPD**
Parviz Minoo (United States)

Chairpersons: Dominique Haumont & Naomi McCallion

Invited Lecture

09.30 - 10.00 **UPDATE ON PATHOGENESIS AND MANAGEMENT OF NEC**
Simon Eaton (United Kingdom)

10.00 - 10.15 **Discussion**

10.15 – 10.45 **Coffee Break**

Chairpersons: Ola Saugstad & Eleanor Molloy

Invited Lecture

10.45 - 11.15 **WHERE NEXT FOR BRAIN PROTECTION?**
Nicola J. Robertson (United Kingdom)

11.15 - 11.30 **Discussion**

Oral Presentations

11.30 - 11.45 **Plasma Metabolite Score Correlates with Hypoxia Time in a Newly Born Piglet Model for Asphyxia**
Maximo Vento (Spain)

11.45 - 12.00 **Docosahexaenoic acid (DHA) augments therapeutic hypothermia in a newborn hypoxia-ischemia model A proton-magnetic-resonance-spectroscopy (H¹-MRS) study in piglets**
Marianne U. Huun (Norway)

12.00 - 12.15 **Effects of Caffeine on Cerebellum Development in an Experimental Model**
Lourdes Lemus-Varela (Mexico)

Chairpersons: Bo Sun & John Kelleher

Invited Lecture

12.15 – 12.45 **HOW TO SAVE 1 MILLION LIVES A YEAR IN LOW AND MIDDLE INCOME COUNTRIES**
Wally Carlo (USA)

12.45 – 13.00 **Discussion**

13.00 – 14.30 **Lunch and Poster Viewing**

Poster Presentations 2

Chairpersons: Martin White & Eren Ozek

13.30 – 13.35 **Urinary intestinal Fatty-acid Binding Protein as a marker of intestinal ischaemia in Necrotising Enterocolitis and Acute Abdomen**
Haris Achilleos (United Kingdom)

13.35 – 13.40 **The effect of intravenous caffeine loading on cerebral blood flow and oxygenation in transitional period of preterm newborns**
Fahri Ovalı (Turkey)

13.40 – 13.45 **Influence of intensive care unit lighting on premature infants to functional brain maturation assessed by aEEG**
Nilufer Guzoglu (Turkey)

13.45 – 13.50 **MEOX2 haploinsufficiency: a novel cause of infantile pulmonary hypertension**
Olivier Danhaive (USA)

13.50 – 13.55 **Polymorphisms in endothelial nitric oxide synthase in persistent pulmonary hypertension of the newborn**
Lourdes Lemus-Varela (Mexico)

13.55 – 14.00 **Rare TBX4 variants are associated with pulmonary hypertension in neonates and infants**
Olivier Danhaive (USA)

14.00 – 14.05 **Multi-dose Vitamin D Supplementation in Preterm Infants: A Prospective Randomized Trial**
Ozlem Bozkurt (Turkey)

14.05 – 14.10 **Effect of maternal/neonatal vitamin D deficiency on development of necrotizing enterocolitis in premature infants**
Merih Cetinkaya (Turkey)

14.10 – 14.15 **Effects of perinatal factors on body mass index and exercise capacity of school-age children**
Irena Štucin Gantar (Slovenia)

14.15 – 14.20 **DNA damage as determined by comet assay in preterm infants correlates with oxygen load received upon stabilization in the delivery room**
Maximo Vento (Spain)

14.20 – 14.25	Radiation doses of Neonates undergoing X-ray Examinations in Intensive Care Units in Korea <i>Min Jee Park (South Korea)</i>
14.25 – 14.30	Turkish national multicentric online registry data for prevention of jaundice associated complications <i>Omer Erdevi (Turkey)</i>

SPiN – UPDATES

Chairpersons: Gene Dempsey & Egbert Herting

14.30 – 15.00	HOW SHOULD WE NOURISH THE PRETERM INFANT? <i>Jatinder Bhatia (USA)</i>
15.00 – 15.30	MODERN MANAGEMENT OF PDA <i>Samir Gupta (United Kingdom)</i>
15.30 – 15.45	Discussion

15.45 – 16.00 **Coffee Break**

Chairpersons: John Murphy & Ben Stenson

16.00 – 16.30	NEONATAL DRUG DEVELOPMENT: SURFACTANTS AND BEYOND <i>Mark Turner (United Kingdom)</i>
16.30 – 16.45	CHARACTERIZATION OF PORACTANT ALFA AND BUDESONIDE EXTEMPORARY COMBINATION FOR SAFE AND EFFECTIVE INTRATRACHEAL ADMINISTRATION <i>Fabrizio Salomone (Italy)</i>
16.45 – 17.15	IGF-1 and ROP <i>Luca Ramenghi (Italy)</i>
17.15 – 17.30	Discussion
17.30	CLOSING REMARKS and INVITATION TO LÜBECK <i>Eleanor Molloy (Ireland)</i>

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POSTER LIST

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COUNTRY: **USA** - ABSTRACT ID: **006**

MEOX2 HAPLOINSUFFICIENCY: A NOVEL CAUSE OF INFANTILE PULMONARY HYPERTENSION

O. Danhaive 1; C. Lizama 2; C. Chapin 1; P. Ursell 3; P. Cogo 4; A. Zovein 2; V. Nagy 5

1. Division of Neonatology, University of California San Francisco, USA; 2. Cardio-Vascular Research Institute, University of California San Francisco, USA; 3. Department of Pathology, University of California San Francisco, USA; 4. Department of Pediatrics, University of Udine, Italy; 5. Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases, Vienna, Austria

INTRODUCTION

Developmental lung disorders are heterogeneous rare diseases characterized by early onset pulmonary hypertension (PH). Mesenchyme homeobox 2 (MEOX2), highly expressed in the lung, down-regulates vascular smooth muscle cell (SMC) proliferation and migration. MEOX2 haploinsufficiency is associated with Alzheimer's disease and MEOX2 polymorphisms increase risk for adult coronary disease.

MATERIALS AND METHODS

A cohort of 40 infants with developmental lung disorders were screened for genetic variants by CGH array and a 28-gene targeted panel. MEOX2 expression was analyzed by multi-channel immunolabeling. We examined lung morphology in MEOX2 heterozygous mice.

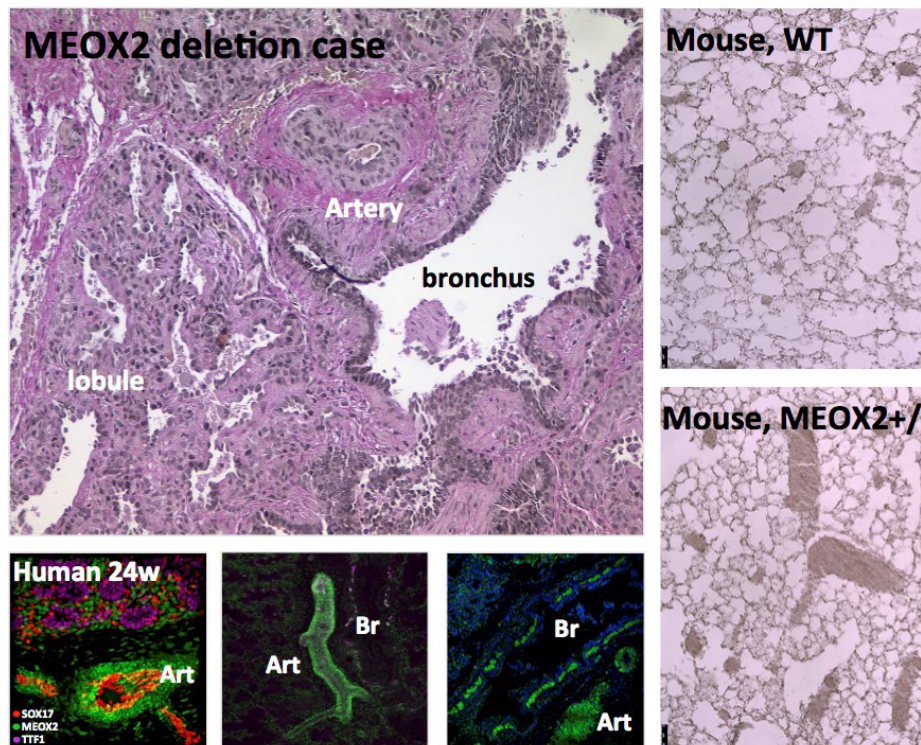
RESULTS

We identified a mono-allelic 7p21.2 deletion encompassing MEOX2 in one infant. No mutations were found in FOXF1 and TBX4, 2 genes associated with developmental lung disorders. Pathology revealed lung arrest at the pseudo glandular stage, an acinar dysplasia phenotype; interlobar and precapillary arteries had smaller lumen diameter, underlying PH. In human normal fetal lung samples, MEOX2 was increasingly expressed from 16 weeks to term in vascular but not bronchial SMC. However, the index case showed decreased/aberrant MEOX2 expression detectable both in airway and vascular SMC, which may reflect primary or secondary changes due to autopsy tissue. Heterozygous MEOX2 knockout mice showed markedly dilated vessels possibly corresponding to pulmonary vein congestion or shunt vessels, thickened pulmonary artery walls and increased radial alveolar counts, suggesting vascular developmental anomalies. Homozygous MEOX2 knockout lead to embryonic/fetal loss or early postnatal death.

