

The 64th Congress of Japan Society
for Neonatal Health and Development

The 3rd Taiwan-Korea-Japan Joint Congress on Neonatology



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Wednesday, November 27, 2019

SHIROYAMA HOTEL kagoshima (formerly Shiroyamakanko Hotel), Japan

President

Satoshi Ibara

(Director, Perinatal Medical Center and Department of Neonatology, Kagoshima City Hospital, Japan)

Secretariat

Perinatal Medical Center Kagoshima City Hospital

37-1, Uearata-Cho, Kagoshima-city, Kagoshima, 890-8760, Japan

Program at a glance

November 27, Wed

2F Crystal garden A

9:30-9:40	Opening Remark Satoshi Ibara (Kagoshima City Hospital)
9:40-10:10	Key Note Speech The need for standardization of neonatal care for the extremely preterm infants among the Joint Congress Countries Lecturer: Satoshi Kusuda (Kyorin University)4 Chairman: Takashi Kusaka (Kagawa University)
10:10-11:20	Oral Presentation 1 Chairmans: Masanori Iwai (Kumamoto University) Hung-Yang Chang (MacKay Children's Hospital)
11:20-12:00	Special Lecture 1 (Taiwan) Hemodynamic instability during postnatal transition and its clinical impact in preterm neonates Lecturer: Reyin Lien (Chang-Gung University School of Medicine/Taiwan Society of Neonatology)8 Chairman: Masahiro Hayakawa (Center for Maternal-Neonatal Care Nagoya University Hospital)
12:00-13:10	Lunch or Poster Viewing
13:10-13:50	Special Lecture 2 (Japan) A diagnostic dilemma for bronchopulmonary dysplasia—Its definition and prognostication— Lecturer: Fumihiko Namba (Saitama Medical University)10 Chairman: Hidehiko Nakanishi (Kitasato University)
13:50-15:00	Oral Presentation 2 Chairmans: Hidetoshi Taniguchi (Osaka University) Chang Ryul Kim (Hanyang University)
15:00-15:40	Special Lecture 3 (Korea) Prevention of human milk acquired cytomegalovirus infection in very low birth weight infants Lecturer: Ellen Ai-Rhan Kim (Asan Medical Center Children's Hospital, University of Ulsan College of Medicine Seoul, Korea)12 Chairman: Shigeharu Hosono (Jichi Medical University Saitama Medical Center)
15:40-16:00	MOU Ceremony and Closing Tomohiko Nakamura (Nagano Children's Hospital)

Master of Ceremony: **Hiroko Iwami** (Osaka City General Hospital)

Key Note Speech

Chairman: Takashi Kusaka (Kagawa University)

The need for standardization of neonatal care for the extremely preterm infants among the Joint Congress Countries

Satoshi Kusuda (Kyorin University)

Key Note Speech

The need for standardization of neonatal care for the extremely preterm infants among the Joint Congress Countries



Satoshi Kusuda

Pediatrics, Kyorin University

Taiwan, South Korea, and Japan have good treatment results for premature infants and are well known internationally. However, treatment methods for preterm infants in each country and between countries are not necessarily standardized. Therefore, many parts depend on the experience of each facility and each country. If treatments are not standardized, research for further prognostic improvement is difficult. Also, the difference in prognosis between facilities remains and increases. Furthermore, international comparison is also difficult. Therefore, in the three countries participating in this Congress, it is important to standardize the treatment of preterm babies under gestational age 28, which requires special experience, among the treatment of preterm infants. The three countries have a system for registering the prognosis of premature infants, and standardization through information exchange is never a difficult task. If standardized, a standardized treatment manual can be created. Furthermore, joint research in the three countries may also be developed. Moreover, since this standardized treatment can be taught, many trainees can be accepted from abroad. Furthermore, standardized treatment methods can be transmitted to the world. This is a valuable organization, so please consider it positively.

EDUCATION

Medical

School of Medicine
Osaka City University
1972 - 1978

PROFESSIONAL EXPERIENCE

Visiting Professor
Pediatrics
Kyorin University
2017-present

DIRECTOR

Professor of Neonatal Medicine
Maternal and Perinatal Center
Tokyo Women's Medical University
2008-2017

Associate Professor of Neonatology
Maternal and Perinatal Center
Tokyo Women's Medical University
2003 - 2005

Staff Neonatologist, Department of Neonatology
Osaka City General Hospital
1993 - 2003

Staff Pediatrician, Department of Pediatrics
Children's Hospital of Osaka City
1988 - 1993

Special Lecture 1 (Taiwan)

Chairman: Masahiro Hayakawa

(Center for Maternal-Neonatal Care Nagoya University Hospital)

Hemodynamic instability during postnatal transition and its clinical impact in preterm neonates

Reyin Lien

(Chang-Gung University School of Medicine/Taiwan Society of Neonatology)

Special Lecture 2 (Japan)

Chairman: Hidehiko Nakanishi

(Kitasato University)

A diagnostic dilemma for bronchopulmonary dysplasia
—Its definition and prognostication—

Fumihiko Namba (Saitama Medical University)

Special Lecture 3 (Korea)

Chairman: Shigeharu Hosono

(Jichi Medical University Saitama Medical Center)

Prevention of human milk acquired cytomegalovirus infection in very low birth weight infants

Ellen Ai-Rhan Kim

(Asan Medical Center Children's Hospital, University of Ulsan College of Medicine Seoul, Korea)

Hemodynamic instability during postnatal transition and its clinical impact in preterm neonates



Reyin Lien

*Dept. of Pediatrics, Chang-Gung University School of Medicine, Taiwan
/Taiwan Society of Neonatology, Taiwan*

Fetal-to-neonatal circulatory transition is a complex process involving termination of fetal-placental circulation, decrease in neonatal pulmonary vascular resistance, and postnatal re-routing/closure of DA, PFO and ductus venosus shunts. Mal-adaptation of such transition may result in compromised end-organ perfusion and disturbed cellular oxygen metabolism. Preservation of hemodynamic homeostasis is especially challenging during transition to extra-uterine life in very preterm neonates. Of utmost concern is the abnormal hemodynamic adaptation, together with suboptimal pulmonary function from immature lungs, which leads to compromised cerebral haemodynamics and insufficient oxygen supply to brain tissue.

In the past decades, pathophysiological linkage of transitioning hemodynamic instability and brain injury in premature birth has been studied, first in animal models and, more recently, by applying sophisticated monitoring devices developed along with fast-advancing technology. Nevertheless, a clear causal-effect relationship between disturbed macro-circulation (cardiovascular performance), end-organ perfusion, cellular injury, and the exact operating mechanisms of maintaining cerebral hemodynamic homeostasis, remain to be elucidated.

A healthy cardiopulmonary system is defined by its ability to adequately deliver sufficient oxygen to meet metabolic demands of the tissues. In care of preterm infants, ensuring hemodynamic stability to provide sufficient oxygen to the brain, and thus minimize brain injury, is our ultimate goal.

Dr. Reyin Lien was born in Taipei, Taiwan and received her medical degree from Taipei Medical College, Taipei, Taiwan in 1981. She then went into the field of pediatrics and further specialized in neonatal-perinatal medicine.

POSTGRADUATE TRAINING

- | | |
|-----------|---|
| 1981-1983 | Resident in Pediatrics, Chang-Gung Memorial Hospital, Taipei, Taiwan |
| 1984-1987 | NIH Post-graduate Trainee, Department of Physiology University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania USA |
| 1987-1990 | Resident in Pediatrics, Milton S. Hershey Medical center, Pennsylvania State University School of Medicine, Hershey, Pennsylvania USA |
| 1990-1993 | Fellow in Neonatal-Perinatal Medicine, Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania USA |

ACADEMIC & HOSPITAL APPOINTMENT

- | | |
|---------------|--|
| 1990-1993: | Clinical Instructor, Department of Pediatrics University of Pennsylvania School of Medicine, Philadelphia, USA. |
| 1993-1995: | Associate Physician, Children's Hospital of Philadelphia, University of Pennsylvania Philadelphia, USA. |
| 1993-1995: | Clinical Assistant Professor, Department of Pediatrics Thomas Jefferson University School of Medicine, Philadelphia, Pennsylvania USA. |
| 1995-present: | Attending Physician, Division of Neonatology Chang-Gung Medical Center, Taoyuan, Taiwan. |
| 1997-2015: | Assistant Professor, Dept. of Pediatrics, Chang-Gung University School of Medicine, Taoyuan, Taiwan. |
| 2005-2014: | Chief, Division of Neonatology, Chang-Gung Medical Center, Taoyuan, Taiwan. |
| 2015-present: | Associate Professor, Dept. of Pediatrics, Chang-Gung University School of Medicine, Taoyuan, Taiwan. |
| 2017-present | Executive Director, Taiwan Society of Neonatology |

RESEARCH INTEREST

- Hypoxic ischemic tissue injury and related diseases in the neonates
- Developmental maturation of breathing mechanics
- Fetal-Neonatal hemodynamic instability and brain injury caused by preterm birth

A diagnostic dilemma for bronchopulmonary dysplasia—Its definition and prognostication—

Fumihiko Namba

Department of Pediatrics, Saitama Medical Center, Saitama Medical University, Japan



Bronchopulmonary dysplasia (BPD) is one of the most common and severe sequelae of extremely preterm birth. The incidence of BPD has remained elevated in Japan despite many advances in neonatal care. BPD not only causes relatively high early infant mortality, but can also result in long-term impairments of pulmonary function. Although there is currently no effective and safe treatment for BPD, novel therapeutics, such as cell-based therapy using mesenchymal stromal cells and treatment with recombinant insulin-like growth factor-1, have been under development. The definition of BPD has gradually evolved, since the initial descriptions of the disease in 1967 by Northway. Shennan suggested definition of utilizing the supplemental oxygen requirements at 36 weeks postmenstrual age (PMA). In 2000, the severity based definition, which categorizes BPD as mild, moderate, or severe according to the respiratory support provided at 36 weeks PMA among very preterm infants treated with supplemental oxygen for at least 28 days, was constructed (NIH consensus definition). However, the validity and utility of these commonly used definitions have been questioned, because it has been reported that (1) there is an inconsistent correlation with long-term respiratory outcomes, (2) oxygen/respiratory support at 40 weeks, not at 36 weeks, is the best predictor for serious respiratory morbidity, and (3) regardless of supplemental oxygen use, respiratory support at 36 weeks PMA best predicted early childhood morbidity. This lecture summarizes the therapeutic potential of novel treatments, in addition to controversies found in the definition of BPD and introducing a prospective multicenter cohort study, which is planned in Japan with the objective of identifying a better definition and perinatal risk factors for BPD.

