28th International Workshop on Surfactant Replacement

Helsinki, Finland

May 31st- June 1st, 2013

Programme

28th International Workshop on Surfactant Replacement

Helsinki, Finland
May 31st- June 1st, 2013

Chiesi
In neonatology for life

Takeda

SCIENTIFIC COMMITEE

Tore Cursedt (Stockholm, Sweden)
Henry L. Halliday (Belfast, UK)
Mikko Hallman (Oulu, Finland)
Ola D. Saugstad (Oslo, Norway)
Christian P. Speer (Wülzburg, Germany)

CHAIRPERSONS

Jatinder Bhatia (Augusta, USA)
Giuseppe Buonocore (Siena, Italy)
Virgilio P. Carnielli (Ancona, Italy)
Howard W. Clark (Southampton,UK)
Tore Curstedt (Stockholm, Sweden)
Henry L. Halliday (Belfast, UK)
Dominique Haumont (Brussels, Belgium)
Egbert Herting (Lübeck, Germany)
Jan Johansson (Stockholm,Sweden)
Boris W. Kramer (Maastricht, The Netherlands)
Eren Özek (Istanbul, Turkey)
Rangasamy Ramanathan (Los Angeles, USA)
Ola D. Saugstad (Oslo, Norway)
Christian P. Speer (Würzburg, Germany)
Bo Sun (Shanghai, China)
David Sweet (Belfast, UK)
Maximo Vento (Valencia, Spain)
Henrik Verder (Copenhagen, Denmark)
Frans Walther (Leiden, The Netherlands)

INVITED SPEAKERS

Sture Andersson (Helsinki, Finland)
Keith Barrington (Montreal, Canada)
Jatinder Bhatia (Augusta, USA)
Mats Blennow (Stockholm, Sweden)
Tore Curstedt (Stockholm, Sweden)
Henry L. Halliday (Belfast, UK)
Mikko Hallman (Oulu,Finland)
Dominique Haumont (Brussels, Belgium)
Eric Shinwell (Jerusalem, Israel)
Roger Soll (Burlington, USA)
Christian P. Speer (Würzburg, Germany)
Ben Stenson (Edinburgh, UK)

PANEL AND ROUND TABLE DISCUSSION

Giuseppe Buonocore (Siena, Italy)
Ugur Dilmen (Ankara, Turkey)
Henry L. Halliday (Belfast, UK)
Rangasamy Ramanathan (Los Angeles, USA)
Eren Özek (Istanbul, Turkey)
Ola D. Saugstad (Oslo, Norway)
Kris Sekar (Oklahoma City, USA)
Christian P. Speer (Würzburg, Germany)
Roger Soll (Burlington, USA)
David Sweet (Belfast, UK)
Maximo Vento (Valencia, Spain)

programma CFM.indd 2 22/05/13 06:52

28th International Workshop on Surfactant Replacement

Helsinki, Finland
May 31st- June 1st, 2013

Chiesi
In neonatology for life

Takeda

Dear Colleagues and Friends,

I am pleased and privileged to welcome you to Helsinki for the ***"28th International Workshop on Surfactant Replacement"***.

Since the first Meeting in 1986 the Workshop has grown. However it has maintained a special, friendly atmosphere and spirit that encourages open discussions and debate concerning safe management practices focusing on respiratory distress and oxygen uptake on our prestigious tiny patients.

The Workshop will be held at the southern tip of Helsinki by the coastline with nearby boats connecting to islands and other great cities of the Baltic Sea; and just footsteps from the center with official buildings including the University of Helsinki. In this time of the year we hope to see the sun even late in the evening.

We are looking forward to having a lively Workshop. Our speakers address the progress in research, describe the state of art and share evidence on new emerging treatment practices. The ongoing research on surfactant has broadened its horizon on systematic studies aiming to increase indications and safer administration techniques. New evidence-based guidelines on management of RDS will be helpful to appreciate where we are today in our continuous efforts to improve the future.

We thank Chiesi Farmaceutici and Takeda for their continued support and the Editors of Neonatology for publishing the proceedings of the Workshop.

Mikko Hallman

programma CFM.indd 3 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

Better Neonatal Outcomes: Oxygen, Surfactant and Drug Delivery

Friday, May 31st

09.00 – 09.20 **Welcome address**
Mikko Hallman
University of Oulu (Oulu,Finland)

Chairpersons: Tore Curstedt *(Stockholm, Sweden),* ***Ola D. Saugstad*** *(Oslo, Norway)*

09.20 – 10.15 **5th Bengt Robertson Lecture**
The Surfactant System Protects Both Fetus and Newborn
Mikko Hallman
University of Oulu (Oulu, Finland)

ORAL PRESENTATIONS

10.15 –10.30 **Modulation of phagocytosis-induced cell death (PICD) of monocytes by tlr-agonists in surfactant**
T. Orlikowski, B.W. Kramer, M Hütten, S.Dreschers
University Childrens' Hospital (Aachen,Germany)

10.30 – 10.45 **Antenatal corticosteroids decrease intra-amniotic LPS-mediated hippocampal inflammation in fetal sheep**
B.W. Kramer, E. Kuypers, R.K. Jellema, D.R.M.G. Ophelders, M. Nikiforou, T.G.A.M. Wolfs, M.W.Kempt, I. Nitsos, J. Pillow G.R. Polglase, J.P. Newnham, A.H. Jobe, S.G. Kallapur
Maastricht University Medical Center (Maastricht, The Netherlands)

10.45 – 11.00 **Can surfactant protein D inhibit HIV infection in the lung?**
J. Madsen, G.D. Gaiha, N. Palaniyar, T. Dong, D.A. Mitchell, H.W. Clark
University of Southampton (Southampton,UK)

11.00-11.30 *Coffee Break*

Chairpersons: Jan Johansson *(Stockholm,Sweden),* ***Howard W. Clark*** *(Southampton,UK)*