CONCLUSIONS

MEOX2 plays a critical role in lung vascular/alveolar development by promoting vascular SMC differentiation and maturation. MEOX2 rare variants may be a novel cause of neonatal PH. By down-regulating essential vascular remodeling processes, MEOX2 could represent a therapeutic target in various forms of PH.

KEY WORDS: PULMONARY HYPERTENSION, GENETICS, LUNG DEVELOPMENT, VASCULAR REMODELING



Targeted Next Generation Sequencing panel (Illumina MySeq)

Pulmonary hypertension-related
and vascular development-
related genes

BMPR2, ENG, SMAD1, SMAD5, SMAD9,
ACVRL1, FOXF1, TBX4, MEOX2, CBLN1,
CRHR1, CRHBP, PPARG

Surfactant homeostasis-related
genes

SFTPA1, SFTPA2, SFTPB, SFTPC,
SFTPD, ABCA3, NKX2.1, CSF2RB

COUNTRY: **USA** - ABSTRACT ID: **009**

RARE TBX4 VARIANTS ARE ASSOCIATED WITH PULMONARY HYPERTENSION IN NEONATES AND INFANTS

O. Danhaive 1; C. Lizama 2; C. Chapin 1; P. Ursell 3; A. VanHeijst 4; F. Brasch 5; M. Griesse 6; A. Zovein 2

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INTRODUCTION

Developmental lung disorders are rare genetic diseases associated with neonatal-onset refractory pulmonary arterial hypertension (PAH), including alveolar capillary dysplasia, acinar dysplasia and others. Whereas FOXF1 variants are found in ~50% of ACD cases, other genetic causes are still largely unknown. Adult PAH TGFSS-related genes are rarely responsible for pediatric PAH (<5%). T-box transcription factor 4 (TBX4) variants were recently reported in children and adults with PAH and in one neonate.

MATERIALS AND METHODS

A cohort of 40 infants with PH and developmental lung disorders (chILD classification) were screened for genetic variants by CGH array and a custom targeted panel. Histology was assessed by two independent pathologists. TBX4 expression was analyzed by multi-channel immunofluorescence.

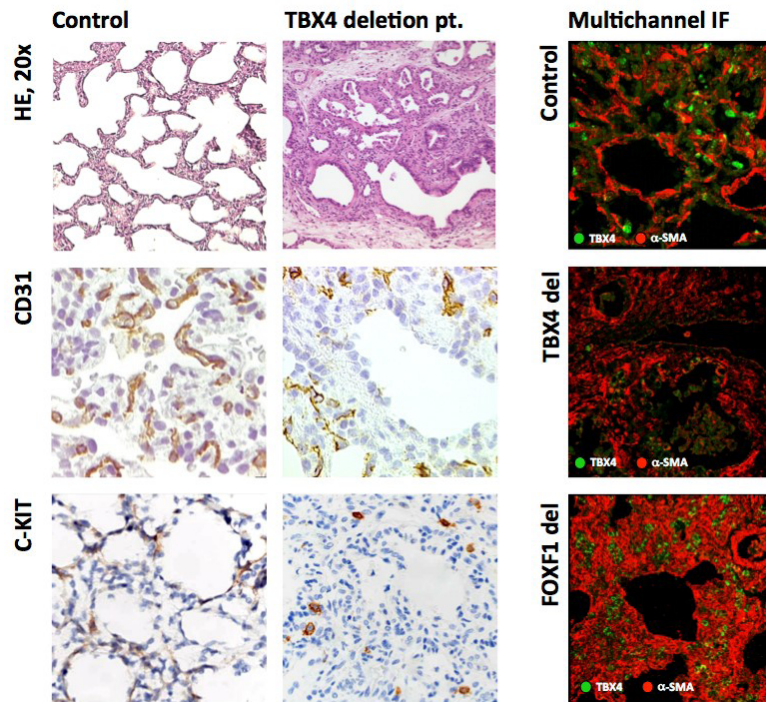
RESULTS

One infant had a 17q23 deletion encompassing 4 genes (table1), of which TBX4 was differentially expressed in lung and associated with adult/pediatric PAH. We re-tested the cohort including TBX and found 2 cases with monoallelic damaging mutations (frameshift and nonsense). Clinical onset and course was variable. Lung pathology was heterogeneous (see table) but consistently including lobular misdevelopment, developmental arrest and vascular remodeling. In fetal lung TBX4 was expressed in mesenchyme since 15 weeks. MEOX2 haploinsufficiency cases showed decreased TBX4 but normal FOXF1 expression whereas FOXF1 mutants had preserved TBX4 expression, suggesting the 2 genes are independent. Capillary density and C-kit expression were decreased, suggesting defective vasculogenesis. TTF-1 expression was markedly decreased in alveolar epithelium, possibly accounting for alveolar misdevelopment.

CONCLUSIONS

TBX4 haploinsufficiency is a novel form of developmental lung disorder resulting in early PAH. The fact that TBX4 variants were also found in later childhood PAH suggest a broad, underrecognized phenotypical and clinical variability for this rare disease.

KEY WORDS: PULMONARY HYPERTENSION, LUNG DEVELOPMENT, GENETICS, ACINAR DYSPLASIA



CASE	CLINICAL ONSET	OUTCOME	PATHOLOGY	TBX4 VARIANT	MECHANISM
#1 female, 40 weeks	3 months, PAH	death, 10 months	Acinar dysplasia	17q23.1-q23.2(58,078,171-60,316,749)x1	deletion (CA4, PPM1D, TBX4 and BRIP1)
#2 female, 36 weeks	2 months, PAH	death, 8 months	Congenital alveolar dysplasia	c.251_delG	frameshift
#3 female, 40 weeks	neonatal transient respiratory failure, PAH	alive, 2.5 years	Alveolar capillary dysplasia + desquamative interstitial pneumonitis	p.R340X	nonsense

Targeted Next Generation Sequencing panel (Illumina MySeq)

Pulmonary hypertension-related and vascular development-related genes

BMPR2, ENG, SMAD1, SMAD5, SMAD9, ACVRL1, FOXF1, TBX4, MEOX2, CBLN1, CRHR1, CRHBP, PPARG

Surfactant homeostasis-related genes

SFTPA1, SFTPA2, SFTPB, SFTPC, SFTPD, ABCA3, NKX2.1, CSF2RB

COUNTRY: **ROMANIA** - ABSTRACT ID: **021**

INTUBATION-SURFACTANT-EXTUBATION ON CONTINUOUS POSITIVE PRESSURE VENTILATION (INSURE) STRATEGY - FIVE YEARS EXPERIENCE IN PRETERM INFANTS ≤ 32 WEEKS GESTATION

M.L. Ognean; O. Boanta; E. Olariu; S. Kovacs; C. Zgârcea; R. Dumitra; D. Andreicut

Clinical County Emergency Hospital Sibiu, Neonatology Department, Sibiu, Romania

Combining early surfactant administration with early CPAP, as INSURE strategy does, has a synergistic effect on alveolar stability, the main scope of RDS therapy.

AIM

To evaluate the experience in using INSURE strategy in preterm infants with $GA \leq 32$ weeks in a regional NICU.

MATERIALS AND METHODS

The study is based on data collected in the Romanian National Registry for RDS between 2011 and 2015. All preterm infants of ≤ 32 weeks GA were included. Prenatal information and data defining the postnatal course of the infants were compared between the preterm infants successfully treated using INSURE strategy and those who needed mechanical ventilation within 72 hours after INSURE. Statistical analysis was done using SPSS for Windows 19; p was considered statistically significant if < 0.05 .

RESULTS

The study group comprised 332 preterm infants with mean GA 29.6 ± 2.2 weeks. INSURE strategy was performed in 108 cases (32.5%), successfully in 61 patients (56.4%). No differences were found as regards the prenatal and intranatal characteristics of the groups. Preterm infants who failed INSURE trial had significantly lower mean Apgar scores at 5 and 10 minutes, lower GA and BW. No differences were found as regards corticosteroid prophylaxis, surfactant dose, and duration of CPAP support. The infants in the INSURE success group had significantly shorter oxygen therapy, lower incidence of BPD ($p=0.0001$; OR 5.70), necrotizing enterocolitis, severe IVH, severe ROP, and decreased risk of death ($p=0.0001$; OR 21.85).