EDUCATION

- 2009 Ph.D. Department of Pediatric and Neonatal- Perinatal Research, Graduate School of Medicine, Osaka University
- 1999 M.D. Faculty of Medicine, Okayama University

PROFESSIONAL EXPERIENCE

- 2018- Associate Professor of Pediatrics, Saitama Medical University
- 2013-2018 Assistant Professor of Pediatrics, Saitama Medical University
- 2009-2013 Postdoctoral Fellow, The Children's Hospital of Philadelphia
- 2009 Research Fellow, Department of Neonatology, Osaka Medical Center and Research Institute for Maternal and Child Health
- 2004-2005 Clinical Fellow, Department of Neonatology, Okayama Medical Center
- 2002-2004 Clinical Fellow, Department of Neonatology, Osaka Medical Center and Research Institute for Maternal and Child Health
- 2002 Resident, Department of Neonatology, Okayama Medical Center

ACADEMIC APPOINTMENTS

- 2018-2021 Councilor, Japan Society of Perinatal and Neonatal Medicine
- 2018- Member, Cochrane
- 2016- Member, Society for Pediatric Research
- 2016-2020 Councilor, Japan Society for Neonatal Health and Development
- 2014-2020 Deputy secretary-general, Japan Society of Perinatal and Neonatal Medicine

HONORS & AWARDS

- 2018 Japan Pediatric Society Academic Research Award
- 2012 Distinguished Research Trainee Awards Nominee, The Children's Hospital of Philadelphia Research Institute

Prevention of human milk acquired cytomegalovirus infection in very low birth weight infants



Ellen Ai-Rhan Kim

*Asan Medical Center Children's Hospital, University of Ulsan College of Medicine Seoul,
Korea*

Human milk is the best source of nutrition for VLBW infants, however, human milk is not always safe due to possible presence of maternal cytomegalovirus (CMV) that can be shed and transferred to their breastfeeding neonate. It has become important to find a preventive method of preparation of human milk to reduce human milk transmitted CMV infection. Some studies report the association of CMV-acquired infection to an increased risk of neurodevelopmental impairment later on. Pasteurization, freezing, ultraviolet-C or microwave irradiation could be used with variable efficacy in reducing human milk acquired CMV infection. We conducted a prospective study to compare the effectiveness of CMV inactivation in human milk of three different preparation methods; Freeze-thawing (FT), low temperature holder pasteurization (LP), and high temperature short-term pasteurization (HP). A total of 158 VLBW infants whose gestational age was less than 32 weeks or birth weight less than 1,500 gram were enrolled. Positivity of CMV PCR of less than 7 days old human milk was 42%. Out of 158 enrolled VLBW infants, 7 infants acquired CMV (4.4%) of which 2 were symptomatic. CMV DNA titer showed unimodal kinetics in most enrolled patients and significantly decreased titers after freezing or pasteurization, however, the acquired rate of CMV via human milk did not show statistical difference among groups of FT, LP, HP preparation. Further research is needed to determine the effectiveness of pasteurization to reduce the risk of CMV infection in VLBW infants, especially in CMV endemic countries.

EDUCATION

1979 Vanderbilt University, B.S. Nashville, Tenn., USA
1984 Yonsei College of Medicine, M.D., Seoul, Korea

CERTIFICATES

Certificate of Medical Doctor, Korea (1984)
Certificate of Pediatric Board, Korea (1988)
Albert Einstein College of Medicine, Montefiore Medical Center, Residency in Pediatrics (1993)
License to practice in New York (1994)
American Board of Pediatrics (1994)
Albert Einstein College of Medicine, Department of Neonatology, Montefiore Medical Center, Fellowship in Neonatology (1996)
American Board of Perinatal - Neonatology Subspeciality (2001)

International Board Certified Lactation Consultant (IBCLC)
Certificate of NRP provider, USA
American Academy of Pediatrics and American Heart Association- Neonatal Resuscitation Program Instructor, Regional Trainer, USA
Certificate of Pediatrics Advanced Life Support, USA
Certificate of Basic Life Support, USA
Certification of attendance (2014 HRPP Symposium): From Policy to Practice

APPOINTMENTS

1997-2001 Assistant professor, University of Ulsan College of Medicine, Asan Medical Center
2001-2006 Associate professor, University of Ulsan College of Medicine, Asan Medical Center
2006-present Professor, University of Ulsan College of Medicine, Asan Medical Center
2009-2011 Chair, Educational Committee, Korean Society of Neonatology
2003-2017 Chief, Division of Neonatology, Asan Medical Center Children's Hospital
2008-2017 Director, Division of Neonatology, Asan Medical Center Children's Hospital
2009-present Chair, NS Committee, Korean Association of Cardiopulmonary Resuscitation
2009-2013 Chair, Subspeciality Board Committee, Korean Society of Neonatology
2015-2017 President, Seoul-Kyung Ki District, Korean Society of Neonatology
2015-present Committee member of Korean Neonatal Network
2017-present Committee member of Baby Friendly Hospital Initiative, Korean committee for UNICEF
2018-present President, Korean Society of Breastfeeding Medicine

Oral Presentation 1

Chairmans: Masanori Iwai (Kumamoto University)
Hung-Yang Chang (MacKay Children's Hospital)

- JO-01** Prognosis of patients with trisomy 18 after cardiac surgery -An analysis of the perinatal medical centers in Hiroshima City -
Masahiro Tahara Tsuchiya General Hospital
- JO-02** Differences in the components of the metabolic syndrome between preschool children who were born prematurely and were born as term infants
Jungha Yun Seoul National University Children's Hospital
- JO-03** Reduced lung function at preschool age in survivors of VLBW preterm infants
Yi-Ya Huang MacKay Children's Hospital
- JO-04** Role of endothelial cells in the ductus arteriosus remodeling
Junichi Saito Yokohama City University/Yale University
- JO-05** Length: An important anthropometric marker for predicting retinopathy of prematurity in preterm infants
Seong Phil Bae Soonchunhyang University Hospital
- JO-06** Ultrasonographic confirmation of endotracheal intubation in extremely-low-birth-weight infants
Syusuke Takeuchi Ibaraki Children's Hospital

Prognosis of patients with trisomy 18 after cardiac surgery -An analysis of the perinatal medical centers in Hiroshima City -

Masahiro Tahara¹, Rie Fukuhara², Yutaka Nishimura³, Norioki Ohno⁴, Risa Morita¹, Kotaro Urayama¹, Mitsunobu Sugino¹, Kazuya Sanada¹, Tetsuya Nitta¹, Saiko Shimozono¹

¹ Department of Pediatrics, Tsuchiya General Hospital, Japan, ² Department of Neonatology, Hiroshima Prefectural Hospital, Japan, ³ Department of Neonatology, Hiroshima City Hiroshima Citizens Hospital, Japan, ⁴ Department of Pediatrics, Hiroshima University Hospital, Japan

The major causes of death in patients with trisomy 18(T18) are heart failure and pulmonary hemorrhage due to congenital heart disease. And we reported that the prevalence of a medial defect of the small pulmonary arteries was high in the patients with T18. To clarify the effectiveness of cardiac surgery in patients with T18, we retrospectively analyzed 47 consecutive patients with T18 and congenital heart diseases who had been hospitalized in perinatal medical centers in Hiroshima city between 2006 and 2015. Thirty patients underwent cardiac surgery (Group C), and the remaining 17 patients did not receive surgical cardiac intervention (Group N). The extubation ratio was significantly higher in Group C(9/15, 60%) than in Group N(3/13, 23%)($p<0.05$). Twenty-eight of the 47 patients presented with apnea (obstructive, $n=21$; central, $n=4$; mixed, $n=3$), and 10 patients underwent tracheotomy. Twenty patients (43%) had a history of convulsions. The discharge rate was significantly higher in Group C (26/30, 87%) than in Group N (2/17, 12%) ($p<0.01$). Survival rates were significantly higher in Group C than in Group N (Group C: 100%, 87%, 84% and 53%; Group N: 77%, 35%, 0% and 0% at the ages of 1month, 6months, 1year, and 3years, respectively; $p<0.01$ each). The major causes of death were cardiac-related (5/15, 33%) and convulsions (3/15: 20%) in Group C, and cardiac-related (11/17, 65%) and infections (3/17, 18%) in Group N. In addition, the ratio of pulmonary to systemic pressure after pulmonary artery banding was significantly higher in the patients who experienced cardiac-related death (0.57 ± 0.12) when compared with others (0.39 ± 0.14)($p<0.01$). Cardiac surgery was effective in patients with T18 in terms of extubation ratio, hospital discharge and prolonged survival. However, several of the patients with T18 died due to cardiac-related complications caused by their distinctive pulmonary histology findings even though cardiac surgeries were performed early.

Differences in the components of the metabolic syndrome between preschool children who were born prematurely and were born as term infants

Jungha Yun¹, YooJinie Kim¹, Eun Sun Lee¹, Seunghyun Shin¹, Hannah Cho¹, Yoo-Jin Kim¹,
Young Hwa Jung², Seung Han Shin¹, Ee-Kyung Kim¹, Han-Suk Kim¹

¹ Division of Neonatology, Department of Pediatrics, Seoul National University Children's Hospital, Republic of Korea,

² Division of Neonatology, Department of Pediatrics, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Republic of Korea

Introduction:

Improvements in neonatal care have dramatically increased survival among premature infants. And recent studies demonstrated that preterm infants appear to be prone to have adverse metabolic outcomes in later life. The objective of the present study was to evaluate components of metabolic syndrome in preschool children who were born prematurely and term infants.

Methods:

This is a retrospective case-control cohort study. Sixty children who were born before 32 weeks of gestation or less than 1,500g at birth between 2008 and 2009 were enrolled as the preterm-cohort group. The term-cohort group consisted of 110 preschoolers infants who were born as term infants at 2009 and enrolled in the healthy preschool children cohort study. Evaluation of study population was conducted at 6~8 years of age including body measurements, body composition, bone age, and blood pressures. Insulin resistance (HOMA-IR), lipid profile, leptin and adiponectin level were also evaluated.

Results:

The Z-scores for body measurement (weight -0.7 ± 1.5 vs. 0.0 ± 1.1 , $p < 0.001$; height -0.4 ± 1.0 vs. 0.3 ± 0.9 , $p < 0.001$) at preschool age were significantly lower in the preterm group. The waist/hip ratio (0.83 vs. 0.75 , $p < 0.001$), systolic blood pressure (107.3 ± 7.8 vs. 96.8 ± 7.8 mmHg, $p < 0.001$), diastolic blood pressure (63.7 ± 8.0 vs. 56.6 ± 6.8 , $p < 0.001$) were higher in the preterm group. In addition, prematurely-born children presented higher values of fasting glucose, insulin, and HOMA-IR in comparison with children born at term. Leptin level was higher and adiponectin level was lower in the preterm group.

Conclusion:

Preschoolers who were born prematurely showed retarded growth. However, blood pressures, fasting glucose and insulin, and leptin were higher in the preterm group. The potential metabolic implications of these findings could be found early before adolescence.

Reduced lung function at preschool age in survivors of VLBW preterm infants

Yi-Ya Huang, Hung-Yang Chang, Hsin-Ju Ko, Jui-Hsing Chang, Chyong-Hsin Hsu, Hsin Chi, Chun-Chin Peng, Wai-Tim Jim, Chia-Ying Lin, Chia-Huei Chen

Department of Pediatrics, MacKay Children's Hospital, Taiwan

Background:

Survivors of preterm birth are at risk of chronic pulmonary disease. The objective of this prospective study was to assess pulmonary function at preschool age in former very low birth weight (VLBW) preterm children at a single tertiary center.

Methods:

We recruited aged 5-6 years children of former VLBW preterm infants from follow up program. Age-matched term controls were recruited from clinics during the same period. Lung function was assessed by spirometry. Forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, and forced expiratory flow rate between 25-75% of FVC (FEF25-75%) were measured. These parameters expressed as z-scores (z-FEV1, z-FVC, z-FEV1/FVC, z-FEF25-75%).