INVITED LECTURE

11.30 – 12.10 **New generation synthetic proteins**
Tore Curstedt
Karolinska Institute (Stockholm, Sweden)

programma CFM.indd 4 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

ORAL PRESENTATIONS

12.10 – 12.25 **New synthetic surfactant containing SP-B and SP-C analogues significantly improves lung function in preterm lambs with severe RDS**
X. Murgia, C. Rey-Santano, V. Mielgo, E. Ruiz-del-Yerro, P. Serna, A. Valls-i-Soler
Cruces University Hospital (Barakaldo, Spain)

12.25 – 12.40 **A spider silk domain for recombinant production of SP-C33 Leu - a surfactant protein C analogue in synthetic surfactant**
J. Johansson, A. Rising, A. Lindqvist, K. Nordling, M. Landreh, T. Curstedt
Karolinska Institute (Stockholm, Sweden)

12.40 – 12.55 **Expanding recognition and genetic diagnosis of lung vascular developmental disorders in children**
O. Danhaive
University of California (San Francisco, USA)

12.55 – 14.30 *Lunch & Poster Session*

***Chairpersons: Dominique Haumont** (Brussels, Belgium), **David Sweet** (Belfast, UK)*

13.55 – 14.30 **POSTER PRESENTATIONS**

Poster 1 **Surfactant use in a European cohort of very-low-gestational age (VLGA) infants. A EuroNeoNet study**
***M. Hallman, Valls-i-Soler, A. Azpeitia** on behalf of the European Neonatal Network (EuroNeoNet)*
Cruces University Hospital (Barakaldo, Spain)

Poster 2 **Surfactant replacement by aerosolisation improves lung function in children with respiratory failure**
M. Hermon, S. Boehme, K. Vergesslich, J. Golej, G. Mostafa, D. Endress, G. Burda, G. Trittenwein
Medical University of Wien (Wien, Austria)

Poster 3 **Nutritional aspects of pulmonary lipidomics - delivery of polyunsaturated fatty acids (PUFA) depending on exogenous supply**
W. Bernhard, M. Raith, R. Kunze, V. Koch, C. Maas, C.F. Poets, A. Franz
Children's Hospital - University of Tübingen (Tübingen, Germany)

Poster 4 **Rescue use of inhaled nitric oxide (iNO) in preterm infants with hypoxemic respiratory failure does not influence outcome**
K. Sekar, M. McCoy, R. Patil, M. Anderson
OU Health Sciences Center (Oklahoma City, USA)

programma CFM.indd 5 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

Poster 5 **Can oxygen saturation after birth predict respiratory distress in term newborns?**
E. Altuncu, A. Topuzoglu, H. Bilgen, E. Ozek
Marmara University School of Medicine (Istanbul, Turkey)

Poster 6 **L/S-ratio on gastric aspirate for prediction of respiratory distress syndrome in the delivery room**
H. Verder, P. Bratholm, C. Eschen, A. Hoskuldsson, M.A.B. Jewen, L. Sorenses
Holbcek Hospital University of Copenhagen (Copenhagen, Denmark)

***Chairpersons: Henry L. Halliday** (Belfast, UK), **Maximo Vento** (Valencia, Spain)*

INVITED LECTURE

14.30 – 15.10 **Delivery room management**
Roger Soll
University of Vermont College of Medicine (Burlington, USA)

ORAL PRESENTATIONS

15.10 – 15.25 **Early intravenous paracetamol therapy associated with closure of patent ductus arteriosus**
O. Aikio, T. Saarela, M. Hallman
University of Oulu (Oulu, Finland)

15.25 – 15.40 **Growth and development of VLBW infants after Less Invasive Surfactant Application under spontaneous breathing: two year follow-up of AMV - trial**
E. Herting, A. Kribs, B. Roth, R. Laux, T. Hoehn, C. Wieg, E. Kattner, S. Avenarius, A. Wense, M. Vochem, P. Groneck, U. Weller, J. Möller, C. Härtel, W. Göpel
University Hospital of Schleswig-Holstein (Lübeck, Germany)

15.40 – 15.55 **Ultrasound for estimation of lung fluid during postnatal adaptation**
L. Martelius, K. Lauerma, C. Janér, L. Süvari, O. Helve, S. Andersson
Helsinki Medical Imaging Center (Helsinki, Finland)

15.55 – 16.25 *Coffee Break*

***Chairpersons: Christian P. Speer** (Würzburg, Germany), **Virgilio P. Carnielli** (Ancona, Italy)*

INVITED LECTURE

16.25 – 17.05 **Optimization of airway medications**
Eric Shinwell
Hebrew University of Jerusalem (Jerusalem, Israel)

programma CFM.indd 6 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

ORAL PRESENTATIONS

17.05 – 17.20 **Amplification of glucocorticoid-mediated SP-B expression by physiologic levels of caffeine *in vitro* and *in vivo***
M. Fehrholz, S. Kunzmann, B.W. Kramer, C.P. Speer
University Children's Hospital (Würzburg, Germany)

17.20 – 17.35 **Surfactants from animal sources directly relax the airway smooth muscle *in vitro***
A. Calkovska, B. Uhliarova, M. Joskova, S. Franova
Comenius University (Martin, Slovakia)

17.35 – 17.50 **Airway expression of serum and glucocorticoid-inducible kinase 1 correlates with cord cortisol in newborn infants**
C. Janér, O Helve, L Süvari, O.M. Pitkänen, S. Andersson
Helsinki University Central Hospital (Helsinki, Finland)

programma CFM.indd 7 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

Saturday, June 1st

Chairpersons: ***Giuseppe Buonocore*** *(Siena, Italy)* ***Ola D. Saugstad*** *(Oslo, Norway)*

INVITED LECTURE

08:30 - 09:10 **Oxygen targets**
Ben Stenson
Simpson Centre for Reproductive Health (Edinburgh, UK)

09.10 – 09.40 **Panel Discussion**
Maximo Vento *(Valencia, Spain),* ***Ola D. Saugstad*** *(Oslo, Norway),*
Rangasamy Ramanathan *(Los Angeles, USA),*
Giuseppe Buonocore *(Siena, Italy)*