CONCLUSIONS

INSURE failure is associated with significantly increased rates of severe postnatal complications - bronchopulmonary dysplasia, severe intraventricular hemorrhage, retinopathy - and death. Lower GA and BW, and perinatal hypoxia are important contributors to unfavorable outcome and are associated both with INSURE failure. Identification of more clinical variables or even a clinical risk score that can be used, rapidly and easily, to select patients with greater chances for INSURE success may reduce the need for re-intubation and mechanical ventilation with their associated risks, including lung and airway trauma, hypoxic episodes, bronchopulmonary dysplasia.

KEY WORDS: INSURE, CPAP, PRETERM INFANT, OUTCOME, BRONCHOPULMONARY DYSPLASIA, INTRAVENTRICULAR HEMORRHAGE, DEATH

COUNTRY: **ITALY** - ABSTRACT ID: **023**

SETTING-UP AND VALIDATION OF A LUNG-LAVAGED SPONTANEOUSLY-BREATHING RABBIT MANAGED IN NCPAP AS A MODEL FOR RESPIRATORY DISTRESS SYNDROME

F. Ricci 1; C. Catozzi 1; X. Murgia 2; B. Rosa 1; D. Amidani 3; L. Lorenzini 1; F. Bianco 1; C. Rivetti 3; S. Catinella 1; G. Villetti 1; M. Civelli 1; B. Pioselli 1; C. Dani 4; F. Salomone 1

1. Chiesi Farmaceutici, R&D Department, Parma, Italy; 2. Department of Drug Delivery, Helmholtz Institute for Pharmaceutical Research Saarland, Saarbrücken, Germany; 3 Department of Life Sciences University of Parma Parco Area delle Scienze, Parma, Italy; 4. Department of Neurosciences, Psychology, Drug Research and Child Health, Careggi University Hospital of Florence, Florence, Italy.

INTRODUCTION

Nasal continuous positive airway pressure (nCPAP) is widely accepted as a primary treatment option in spontaneously-breathing premature infants with respiratory distress syndrome (RDS). Novel non-invasive surfactant administration methods are actively investigated for coupling surfactant replacement therapy (SRT) with nCPAP. We aim here to set up and validate a reliable RDS animal model managed on nCPAP for testing non-invasive SRTs.

MATERIALS AND METHODS

Lung injury was induced on adult rabbits by repeated bronchoalveolar lavages (BALs). To assess effective depletion, the chemical composition and biophysical properties of surfactant were monitored in BALs. Animals were randomized into two groups: no treatment (nCPAP only) and InSurE Poractant Alfa (Curosurf®) treatment. Physiological parameters were monitored at baseline, after surfactant depletion, and every 30 min after the start of nCPAP until sacrifice (180 min). Lung mechanics were evaluated at baseline, after BALs, and before sacrifice.

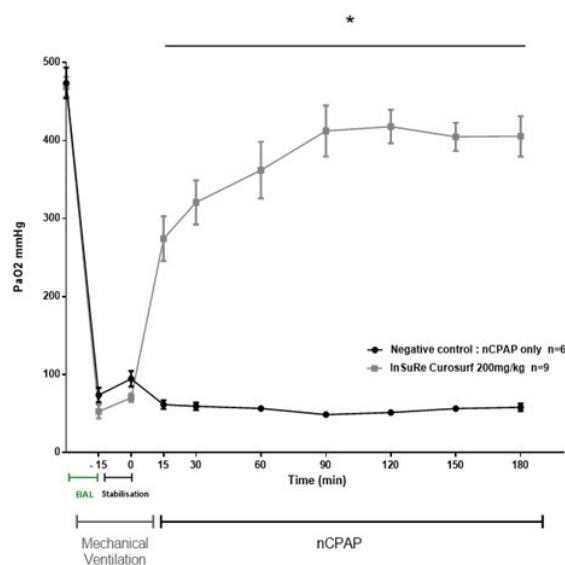
RESULTS

Surfactant depletion is a progressive process involving a gradual removal of the surfactant components. Only after the fifth BAL were the amounts of surfactant phospholipids and proteins all consistently decreased indicating effective depletion. The InSurE group showed a steep improvement of the arterial oxygen and a final pressure/volume curve indicating a higher pulmonary compliance compared to the nCPAP group (Fig.1). No signs of recovery were observed in the no treatment group. At the end of the observation period, all respiratory indices had significantly improved only in the InSurE group (Tab.1).

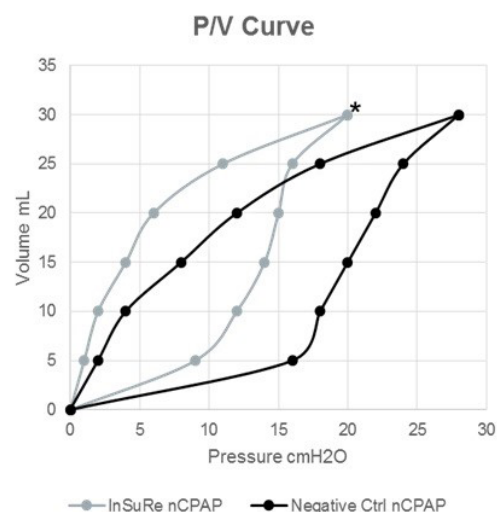
CONCLUSIONS

The lung-lavaged spontaneously-breathing adult rabbit RDS model proved to be a valuable preclinical tool for mimicking the clinical scenario of preterm infants affected by mild RDS who spontaneously breathe and do not require mechanical ventilation. This population might be of particular interest for the application of non-invasive SRTs.

KEY WORDS: NCPAP, BRONCHO-ALVEOLAR LAVAGE, SPONTANEOUSLY-BREATHING RABBIT, SURFACTANT, RDS



Statistical analysis: 2-ways ANOVA with Tukey's test
Improved oxygenation value compared to Negative control group * $p < 0.01$



* P vs. Control < 0.01

	GROUP	BASAL	RESPIRATORY DISTRESS	180 MIN
A – aDO ₂	Control	165 ± 21	488 ± 17#	504 ± 35
	InSurE	168 ± 11	529 ± 14#	244 ± 60§*
A – aDO ₂	Control	0.74 ± 0.03	0.16 ± 0.02#	0.10 ± 0.11
	InSurE	0.74 ± 0.02	0.15 ± 0.01#	0.68 ± 0.06§*
VEI	Control	0.22 ± 0.02	0.05 ± 0.01#	0.06 ± 0.02
	InSurE	0.23 ± 0.01	0.06 ± 0.01#	0.13 ± 0.02§*
OI	Control	1.2 ± 0.1	10.1 ± 1#	14.78 ± 2.23
	InSurE	1.1 ± 0	13.3 ± 1.1#	1.66 ± 0.14§*
Cdyn (ml/cmH ₂ O/kg)	Control	0.88 ± 0.05	0.2 ± 0.02#	0.45 ± 0.09
	InSurE	1.09 ± 0.02	0.31 ± 0.04#	0.80 ± 0.04§*

Table 1 Ventilation indices and dynamic compliance of surfactant- depleted rabbit. Mean Alveolar-arterial Oxygen Pressure Difference (A-aDO₂), Arterial/alveolar Ratio (a/ADO₂), Ventilation Efficiency Index (VEI), Oxygenation Index (OI), and Dynamic Compliance (Cdyn) in animals managed just with nasal CPAP (Control) and in animals treated with surfactant (InSurE) followed by nasal CPAP management. Values were recorded upon intubation (Basal), after the bronchoalveolar-lavage induced respiratory distress, and at the end of the experimental period (180 min). N=6 and N=9 in the Control and InSurE groups, respectively. # P vs. Basal values < 0.05 ; § P vs. Respiratory Distress Values < 0.05 ; * P vs. Control Group < 0.05 .

COUNTRY: **TURKEY** - ABSTRACT ID: **026**

MULTI-DOSE VITAMIN D SUPPLEMENTATION IN PRETERM INFANTS: A PROSPECTIVE RANDOMIZED TRIAL

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Department of Neonatology, Zekai Tahir Burak Maternity Teaching Hospital, Ankara, Turkey

INTRODUCTION

Preterm newborns are born with lower vitamin D stores. Although vitamin D supplementation is recommended there is no consensus regarding the adequate dose of supplementation for preterm infants. The aim is to assess the effect of three different doses of vitamin D supplementation (400, 800 and 1000 IU/d) in preterm infants ≤ 32 weeks gestation on the prevalence of vitamin D deficiency and 25 (OH) D levels at 36 weeks postmenstrual age (PMA).

MATERIALS AND METHODS

121 preterm infants with gestational age of 24-32 weeks were randomly allocated to either receive 400, 800 or 1000 IU/d vitamin D. After blood sampling for baseline 25 (OH) D, PTH, Ca, phosphorus and ALP levels daily supplementation was started and continued until 36 weeks PMA. Vitamin D deficiency was defined as serum 25 (OH) D level <20 ng/ml.