Results:

Twenty-four term controls and 54 surviving VLBW preterm children (preterm group mean gestational age: 28.6 ± 2.6 weeks, birth weight: 1047 ± 273 gm) were studied. Preterm group children had significantly lower values of z-FEV1, z-FVC, and z-FEF25-75%, compared with term controls (-0.79 vs -0.02, $p=.003$; -0.71 vs -0.11, $p=.023$; -0.95 vs -0.13, $p=.004$; respectively). Further segregation of participants by birth weight and gestation revealed significantly impaired z-FEV1, z-FVC, and z-FEF25-75% in children lighter at birth (≤ 1000 gm) as compared to those born heavier (1001-1500gm) or born at term ($p<.05$). The values of z-FEV1, z-FVC, and z-FEF25-75% were significantly reduced in children born at earlier gestation (≤ 28 weeks) versus those born at term ($p<.05$). Preterm infants with a history of bronchopulmonary dysplasia (BPD, $n=30$) also had significantly lower z-FEV1, z-FVC, and z-FEF25-75% compared with non-BPD patients and term controls ($p<.05$).

Conclusions:

Children born preterm with VLBW have reduced lung function at preschool age, especially among those with younger gestational age, lower birth weight and BPD. Additional long-term follow-up of respiratory outcomes are needed in this vulnerable population.

Role of endothelial cells in the ductus arteriosus remodeling

Junichi Saito^{1,2}, Utako Yokoyama^{1,3}, Yoshihiro Ishikawa¹

¹Cardiovascular Research Institute, School of Medicine, Yokohama City University, Japan, ²Department of Cardiovascular Medicine, School of Medicine, Yale University, USA, ³Department of Physiology, School of Medicine, Tokyo medical University, Japan

Aims:

Intimal thickening (IT) formation is required to lead complete closure of the ductus arteriosus (DA). Disruption of the internal elastic lamina (IEL) is one of early processes of IT formation. We have demonstrated that smooth muscle cells of the DA play important roles in IT formation. However, the roles of DA ECs have not been fully investigated. We herein focused on tissue-type plasminogen activator (t-PA), which is a DA EC dominant gene, and investigated its contribution to the IT formation.

Methods and results:

ECs from the DA and aorta were isolated from full-term rat fetuses (gestational day 21) using fluorescence-activated cell sorting. RT-PCR showed that the t-PA mRNA expression was 2.7-fold higher in DA ECs than in aortic ECs. A strong immunoreaction for t-PA was detected in pre-term and full-term rat DA ECs. It has been reported that t-PA-mediated plasminogen-plasmin conversion activates gelatinase matrix metalloproteinases (MMPs). We then performed gelatin zymography and found that plasminogen significantly promoted activation of the elastolytic enzyme MMP-2 in rat DA ECs. In situ zymography demonstrated that marked gelatinase activity was observed at the site of disrupted IEL in the full-term rat DA. In a three-dimensional vascular model, EC-mediated plasminogen-plasmin conversion augmented the IEL disruption. In vivo administration of plasminogen to pre-term rat fetuses (gestational day 19), in which IT is poorly formed, promoted IEL disruption accompanied by gelatinase activation and enhanced IT formation in the DA. Additionally, experiments using five human DA tissues demonstrated that the t-PA expression level was 3.7-fold higher in the IT area than in the tunica media. t-PA protein expression and gelatinase activity were detected in the IT area of the human DAs.

Conclusion:

EC-derived t-PA may help to form IT of the DA via activation of MMP-2 and subsequent IEL disruption.

Length: An important anthropometric marker for predicting retinopathy of prematurity in preterm infants

Seong Phil Bae¹, Ee-Kyung Kim², Seung Han Shin², Soo Yeon Park³

¹Department of Pediatrics, Soonchunhyang University College of Medicine, Soonchunhyang University Hospital, Republic of Korea, ²Department of Pediatrics, Seoul National University College of Medicine, Seoul National University Children's Hospital, Republic of Korea, ³Department of Biostatistics, Soonchunhyang University College of Medicine, Soonchunhyang University Hospital, Republic of Korea

Objective:

Low gestational age (GA) and intrauterine growth restriction are reported to be important risk factors for retinopathy of prematurity (ROP) requiring treatment. However, few studies have explored the relationship between linear growth and ROP requiring treatment. We sought to investigate how intrauterine growth, postnatal weight gain and length growth affect the risk of ROP requiring treatment.

Methods:

From the cohort of very-low-birth-weight (VLBW) infants registered in the Korean Neonatal Network (KNN) from January 2013 to December 2016, 2634 with GAs between 24 and 28 weeks were included. According to the INTERGROWTH-21st standards, infants were classified into 4 groups: Small for gestational age (SGA) (WL)-birth weight (BW)<the 10th percentile (%) and birth length (BL)<10%; SGA (W)-BW<10% and BL ≥ 10%; SGA (L)-BW ≥ 10% and BL<10%; and AGA- BW ≥ 10% and BL ≥ 10%. We performed an analysis of the risk factors in intrauterine growth for ROP requiring treatment while adjusting for other risk factors. Extrauterine growth restriction of weight (EUGR (W)) and length (EUGR (L)) were also analyzed with the risk factors for ROP requiring treatment.

Result:

Among infants with GAs above 26 weeks, SGA (L) had a higher odds ratio than SGA (WL) for increasing the incidence of ROP requiring treatment, but both were significant risk factors compared to AGA (OR, 1.949; CI, 1.145-3.32; P=0.014 vs OR, 1.616; CI, 1.002-2.554; P=0.04). EUGR (L) was associated with ROP requiring treatment in both the SGA (WL, W, L; OR, 1.43; CI, 1.046-1.956; P=0.025) and AGA (OR, 2.795; CI, 1.172-6.666; P=0.02) group, but EUGR (W) was significant in only the AGA group (OR, 1.658; CI, 1.243-2.212; P=0.001).

Conclusion:

More research is needed to understand the physiology and clinical significance of linear growth in these infants.

Ultrasonographic confirmation of endotracheal intubation in extremely-low-birth-weight infants

Syusuke Takeuchi^{1,2}, Junichi Arai¹, Motomichi Nagafuji^{1,2}, Ayako Hinata^{1,3}, Tae Kamakura¹,
Yusuke Hoshino¹, Yoshiya Yukitake¹, Yasuyuki Miyamoto¹

¹Department of Neonatology, Ibaraki Children's Hospital, Japan, ²Department of Pediatrics, University of Tsukuba, Japan, ³Department of Neonatal Health and Development, Aomori Prefectural Central Hospital, Japan

Background:

Neonatal endotracheal intubation is an important procedure for the management of extremely-low-birth-weight (ELBW) infants. The endotracheal intubation should be confirmed using a colorimetric exhaled CO₂ detector (colorimetry, below) to confirm intubation. But use of colorimetry in ELBW infants especially in infants weighing less than 600g, may lead to false negative results leading to unnecessary reintubation and delayed decisions. Another reliable method for confirming intubation in these infants is needed. The purpose of this study was to investigate the usefulness of ultrasonography (US) for confirmation of endotracheal tube (ETT) placement during resuscitation in ELBW infants.

Methods:

We conducted a retrospective review of the medical records of ELBW infants in whom ETT position was verified using US between June 2016 and September 2017. We investigated the background of the patients and US investigators, and the time required for the detection of exhaled carbon dioxide using the colorimetric method and US.

Results:

Eleven ELBW infants were examined using US by 4 neonatologists. The median gestational age was 27 weeks 2days (rang 23weeks 5days to 30 weeks 4days) and median birth weight was 661g (400g to 996g). The median durations required for determining ETT position by the colorimetric method and US were 9 and 3 seconds, respectively. In 6 ELBW infants, we could verify ETT position more rapidly using US than by using the colorimetric method and thus perform prompt resuscitation. Unnecessary reintubations were avoided in 3 ELBW infants.

Conclusion:

US allowed determination of tracheal intubation. The colorimetric method yielded false-negative results; in such cases, unnecessary reintubation could have been avoided if US was used. When it was judged as false, we were able to perform appropriate resuscitation by evaluating the cause.

Oral Presentation 2

Chairmans: Hidetoshi Taniguchi (Osaka University)
Chang Ryul Kim (Hanyang University)

- J0-07** Benefits of umbilical cord milking versus delayed cord clamping on neonatal outcomes in preterm infants: A systematic review and meta-analysis
Nobuhiko Nagano Nihon University
- J0-08** Serial lung ultrasonography for the assessment and follow up of TTN progress
Chung-Sing Li Chang Gung Memorial Hospital
- J0-09** FADS gene polymorphisms modulate DHA content between maternal diet and breast milk in Taiwan
Hsiang-Yu Lin China Medical University, Children's Hospital
- J0-10** Necrotizing enterocolitis predict delayed white matter maturation and poor neuodevelopment
Jong Ho Cha Hanyang University
- J0-11** Caffeine versus theophylline: Comparison the efficacy and side effects in apnea of prematurity
Yi-Chieh Lin National Taiwan University Children Hospital
- J0-12** Cerebral oxygenation and oxygen extraction during apnea in preterm infants: Effects of accompanied desaturation
Soo Kyung Nam Inha University Hospital

Benefits of umbilical cord milking versus delayed cord clamping on neonatal outcomes in preterm infants: A systematic review and meta-analysis

Nobuhiko Nagano¹, Makoto Saito², Takahiro Sugiura³, Fumiko Miyahara⁴, Fumihiko Namba⁵, Erika Ota⁶

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Background:

Optimum timing of umbilical cord clamping has not been established in preterm infants.

Objectives:

We compared the short- and long-term effects of umbilical cord milking (UCM) versus delayed cord clamping (DCC) on infants born at less than 37 weeks of gestation.

Search methods:

A systematic review and meta-analysis was conducted according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" statement. We searched CINAHL, CENTRAL, EMBASE, MEDLINE, PubMed and ClinicalTrials.gov for relevant randomized controlled trials (RCTs).

Selection criteria:

We included individual and clustered RCTs comparing UCM to DCC for infants born before 37 weeks of gestation.

Data collection and analysis:

Four reviewers independently assessed trial quality and eligibility for inclusion.

Main results:

Two trials (255 preterm infants, 23 0/7 to 32 6/7 weeks of gestation) were included in the analysis. UCM was associated with fewer intraventricular hemorrhages (IVHs) (two trials, 255 infants; relative risk [RR] 0.45, 95% confidence interval [CI] 0.20 to 0.98, low quality of evidence) and UCM was an increased proportion of infants with a Bayley score at 2 years of age (two trials, 174 infants; Cognitive: RR 1.14, 95% CI 1.03 to 1.26, Language: RR 1.24, 95% CI 1.03 to 1.49, low quality of evidence) compared to DCC.

Authors' conclusions:

UCM wasn't reduced in-hospital mortality and need for transfusion compared to DCC. But our study suggests that UCM may lower the risk of IVH and improve certain neurodevelopmental outcomes compared to DCC in preterm infants.

Serial lung ultrasonography for the assessment and follow up of TTN progress

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Background:

Transient tachypnea of the newborn (TTN) is one of the most common causes of respiratory distress in neonates. In general, TTN is diagnosed based on typical medical history, clinical manifestations, and chest radiographic finding. Previous studies have shown that lung ultrasonography has high sensitivity and specificity for diagnosing TTN; however, there is limited using reports on sonographic image to monitor clinical evolution of TTN. This prospective study aims to assess and follow the TTN severity via serial lung ultrasonography.