ORAL PRESENTATIONS

09.40 – 09.55 **DNA glycosylases protect the newborn mouse lung from apoptosis, cell cycle arrest and inflammation**
G.W. Rognlien, E.J. Wollen, M. Bjørås, O.D. Saugstad
University of Oslo (Oslo, Norway)

09.55 – 10.10 **Hyperoxia-mediated pulmonary inflammation in neonatal rats: protective effects of caffeine**
C. Bührer, U. Weichelt, R. Cay, T. Schmitz, M. Sifringer, E. Strauss, S. Endesfelder
Charité University Medical Center (Berlin, Germany)

10.10 – 10.25 **Caffeine and rolipram down-regulate SMAD signalling and TGF-β - stimulated CTGF and transgelin expression in lung epithelial cells**
S. Kunzmann, M. Fehrholz, I. Bersani, C.P. Speer
University Children's Hospital (Würzburg, Germany)

10.25 – 10.40 **Gene encoding kit ligand associates with bronchopulmonary dysplasia**
M.K. Karjalainen, J. Huusko, M. Mahlman, G. Toldi, M. Szabó, M. Rämet, P.M. Lavoie, M. Hallman *on behalf of Gen-BPD Study Group*
University of Oulu (Oulu, Finland)

10.40 – 11.10 *Coffee Break*

Chairpersons: ***Rangasamy Ramanathan*** *(Los Angeles, USA),* ***Bo Sun*** *(Shanghai, China)*

INVITED LECTURE

11:10-11:50 **Hemodynamics**
Keith *Barrington*
University of Montreal (Montreal, Canada)

programma CFM.indd 8 22/05/13 06:52

11:50-12:20 **Round table discussion**
Roger Soll *(Burlington, USA),* ***Kris Sekar*** *(Oklahoma City, USA),*
Ugur Dilmen *(Ankara, Turkey)*

12.20 – 14.00 *Lunch & Poster Session*

Chairpersons: ***Boris W. Kramer*** *(Maastricht, The Netherlands)*
Frans Walther *(Leiden, The Netherlands)*

13.20 – 14.00 **POSTER PRESENTATION**

Poster 7 **Is higher 25 (OH)-vitamin D level preventive for respiratory distress syndrome in preterm infants?**
S. Beken, N. Dinlen Fettah, D. Dilli, A. Zenciroğlu, N. Okumuş
Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital (Ankara, Turkey)

Poster 8 **Porcine surfactant abolishes exocytosis of alveolar type II cells induced by polymyxin B**
G. Stichtenoth, E. Herting, M. Rüdiger, A. Wemhöner
University of Lübeck (Lübeck, Germany)

Poster 9 **Valproic acid-mediated protection against hyperoxic lung injury via histone deacetylase inhibition in a neonatal rat model**
M. Cetinkaya, M. Cansev, F. Cekmez, C. Tayman, F.E. Canpolat, I.M. Kafa, E.O. Yaylagul, S.U. Sarici
Kanuni Sultan Suleyman Teaching and Research Hospital (Istanbul, Turkey)

Poster 10 **The early predictive significance of interleukin-33 (IL-33), soluble ST2 (SST2) and soluble urokinase-type plasminogen activator receptor (SUPAR) in bronchopulmonary dysplasia**
T. Tunc, F. Cekmez, E. Ince, S. Yildimir, G. Aydemir, O. Bulbut, H. Yaman, A. Coban
Gulhane Military Medical Academy (Ankara,Turkey)

Poster 11 **Molecular and ultrastructural correlates of diffuse lung disease associated with SP-C mutations**
O. Danhaive
University of California, San Francisco (San Francisco, USA)

Poster 12 **Does a brief trial of endotracheal CPAP before extubation increase the work of breathing in preterm infants?**
G. Dimitriou, A. Vervenioti, X. Sinopidis, S. Mantagos
University of Patras (Patras, Greece)

programma CFM.indd 9 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

POST CONFERENCE WORKSHOP

Chairpersons: ***Egbert Herting*** *(Lübeck, Germany),* ***Henrik Verder*** *(Copenhagen, Denmark)*

14:00-14.30 **Regionalization of neonatal medicine**
Sture Andersson
University Children's Hospital (Helsinki, Finland)
Mats Blennow
Karolinska University Hospital (Stockholm, Sweden)

14.30-15.00 **Online registration of nosocomial infections in the NICU**
Dominique Haumont
Saint-Pierre University Hospital (Brussels, Belgium)

15.00-15.15 *Discussion*

Chairpersons: ***Eren Özek*** *(Istanbul, Turkey),* ***Jatinder Bhatia*** *(Augusta, USA)*

15:15-15.45 **RBC transfusion practice and EPO**
Roger Soll
University of Vermont College of Medicine (Burlington, USA)

15:45-16:15 **Nutrient intake and neurologic outcomes of preterm infants**
Jatinder Bhatia
Georgia Health Sciences University (Augusta, USA)

16:15-16:45 *Coffee Break*

Chairpersons: ***Henry L. Halliday*** *(Belfast, UK),* ***Christian P. Speer*** *(Würzburg, Germany)*

16:45-17:15 **RDS Guidelines**
David Sweet
Royal Maternity Hospital (Belfast, UK)

17:15-17:45 **Round table discussion**
Henry L. Halliday *(Belfast, UK),* ***Christian P. Speer*** *(Würzburg, Germany),*
Roger Soll *(Burlington, USA),* ***Eren Özek*** *(Istanbul, Turkey)* ***David Sweet***
(Belfast, UK)

17:45-18:00 **Closing remarks and invitation to Valencia**
Mikko Hallman *(Oulu, Finland),* ***Maximo Vento*** *(Valencia, Spain)*

programma CFM.indd 10 22/05/13 06:52

28th International Workshop on Surfactant Replacement

Helsinki, Finland

May 31st- June 1st, 2013

Poster List

programma CFM.indd 11 22/05/13 06:52

POSTER 1

SURFACTANT (SF) USE IN A EUROPEAN COHORT OF VERY-LOW-GESTATIONAL-AGE (VLGA) INFANTS. A EURONEONET STUDY

M. Hallman, Valls-i-Soler, A. Azpeitia *on behalf of the European Neonatal Network (EuroNeoNet)*
Cruces University Hospital, Barakaldo, Spain