RESULTS

Of the 121 infants 71.9% had deficient vitamin D levels before supplementation. The average 25 (OH) vitamin D levels at 36 weeks PMA were significantly higher in 800 IU (40 ± 21.4) and 1000 IU group (43 ± 18.9) when compared to 400 IU group (29.4 ± 13). The rate of vitamin D deficiency (2.5 vs 22.5 ; RR: 0.09; CI:0.01-0.74) and insufficiency (30 vs 57.5 ; RR:0.32; CI:0.13-0.80) was significantly lower in 1000 IU group when compared to 400 IU group at 36 weeks PMA. The rates of respiratory distress syndrome, bronchopulmonary dysplasia and late onset sepsis were similar between 3 groups.

CONCLUSIONS

Higher doses (1000 IU/d) of vitamin D supplementation in preterm infants ≤ 32 weeks gestation age effectively decreases the prevalence of vitamin D deficiency and leads to better levels of 25 (OH) vitamin D at 36 weeks PMA. The clinical importance of biochemically sufficient levels of vitamin D need to be further assessed in preterm infants.

KEY WORDS: VITAMIN D DEFICIENCY, SUPPLEMENTATION, PRETERM, HIGH DOSE

COUNTRY: **TURKEY** - ABSTRACT ID: **034**

THE EFFECT OF INTRAVENOUS CAFFEINE LOADING ON CEREBRAL BLOOD FLOW AND OXYGENATION IN TRANSITIONAL PERIOD OF PRETERM NEWBORNS

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INTRODUCTION

Early caffeine initiation is associated with reduced rates of BPD and treatment requirement of PDA in very low birthweight infants. The aim of this study was to show whether or not early caffeine use at 4 hours of age impairs cerebral blood flow and oxygenation/hemodynamics in the transitional period of very low birthweight preterm infants.

METHODS

Caffeine was administered at an intravenous loading dose of 20 mg/kg at 4 hours of life in preterm infants born <32 weeks gestation and <1500 g. Changes of heart rate, mean systemic arterial pressure, cardiac outputs, transcutaneous oxygen saturation, cerebral blood flow, cerebral tissue oxygenation index and cerebral fractional tissue oxygen extraction were investigated before and 1, 2 and 4 hours after caffeine loading, using pulse oximeters, cranial doppler imaging and near infrared spectroscopy where appropriate. The primary outcome was the effect of caffeine on cerebral blood flow and oxygenation.

RESULTS

Twenty-two infants were studied with a mean gestational age of 28.6 ± 2 weeks and birth weight of 1054 ± 270 gram. One hour after intravenous caffeine administration, the peak systolic and mean blood flow velocity in the middle cerebral artery had decreased by approximately 19% and 18%, respectively, compared with the basal values ($p=0.002$ and $p=0.05$, respectively) and partially recovered four hours after the caffeine treatment. Although statistical significance was not found ($p=0.345$), superior vena cava flow velocity was increased 21.3% after four hours caffeine loading compared to basal value. Other serial measurements did not differ significantly.

CONCLUSIONS

This is the first observational case study to show the effect of intravenous caffeine therapy on cerebral blood flow and oxygenation in the transitional period of preterm newborn infants. Early caffeine prophylaxis increased systemic blood flow, decreased cerebral blood flow transiently and did not change cerebral tissue oxygenation index significantly.

KEY WORDS: VERY LOW BIRTH WEIGHT, CEREBRAL HEMODYNAMICS, CAFFEINE, CEREBRAL BLOOD FLOW

COUNTRY: **SPAIN** - ABSTRACT ID: **037**

DNA DAMAGE AS DETERMINED BY COMET ASSAY IN PRETERM INFANTS CORRELATES WITH OXYGEN LOAD RECEIVED UPON STABILIZATION IN THE DELIVERY ROOM

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INTRODUCTION

Oxidized DNA is increased in preterm infants resuscitated with higher oxygen concentrations. Moreover, premature infants have an immature glycosylase DNA-repair enzyme system. The alkaline comet assay detects DNA strand breaks and alkali-labile sites based on the electrophoresis of single nucleoids that if digested with specific endonucleases an ample array of DNA lesions can be detected. The nature of the substrate lesions defines the repair pathway to be studied. Therefore, identifying DNA lesions in preterm infants will allow to define which repair pathways may be immature and what type of lesions will linger and cause longterm morbidities. We aimed to assess DNA damage using comet assay in preterm infants receiving different oxygen loads during delivery room stabilization.

MATERIALS AND METHODS

Pilot study performed in preterm infants randomly assigned to lower (0.3; LowOx) or higher (0.6; HiOx) initial FiO₂ during stabilization. 500 µL of blood was obtained at 2 h after birth and 287,5 µL of PBS added to an 25µL blood aliquot.

Samples were analyzed under three conditions: lysis (Triton 100X buffer), alkaline buffer and alkaline buffer plus FPG (formamido-pyrimidine glycosylase). As negative controls THP-1 cell line (European Collection of Authenticated Cell Cultures) and as positive controls FSK cell line irradiated with X-rays were employed.

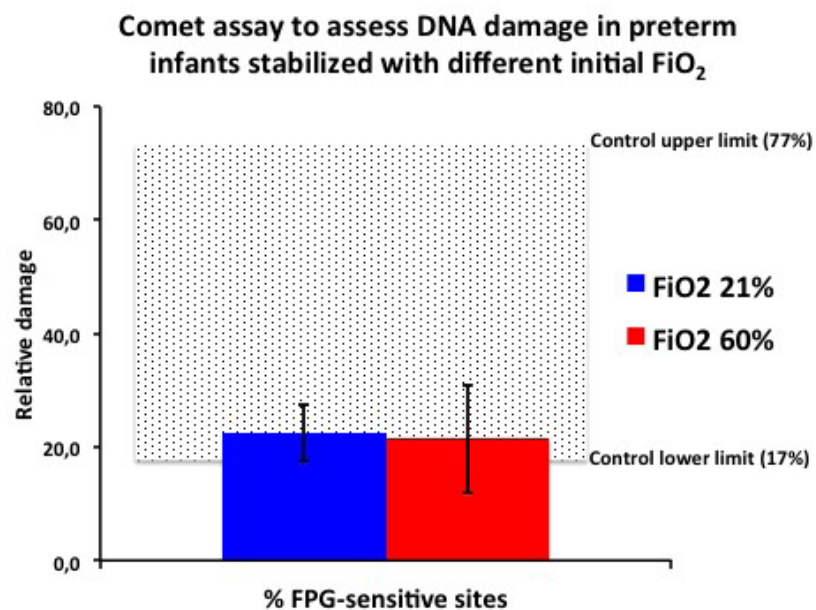
RESULTS

Degree of damage to DNA is shown in figure 1. No differences regarding perinatal characteristics were assessed. Values for lysis, buffer and buffer FPG in controls, LowOx and HiOx groups are shown in table 1. There were no differences between LowOx and HiOx groups. However, LowOx had 34.1 and HiOx 33.8% of DNA damage of higher limit buffer-FPG DNA damage. These RESULTS were 8.3% and 8.6% higher that the lower limit buffer-FPG DNA damage.

CONCLUSIONS

Preterm birth stabilization is associated with increased damage to DNA as determined by the comet assay. However, there are no differences in DNA-damage when higher (>0.6) or lower (<0.3) initial FiO₂ are employed. This is in accordance with previous RCT performed in preterm infants (Rook D et al J Pediatr 2014).

KEY WORDS: OXYGEN, PRETERM, DNA-DAMAGE, COMET ASSAY, GLYCOSYLASES



Comet assay of DNA in preterm with different initial FiO₂s

	Lysis	Buffer	FPG	% FPG Sensitive sites
LowOx iFiO ₂ (>0.3)	6.04	14.05	28.2	22.50
HiOx iFiO ₂ (>0.6)	7.50	16.14	28.93	21.45
Negative control	0	3.03	17.08	17.08
Positive control	73.3	76.16	76.56	76.56

FPG = Formamido-pyrimidine glycosylase

COUNTRY: **TURKEY** - ABSTRACT ID: **039**

RESCUE HIGH FREQUENCY OSCILLATORY VENTILATION IN NEWBORNS WHO FAIL CONVENTIONAL VENTILATION: PRELIMINARY DATA

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INTRODUCTION

High frequency oscillatory ventilation (HFOV) has been shown in experimental studies to result in less lung injury. HFOV is also used in critically ill newborns oftenly when CV fails, especially in units with lack of NO and ECMO. There is no data on the response of newborns to rescue HFOV management in the literature. We have conducted an online registry database for our country and aimed to evaluate the factors that affect the response to rescue HFOV in newborns who had CV failure in respiratory support.