Methods:

Between November 2018 and August 2019, Neonates ≥ 34 weeks of gestation admitted to newborn center of Chang Gung Memorial Hospital diagnosed of TTN and needing ventilatory support of any kind were enrolled in the study group, and those without respiratory disease as the control group. Trans-thoracic lung ultrasound was performed and scores based on self-defined scoring system were recorded within 4 hours of admission and followed up at 24 and 48 hours later. The ultrasound scores were analyzed in both groups.

Results:

A total of 41 infants were included in this study. Twenty-four infants (59%) were enrolled in the study group, seventeen (41%) in the control group. The ultrasound scores were highest on the first day, then declined gradually on the second and third in most cases of both groups. On the first and second day, the ultrasound scores of the TTN group were significantly higher than those of the control group.

Conclusions:

The relatively higher lung ultrasound scores reflect delayed lung fluid clearance in neonates with TTN. Late preterm or term infants who did not show decrement of scores might have neonatal pathologies other than TTN, such as mild RDS. Although the sample size was limited, this prospective study showed the potential of lung ultrasonography to be a practical tool to assess and follow the TTN severity.

FADS gene polymorphisms modulate DHA content between maternal diet and breast milk in Taiwan

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Carriers of the minor alleles of Fatty acid desaturases (FADS) single nucleotide polymorphisms (SNPs) tend to have a lower Long-Chain Polyunsaturated Fatty Acids (LCPUFAs) content in RBC membrane and in breast milk of mother in Caucasians. This study aimed to explore whether gene polymorphisms modulated DHA content between maternal diet and breast milk in Taiwan.

From 2017 Jan to 2018 Dec, Taiwanese women who just having delivered full-term baby were enrolled. DNA was obtained by oral mucosa swab at the first visit. Dietary information was obtained by Food frequency questionnaire. This questionnaire and breast-milk were collected twice in this study. Four SNPs(rs1535, rs174575, rs174448, rs174561) from the FADS1 and FADS2 gene cluster were selected. We also inquired Fish intake frequency questionnaire (FFQ).

One hundred ninety one postpartum women were enrolled. The genotypes of the 4 SNPs were determined. The minor allele frequency were in agreement with data from Taiwan biobank. The average DHA level in breast milk of Taiwanese women is about 0.42%. There was no difference in DHA levels when subjects were classified according to their genotypes. When the correlation of DHA levels between dietary intake and breast milk assessed according to genotype, a gene-diet positive correlation is found in homozygous for the major allele.

Conclusions:

DHA content in breast milk of Taiwanese women is 0.42%. Lower proportions of DHA in breast milk from women who were homozygous for the minor allele might not be compensated for by increasing fish and fish-oil intake.

Necrotizing enterocolitis predict delayed white matter maturation and poor neurodevelopment

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Background:

Necrotizing enterocolitis (NEC), known as the main cause of premature infant death and disability from gastrointestinal disease, is associated with adverse neurodevelopmental outcome in preterm infants.

Objective:

This study examined (1) the brain volume and (2) white matter (WM) microstructure in preterm infants at term-equivalent age and (3) neurodevelopmental outcomes at 18 months' corrected age (CA) to explore the effects of NEC on brain development.

Method:

We studied 86 preterm infants (20 with NEC \geq stage II and 66 without NEC) with no evidence of focal abnormalities on conventional magnetic resonance imaging (MRI) at term-equivalent age. White matter maturation was assessed by magnetic resonance diffusion tensor imaging (DTI) and volume analysis. Probabilistic maps were created for pathways related to cognition, motor and language such as corpus callosum, cortical spinal tract and inferior longitudinal fiber. Neurodevelopmental outcomes were assessed with Bayley Scales of Infant and Toddler Development-III (Bayley-III).

Results:

The preterm infants with NEC \geq stage II had smaller deep gray matter ($p=0.034$), cerebral white matter ($p=0.022$) volumes than the preterm infants without NEC, independent of gestational age, PMA at MRI scan, and total intracranial volume. When adjusted with GA, PMA at MRI and total parenteral nutrition, the preterm infants with NEC exhibited marked increments in mean diffusivity in the corpus callosum splenium ($p=0.006$) and Lt. cortical spinal tract ($p=0.004$) compared with the infants with no NEC, with a significance level of $p \leq 0.008$ as a Bonferroni correction for multiple comparisons. Notably, on the multiple regression analyses, the MD value of the corpus callosum splenium were correlated with the motor scores ($p=0.002$) and the language scores ($p=0.025$) on Bayley-III at the 18-month corrected age.

Conclusion:

Our study highlights the adverse impact on corpus callosum splenium in preterm infants with NEC \geq stage II compared with those without NEC at term-equivalent age, relating to poor motor and language development in preterm infants with NEC.

Caffeine versus theophylline: Comparison the efficacy and side effects in apnea of prematurity

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Background:

Apnea of prematurity is one of the most common phenomenon in neonatal intensive care unit(NICU). Periodic hypoxia/hypoxemia then bradycardia episodes make injury to the vulnerable brain of premature infants. Methylxanthine is the main medication of choice for apnea, especially caffeine and aminophylline/theophylline. Caffeine has just been introduced into Taiwan at 2018. This study is aimed to compare the efficacy and side effects between caffeine and theophylline.

Methods:

This was a retrospective, case control, gestational age matched study, with one case received caffeine and two cases received theophylline. We enrolled patients born during the period of 2017/01-2018/12, who were admitted at NICU of our hospital within 3 days after birth. We included infants of 23-35 weeks of gestational age, and birth body weight above 500gm. Infants with congenital abnormalities, or expired before discharge were excluded.

Result:

There were 48 cases in caffeine group, and 96 cases in the theophylline group. The mean of gestational age and birth weight between two groups were 30.08 ± 2.75 vs. 29.95 ± 2.57 weeks and 1293.12 ± 392.03 vs. 1329 ± 453.84 gm.

The treatment duration was significantly shorter in caffeine group than that of in theophylline group (15.43 ± 10.85 vs. 24.77 ± 19.81 d, $p < 0.000$), especially in gestational age less 30 weeks of gestational age and among male.

Conclusion:

Caffeine is more effective and less side effects than theophylline in treatment of apnea of prematurity. Further large prospective control study may be needed.

Cerebral oxygenation and oxygen extraction during apnea in preterm infants: Effects of accompanied desaturation

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Purpose:

Preterm infants have immature respiratory control and cerebral autoregulation. This study aimed to investigate cerebral oxygenation and oxygen extraction during apnea and its difference based on the presence of desaturation.

Methods:

The prospective observational study was conducted at Inha University hospital. Near-infrared spectroscopy (NIRS)-monitored cerebral regional saturation (crSO₂) and cerebral fractional oxygen extraction (cFTOE) were measured in the first 1 week of life during 3 to 4 apneic episodes in each of 17 stable spontaneously breathing preterm infants. Their median (IQR) gestational age and birth weight were 28.9 (26.4 – 30.0) weeks and 990 (930 – 1,220)g, respectively. Apneas lasting ≥ 20 seconds or accompanying desaturation (SpO₂<85%) or bradycardia (heart rate (HR), <100 bpm) even at shorter times were included. The mean of 30 min before apnea (baseline), lowest or highest value following apnea (nadir) and the difference from baseline (Δ) in crSO₂, cFTOE and HR were analyzed.

Results:

A total of 55 apneas were recorded. Median (IQR) postmenstrual and postnatal age at episodes were 29.1 (27.1 – 30.4) weeks and 2 (2 – 5) days, respectively. Baseline, nadir, Δ value and repeated-measures analysis of variance factor (F) of each parameters were as follow: crSO₂ 73.5 (67.5 – 80.3)%, 64.0 (51.0 – 67.0)%, -11.6 (-24.0 – -6.5)% and F 76.85 (P<0.001); cFTOE 0.23 (0.17 – 0.29), 0.33 (0.26 – 0.43), 0.11 (0.03 – 0.22) and F 28.62 (P<0.001). When we divided apneic episodes with or without desaturation, Δ HR was significantly lower in episodes with desaturation compared to episodes without desaturation (F 26.77, P<0.001). However, Δ crSO₂ and Δ cFTOE were not different between two groups (F 0.385, P=0.537; F 1.648, P=0.205).

Conclusion:

Whether or not reduced SpO₂ (<85%), apneas were associated with decrease in cerebral oxygenation and increase in cerebral oxygen extraction in preterm infants. Cerebral regulatory mechanism is insufficient in preterm infants and desaturation may not be an effective indicator for cerebral circulation during apneas for this immature population.

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Using platelet parameters to anticipate morbidity and mortality among preterm neonates: A retrospective study

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We aimed to investigate whether platelet parameters could predict bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), and NICU mortality. We retrospectively investigated platelet count, plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) on the first day of life in preterm newborns born less than 32 weeks' gestation admitted to our NICU from 2006 through 2017. Receiver operating characteristic (ROC) and multiple regression analyses, along with Cox proportional hazard modeling, identified independent predictors of morbidities and mortality in preterm newborns. A total of 305 preterm newborns were included in this study. Gestational age, birth weight, and Apgar score were significantly lower in non-survivors than in survivors. Platelet count, PCT, PDW and PMI did not differ significantly between the two groups, whereas mean MPV in non-survivors was significantly higher than in survivors (10.5 fl versus 10.0 fl, $p=0.001$). Per ROC curve, an MPV threshold of 10.2 fl. MPV predicts prognosis in neonates with a sensitivity of 72.4% and a specificity of 58.6% (AUC=0.685, 95% CI: 0.592-0.777, $p=0.001$). Multivariate Cox hazard modeling showed that shorter GA [HR:0.612, 95% CI: 0.464-0.840, $p=0.001$], male sex [HR:0.239, 95% CI: 0.100-0.570, $p=0.001$], NEC [HR:0.257, 95% CI: 0.084-0.785, $p=0.017$], PA [HR:0.301, 95% CI: 0.119-0.761, $p=0.011$], and $MPV \geq 10.2$ fl [HR:0.298, 95% CI: 0.126-0.702, $p=0.006$] independently predicted overall survival. Furthermore, multivariate analysis revealed that platelet parameters were not associated with BPD and NEC, whereas small for gestational age (SGA), Apgar score at 5 minutes, and low PCT were associated with IVH. This study demonstrates that low PCT predicts IVH, and $MPV \geq 10.2$ fl correlates with mortality among infants born after less than 32 weeks' gestation.

Comparison the effect of using alcohol and natural drying application on newborn umbilical cord care in recent 10 years: A systematic review

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Background:

Umbilical cord is made up of blood vessels and connective tissue which connects the neonate and placenta in uterus. The mother and her baby was separated by cutting the cord after birth. Umbilical care of the neonate is unique to human beings, practically varies according to geographic, cultural and economic factors.

Objective:

This study compares the efficacy of alcohol and natural drying on umbilical separation time and the incidence rate of omphalitis.

Method:

We identified suitable keywords and built a PICO, then we searched database from Cochrane Library, Up To Date, CINAHL Plus with Full Text [EBSCOhost], Medline and PubMed between 2008-2018. Our Search criteria included quasi-randomized trials, RCT and systematic review of different forms of umbilical cord care. We used oxford centre for evidence-based medicine and critical appraisals skills programme to appraise of its validity and usefulness.

Result:

In this study, we realized natural drying application on newborn umbilical cord markedly shortened the cord separation time compare to alcohol using. In addition, the incidence rate of omphalitis has no significant difference between drying and Alcohol.