Background: Surfactant therapy has proven its efficacy in improving survival and decreasing morbidities in VLGA infants. However, the wide prenatal exposure to corticosteroids is believed to have reduced its need.
Aim: To determine the patterns of SF administration in over 150 NICU´s belonging to EuroNeoNet. and to evaluate the variations in practice affecting its use in a 5 year period.
Methods: SF use rate and associated risk factors were analysed in a cohort of 25,916 VLGA infants (mean GA and BW: 28.2 ± 2.4 wks and 1,132 ± 366 g) from 2006 to 2010 admitted to one of the 185 EuroNeoNet NICUs. Independent comparisons with non-parametric tests and logistic regression models were performed to predict SF use, using crude and adjusted Odd Ratios (OR) to determine perinatal and early neonatal associations; $p<0.05$. Predictive capacity of models was assessed by Hosmer- Lemeshow test and discrimination by area under ROC curve (AUC).
Results: SF therapy was required by 54.8% of all VLGA infants, percentage that remained stable throughout in the period studied (min. max values: 53.4-55.9%). Infants requiring SF therapy had a lower GA (27.3 ± 2.2 vs. 29.1 ± 2.2 wks), BW (1022 ± 328 g and 1265 ± 366 g) and 1- and 5-min Apgar scores. They were more frequently male, were less often born by C-Section, had less congenital anomalies and less exposure to prenatal corticosteroids [54.4% vs. 56.5%, OR (95%CI): 1.1 (1.02 – 1.16)]. There was a significant increase of corticosteroid use and C-section in the study's period.
The median age at SF instillation was 45 [15-132] min. Early SF instillation (<1 hr of life) was used in 31.9% of infants, proportion that remain unchanged. Adjusting for prenatal risk factors (BW, GA, Gender, 1-min and 5-min Apgar scores, mode of delivery, congenital abnormalities and corticosteroids use) Early SF-requirement was related to both, higher risk of BPD and decrease survival [OR (95%CI) : BPD: 1.6 (2.2 – 2.9); Non-Survivors 1.8 (1.6 – 2)].
Conclusion: In this large cohort of VLGA, SF use remained stable, as it was its early administration, a strong indicator for increase mortality and BDP.
Acknowledgements: We thank patients and participating NICU´s. EuroNeoNet is supported by the DG SANCO funded project EuroNeoStat II (Agreement 2008/1311).

programma CFM.indd 12 22/05/13 06:52

Chiesi
In neonatology for life
Takeda

POSTER 2

SURFACTANT REPLACEMENT BY AEROLISATION IMPROVES LUNG FUNCTION IN CHILDREN WITH RESPIRATORY FAILURE

M. Hermon*, *S. Boehme, K. Vergesslich, J. Golej, G. Mostafa, D. Endress, G. Burda, Trittenwein
Medical University of Wien, Wien, Austria

Background: Tracheal surfactant instillation has been shown to be a beneficial supportive therapy in children with surfactant dysfunction-related in case of respiratory failure and ARDS. In this context, aerosolized surfactant application is under discussion to improve alveolar deposition even with reduced surfactant doses.
Objective: The objective of this study was to investigate pulmonary function in children with respiratory failure treated with nebulization of diluted surfactant. Therefore we used Electrical Impedance Tomography (EIT), a well established technique for assessment of regional ventilation distribution.
Methods: Nine mechanically ventilated infants with respiratory failure received aerolized surfactant (Curosurf, Chiesi Pharmaceutics; 60 mg/kg BW, diluted in 10 mL 0.9% NaCl) applied endotrachealy using an Aeroneb® Solo nebulizer. Next to spirometry and hemodynamic, relative impedance changes (rel.ΔZ) by EIT as surrogate lung function parameters were recorded and analysed for right - left, ventral – dorsal, apical – middle – basal lung regions of interest (ROI). Reflecting regional distribution of VT (amplitude of rel.ΔZ) and changes in end-expiratory lung volume (EELV) by minima of rel.ΔZ. Data was recorded before, 1, 6, and 12 hours after surfactant application. Respirator settings were kept unchanged. For statistical analysis we used: mixed linear model, and a Sidak correction for multiple testing. Furthermore, RDS-score was assessed descriptively by chest X-ray before, 1 and 3 days after the intervention.
Results: Next to improved oxygenation, aerolisation of surfactant resulted in redistribution of regional ventilation**.** After surfactant application, EELV increased significantly ($p < 0.001$), especially in the dorsal lung areas as detected by EIT. Furthermore, regional ventilation distribution analysis observed a shift from ventral towards dorsal lung areas, while **t**otal lung volume was almost equally distributed between the left and right lung. Surfactant aerolisation led to an increase of regional ventilation in dorsal ROI from 34.5±5.6 % before to 51.1±9.5 % at 12 hours post aerolisation ($p < 0.001$). No changes in apical ROI could be observed, while regional aeration shifted significantly from middle (45.2±3.1 % before to 35.8±7.2 % at 12 h post aerolisation) towards basal lung areas (37.4±5.6 % before to 49.0±8.5 % at 12h post aerolisation). These findings were followed by RDS score.
Conclusions: These results implicate that aerolisation of surfactant induces an amelioration of surrogate parameters of lung function. These beneficial effects upon lung function stayed present for at least 12h. Nevertheless, in a next step the clinical relevance of surfactant aerolisation has to be proofed in comparison to tracheal bolus application.
Ethical approval: All study procedures were performed after parenteral informed consent and in accordance to the local ethical committee.

programma CFM.indd 13 22/05/13 06:52

POSTER 3

NUTRITIONAL ASPECTS OF PULMONARY LIPIDOMICS – DELIVERY OF POLYUNSATURATED FATTY ACIDS (PUFA) DEPENDING ON EXOGENOUS SUPPLY