MATERIALS AND METHODS

A multicentric prospective study in infants who still had respiratory failure in case of CV and switched to rescue HFOV has been conducted since May 2016. The online records of 22 collaborator NICUs around the country for the first 8 months were evaluated. Patients were grouped as survived (Group S) and dead (Group D). Characteristics of the patients such as birth weight (BW), gestational age (GA) and disease in addition to ventilator settings, arterial blood gas analysis, ventilation duration and side effects were compared between groups.

RESULTS

Two-hundred-fourty-seven patients with mean GA of 31 ± 5.3 week and mean BW of 1653 ± 1016 g were enrolled in the study. Major diseases requiring rescue HFOV were listed as respiratory distress syndrome (66%), congenital pneumonia (20.2%), sepsis (6.5%), congenital diaphragmatic hernia (4.5%), meconium aspiration syndrome (4.5%) and persistent pulmonary hypertension (4%). Patients were switched to rescue HFOV at median 36 hour of life and 78.9% of them received surfactant.

Infants who died (Group D) had lower BW (1508 ± 1031 g vs 1779 ± 989 g, $p=0.049$) and GA (30.3 ± 5.6 week vs 31.5 ± 4.9 week, $p=0.03$) in comparison to infants who survived (Group S). Cut-off levels for GA and BW in HFOV response were found to be 28.1 wk with and 1017 g. There were no correlation between side effects such as IVH, PDA, ROP and BPD could be demonstrated with the duration of rescue HFOV in groups.

CONCLUSIONS

Rescue HFOV in case of CV fail is more effective in patients with GA greater than 28 wks and BW larger than 1000 g, independent of the disease and initial rescue ventilator settings.

KEY WORDS: HIGH FREQUENCY OSCILLATORY VENTILATION, CONVENTIONAL VENTILATION, RESCUE

COUNTRY: **TURKEY** - ABSTRACT ID: **040****TURKISH NATIONAL MULTICENTRIC ONLINE REGISTRY DATA FOR PREVENTION OF JAUNDICE ASSOCIATED COMPLICATIONS**

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INTRODUCTION

The incidence and complication rates of jaundice are unknown in Turkey. We conducted an online registry database to determine the risk factors in infants who were hospitalized for jaundice, and the rate of complications due to acute bilirubin encephalopathy and kernicterus.

MATERIALS AND METHODS

A multicentric prospective study in infants born ≥ 35 weeks' gestation and hospitalized for jaundice was conducted between 2015 and 2016. The online records of 5620 patients from 50 collaborator NICUs all around the country for 12 months were evaluated.

RESULTS

The mean gestational age of patients and birth weight were 38 ± 1.6 weeks and 3102 ± 517 g, respectively. The history of siblings treated for jaundice was present in 3.4% of patients. The leading etiological entities were hemolytic jaundice (28.9%), dehydration (27.6%), breast milk jaundice (12.6%) and prematurity (8.5%). ABO blood incompatibility was the most common cause (73.7%) of the hemolytic jaundice. Two-hundred-sixty-nine infants (4.8%) received intravenous immunoglobulin in addition to phototherapy. Exchange transfusion was performed to 132 (2.3%) patients. Patients who had exchange transfusion had higher rate of hemolytic jaundice, higher reticulocyte count, longer duration of phototherapy and higher bilirubin/albumin ratio ($p < 0.05$). Logistic regression analysis demonstrated that having reticulocyte count ≥ 7 (OR: 8.83, 95% CI 3.57-21.87, $p = 0.001$) and bilirubin/albumin ratio ≥ 6.5 (OR: 21.1, 95% CI 9.6-46.3, $p = 0.001$) increased the exchange transfusion rate significantly.

Kernicterus was reported in 14 patients (0.25%). Male (85.7%) gender, hemolytic jaundice, higher reticulocyte count (≥ 7) and bilirubin/albumin ratio (≥ 6.5) were the major risk factors for the kernicterus ($p < 0.05$). Hearing loss and neurological deficiency were detected as complications in 0.35% and 0.25%, respectively.

CONCLUSIONS

Dehydration related to lack of proper feeding is one of the most common etiological factors after hemolytic jaundice. Kernicterus and neurological complications reported in our study show that jaundice is still an important public health problem among newborns, and more concentration is needed to prevent its complications.

KEY WORDS: JAUNDICE, KERNICTERUS, COMPLICATION, DATABASE

COUNTRY: **TURKEY** - ABSTRACT ID: **043**

INFLUENCE OF INTENSIVE CARE UNIT LIGHTING ON PREMATURE INFANTS TO FUNCTIONAL BRAIN MATURATION ASSESSED BY AEEG

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INTRODUCTION

Amplitude-integrated EEG (aEEG) presents a valuable tool for functional brain maturation of preterms. However the effects of enlightenment on functional brain maturation of prematures has not been investigated. In this study, the relationship between light exposure and functional brain maturation in prematures were investigated using an aEEG.

MATERIALS AND METHODS

33 prematures with gestational weeks between 30-35 weeks are involved in this study. They were randomly distributed into three groups in which different lighting protocols were applied. In group 1, the babies' incubator is covered for 24 hours. In group 2 the babies' incubator is open for 24 hours. In group 3 the babies incubator is covered for 12 hours and open for another 12 hours. The babies are evaluated with an aEEG on the third (first measurement) and tenth days (second measurement) and the Burdjalov scoring is done. Anaysis of the aEEG recordings were performed, based on the sleep-wake cycles (SWC), the upper and lower margin amplitudes, the narrowband, broadband and bandwidth of the SWC.

RESULTS

At the first measurements, the narrow band lower amplitudes in group 1 were higher than in the other groups ($p:0.03$), but the difference was not significant in the second measurement ($p:0.07$). The Burdjalov scores were higher in group 1 and group 3 on the tenth day, though this was not statistically significant ($p:0.92$). Finally, when the babies were re-evaluated according to their gestational weeks, the two groups under 34 weeks (30-31 weeks, 32-33 weeks) were similar in their Burdjalov scores, whereas 34-35 weeks had higher scores.

CONCLUSIONS

The difference observed between groups in terms of narrow band lower amplitude in the first measurement, may reflect the effect of intrauterine environment rather than enlightenment; because the measurement was made on the third day. However the fact that all groups have similar results on day 10 suggests that other factors in the intensive care setting may diminish the effect of enlightenment. Burdjalov scores are associated with maturation, and high scores in the 34-35-week group suggest a 34-week threshold for the SWC and development.

KEY WORDS: PREMATURE, AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY, NEONATAL INTENSIVE CARE UNIT, ENLIGHTMENT

COUNTRY: **TURKEY** - ABSTRACT ID: **048**

ACCURACY OF LUNG ULTRASONOGRAPHY IN THE DIAGNOSIS OF RESPIRATORY DISTRESS SYNDROME IN NEWBORNS

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INTRODUCTION

Lung ultrasonography has become an important tool in the diagnosis and follow-up of lung diseases in newborn period in recent years. Lung diseases such as pneumonia, transient tachypnea of the newborn and RDS can be diagnosed with lung ultrasound. This study is planned to see acute ultrasonographic changes after surfactant treatment in premature newborns.

MATERIALS AND METHODS

This study was performed in Hacettepe University NICU. Forty patients who were diagnosed as RDS and given surfactant were included in the study. Lung ultrasonography was performed once before surfactant treatment and three times after surfactant treatment. Post treatment ultrasonographic examinations were carried out at two hours, four hours and six hours after surfactant treatment.

RESULTS

Before surfactant treatment lung USG findings of patients were as follows; lung consolidation with air bronchograms (40/40), alveolar interstitial syndrome (36/40), pleural line abnormalities (37/40), lung pulse (37/40), decrease of lung sliding and disappearance of A-lines and spared areas (36/40) in all USG of patients. Second hour of treatment only change was disappearance of air bronchograms and lung consolidation in five patients. Four hours after treatment we have seen reduction in lung consolidation in fifteen patients, AIS partially changed to B-lines in 21 patients, appearance of A-lines and spared areas. But after six hours we started to see A-lines clearly, lost of AIS, appearance of pleural line and lung sliding nearly in all patients except four patients (Table I).

CONCLUSIONS

Lung USG is a simple, practical and low cost method in diagnosing neonatal RDS. This study further confirms that a lung ultrasound has a great significance in diagnosing neonatal RDS. However more experience is needed to replace chest X ray by lung USG in the diagnosis and treatment of RDS.