Conclusion:

Using sterilized cotton without addition of any antibacterial agents and keeping the cord area dry seems to be more effective and convenient than using alcohol.

Improving neonatal infusion safety

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Intravenous infusion catheter therapy is the most common and necessary medical treatment during hospitalization. But in clinical work, drug leakage often occurs to peripheral tissues when intravenous administration is used. Especially the premature infants in neonatal intensive care unit, because the skin structure is not yet fully developed, which increases the risk of drug leakage. Neonates with the small and fragile blood vessels have low blood flow, resulting less blood to dilute infusion drugs. Neonates have poor tolerance to drugs, and are prone to unexpected events such as drug extravasation, skin necrosis and organ injury during infusion. It is an important issue to improve the safety of neonatal infusion.

Through the cooperation of medical care team (physicians, pharmacists, nurses and information personnel), we established: (1) Information system construction standard care process: high-warning drug formulation, format prescription mode of doctor's advice and continuous infusion and multiple pipeline care, operation of warning system for early pressure changes, feedback mechanism for abnormal events (2) Education training and verification mechanism: Drug safety, pipeline safety, instrument operation, etc. (3) Medical equipment introduction: Infusion device (Syringe, Pump, Set and 3-way) is accurate and stable in line with neonatal vascular characteristics, which will effectively improve the safety of neonatal infusion.

Comparison of decision-making in neonatal care between China and Japan

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Background:

Various differences between China and Japan in approaches to medical treatment have been noted, but a few studies have examined differences in medical decision-making, especially in neonatal care. The aim of this study was to clarify these differences by means of a questionnaire.

Methods:

The subjects were physicians on the staff of NICUs in China and Japan. The study questionnaire consisted of three parts dealing with the general characteristics of the participants, questions about treatment strategies for hypothetical, critically ill infants, and general questions about the treatment of foreign patients. The Likert scale was used to assess the treatment strategies and the results were analyzed statistically. Subgroup analysis by age, sex, and medical and NICU experience was also performed.

Results:

The proportion of respondents in the Chinese and Japanese groups was 26/26 (100%) and 26/31 (84%), respectively. There was a significant difference between the Chinese and Japanese groups for 8 of 75 questions; Chinese physicians chose the positive treatment or examination options for these eight questions unlike their Japanese counterparts. The responses of the younger, less experienced physicians in both countries were more similar to each other, and more positive than those of their older, more experienced colleagues.

Conclusion:

Chinese physicians showed a more positive attitude toward examination and treatment, whereas Japanese physicians showed a more cautious attitude.

Neonatology seminar retreat for medical students and residents in Osaka Prefecture (TOKOTON neonatal seminar): An eight-year experience

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Background:

In Osaka prefecture, Japan, significant improvement of neonatal care has been achieved in last few decades. Neonatal Mutual Cooperative System (NMCS) is the neonatal transport system which was established in 1977 and is supported by 27 NICUs. NMCS has been serving not only to save the neonates in need but also to enhance academic and social exchange among neonatologists in Osaka over the many years. Thus NMCS contributed to increase the number of NICU beds as well as neonatologists. However, there is growing concern that the number of neonatologists may not meet NICU beds and in 2011, Osaka prefecture started Osaka medical career development program to encourage pediatric residents to become established neonatologists. In this context, NMCS and Osaka prefecture planned to hold annual neonatology seminar retreat for medical students and residents and named TOKOTON (meaning “thoroughly” in Japanese) neonatal seminar. In this report, we discuss if this seminar retreat would contribute to increase the number of young neonatologists in Osaka prefecture.

Methods:

TOKOTON neonatal seminar is an overnight seminar retreat that includes a life story talk by an established neonatologist, lectures, hands-on training, small group discussions and social gatherings. Questionnaires were performed to attendees and collected right after the seminars to obtain satisfactory scores (rating 1 to 5, 5 means more than satisfactory) and follow-up surveys were performed for medical students and junior residents three years after the seminars.

Results:

Questionnaires showed overall satisfactory scores (1 to 5) of 3.9-4.4 (median 4.3). Follow-up surveys showed that 85% of medical students and junior residents chose to become pediatrician and 80% of all surveyed had been trained at NICUs in Osaka prefecture.

Conclusion:

Neonatology seminar retreats for medical students and residents by local neonatologists and Osaka prefecture might have caused favorable impact on working at NICU in this region.

Successful transition process of attachment between mother with congenital heart disease and preterm baby

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High-risk pregnant mothers and newborns are often separated by mother's diseases, leading to a higher difficulty in attachment establishment between mother and baby. The purpose of this report is to describe the transition process of attachment relationship between mothers with congenital heart disease and her preterm babies. With the help of caring theory, the mothers can connect with babies and successfully change roles successfully.

Through in-depth interviews to understand the mother's postpartum hospitalization due to congenital heart disease, and neonatal care of neonates in intensive care unit, resulting in the separation of mother and infant, and causing the stress of establishment process of mother's role.

This study found that the attachment of high-risk pregnant mothers to newborns is far greater than that of ordinary mothers. The transition of attachment can be summarized into four stages: expecting new life, worrying about genetic diseases, recognizing health and aggressive participation.

Using caring theory to help their successful transition, the process can be divided into three stages: 1. Identifying feelings, giving preparation period and no compulsion. 2. Provide support and information. 3. Offer opportunities and learning. 4. Enhance confidence and make the impossible mission possible.

Mothers with high-risk pregnancies are more difficult to get adjusted because of their worries and uncertainties. A complete prenatal and postnatal care plan is useful in shortening the separation time between mother and baby. Appropriate resources can be provided, and effective attachment relationships can be established, which will help to alleviate the pressure of mothers and establish the character of mothers.

From neonatologist to home doctor for individuals with severe motor and intellectual disabilities

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Regardless of the progress of neonatology, some of the patients should have medical treatment and care at home after discharge which should be the event of happiness. Parents will take the children to the hospital regularly for physical (and/or mental) check, maintenance including changing devices and so on.

I had been worked as a Neonatologist for more than 15 years with following up severe cases at outpatient clinic. After that, I encountered the home medical treatment (HMT) which could decrease the stress of the patients and the families. We the staff of HMT go to their home every one or two weeks. We can examine the patients, prescribe medicines, change the devices and listen to the voices of the families regularly. The time for those could be put more slowly than that at the hospitals.

During five years of HMT, I have learned some points as a former neonatologist; 1) Home care should be so hard for the families that team approach for multidisciplinary support should be needed, as much as that of NICU. 2) We the staff should have respect to the families for starting and continuing their lives at home. 3) Preparation for lives at home would need some period and place; transitional facilities should be needed in our country, too. 4) Families (and maybe the patients) should have grief, losing the future looking ahead so that visiting staff should understand it for keeping going and empathizing with the families. Neonatologist should be one of the best supporters for the families, who knows their grief.

I give thanks to the doctors and the staff of acute care hospitals with NICU who treat the patients in acute exacerbation. And we the staff of HMT would like to keep good cooperation with them for the children and families of SMID.

Lung ultrasonography in predicting the prognosis of bronchopulmonary dysplasia in neonates

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Objective:

Neonatal lung ultrasonography (LUS) is widely used, but its usefulness in bronchopulmonary dysplasia (BPD) has not been fully discussed. Our aim of this study is to investigate the usefulness of LUS scores in predicting respiratory prognosis in BPD.

Methods:

We performed a prospective cohort diagnostic accuracy study between 2017 and 2019 in level III neonatal intensive care units. 87 neonates requiring oxygen therapy at 28 days of life were included. LUS was performed on day 28, at the 36 weeks' postmenstrual age (PMA), and at the time of discharge. 0-3 point LUS score was given in three regions of each lung (midclavicular line, midaxillary line, scapular line); total score range 0-18 point. Classification of BPD severity was based on the National Institute of Child and Human Development. A receiver operating characteristic curve was constructed to assess the LUS score for the prediction of moderate-severe BPD and home oxygen therapy.

Results:

Of the 87 neonates, 39, 33, and 15 neonates had mild, moderate, and severe BPD, respectively. The LUS score significantly correlated with BPD severity and improved with time (median [interquartile range] scores for each group: Day 28, 5 [4-6] vs. 7 [6-8] vs. 9 [8-12], $P < .001$; 36 weeks' PMA, 3 [2-4] vs. 6 [5-7] vs. 9 [8-10], $P < .001$; and Discharge, 2 [1-2] vs. 4 [4-5] vs. 6 [5-6], $P < .001$). The LUS score cutoff of 7 on day 28 in predicting moderate-severe BPD had a sensitivity of 87% and specificity of 93% with area under the curve of 0.95 (95% confidence interval: 0.91-0.99), and cutoff of 10 on day 28 in predicting home oxygen therapy had a sensitivity of 86% and specificity of 91% with area under the curve of 0.95 (95% confidence interval: 0.88-1.0).

Conclusion:

LUS scores can predict respiratory prognosis in BPD.

Applying data mining techniques to predict bronchopulmonary dysplasia in very-low-birth-weight (VLBW) infants- A population-based study

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Background:

Predicting risk for bronchopulmonary dysplasia (BPD) provides aid in resource planning, family counseling, and stimulates quality-improvement initiatives. It also supports patient selection for new clinical trials. However, it remains a challenge to provide accurate prediction.

Objective:

The present study aims to find models with better performance in predicting BPD via data mining techniques.

Design/Methods:

Cohort data of VLBW preterm from 2001 to 2013 were used. BPD was defined as O₂ requirement at 36 wks PMA. Exclusion criteria were 1) Transferred to/from other hospital; 2) GA < 23 wks or > 32 wks. Ten out of 36 perinatal and hospitalization risk factors were selected for analysis by CfsSubsetEval in Weka 3.8 (University of Waikato, NZ). The database was randomly divided into training (n=5240) and test datasets (n=2620). In the training cohort, performance of these techniques was evaluated by 10-fold cross validation. The model with the best prediction was subsequently used to predict BPD on the test set.

Results:

A total of 7860 infants were included in this study. The performance of each data mining method is shown in Table 1.

Conclusions:

Each of Naïve Bayes, neural network and logistic regression provides good performance in predicting BPD. They have accuracy around 80% and ROC area: 0.85 to 0.86.

Table 1. Performance (Weighted Average) of different data mining methods in predicting BPD in Test dataset and Training dataset (in parentheses)

Methods	Logistic Regression	Neural Network	Decision Tree	K-NN	Naïve Bayes	SVM
Accuracy (TP rate)	0.785 (0.794)	0.787 (0.783)	0.782 (0.781)	0.687 (0.691)	0.785 (0.785)	0.749 (0.75)
ROC area	0.851 (0.859)	0.847 (0.85)	0.793 (0.804)	0.688 (0.697)	0.848 (0.85)	0.737 (0.741)

Development of a novel treatment for neonatal bronchopulmonary dysplasia by multilineage-differentiating stress-enduring cells

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Neonatal bronchopulmonary dysplasia (BPD) is still a critical complication in low birth weight infants. Multilineage-differentiating stress-enduring (Muse) cells are a novel type of endogenous stem cells, which can migrate into the injured sites after intravenously injection and spontaneously differentiate into functional cells. In the present study, we evaluated whether the Muse cells could exert a treatment effect on BPD model rats.