W. Bernhard, M. Raith, R. Kunze, V. Koch, C. Maas, C.F. Poets, A. Franz
Children's Hospital - University of Tübingen, Tübingen, Germany

Background: Exogenous linoleic (LA), arachidonic (AA) and docosahexaenoic acid (DHA) are enriched in the lungs. Their supply via plasma impacts on pulmonary tissue, surfactant and macrophage homeostasis and functions. Plasma phosphatidylcholine (PC) is a major PUFA carrier, particularly of DHA.
Objective: To assess plasma concentrations of PC components as a determinant of peripheral supply with PUFA in preterm infants undergoing neonatal intensive care.
Methods: Plasma from cord blood (24-42 weeks gestational age(GA); N=144) and clinically indicated postnatal blood samples of preterm infants (24-35w GA; N=173 samples of 55 patients) were extracted and phospholipids analysed with tandem mass spectrometry. The study was approved by the local ethics committee. Data are shown as median (25^{th}-75^{th} percentile).
Results: Compared to cord plasma comprising low PC (1.09(0.91-1.28)mmol/L), plasma PC rapidly increased postnatally, comprizing 1.88 mmol/L(1.75-2.33) at d0-2, and reaching 2.76(2.24-3.03) at d3-7. This postnatal increase was independent of gestational age, and was due to an increase in PC components containing LA. In cord plasma, LA-PC comprised 27(26-29)% of total PC throughout gestation. In preterm infants, however, LA-PC rapidly increased postnatally: corrected for GA, LA-PC increased from 36(31-38)% at 24-27w to 47(41-50)% at 37-42w. This increase was at the expense of AA-PC and DHA-PC levels. In preterm infants AA-PC was 25(21-28)%, compared to 35(33-38)% in cord blood. DHA-PC was 5.2(4.5-6.1)% in preterm infants, whereas in cord blood it increased from 8(7-9)% at 24-27w to 14(9-16)% at 37-42w.
Conclusions: Plasma phospholipid homeostasis in preterm infants is markedly different from gestational age-matched fetuses in utero, which may be caused by inadequate lipid nutrition. These differences may alter pulmonary lipid homeostasis, and, therefore, might impact on surfactant lipids, mediators of pulmonary immunity and lung development.

programma CFM.indd 14 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

POSTER 4

RESCUE USE OF INHALED NITRIC OXIDE (iNO) IN PRETERM INFANTS WITH HYPOXEMIC RESPIRATORY FAILURE DOES NOT INFLUENCE OUTCOME

K. Sekar, M. McCoy, R. Patil, M. Anderson
OU Health Sciences Center, Oklahoma City, USA

Background: Routine use of iNO in preterm infants with hypoxemic respiratory failure (HRF) has shown inconsistent results.
Aim: To compare Bronchopulmonary dysplasia (BPD) and mortality outcomes in infants who received iNO as a rescue therapy for HRF.
Methods: A retrospective chart review was conducted from 01/ 2005 to 04/ 2011 from the neonatal intensive care data base. Data regarding birth weight, gestational age less than 36 weeks, date to start iNO, duration of iNO use, length of stay, number of ventilator days, type of ventilation, Oxygenation index (OI) before and after initiation of iNO observed from the closest blood gas, BPD outcomes, mortality and comorbidities such as pulmonary hypertension, necrotizing enterocolitis, grade 3 and 4 intraventricular hemorrhage were collected (n= 91). Infant were grouped as follows: those who received iNO early (started and stopped < 7 days after birth, n=51), late (started >7 days, n= 40). Analysis of the continuous variables consisted of the Wilcoxon- Mann- Whitney test and multiple logistic regression to compare outcomes.
Results: Among the survivors, incidence of BPD (oxygen requirement at discharge or 36 weeks post menstrual age) was 58.3 % in the early group and 78.9% in the late group (p= 0.15) The mortality was 53.9% in the early group and 53.7% in the late group (p=NS). Infants in the early group had a higher OI prior to initiation of iNO (Median OI= 44.4), than the late group (Median OI= 37.64), but had better response as evidenced by larger decrease in OI after iNO initiation (p=0.02) versus the late group (p= 0.06). Multiple logistic regression showed no difference in the odds of developing BPD or mortality among the two groups controlling for birth weight and comorbidities (p=0.864).
Conclusion: Use of iNO as a rescue therapy in sick preterm infants with HRF does not influence the odds of developing BPD or mortality whether administered early (< 7 days) or late (>7 days). The change in OI noted in both groups did not influence BPD outcome or mortality. Routine use of iNO in sick preterm infants with HRF should be discouraged.

programma CFM.indd 15 22/05/13 06:53

POSTER 5

CAN OXYGEN SATURATION AFTER BIRTH PREDICT RESPIRATORY DISTRESS IN TERM NEWBORNS?

E. Altuncu, A. Topuzoglu, H. Bilgen, E. Ozek
Marmara University School of Medicine, Istanbul, Turkey

Background: Studies performed in term neonates have shown that oxygen saturation (SpO2) does not reach stable values of 85% or higher until 5 minutes after birth and some healthy newborn infants need even more time. The pulse oxymetry is a noninvasive and useful approach for immediate neonatal monitoring and it gives much information not only for the assessment, but also the therapeutic decision making.
Objective: In this study, we aimed to assess if delayed increase in SpO_2 immediately after birth may predict the developing respiratory distress (RD) in healthy term newborns.
Methods: Neonates who were healthy, active with regular respiratory pattern, without a remarkable obstetric history and eligible within two minutes of life were evaluated. After cord clamping, the pulse oxymeter probe was applied to the right hand within the first two minutes of life and then SpO_2 and heart rate (HR) recordings were obtained continuously during the first 10 minutes. Infants who developed RD during follow up were assigned as “RD group”. Their SpO_2 levels at birth were compared with the SpO_2 levels of babies without any postnatal respiratory problem (normal group).
Results: There were 200 babies (vaginal:150; cesarean: 50) in the normal group and 26 infants (vaginal:15 ; cesarean: 11) in the RD group. The two groups were well balanced in terms of birthweight, length, sex and gestational age. The median SpO_2 in the first min were 69% in RD group and 70% in normal group. It was increased to 72% and 90% at five minutes, and 89% and 98% at 10 minutes in RD and normal groups, respectively. SpO_2 levels were significantly lower in infants with postnatal RD in both vaginal and cesarean deliveries compared to babies without RD which became apparent after 3 minutes of life ($p<0.0001$). Tachypnea resolved spontaneously in 22 of them within one hour. Two newborns were given supplemental oxygen in the nursery and one necessitated nasal continuous positive pressure for two days and was diagnosed as transient tachypnea of the newborn. One neonate had coarctation of the aorta. None of the infants were intubated. There were no significant differences between the median HR for each min of life among the two groups ($p<0.05$).
Conclusions: This study showed that the median SpO_2 values were lower in infants who developed RD when compared with the normal group. Application of this finding to the clinical practice might help to detect babies who may require close follow-up in the immediate postnatal period.