KEY WORDS: LUNG ULTRASONOGRAPHY, RESPIRATORY DISTRESS SYNDROME, SURFACTANT TREATMENT, NEWBORN

	Air bronchograms and lung consolidation	Alveolar interstitial syndrome (AIS)	Abnormal pleural line	Lung pulse	Reduction of A-lines and spared areas
Before surfactant therapy	40 (40)	36 (40)	37 (40)	37 (40)	36 (40)
2 hours after surfactant therapy	35 (40)	36 (40)	36 (40)	35 (40)	36 (40)
4 hours after surfactant therapy	25 (40)	15 (40)	18 (40)	16 (40)	22 (40)
6 hours after surfactant therapy	4 (40)	3 (40)	4 (40)	2 (40)	4 (40)

COUNTRY: **TURKEY** - ABSTRACT ID: **049**

COMPARISON OF SYNCHRONIZED NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION VS NASAL CPAP VS HIGH FLOW NASAL CANULA IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME: PROSPECTIVE RANDOMIZED STUDY

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INTRODUCTION

Non-invasive respiratory support has been increasingly used as primary ventilation mode for early management of respiratory distress syndrome (RDS) as an alternative for intubation and mechanical ventilation. The aim of this study was to compare the effects of three non-invasive respiratory support, synchronized nasal intermittent positive pressure ventilation (NIPPV), nasal continuous positive pressure (nCPAP) and high flow nasal canula (HFNC) for initial treatment of RDS in preterm infants.

MATERIALS AND METHODS

Preterm infants admitted to NICU with clinical findings of RDS were randomized into three different non-invasive respiratory support: NIPPV vs. nCPAP vs. HFNC. The primary outcome was the need of intubation within 72 hours of life. The secondary outcomes were duration of noninvasive respiratory support, duration of total oxygen usage, duration of hospitalization, death, air leaks, nasal trauma, and frequency of neonatal morbidities including bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC) and nosocomial sepsis.

RESULTS

A total of 55 infants were randomized to NIPPV (n=18), nCPAP (n=20) and HFNC (n=17). No significant differences were detected between 3 groups in terms of demographical features. The need of intubation within 72 hours of life were similar for 3 groups. Although no significant differences were detected between 3 groups in terms of BPD, ROP, IVH, NEC, sepsis, and air leaks, the duration of non-invasive respiratory support was significantly higher in HFNC group compared with NIPPV and NCPAP groups (p=0.002).

CONCLUSIONS

As initial respiratory support NIPPV, NCPAP and HFNC showed similar efficacy for prevention of intubation in preterm infants with RDS. However, infants in HFNC group had higher duration of non-invasive ventilation. We may suggest that both NIPPV and NCPAP may be preferred as initial non-invasive respiratory support in preterm infants with RDS to shorten duration of ventilation. Although HFNC has similar efficacy, the duration of this technique may limit its usage.

KEY WORDS: NON INVASIVE VENTILATION, RESPIRATORY DISTRESS SYNDROME, CPAP, HIGH FLOW NASAL CANULA, NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION

COUNTRY: **TURKEY** - ABSTRACT ID: **061**

THE EFFECT OF CONTINUOUS PEEP ADMINISTRATION DURING SURFACTANT TREATMENT ON CEREBRAL HEMODYNAMICS IN INTUBATED PRETERM INFANTS: A NIRS STUDY

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INTRODUCTION

Surfactant is a cornerstone in the treatment of respiratory distress syndrome, however there is an ongoing debate about the best and comfortable way to administer it. We hypothesized that uninterrupted respiratory support and continuous PEEP implementation while instilling surfactant via a double lumen endotracheal tube (ETT) will result in higher regional cerebral tissue oxygenation (rcSO₂) and the alteration in cerebral hemodynamics will be minimal.

MATERIALS AND METHODS

Preterm infants who required intubation in the delivery suit and with gestational age ≤ 32 weeks were enrolled. Patients whose parents' consent obtained intubated either via single lumen or double lumen ETT (Vygon®) with appropriate sizes. Following NICU admission a NIRS probe placed on the forehead and each infant monitored with INVOS 5100 device for 15 minutes and then 200mg/kg poractant alpha instilled to the patients. In single lumen ETT group, patients separated from the ventilator an orogastric tube placed in ETT tube and surfactant was instilled. In double lumen group respiratory support was not interrupted during instillation.

RESULTS

A total of 43 infants analyzed. Surfactant was instilled via single lumen ETT in 20 and double lumen ETT in 23 infants. Birthweights (1037 ± 238 vs 1152 ± 277 g) and gestational ages (28 ± 2.3 vs 29 ± 1.6 weeks) did not differed between groups. During instillation rcSO₂ levels [61.5 ($49-76$) vs 63 ($48-76$)] and ftOe levels [0.16 ($0.06-0.39$) vs 0.27 ($0.1-0.44$)] were similar ($p=0.68$ and 0.35 respectively). Baseline rcSO₂ and minimum, maximum, average rcSO₂ levels recorded two hours following surfactant instillation were similar ($p=0.73$, 0.52 , 0.16 and 0.94 respectively). Grade ≥ 3 IVH was observed in 3 (15%) vs 2 (8,6%) the difference was not statistically significant ($p=0.27$).

CONCLUSIONS

Interruption of respiratory support during surfactant instillation did not significantly altered the cerebral tissue oxygenation. These results did not support our hypothesis possibly due to small sample size and should be confirmed with further studies.

KEY WORDS: REGIONAL CEREBRAL TISSUE OXYGENATION, RESPIRATORY DISTRESS SYNDROME, INSTILLING SURFACTANT

COUNTRY: **TURKEY** - ABSTRACT ID: **062**

NIPPV VERSUS BI-LEVEL CPAP FOR EARLY RESCUE TREATMENT OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS: PRELIMINARY REPORT

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INTRODUCTION

To compare the effectiveness of nasal intermittent positive-pressure ventilation (NIPPV) with bi-level nasal CPAP (BiPAP) as a primary mode of treatment for RDS in preterm infants.

MATERIALS AND METHODS

In this prospective randomized study, preterm infants of 26-30 weeks of gestational age who were admitted to neonatal intensive care unit were screened for eligibility following parental consent. Preterm infants who suffered from RDS requiring non-invasive respiratory support were enrolled. Enrolled infants were randomized into two study groups; NIPPV or BiPAP group. Non-invasive respiratory support was delivered using the device of SLE 5000 (Specialised Laboratory Equipment, South Croydon, United Kingdom) in NIPPV group and infant flow-deriver device (Viasys Corp, Care Fusion, CA) in BiPAP group. Surfactant therapy requirement was evaluated in all preterm infants after admission. Poractant alfa was administered using MIST approach. The primary end-point, failure of non-invasive respiratory support, was compared between the groups. Short and long-term neonatal outcomes were also evaluated.

RESULTS

A total of 148 infants were enrolled for the study. There was no significant difference between NIPPV and BiPAP groups in terms of demographic characteristics. Statistically significant difference was observed between NIPPV and BiPAP groups with regard to failure of non-invasive respiratory support (30% vs 15.4%; $p=0.033$). More infants in NIPPV group required poractant alfa therapy compared to BiPAP group, however no significant difference was found (62.9% vs 50%; $p=0.12$). There was no difference between NIPPV and BiPAP group on postnatal 28th day in terms of oxygen demand and moderate to severe BPD.

CONCLUSIONS

Preliminary results showed that fewer infants required mechanical ventilation in the BiPAP group compared to the NIPPV group. Neonatal outcomes will be more clearly defined after completion of the study.

KEY WORDS: RESPIRATORY DISTRESS SYNDROME, PRETERM INFANT, NONINVASIVE VENTILATION
BiPAP, NIPPV

COUNTRY: **TURKEY** - ABSTRACT ID: **064**

EFFECT OF MATERNAL/NEONATAL VITAMIN D DEFICIENCY ON DEVELOPMENT OF NECROTIZING ENTEROCOLITIS IN PREMATURE INFANTS

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INTRODUCTION

Recent studies show that vitamin D is a key modulator of immune function and inflammation with broad regulatory effects on cells of the adaptive and innate immune system. The aim of this study was to investigate the possible association between maternal/neonatal 25-hydroxy vitamin D (25-OHD) levels and development of necrotising enterocolitis (NEC) in premature infants.

MATERIALS AND METHODS

One hundred and forty five preterm infants ≤ 36 weeks of gestation were enrolled. 25-OHD levels were determined in maternal/neonatal blood samples that were obtained at the time of admission to the neonatal intensive care unit.

RESULTS

Of the 145 enrolled patients, 26 (18 %) developed NEC. Maternal/neonatal 25-OHD levels in the NEC group were significantly lower than those of the no-NEC group ($p=0.001$ and 0.004 , respectively). In univariate logistic regression analysis, both maternal/neonatal vitamin D levels were a significant predictor of NEC (OR: 0.92 and 0.89; $p<0.001$ and $p<0.005$, respectively). However, multivariate logistic regression analysis revealed that only maternal vitamin D level was a significant predictor of NEC (OR: 0.86, $p<0.0009$).