The BPD model included rats that were exposed to 80% oxygen for 14 days. At postnatal day 5 (P5), GFP labeled Muse (M group), non-Muse mesenchymal stem cells (non-M group) (1×10^4 cells in each group), or vehicle (HBSS) (V group) was administered *via* the right external jugular vein. Immediately (P15) and 2 weeks (P29) after exposure to hyperoxia, the treatment effect on lung maldevelopment and inflammation, and pulmonary hypertension was evaluated.

Compared to the non-Muse cells, more GFP-positive Muse cells were detected in the sections of the lung parenchyma at P29. The tissue volume density of the lung was ameliorated in the M group, but not in the non-M group (P29). The medial wall thickness of pulmonary arteries was lower in the M group, but in the non-M group than that in the V group, and the dry weight ratio of the right ventricle free wall to the interventricular septum plus the left ventricle in the M group was lower than those in V and non-M groups (P15 and 29). The numbers of macrophages and lymphocytes in BALF were significantly smaller in the M group, but not in the non-M group than those in the V group (P15).

In conclusion, the present study indicated that compared to non-muse cells, more Muse cells migrated into the lung, and that the treatment effect of Muse cells on lung maldevelopment and pulmonary hypertension was stronger than that of non-Muse cells.

Neonatal outcomes in extremely preterm infants with prolonged preterm premature rupture of membrane

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Subject:

The management with preterm premature rupture of membrane (PPROM) during second trimester is controversial in perinatal medicine. This observational cohort study was conducted to assess the prolonged PPRM as a risk factor for neonatal outcomes in extremely preterm infants.

Methods:

Of the 3,170 extremely preterm infants born at 23-27 weeks' gestation between 2014 and 2017, who were registered in Korean Neonatal Network, 1,427 infants were born to women with PPRM. Compared with control group (PPROM of ≤ 2 days, $n=684$), prolonged PPRM group was arbitrarily defined by latency period between PPRM and delivery ≥ 7 days ($n=431$). Because of uncertainty about the expectant management of PPRM, 229 infants with latent period of PPRM between 3 and 6 days were excluded.

Results:

Mean gestational age at PPRM and latency period in prolonged PPRM group were significantly different with in control group (22.7 ± 2.5 vs 25.6 ± 1.4 weeks, 21.5 ± 14.8 vs 0.7 ± 0.8 days, respectively, $p < 0.05$). The incidence of vaginal delivery, oligohydramnios (amniotic fluid index < 5) and histologic chorioamnionitis was also significantly higher than in control group ($p < 0.05$). However, there was not a significant difference in gestational age at delivery and birth weight. The mortality before discharge in prolonged PPRM group was not significantly different with in control group ($124/431$ [28.8%] vs $207/684$ [30.3%], $p = 0.82$). The incidence of moderate to severe bronchopulmonary dysplasia (BPD) and pulmonary hypertension with treatment in prolonged PPRM was higher than in control group ($190/314$ [60.5%] vs $255/487$ [52.4%], $113/431$ [26.2%] vs $103/684$ [15.1%], respectively, $p < 0.05$). Conversely, the incidence of necrotizing enterocolitis, sepsis, and retinopathy of prematurity was not significantly different between two groups. In multivariate regression analysis, the prolonged PPRM was the independent risk factor of moderate to severe BPD (RR=2.44, 95% CI=1.62-3.66).

Conclusion:

Prolonged PPRM in extremely preterm infants was associated with BPD, but not with mortality before discharge.

Comparison of thyroid function at birth in preterm infants with respiratory distress syndrome of newborn

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Purpose:

Thyroid hormones are essential for normal growth and development of fetus. Association between Thyroid hormones and lung maturation in several species have been reported. But there is few reports about the relationship between Thyroid hormones and respiratory distress syndrome of newborn(RDS). We compared the thyroid function of preterm infants who had RDS

Methods:

this study is the Retrospective cohort study of preterm infants who were born before 34 weeks of gestation and admitted at neonatal intensive care unit of Wonju Severance Christian Hospital from March 2017 to February 2019. Thyroid function test including thyroid stimulating hormone(TSH), free serum thyroxine(fT4) and triiodothyronine(T3) is performed 0, 1, 3 weeks after birth in preterm infants.

Results:

Total 132 preterm infants were enrolled and infants with RDS were 60. TSH and T3 level were lower in RDS group than in control group. Logistic regression analysis showed that TSH levels are significantly lower in RDS group.

Conclusion:

we suggest that lower TSH levels Infants in RDS group mean a relationship between immature functions of thyroid function and surfactant secretion of lung.

The application of instantaneous CO₂ mode to exhaled carbon dioxide monitoring during high frequency oscillatory ventilation in very low birth weight infants

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Background and aims:

We examined the correlation and agreement between blood carbon dioxide partial pressure (PCO₂) and carbon dioxide (CO₂) concentrations in exhaled breath measured by instantaneous CO₂ (InstCO₂) during high frequency oscillatory ventilation (HFOV) in very low birth weight infants (VLBWI).

Methods:

InstCO₂ mode was installed on the mainstream end-tidal carbon dioxide (ETCO₂) monitor "OLG-3800 (NIHON KOHDEN CORPORATION, Japan)" to measure the CO₂ concentration in the constant air stream using the same sensor as ETCO₂. With the rise time of 55 ms, the CO₂ concentration was displayed and recorded on the monitor every second. We applied InstCO₂ to measure exhaled CO₂ during HFOV. The maximum value of InstCO₂ for 3 minutes before and after blood sampling (InstCO₂MAX) was adopted since InstCO₂ fluctuates frequently. Furthermore, the degree of coincidence (DOC) was defined as " $(PCO_2 - |PCO_2 - InstCO_2MAX|) / PCO_2 * 100(\%)$ ". PCO₂, InstCO₂MAX, DOC, ventilator settings and respiratory conditions were examined statistically.

Results:

A total of 216 simultaneous data of PCO₂, InstCO₂, ventilator settings and respiratory conditions were obtained from 7 HFOV-ventilated VLBWI. There was a significant correlation ($r^2 = 0.57$, $P < 0.0001$) between InstCO₂MAX and PCO₂. The median DOC was 80.75%, and the ratio of more than DOC 80% was 57.4%. In multivariate analysis, fraction of inspiratory oxygen ($p = 0.00246$), minute volume ($p = 0.00283$), mean airway pressure ($p = 0.01524$) and postnatal day ($p = 0.02615$) significantly affected InstCO₂MAX if DOC 80% or more was clinically applied.

Conclusions:

The value of InstCO₂ correlates with PCO₂ when the conditions are met. For the clinical application of InstCO₂, further studies are needed.

Measurement of oxygen diffusivity through cell layers using biomimetic microfluidic device

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Background:

In mammals, inhaled oxygen moves from the alveoli to the blood through alveolar epithelium into pulmonary capillaries. Different studies have been reported to examine experimental oxygen diffusivity for simple membrane or single-celled organisms; however, suitable devices have not been developed to demonstrate for the oxygen transportation through cell layers.

Methods:

We have established a multi-layer biomimetic microfluidic device with the relative fluorescence lifetime detection apparatus to measure oxygen diffusivity through a cell layer. The oxygen tension profile with and without the cells cultured on top of the membrane is measured and compared. The differentiated type I pneumocytes-like cells from mouse pulmonary stem/progenitor cells (CAR+mPSCs), A549 (type II cancer cell) and 3T3 (fibroblast) cell lines are used to form cell layers within the device to evaluate their oxygen diffusivity.

Results:

The quantitative results show that the normalized diffusivity is lowered approximately 40% with the A549 cells culture on top of the membrane, suggesting the A549 cells impede the oxygen transportation through the cell layers and act as oxygen diffusion barriers. In contrast, the normalized diffusivities are slightly less than 1 for the membranes with 3T3 (0.99) and undifferentiated CAR⁺ (0.93) cells, which have no effects or minimal on oxygen transportation, culture on top of them. It is notable that the membrane with type I pneumocytes differentiated from the CAR⁺ cells has the normalized oxygen diffusivity greater than one (1.57), which indicating the speed of oxygen transportation through the membrane is facilitated for more than 50% with the presence of the cells comparing to the bare membrane.

Conclusion:

The study offered a new in vitro approach to evaluate the oxygen diffusivity across cell layers in biomimetic device, and the results show a distinct facilitated oxygen diffusion behavior of the differentiated type I pneumocytes-like cells that has never been discussed before.

Leri-Weill dyschondrosteosis in a newborn presenting with respiratory failure due to severe micrognathia

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Haploinsufficiency of the SHOX gene (short stature homeobox-containing gene, NM_000451) in the pseudoautosomal region (PAR1) of the X and Y chromosomes can result in a wide spectrum of short stature phenotypes, including patients with Turner syndrome, Leri-Weill dyschondrosteosis (LWD) and short stature without any specific features. LWD has rarely been diagnosed with respiratory failure in the neonatal period. A female infant had been born to a 39-year-old woman. The mother was referred for evaluation of intrauterine fetal growth restriction complicated with oligohydramnios and micrognathia detected on routine sonography. The baby was born at a gestational age of 36 weeks 4 days by cesarean section and weighed 2,000 g. She was lethargic with a weak cry at birth and needed positive pressure ventilation. She was in marked respiratory distress with cyanosis and chest wall retractions. The nasal continuous positive airway pressure was initially applied and she was weaned to room air by the 3rd hospital day. Pulse oxygen saturation was kept relatively stable when she was placed in the prone position. She presented with dysmorphic features including micrognathia, retrognathia, hypotelorism, cleft soft palate and clitoromegaly considered as a mild ambiguous genitalia. The growth profiles of birth weight, height, and head circumference were 3rd, 10th and 10-50th percentile, respectively. Chromosome analysis of the patient confirmed 46, XX karyotype. 947 Kb deletion at Xp22.33 was delineated by chromosomal microarray. A magnetic resonance imaging (MRI) scan of the brain demonstrated diffusion restriction foci in left side genu of the corpus callosum suggesting hypoxic-ischemic injury. There was no remarkable bony abnormality on radiographs of the hand, wrist and forearm. On the 42nd hospital day, she underwent elective tracheostomy due to persistent airway obstruction secondary to micrognathia. After educating and training caregivers for feeding and tracheostomy care, she was discharged on the 76th hospital day.

Intraoperative indocyanine green fluorescence lymphangiography to visualize chylous leakage spots after surgeries

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Chylous leakage is a complication that can occur after surgeries. Patients can be treated with conventional therapies. Additionally, there are various procedures that treat chylous leakage, though they sometimes ended in failure due to difficulty in detecting leakage spots. To remedy this problem, we have adopted intraoperative Indocyanine green fluorescence lymphangiography (ICGFL). We hereby present two cases of successfully treated patients with refractory chylous leakages.

Case.1:

A male infant was delivered at 26 weeks' gestation, weighing 533 grams. He underwent an enterostomy procedure for his meconium-related ileus on day 15. He presented with chylous ascites after the surgery and did not improve despite conventional therapies. He underwent another operation to stop the chylous leakage on the 37th day after the surgery. We adopted the technique of intraoperative ICGFL to search for the leakage spot. We could see it clearly inscribed on the surface of his intestine, thanks to the visualization. We sprinkled the region with fibrin sealant. The chylous drainage ceased after the operation.