programma CFM.indd 16 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

POSTER 6

L/S-RATIO ON GASTRIC ASPIRATE FOR PREDICTION OF RESPIRATORY DISTRESS SYNDROME IN THE DELIVERY ROOM

H.Verder, P.Bratholm P, C. Eschen, A. Hoskuldsson, M.A.B. Jensen, L. Sorensen
Department of Pediatrics, and Department of Clinical Biochemistry, Holbaek Hospital, University of Copenhagen, Denmark

Background: Early rescue treatment of respiratory distress syndrome (RDS) with surfactant better the outcome. But only half of infants <30 weeks' gestation need surfactant. Consequently, there is need for a rapid method to identify which preterm infants have a need of surfactant treatment and should therefore be given this treatment early. Lecithin-sphingomyelin (L/S)-ratio measured on gastric aspirate by Fourier transform infra-red spectroscopy (FTIR) seem to fulfill this condition.
Methods: gastric aspirate from 40 newborns with gestational age 27 to 41 weeks were frozen at -20 C and analyzed later. Before analyses gastric aspirates were mixed in 5 sec by a vortex mixer, and 50 µL was placed in a Tensor 27 FTIR spectrometer from Bucker Optics with a BioATR unit from Micro Biolytics Inc.
Results: Different concentrations of lecithin and sphingomyelin assay kits from Cayman Chemical, AH-Diagnostics were measured by a Konelab Prime 30i instrument. The lecithin and sphingomyelin values were measured by the FTIR instrument with good results compared to the standard values. L/S-ratio is determined satisfactorily with R x R: 0,99 for the computed values (squared correlation between measured values and computed ones) and R x R: 0,89 for 10-fold cross-validation.
Conclusion: L/S values measured by FTIR may be available within a few minutes and may be used in the delivery room as guide for surfactant treatment. The next step is validation in clinical studies.

programma CFM.indd 17 22/05/13 06:53

POSTER 7

IS HIGHER 25 (OH)-VITAMIN D LEVEL PREVENTIVE FOR RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS?

S. Beken, N. Dinlen Fettah, D. Dilli, A. Zenciroğlu, N. Okumuş
Neonatal Intensive Care Unit of Dr Sami Ulus Maternity and Children Training & Research Hospital, Ankara, Turkey

Background: Experimental and observational studies have shown that vitamin D deficiency may be associated with an increased risk for non-bone diseases and/or abnormal development for the other systems of fetus.
Objective: The aim of this study is to determine the relationship between cord blood 25-hydroxyvitamin D [25 (OH) D] concentrations and the subsequent risk of respiratory distress syndrome (RDS) in preterm infants.
Methods: Between January 2012 and January 2013; 52 preterm infants, gestational age below 32 weeks, were prospectively enrolled. All babies were followed on nCPAP as an initial respiratory support and surfactant was given as an early rescue therapy. Cord blood from these newborns was tested for 25 (OH) D (Vit-D) level and low level is defined as <20 ng/mL. The patients were divided into two groups according to Vit-D status as low group (Lo-G) and normal group (No-G).
Results: Thirty-eight infants had low levels of 25 (OH) D [Lo-G: med; 6,0ng/mL (IQR:4-12), No-G: med; 21,5ng/mL (IQR:21-22,7)]. Two groups were similar for gestational age (GA) and birth weights (BW). RDS rate was significantly higher in Lo-G (n=32, 84%) compared to No-G (n=2, 17%) (p=0.001). There was a positive correlation between 25 (OH) D levels and GA (r=0.42, p=0.002). Length of hospital stay (r=-0.52, p=0.001) and duration of mechanical ventilatory support (r=-0.79, p=0.001) were negatively correlated with 25 (OH) D levels. When BW, gender, use of antenatal steroid, and 25 (OH) D level were assigned as possible risk factors, multivariate analysis showed that higher 25 (OH) D level has a two fold decreased risk for RDS [OR: 0.5, 95% CI (0.3-0.8), p=0.006].
Conclusion: Higher cord blood 25 (OH) D levels seem to be associated with decreased risk of RDS in preterms.

programma CFM.indd 18 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

POSTER 8

PORCINE SURFACTANT ABOLISHES EXOCYTOSIS OF ALVEOLAR TYPE II CELLS INDUCED BY POLYMYXIN B

G. Stichtenoth, E. Herting, M. Rüdiger, A. Wemhöner
Departments of Pediatrics, (a) University of Lübeck and (b) Technical University of Dresden

Background: Pulmonary surfactant can be used as a vehicle to transport pharmaceutical agents to the terminal air spaces of the lung. In combination with the polypeptide antibiotic Polymyxin B (PxB), modified porcine surfactant maintains surface activity while antimicrobiotic activity is preserved in vitro and in animal experiments. This combination could be useful for local treatment of severe Gram negative pneumonia. Objective: To investigate effects of Pxb/surfactant mixtures on endogenous surfactant exocytosis of alveolar type II cells (ATIIC). Methods: ATIIC were isolated from rat lungs and cultivated during 48h. Subsequently, cells were exposed to PxB and/or modified porcine surfactant for 1-5h. For comparison, negative controls were exposed to culture medium. Exocytosis was determined by the decay of intracellular stained surfactant by means of a fluorescence assay. Results: In absence of surfactant, PxB (0.1 mg/ml) significantly reduces fluorescence in ATIIC. In comparison fluorescence in negative controls remains stable. In presence of surfactant (5 or 10 mg/ml) the stimulating effects of PxB on exocytosis are reduced. Conclusion: In vitro, PxB stimulates exocytosis of ATIIC. This effect is counterbalanced by addition of modified porcine surfactant. So far, our studies are not discouraging the concept of combined treatment of PxB and surfactant.