CONCLUSIONS

This is the first study to propose a possible association between maternal/neonatal 25-OHD levels and subsequent development of NEC in preterm infants.

KEY WORDS: NECROTIZING ENTEROCOLITIS, PREMATURE INFANT, MATERNAL VITAMIN D, NEONATAL VITAMIN D

COUNTRY: **ITALY** - ABSTRACT ID: **070**

BRONCHOSCOPIC SURFACTANT ADMINISTRATION IN NEWBORN INFANTS WITH RESPIRATORY DISTRESS SYNDROME: A RETROSPECTIVE STUDY

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INTRODUCTION

we evaluated the safety, feasibility and effectiveness of surfactant administration by fiberoptic bronchoscopy in infants with respiratory distress syndrome (RDS).

MATERIALS AND METHODS

We retrospectively analyzed data of term and preterm infants with RDS admitted to our NICU/PICU (from 2003 to 2015), treated with surfactant therapy (Curosurf, Chiesi Farmaceutici, Italy) via endoscopy. Three types of flexible fiberoptic bronchoscope (outer diameter 2.5 - 3.5 mm, operative channel 1.2 mm) were used. All subjects were spontaneously breathing and supported in nCPAP. Clinical characteristics, ventilatory support modes, technical problems and complications during the procedure were evaluated.

RESULTS

Data of 59 subjects (37 M, 22 F) were reviewed. Gestational age (GA) was 32.6 ± 2.6 SD weeks (26.4-40.2). Birth weight (BW) was 2031 ± 804 SD grams (800-4190). FiO₂ before surfactant was 45% (± 9.5). FiO₂ significantly decreased by 16% after surfactant ($p < 0.001$). Oxygenation significantly improved after the procedure: PaO₂/FiO₂ ratio increased from 107 (± 29) to 218 (± 83). A-aDO₂ improved from 237 mmHg (± 69) to 94 mmHg (± 52) ($p < 0.001$). The bronchoscopic procedure lasted 4.3 ± 3.7 minutes. Minor difficulties were observed in 4 patients (6.8%) during bronchoscopy. Transient episodes of desaturation (SpO₂ $< 80\%$) were observed in 9 infants (15.3%). Eight out of 59 infants (13.6%) eventually underwent endotracheal intubation and mechanical ventilation (MV), 39.7 ± 46.7 hours after surfactant administration. Six infants (10%) developed bronchopulmonary dysplasia (BPD). Fifty-one (86.5%) patients were discharged, 7 (11.9%) transferred. One patient eventually died.

CONCLUSIONS

Bronchoscopic surfactant administration may be a safe and effective technique to improve oxygenation in neonates with RDS, as an alternative to other techniques that require direct laryngoscopy. Further controlled studies are required to confirm our preliminary observation.

KEY WORDS: SURFACTANT THERAPY, RESPIRATORY DISTRESS SYNDROME, FLEXIBLE BRONCHOSCOPY, NEWBORN

COUNTRY: **GERMANY** - ABSTRACT ID: **074**

CUROSURF® REDUCES GROWTH OF E.COLI IN NEONATAL RABBIT PNEUMONIA

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BACKGROUND

E.coli and group B streptococci (GBS) are a frequent cause of neonatal pneumonia worldwide. Clinical presentation of neonatal pneumonia and respiratory distress is similar. Both diseases are treated with surfactant and antibiotics. In neonatal GBS pneumonia surfactant treatment improves oxygenation, lung function and reduces bacterial growth.

OBJECTIVE

To study the effects of porcine surfactant on bacterial growth in an animal model of neonatal E.coli pneumonia. Methods: Neonatal near-term rabbits were tracheotomised and treated with modified porcine surfactant (200 mg/kg) or an equal volume of saline. After opening the lungs during 15 min of ventilation animals were inoculated with 5 ml/kg E.coli-suspension (108 CFU/ml). Animals were ventilated with standardized individual tidal volumes for 4h. Then, lungs were lavaged 4 times using 20 ml/kg saline. Bacterial concentration of the lavage fluid was determined.

RESULTS

The recovery of the lavage was $89 \pm 14\%$ in the control and $92 \pm 19\%$ in the surfactant treated group (mean \pm SD; n=11-12 animals per treatment group). The log 10 of bacterial concentration in the lavage fluid was 8.0 ± 0.5 in the control and 7.6 ± 0.38 in the surfactant group.

CONCLUSIONS

Porcine surfactant reduces bacterial growth in E.coli pneumonia in neonatal ventilated rabbits. Besides improvement of respiratory failure, surfactant-treatment in neonatal Gram-negative pneumonia might contribute to bacterial clearance.

KEY WORDS: N/A

COUNTRY: **UNITED STATES** - ABSTRACT ID: **081**

IDENTIFICATION OF A REGULATORY ALVEOGENESIS GENES CLUSTER USING A NOVEL GENETIC APPROACH

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Elucidation of biological pathways & key regulatory genes governing lung alveolar formation represent a major challenge. This information is necessary for developing effective & novel therapies for both neonatal(BPD) & adult(COPD) lung diseases. To elucidate the molecular networks that regulate alveogenesis, we developed a novel genetic-based approach. We generated two independent strains of mutant mice. In strain #1,TGF & in #2,PDGFA signaling were abrogated by conditional inactivation of their receptors in secondary crest myofibroblasts (SCMFs), the key mesodermal cells that drive alveogenesis, specifically during postnatal life. Both mutations produced an identical phenotype; profound alveolar hypoplasia akin to human neonatal BPD. Analysis by RNAseq of FACS-isolated SCMFs for each mutant strain identified 624 genes (405 decreased/219 increased) in the TGF&201 (143 decreased/58 increased) genes in the PDGFA lungs that were differentially expressed. Importantly, 117 of these genes are in common between the two mutant models.The 117 genes represent a cluster of potential candidate genes with key regulatory function in alveogenesis. Functional Grouping analysis revealed genes belonging to extracellular matrix (ECM), transcription factors & signaling molecules (ligands & receptors). The predominantly affected genes include various Integrins and ECM. A number of the genes represent targets of IGF1, & WNT pathways. One of these,Cyr61 is a target of IGF1. Cyr61 encodes a matricellular protein that has not been studied in the lung. We show that Cyr61 is differentially affected in a preterm lamb model of BPD in response to Mechanical Ventilation versus High Frequency Nasal Ventilation (HFNV). Importantly, homozygous deletion of Cyr61 in SCMFs results in a severe BPD phenotype. Phase II clinical trials of IGF1 have shown significant reduction in BPD and IVH. The novel approach developed by this study represents an unprecedented opportunity to elucidate the detailed mechanisms of how IGF1 and its target Cyr61 & other key regulatory pathways control alveogenesis. This information will be critical for development of effective preventive or therapeutic strategies for BPD.

KEY WORDS: N/A

COUNTRY: **UNITED KINGDOM** - ABSTRACT ID: **082**

URINARY INTESTINAL FATTY-ACID BINDING PROTEIN AS A MARKER OF INTESTINAL ISCHAEMIA IN NECROTISING ENTEROCOLITIS AND ACUTE ABDOMEN

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INTRODUCTION

Early diagnosis and prediction of severity in Necrotising Enterocolitis (NEC) and intestinal ischaemia is challenging. No specific biomarkers are currently in clinical use. We aimed to study the performance of intestinal Fatty-acid Binding Protein (iFABP), which is known to be elevated following mucosal damage, for identifying intestinal ischaemia. Secondary aims were to compare iFABP levels between NEC, other abdominal pathologies and controls, compare levels of patients treated medically or surgically, and compare pre-operative and post-operative iFABP levels.

METHODS

This was an ethically approved prospective observational study. Four groups of patients were recruited: (i) babies with NEC (Bell stage II-III); (ii) children <16 years with other acute abdominal pathologies and suspected intestinal ischaemia; (iii) term infants having a laparotomy/laparoscopy without evidence of intestinal pathology (term controls); (iv) preterm control infants, born at <32 weeks, with no suspected NEC. Patients were recruited from two centres, between May 2013 and September 2016. Urine samples were collected at different timings (recruitment, pre-operatively, post-operatively, recovery). iFABP was measured by ELISA and creatinine was measured spectrophotometrically.