Case.2:

A female infant with hypoplastic left heart syndrome was delivered at 39 weeks' gestation, weighing 2,726 grams. She underwent pulmonary artery banding on day 6. We conducted the Norwood procedure and Glenn procedure when she was 3 months and 9 months old, respectively. After the third surgery, she developed chylothorax. Various interventions were performed, including pleurodesis, thoracic duct (TD) ligation and TD interruption, though they ended in failure. She underwent the second TD ligation with intraoperative ICGFL at the age of 15 months. Her TD was visualized clearly, and the duct was definitively ligated. The amount of chylous leakage decreased dramatically after the surgery.

In our experiences, intraoperative ICGFL visualized chylous leakage regions distinctly, be it the chylothorax or chylous ascites. Hence, this procedure may have great potential in treating patients with refractory chylous leakage.

Effect of antenatal steroid on postnatal hemodynamics in extremely low birth weight infants

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Background:

Antenatal steroid (AS) has been reported to decrease the incidence of intraventricular hemorrhage in pre-term infants. The mechanisms responsible for this effect may include circulatory stabilization including cerebral perfusion during the transitional period.

Objectives:

To determine circulatory changes in the early postnatal period after AS, focusing on cerebral and peripheral perfusion.

Study design:

In this prospective observational study, 54 extremely low birth weight infants (gestational age 26.1 ± 1.8 weeks; birth body weight 695 ± 171 g) were monitored for cerebral blood volume (CBV) and lower-limb skin blood flow (LBF) between 6 and 30 h after birth using near-infrared spectroscopy and laser Doppler flowmetry, respectively. Changes in CBV were evaluated by assessing changes in the ratio of total hemoglobin (T-Hb) to those at 72 h when circulatory status in the majority of infants was stabilized. Peripheral vascular resistance index was also calculated using mean arterial blood pressure (MABP) and LBF using the following formula: $MABP/LBF$. Infants were divided into infants with antenatal steroid (AS group, $n=31$) and infants without antenatal steroid (non-AS group, $n=23$) and were compared to changes in circulatory parameters between groups using t-tests with Bonferroni correction.

Results:

The ratio of T-Hb started to decrease after 10 h in the non-AS group but not in the AS group, and was significantly higher in the AS group at 22 h after birth. LBF and MABP did not differ significantly between groups, but calculated peripheral vascular resistance was significantly higher at 22 h in the ANS group.

Conclusion:

The mechanisms by which AS decreased the incidence of intraventricular hemorrhage might include increases in and/or stabilization of cerebral blood volume via increased peripheral vascular resistance. This study was funded by JSPS KAKENHI grant number JP15K09722.

The reference range for blood pressure of preterm infants born before GA30wk: Data from PLASE study

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The purpose of the study:

To investigate the appropriate range of blood pressures (BPs) for preterm infants born before GA30wk, at each gestational age, and days after birth.

Background:

There is a lack of evidence for the normal BP range for preterm infants. Previous studies focused on BPs of preterm infants were relatively old and mostly single-center studies. The BP data applied for this study were derived from PLASE study database. We prospectively corrected clinical and echocardiographic data of infants with gestational ages between 23 and 29 weeks in 34 Japanese NICUs over 14 months in PLASE study. Data points were 1, 3, 7 and 14 days of age to assess echo measurements and vital signs including blood pressure measured by either intra-arterial line and oscillometric method. BP data were analyzed with divided two groups, BPs of infants developed neonatal adverse outcomes related to cardiovascular instability and BPs of infants without those outcomes.

Results:

In total, 710 patients were analyzed for this study. Mean BPs of 23, 26 and 29 wkGA infants without certain neonatal adverse outcomes were: 23wk (n=40, 30.2mmHg(SD6.8) on Day1, 30.9mmHg(SD6.0) on Day3, 34.5 mmHg(SD6.6) on Day7, and 37.9mmHg(SD7.3) on Day14), 26wk (n=101, 31.6mmHg(SD4.5) on Day1, 34.5mmHg (SD6.4) on Day3, 37.4mmHg(SD8.1) on Day7, and 41.3mmHg(SD7.1) on Day14), and 29wk (n=125, 37.4mmHg (SD7.7) on Day1, 41.7mmHg(SD9.3) on Day3, 43.8mmHg(SD8.0) on Day7, and 45.9mmHg(SD9.1) on Day14). There was no significant difference between BPs of infants with and without neonatal adverse outcomes at almost all measuring points.

Conclusion(s):

The reference BPs of preterm infants increased as GA and days after birth. Further prospective clinical studies originally planned to investigate an optimal BP range of preterm infants are required to confirm this data.

Brain MRI and clinical outcomes of cerebral palsy patients of preterm infants

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Introduction:

We analyzed MRI scans of cerebral palsy (CP) patients of preterm babies by periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and cerebellar hemorrhage (CBH). We also assessed motor and neurocognitive outcomes associated with these findings.

Methods:

Retrospective study was done with preterm babies diagnosed with CP at 2 years of age. Neonates of 23-32 weeks' gestation born at Seoul National University Hospital in 2009 to 2015 without major congenital anomalies were included. The brain MRI scans at almost term-equivalent age were graded by their severity. Motor function was scored based on Gross function classification scale (GMFCS) and neurodevelopmental outcomes were assessed by using the *Bayley Scales of Infant and Toddler Development, Third Edition* (Bayley-III) or *Korean Ages and Stages Questionnaire (K-ASQ)* or *Korean Wechsler Intelligence Scale for Children, Fourth Edition (K-WISC-IV)*.

Results:

Among 618 survivors born between 23 to 32 weeks' gestation, 5.2% were diagnosed with CP. 37 infants were eligible for the study. The prevalence of CP was 11% in infants born between 23 to 28 week's gestation and 3.4% with gestational age of 28-32 weeks. 35 underwent MRI and 42.9% showed non-cystic PVL. Majority had brain insult postnatally (78.4%) by hypoxic events (86.2%). 74.3% were diagnosed with spastic diplegia. All spastic quadriplegia patients had walking and sitting dysfunction with cognitive and communication problems at 2 years of age, while 50% of spastic diplegia patients showed walking and communication problems. More patients with cystic PVL had poor motor and neurocognitive function than non-cystic PVL group.

Conclusion:

The prevalence of CP was 4.8% in 1993 to 1994, while 5.2% in our study. Non-cystic PVL and spastic diplegia type of CP were predominant. Severe motor and neurocognitive dysfunction were more observed in spastic quadriplegia and cystic PVL groups, which was also reported in previous data of 1993 and 1994.

Predictive value of F-18 FDG PET/CT for poor neurodevelopmental outcome in very-low-birth-weight infants without structural abnormalities

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Subject:

Although structural abnormalities are not observed on the brain magnetic resonance images (MRI) of very low-birth-weight (VLBW) infants, neurodevelopmental outcomes in such infants are still questionable. This study investigated the predictive value of F-18 fluorodeoxyglucose (F-18 FDG) brain positron emission tomography (PET) for neurodevelopmental outcomes in VLBW infants without structural abnormality.

Methods:

Twenty-seven VLBW infants without structural abnormality on the brain MRI were prospectively enrolled. All infants underwent F-18 fluorodeoxyglucose (F-18 FDG) brain PET and MRI at term-equivalent age. The regional glucose metabolic ratio and asymmetry index were calculated. Neurodevelopmental outcomes were assessed using Bayley Scales of Infant Development-II (BSID-II) of the Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) at a corrected age of 18-24 months. The poor neurodevelopmental outcome was defined as MDI or PDI < 85 on BSID-II. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC) of F-18 FDG PET/CT for predicting poor neurodevelopmental outcome were calculated using combination model of asymmetric index.

Results:

The glucose metabolic ratio of the right central region was significantly correlated with MDI ($r=0.505$, $p < 0.05$). The asymmetric indices of the central, lateral frontal, and thalamic regions were significantly correlated with MDI ($r=0.477$, 0.467 , and 0.451 , respectively, $p < 0.05$). The asymmetry index of the thalamus was significantly correlated with PDI ($r=0.410$, $p < 0.05$). The sensitivity, specificity, accuracy, PPV, NPV and AUC of F-18 FDG PET/CT are 100%, 58.8%, 74.1%, 58.8%, 100% and 0.75.

Conclusion:

The cerebral glucose metabolism measured by F-18 FDG PET at term-equivalent age was significantly correlated with MDI and PDI at a corrected age of 18-24 months. F-18 FDG brain PET could be used as a diagnostic tool to predict neurodevelopmental outcomes in VLBW infants without structural abnormality.

Lenticulostriate vasculopathy in very-low-birth-weight preterm infants: Presentations, evolutions and associated perinatal risk factors

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Background/Objectives:

Lenticulostriate vasculopathy (LSV) was first identified by cranial ultrasound (cUS) as vasculopathy of neonates over basal ganglia nearly 30 years ago but its pathogenesis and clinical significance remains unclear especially in preterm infants. The aim of our study is to determine the prevalence, the evolution and the associated perinatal risk factors among very low birth weight (VLBW) preterm infants with LSV.

Material/Methods:

One hundred and thirty VLBW preterm infants admitted at our NICU from January 2011 to March 2018 were enrolled. Serial cUS had been regularly performed since birth till corrected age of 1 year. LSV was divided into early-onset (≤ 10 postnatal days; PND) and late-onset (> 10 PND). Perinatal characters, placental pathology and neonatal morbidities were collected and compared between groups.

Results:

The prevalence of LSV before 1 year among these preterm infants was 39.2% (51/130). Bilateral linear type LSV was the most common presentation. The first detection timing of LSV were 44 ± 11.5 weeks of post-menstrual age and persistent for average 6 months. The PND at LSV first detection were 112 ± 83 days and was negatively correlated with the gestational age (GA) (R-square=0.153, $p=0.005$). Infants with LSV had similar perinatal characteristics, placenta pathology, incidence of cytomegalovirus infection and clinical morbidities with infants without LSV. Forty-five (88.2%) infants belonged to late-onset LSV. Infants with late-onset LSV had a significant higher rate of small for gestational age (SGA) and longer post-natal oxygen usage durations compared with infants without LSV. In a multivariable regression model adjusting GA and SGA, longer oxygen usage durations remains an independent risk factors for the development of late-onset LSV in VLBW infants. (OR=1.030, $p=0.032$)

Conclusion:

LSV maybe a nonspecific marker of perinatal insult to the developing brain of preterm infants. Prolong post-natal oxygen usage is one of the predisposing risk factors to develop late-onset LSV in VLBW preterm infants.

The application of continuous video electroencephalographic (cEEG) monitoring in the neonatal intensive care unit: A single center experience in Taiwan

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Background:

Neonates with seizures are frequently associated with acute brain injuries. The diagnosis of neonatal seizure remains challenging. Continuous video electroencephalographic (cEEG) monitoring is the gold standard for the diagnosis of neonatal seizures. The aim of this study is to identify the prevalence of electrographic seizures and analyze the clinical features of high-risk newborn infants with suspected seizures.

Methods:

We conducted this prospective cohort study in a tertiary neonatal intensive care unit between September 1, 2016 and December 31, 2018. Neonates with high risk of encephalopathy and receiving cEEG monitoring were eligible. Patients' demographic characteristics, indication for cEEG monitoring and presence of electrographic seizures were collected and analyzed.

Results:

A total of 82 neonates with high risk of encephalopathy underwent cEEG monitoring were enrolled. The majority of enrolled neonates were born at term (57%). Seventeen out of the 82 neonates (20.7%) were hypoxic ischemic encephalopathy (HIE) receiving therapeutic hypothermia. The median duration of cEEG monitoring in the current study was 22 hours. Neonates who received therapeutic hypothermia for HIE were monitored for a median duration of 42 hours. Electrographic seizures were captured in 21/82 (25.6% of monitored patients) and of those, 13/21(61.9%) had no clinical correlation. In addition, 51/82 subjects (62.2%) were monitored due to paroxysmal events concerning for seizures, but never had electrographic seizures.