programma CFM.indd 19 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

POSTER 9

VALPROIC ACID-MEDIATED PROTECTION AGAINST HYPEROXIC LUNG INJURY VIA HISTONE DEACETYLASE INHIBITION IN A NEONATAL RAT MODEL

M. Cetinkaya, M. Cansev, F. Cekmez, C. Tayman, F. E. Canpolat, I. Mustafa Kafa, E. Orenlili Yaylagul, S. Umit
Kanuni Sultan Suleyman Teaching and Research Hospital, Istanbul, Turkey

Background: Histone acetylation and deacetylation may play an important role in the pathogenesis of inflammatory lung diseases.
Objective: The aim of this study was to evaluate the preventive effect of valproic acid (VPA), a histone deacetylase (HDAC) inhibitor, on neonatal hyperoxic lung injury.
Methods: Thirty newborn pups were arranged in control, hyperoxia, and hyperoxia + VPA groups. Pups in the control group were kept in room air and received daily saline injections, while those in hyperoxia and hyperoxia+VPA groups were exposed to 95% O_2 and received daily saline and VPA (30 mg/kg) injections respectively, for 10 days. Histopathological, biochemical and molecular biological indicators of lung injury, apoptosis, inflammation, fibrosis and histone acetylation were evaluated in lung tissue specimens of pups in different treatment groups.
Results: VPA treatment significantly improved histopathologic grade, radial alveolar count and lamellar body membrane protein expression, while it decreased number of TUNEL(+) cells and active Caspase-3 expression. Expressions of TGFβ3 and phospho-SMAD2 proteins and levels of tissue proinflammatory cytokines as well as lipid peroxidation biomarkers were significantly reduced while anti-oxidative enzyme activities were enhanced by VPA treatment. VPA administration also reduced HDAC activity while increasing acetylated H4 protein expression.
Conclusion: The present study shows for the first time that VPA treatment ameliorates lung damage in a neonatal rat model of hyperoxic lung injury. The preventive effect of VPA against hyperoxic lung injury might involve HDAC inhibition.

programma CFM.indd 20 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

POSTER 10

THE EARLY PREDICTIVE SIGNIFICANCE OF INTERLEUKIN-33 (IL-33), SOLUBLE ST2 (sST2) AND SOLUBLE UROKINASE-TYPE PLASMINOGEN ACTIVATOR RECEPTOR (suPAR) IN BRONCHOPULMONARY DYSPLASIA

T. Tunc, F. Cekmez, E. Zeynep Ince, S. Yildirim, G. Aydemir, O. Bulut, H. Yaman, A. Coban
Department of Neonatology, Gulhane Military Medical Academy, Ankara, Turkey

Background: Serum IL-33, sST2 and suPAR have been investigated as prognostic biomarkers of inflammation.
Objective: To assess the predictive value of sST2, IL-33 and suPAR levels in preterm babies at risk of developing BPD.
Methods: In preterm babies minor than 32 weeks (n:38) serum IL-33, sST2 and suPAR levels were measured in cord blood and on postnatal 14th day. The correlation between these levels and the development and severity of BPD were analyzed.
Results: The mean gestational age (GA) and birth weight (BW) were 28,4 +- 1,5 weeks and 974 +- 153 g respectively. The BPD group (n:25) and non BPD group (n:13) were similar in regard to mean GA, BW, antenatal steroid use, chorioamnionitis, incidence of sepsis and NEC; whereas the incidence of PPROM, PDA, duration of mechanical ventilation, RDS were significantly higher in the BPD group. The mean cord blood levels of IL-33, sST2 and suPAR were not significantly different between the two groups. The mean 14th day levels of suPAR and sST2 were significantly higher in the BPD group (0,79 vs 2,33 ng/mL, p minor than 0,001; 0,32 vs 0,75 ng/mL respectively; p:0,028). IL-33 levels were also higher but not significantly (0.60 vs 1,30 ng/mL, p: 0,077). There was a significant difference between suPAR levels in patients with mild-moderate and severe BPD (p minor than 0.001). Using the ROC curve the optimum cut-off level for suPAR was 1,55 ng/mL. The correlation between 14th day suPAR levels and the severity of BPD was significant (r:0,781, p minor 0,001).
Conclusions: Postnatal 14th day serum suPAR and sST2 levels may be sensitive biomarkers in the prediction of BPD and their severity which could facilitate targeting of early prophylactic interventions. (Istanbul Medical Faculty Ethic Committee)