RESULTS

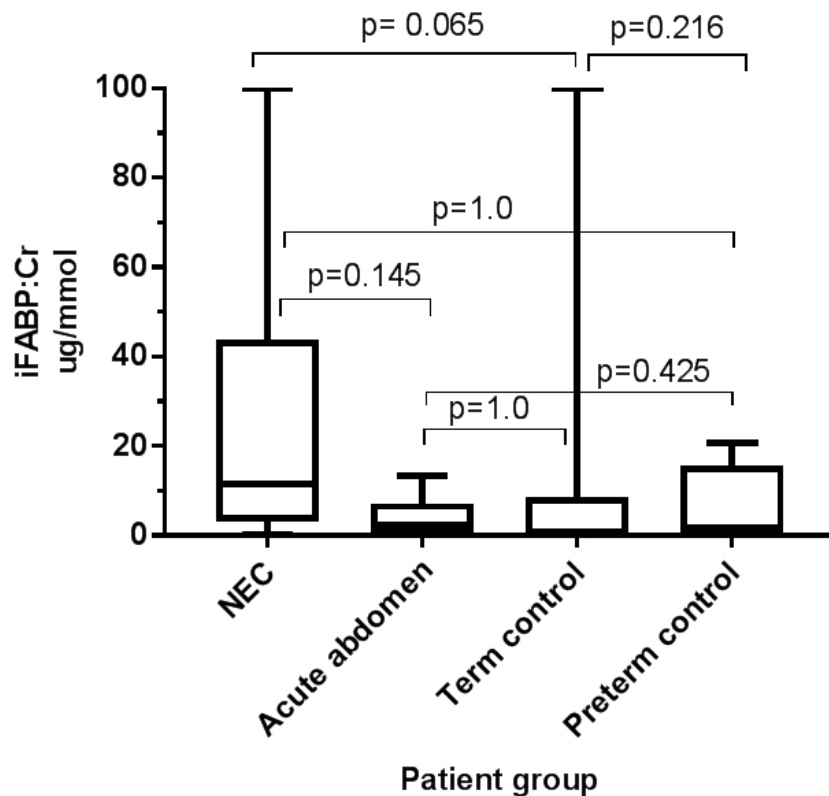
iFABP was quite variable in all groups of patients (Figure). Although the infants with NEC or acute abdomen had higher median iFABP:Cr levels, there were no significant differences between the groups. Median iFABP:Cr was higher pre-operatively vs post-operatively (Table), although the differences were not significant due to the wide variability.

CONCLUSIONS

Although iFABP is potentially useful as a marker of ischaemic bowel in conditions such as NEC and acute abdomen, the wide variation in iFABP levels in control infants may hinder the prognostic value of this test, unless combined with other markers.

KEY WORDS: IFABP, INTESTINAL FATTY-ACID BINDING PROTEIN, NECROTISING ENTEROCOLITIS, ACUTE ABDOMEN, INTESTINAL ISCHAEMIA

Figure: Initial iFABP:Cr values per patient group
(medians, 2.5th – 97.5th percentiles, Kruskal-Wallis test)



Pre-operative and post-operative iFABP:Cr values

	Median pre-operative iFABP:Cr	Median post-operative iFABP:Cr	p-value (Wilcoxon Signed-Rank test)
NEC group	12.23	4.07	0.34
Acute abdomen group	0.85	0.67	0.87
Both groups	5.43	1.67	0.48

COUNTRY: **KOREA, SOUTH** - ABSTRACT ID: **083**

RADIATION DOSES OF NEONATES UNDERGOING X-RAY EXAMINATIONS IN INTENSIVE CARE UNITS IN KOREA

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INTRODUCTION

With medical advances, the survival of preterm infants has increased and they often require multiple radiographic examinations. There are no reports on the radiation doses of neonates admitted to Neonatal Intensive Care Units (NICUs) in Korea. Therefore, this study evaluated the radiation dose of diagnostic x-rays performed in NICUs using mobile x-ray machines.

MATERIALS AND METHODS

We retrospectively analyzed the radiographs of all low-birth-weight infants (Weight <1,500g) who were admitted to Soonchunhyang University Bucheon Hospital from 2011 to 2016 regardless of whether they were discharged alive. The entrance surface doses were calculated using the non-dosimeter dosimetry formula.

RESULTS

Of 296 infants (birth weight 350–1490 g), all required at least one chest including abdomen radiograph. The subjects required a mean of 37.28 ± 6.19 radiographs per infant and 25% of the infants had more than 50 radiographs. The variation in number of radiographs taken might result from the birth weight, morbidity (e.g., respiratory distress syndrome, patent ductus arteriosus, bronchopulmonary dysplasia, necrotizing enterocolitis, and sepsis), and durations of central venous catheter insertion and hospital stay (all $p < 0.001$).

CONCLUSIONS

Low-birth-weight infants treated in our NICU had high frequency of radiation and gonad exposures compared with previous studies. Additional studies should examine how to minimize the cumulative exposure dose and how to achieve optimal image quality.

KEY WORDS: RADIATION DOSES, X-RAY, NEONATAL INTENSIVE CARE UNITS (NICUS), LOW-BIRTH-WEIGHT INFANTS

COUNTRY: **MEXICO** - ABSTRACT ID: **087**

POLYMORPHISMS IN ENDOTHELIAL NITRIC OXIDE SYNTHASE IN PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

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INTRODUCTION

Persistent pulmonary hypertension of the newborn (PPHN) is a serious condition with high morbidity and mortality, with a complex therapeutic approach. There is considerable interest in the identification of alterations in the signaling pathways that regulate pulmonary vasoconstriction, but the role of some polymorphisms has not been well defined.

OBJECTIVE

To identify polymorphisms that are involved in endothelial nitric oxide synthase (eNOS) function in newborns with PPHN.

METHODS

We included 42 infants; 21 with PPHN, confirmed by echocardiography (study group) and 21 healthy newborns (control group). DNA extraction was performed from 1 ml peripheral blood by polymerase chain reaction (PCR), with specific primers for eNOS. Prior to PCR, polymorphisms T786C and I/D (insertion/deletion) (VNTR 27 base pairs), were identified by electrophoresis in polyacrylamide gels stained with silver nitrate. For statistical analysis, we used Student's t, X² and Hardy-Weinberg equilibrium test. Statistical significance was considered when $p < 0.05$ with confidence intervals of 95%.

RESULTS

The group with PPHN had lower gestational age and lower mean body weight than the controls (35.6 ± 2.8 weeks versus 38.1 ± 1.9 ($p=0.008$) and $2,622 \pm 626$ g versus $2,992 \pm 565$ g ($p=0.05$), respectively. T/T-C/C genotype was present in 59% (13/21) of the newborns with PPHN and in 25% (5/21) of the controls [OR 4.33 (95% CI 1.15-16.2); $p=0.029$]. The I/D genotype was observed in 50% (11/21) in PPHN compared to 10% (2/21) in the control group [OR 10.4 (95% CI 1.9- 76.38); $p=0.002$]. In contrast, genotype T/T was observed in 43% (9/21) of newborns with PPHN and in 76% (16/21) of the controls [OR 0.23 (95% CI 0.06 to 0.88); $p=0.029$]

CONCLUSIONS

We found statistically significant differences in the prevalence of eNOS gene's polymorphisms in infants with PPHN. These mutations alter eNOS function and can be partially responsible for the vaso-reactivity with enhanced pulmonary vasoconstriction and the vascular remodeling present in this condition. Presence of TT/CC, I/D genotype and absence of genotype T/T can be risk factors and we speculate that they could be related to the poor response to inhaled nitric oxide shown by some infants.

KEY WORDS: PPHN, Polymorphisms, eNOS

COUNTRY: **SLOVENIA** - ABSTRACT ID: **089**

EFFECTS OF PERINATAL FACTORS ON BODY MASS INDEX AND EXERCISE CAPACITY OF SCHOOL-AGE CHILDREN

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OBJECTIVE

To identify the possible long term effects of perinatal factors on child's body mass index (BMI) and fitness capacity.

METHODS

Data from two registries, the SLOFIT database and NPIS, were linked to evaluate the potential effects of perinatal factors on children's body mass index (BMI) and exercise capacity (PFI). We analyzed SLOFIT data of 2929 children from 2016 and linked them to data of 6894 born infants (90 stillbirths and neonatal deaths excluded) at our institution in 2008. Our subjects were thus 8 (SD) years old on average. Linear regression analysis was used to assess the potential relationship between child's BMI or child's physical fitness index (PFI) and perinatal factors.

RESULTS

We identified 2929 (43%) of children in the SLOFIT database born in our institution in 2008. Child's BMI at school-age was positively associated with maternal pre-pregnancy BMI ($p<0.001$), and inversely associated with term birth ($p=0.02$) and mother's education level ($p<0.001$). Child's PFI at school-age was positively associated with school grade ($p<0.001$), birth weight ($p=0.006$), and maternal education ($p<0.001$). PFI was inversely associated with nulliparity ($p<0.001$), lower maternal education ($p=0.003$), maternal pre-pregnancy BMI ($p<0.001$), and Neonatal Intensive Care Unit (NICU) admission ($p=0.020$).

CONCLUSIONS

Maternal pre-pregnancy BMI and education level are associated with BMI and fitness capacity at the age of 8 years. Firstborns and those admitted to NICU had lower fitness capacity. Being born very preterm had no significant impact neither on BMI or PFI.

KEY WORDS: N/A

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