programma CFM.indd 21 22/05/13 06:53

POSTER 11

MOLECULAR AND ULTRASTRUCTURAL CORRELATES OF DIFFUSE LUNG DISEASE ASSOCIATED WITH SP-C MUTATIONS

O. Danhaive
University of California, San Francisco, USA

Background: SP-C mutations manifestations span from neonatal respiratory distress syndrome to adult familial pulmonary fibrosis. Besides transplant, early therapies may stabilize or improve symptoms but diagnosis is often delayed due to phenotypic and genotypic variability. Objectives: to identify SP-C mutations in a cohort of 87 children and 63 adults with idiopathic diffuse lung diseases and determine their phenotypical correlates.
Methods: we sequenced the SFTPC (SP-C) gene plus SFTPB, ABCA3 and NKX2.1 (TTF-1) and correlated genetic findings with lung tissue morphology, ultrastructure and surfactant proteins expression.
Results: 7/87 children (8%) were heterozygous SP-C mutation carriers. ABCA3 mutations were found in 14 (16%), TTF-1 deficiency in two (2%) and other genetic conditions in six (7%). No mutations were found among adults. Among SP-C mutants, median age at onset was 6 months, in occasion of a bronchiolitis episode in 4; 2 patients died, 3 were on oxygen and 2 on room air at a median follow-up of 25 months. 3 carried the I73T mutation and 1 E66K, both located in the non-BRICHOS sequence of the C-terminus propeptide. We identified 3 new mutations, A155P, P173H and V102M, all in the BRICHOS domain. Lung morphology consisted of desquamative interstitial pneumonia, but immunolabeling and transmission electron microscopy showed specific anomalies, consisting of abnormal intracellular surfactant, plus misfolded protein response in BRICHOS mutants, and aberrant proSP-C trafficking in non-BRICHOS.
Conclusions: In the Italian population SP-C mutations typically present in infancy, with variable clinical course and outcomes in part due to environmental factors. Electron microscopy studies showed specific type II cell anomalies that may be useful for early diagnosis if validated in future studies.

programma CFM.indd 22 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

POSTER 12

DOES A BRIEF TRIAL OF ENDOTRACHEAL CPAP BEFORE EXTUBATION INCREASE THE WORK OF BREATHING IN PRETERM INFANTS?

G. Dimitriou, A. Vervenioti, X. Sinopidis, S. Mantagos
Neonatal Intensive Care Unit, Department of Paediatrics, School of Medicine, University of Patras, Greece

Background: It has been suggested that preterm infants should be extubated from low-rate of intermittent mandatory ventilation, as a period of endotracheal continuous positive airway pressure (ETT-CPAP) increases the work of breathing and the likelihood of extubation failure. However, measurement of spontaneous breathing performance during a brief period of ETT-CPAP was shown to be useful in predicting the likelihood of successful extubation. The diaphragmatic pressure-time product (PTPdi), the integration of transdiaphragmatic pressure over time, reflects the energy expenditure of the diaphragm and it has been used as a measure of the work of breathing.
Objective: To compare the PTPdi in preterm infants supported by low-rate synchronous intermittent mandatory ventilation (SIMV) and ETT-CPAP. Methods: Twenty-five infants (median gestational age 29 weeks) ready to be extubated, were studied on each mode of ventilatory support for 30 minutes, in a random order. The mean PTPdi was calculated during the last minute of each period. Results: The PTPdi on ETT-CPAP compared to the PTPdi on SIMV was not significantly higher (median 163.6 vs 163.4 cmH2O*sec/min, respectively, p=0.146). Conclusion: A brief trial of endotracheal CPAP before extubation, compared to low-rate SIMV, does not increase the work of breathing in preterm infants.

programma CFM.indd 23 22/05/13 06:53

USEFUL INFORMATION

CONGRESS VENUE

Marina Congress Center

Katajanokanlaituri 6 | 00160 Helsinki - FINLAND

tel. +358 9 16661 | fax. +358 9 1666734

CONGRESS MATERIAL

BADGES

Participants will receive their names badges when collecting their Congress documents. They are kindly requested to wear their names badge during all Congress.
Please note that admission to Scietific Session is resctricted to Participants wearing their badge.

CERTIFICATE OF ATTENDANCE

The Certificate of Attendance will be distributed at the end of the Congress.

CONTINUING MEDICAL EDUCATION ACCREDITATION

UEMS – European Union of Medical Specialists: 12 credits recognized.
The "28th International Workshop on Surfactant Replacement" has been accredited by the European Accreditation Council for Continuing Medical Educational (EACCME) for the entire congress. EACCME credits are recognized Europe-wide and in North America can be exchanged for their national equivalent by contacting your national CME authority.

ORAL PRESENTATION

Speakers are kindly requested to hand their presentation to MCA Events technicians the day before their presentation, 15 minutes before the beginning of the scientific programme.

POSTERS PRESENTATION

Poster Presenters are kindly requested to hang their poster at the beginning of the first day of the Congress (May 31st) and they will take them off at the end of the last day (June 1st).
Poster number will be located on the poster panel.

OFFICIAL LANGUAGE

English is the official language of the Congress.

ORGANIZING SECRETARIAT

MCA Events srl
Via A. Binda, 34 | 20143 Milan, Italy
Tel: +39 (0) 02 34934404 | Fax: +39 (0) 02 34934397
www.mcascientificevents.eu | www.mca-group.eu

28th International Workshop on Surfactant Replacement has been organized with the unrestricted grant of Chiesi and Takeda.

programma CFM.indd 24 22/05/13 06:53

28th International Workshop on Surfactant Replacement

Helsinki, Finland
May 31st- June 1st, 2013

Chiesi
In neonatology for life

Takeda

1986.....Amsterdam, The Netherlands
1987.....Mantua, Italy
1988.....Belfast, UK
1989.....Göttingen, Germany
1990.....Sestri Levante, Italy
1991.....Heviz, Hungary
1992.....San Sebastian, Spain
1993.....Oslo, Norway
1994.....Jerusalem, Israel
1995.....Versailles, France
1996.....Tübingen, Germany
1997.....Stockholm, Sweden
1998.....Belfast, UK
1999.....Skagen, Denmark
2000.....Kos, Greece
2001.....Edinburg, UK
2002.....Cagliari, Italy
2003.....Prague, Czech Republic
2004.....Vienna, Austria
2005.....Belfast, UK
2006.....Oslo, Norway
2007.....Ancona, Italy
2008.....Brugge, Belgium
2009.....Ljubljana, Slovenia
2010.....Moscow, Russia
2011.....Istanbul, Turkey
2012.....Lisbon, Portugal
2013.....Helsinki, Finland
2014.....Valencia, Spain

programma CFM.indd 25 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

NOTES

programma CFM.indd 26 22/05/13 06:53

Chiesi
In neonatology for life
Takeda

NOTES

programma CFM.indd 27 22/05/13 06:53

29th International Workshop on Surfactant Replacement

Chiesi
In neonatology for life

Takeda

programma CFM.indd 28 22/05/13 06:53