Conclusion:

Electrographic seizures occurred in 25.6% of neonates with high risk of encephalopathy and were often electrographic-only in this study. We have demonstrated that continuous video electroencephalographic monitoring could help exclude neonatal seizures in more than one half of the cases.

A sporadic case of currarino syndrome with intraspinal tumor

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Introduction:

Currarino syndrome (CS) is an autosomal dominant disease characterized by anorectal malformation, sacroccocygeal defect, and presacral mass as triad. The condition is associated with a mutation of the MNX1 gene. While one of the common CNS manifestations is tethering of the cord, intraspinal tumor is very rare. We report a newborn case of CS with intraspinal tumor.

Case report:

A male newborn was born by NSVD at 38⁺² weeks gestational age. Fetal sonography showed ambiguous genitalia and ill-defined anus. The family history was irrelevant. Body weight was 3,230 g (50-90 p), height was 49.5 cm (50 p), head circumference was 34.1 cm (50 p). Imperforated anus, bifid scrotum, hypospadias and simian crease on right hand were observed. Meconium was excreted through fold at perineum and urination via urethral end at left side of penis. Pelvic MRI showed irregular shaped presacral mass with heterogeneous enhancement; urethra was intact. Spine MRI showed expansile intramedullary thickening of spinal cord with diffuse enhancement of its surface below T 7-8 and tethered spinal cord. AFP 42,632 ng/mL, Beta-hCG 0.3 mIU/mL were confirmed. SRY gene was positive and karyotype was 46 XY. Genetic analysis to identify a pathogenic mutation in the MNX1 gene is pending. Colostomy and surgical resection of presacral mass was performed on the 5th and 14th day after birth, respectively. Spinal cord biopsy was also done. On pathology, the presacral mass was confirmed to be immature teratoma grade 3 with yolk sac tumor and embryonal carcinoma components. Tissue from the spinal cord was revealed to be involvement of immature teratoma. AFP declined to 1,356 ng/mL 12 days after operation.

Conclusion:

Although not part of the original triad, spinal abnormalities including tumor can occur in CS. Lumbosacral imaging and or biopsy should be included for investigation of CS.

Effect of oral care on the incidence of early-onset ventilator-associated pneumonia in preterm infants

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Background:

Ventilator-associated pneumonia (VAP) is a potentially serious complication related to mechanical ventilation in critically ill patients. However, few studies have investigated the efficacy of an oral care protocol in reducing VAP in preterm infants. This study aimed to investigate the efficacy of an oral care protocol in reducing the number of oral bacteria and incidence of early-onset (within 4 days of intubation) VAP in preterm infants.

Methods:

We conducted a prospective study on preterm infants born between 2014 and 2019. Oral hygiene care was performed by swabbing the oral cavity in six locations using a sponge brush moistened with sterile water. The number of oral bacteria was measured for approximately 1 min on-site using the Bacterial Counter (PHC) before and after oral care in preterm infants supported by endotracheal intubation (ETI), continuous positive airway pressure (CPAP), or high-flow nasal cannula (HFNC). The incidence of early-onset VAP in infants undergoing oral care prior to re-intubation was compared with that of infants without performing oral care.

Results:

Mean (SD) gestational age and birthweight for our study population (comparison of oral bacterial number) were 27.0 (3.2) wks and 1023 (490) g, respectively. The mean number of oral bacteria was significantly lower ($p < 0.01$) after the oral care, respectively : 4.46×10^7 vs 1.25×10^6 , ETI, $n=23$; 1.32×10^7 vs 6.82×10^5 , CPAP, $n=38$, and 1.68×10^7 vs 6.50×10^5 , HFNC, $n=22$). The incidence of early-onset VAP was 51% (19/37) after re-intubation without performing oral care and significantly decreased to 20% (6/30; $p=0.008$) with our oral care protocol.

Conclusion:

Oral hygiene care using a sponge brush moistened with sterile water appears to be effective in reducing the number of oral bacteria and the incidence of early-onset VAP in preterm infants.

The impact of early empiric antibiotics use on gut microbiota in very low birth weight preterm infants

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Introduction:

Antibiotics are known to disrupt microbial balance. Our objective was to determine the impact of different empiric antibiotics use in the first week of life on microbial colonization and diversity in very low birth weight (VLBW) preterm infants.

Methods:

Breast fed VLBW infants were divided into two groups, including those who received 3 d of combination treatment of ampicillin and gentamicin (AG group), and those received 7 d of ampicillin and cefotaxime (AC group). Infants with any antibiotics use after age of 7d and infants on exclusive formula feeding were excluded. Stool samples were collected at age of 7d, 14d, and 30d. The 16s ribosomal DNA community profiling was used to compare the microbiota between two groups.

Results:

Twenty-four infants were enrolled in our study (AG group=10, AC group=14). The gestation age and birth weight were 30.0 ± 2.5 weeks and 1286 ± 190 gm in the AG group versus 28.9 ± 2.5 weeks and 1099 ± 280 gm in the AC group, respectively. Infants of AC group had significantly increased abundance of *Enterococcus* in the 7th day of life compared to those of AG group (12.3% vs 0.6%, $P=.032$). The richness of species in AC group significantly decreased in the 14d ($p=.038$) and 30 d ($p=.030$) samples as compared to that in the 7d sample. The evenness was lowest in the 7d sample of AC group comparing to the 14d and 30 d samples ($p=.041$). The diversity within group had no significant difference between two groups in each time period samples.

Conclusions:

Different antibiotic treatments affect the early development of gut microbiota in VLBW preterm infants. A combination of ampicillin and cefotaxime resulted in an overgrowth of *Enterococcus* and a decreased in richness and evenness. The clinical relevance of these findings is to be elucidated in further studies.

Cord blood procalcitonin level predicts the severity of early-onset sepsis in extremely preterm infants

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Background:

Early-onset sepsis (EOS) is a major cause of morbidity in preterm infants. Particularly in extremely preterm infants, severe cases have a high mortality rate. As options such as PMX-DHP are available for severe sepsis, early prediction of the severity of EOS is important. Although some reports have indicated that serum procalcitonin (PCT) level is useful as a marker of neonatal sepsis, no studies have reported on the prediction of the severity of these sepsis using PCT level. We analyzed the transition of PCT levels after birth and examined the prediction of severe cases in extremely preterm infants

Methods:

This was a retrospective case-control study of extremely preterm infants (26.0 weeks of gestation, IQR: 24.6-26.9) who were <12 h of age at admission to our hospital between January 2011 and December 2018. The patients were categorized using culture, laboratory, and clinical data into the EOS or non-EOS group. We further divided the EOS group into death and survival cases and compared the course of the PCT.

Results:

Among 102 infants, 15 (14.7%) were classified as EOS. We found no difference in median in cord blood PCT level between the EOS and non-EOS groups (median, 0.7 ng/mL vs 0.4 ng/mL) and a significant difference in PCT level on day 1 (median, 94.0 ng/mL vs 4.8 ng/mL). Within the EOS group, we found a marked difference in cord blood PCT level between EOS death and EOS survival (median, 89.4 ng/mL vs 0.5 ng/mL).

Conclusions:

In the comparison between EOS and non-EOS, the difference was more noticeable in day 1 PCT than in cord blood PCT. However, cord blood PCT may be a sensitive indicator of the severity of EOS.

Emerging serotype III Sequence type 17 group B streptococcus invasive infection in infants: The clinical characteristics and impacts on outcomes

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Background:

Group B Streptococcus (GBS) is an important pathogen that causes high mortality and morbidity in young infants. However, data on clinical manifestations between different GBS serotypes and correlation with molecular epidemiology are largely incomplete. The aim of this study was to determine the serotype distribution, antimicrobial resistance, clinical features and molecular characteristics of invasive GBS isolates recovered from Taiwanese infants.

Methods:

From 2003 to 2017, 182 non-duplicate GBS isolates that caused invasive disease in infants less than one year of age underwent serotyping, multilocus sequence typing (MLST) and antibiotic susceptibility testing. The clinical features of these infants with GBS disease were also reviewed.

Results:

Of the 182 patients with invasive GBS disease, 41 (22.5%) were early-onset disease, 121 (66.5%) were late-onset disease and 20 (11.0%) were late late-onset disease (>90 days of age). All these patients were treated with effective antibiotics on time. Among them, 51 (28.0%) had meningitis, 29 (16.0%) had neurological complications, 12 (6.6%) died during hospitalization, and 15 (8.8%) out of 170 patients who survived had long-term neurological sequelae at discharge. Serotype III GBS strains accounted for 64.8%, followed by serotype Ia (18.1%) and Ib (8.2%). MLST analysis revealed 11 different sequence types among the 182 isolates and ST-17 was the most dominant sequence type (56.6%). The correlation between serotype III and ST17 was evident, as ST17 accounted for 87.3% of all serotype III isolates. There was an obvious increasing trend of type III/ST-17 GBS that caused invasive disease in infants. All isolates were susceptible to penicillin, cefotaxime, and vancomycin, while 68.1% and 65.9% were resistant to erythromycin and clindamycin, respectively.

Conclusions:

Despite timely and appropriate antibiotic treatment, a significant proportion of invasive GBS disease still inevitably causes adverse outcomes. Further study to explore preventive strategies and development of serotype-based vaccines will be necessary in the future.

Prevalence, carriage duration, serotype and genotypic variations of neonatal group B streptococcus colonization in Taiwan

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Background:

Group B Streptococcus (GBS) commonly colonizes in the vaginal tract of a pregnant woman, and GBS infection in neonates can be life-threatening. We aimed to study the prevalence of GBS colonization after implementation of IAP, the duration of GBS carriage, and the serotypes and genotypic variations among GBS strains at a single medical center in Taiwan.

Methods:

From August 2015 to July 2018, 1055 neonates born in the Chang Gung Memorial Hospital were randomly enrolled in our study. For all the enrolled neonates with maternal GBS screening, nasal and rectal swabs were taken within 24 hours after birth, and the subsequent GBS-positive participants would be pursued for GBS carriage until cultures proven negative. Capsular serotyping, multilocus sequence typing (MLST) and pulsed-field gel electrophoresis (PFGE), were taken to analyze the GBS positive neonates.

Results:

Among the 1055 enrolled neonates, only 16 (1.5 %) were found to be GBS-positive. The GBS carriage rates in the vaginal tract of the mothers were 14.7% (155/1055). A total of three patients (18.8%, 3/16) were found to have long-term GBS colonization for more than 6 months. The predominant serotype among the 16 GBS isolates was III (25%). Amongst the three long-term GBS carriers, two were serotype II and one was serotype III (two were born to non-carrier mothers). The major sequence type was ST1 (56%, 9/16). In PFGE patterning, there were three pairs of PFGE-various strains sharing the same serotypes and sequence types.

Conclusions:

Neonatal GBS colonization is greatly associated with maternal GBS status. For IAP indicated mothers, complete antibiotic treatment could significantly reduce the rate of neonatal colonization. GBS colonization in neonates may last up to 6 months. On the other hand, the genetic discrimination by serotyping and sequence typing seems to be insufficient and may work better with the help of PFGE patterning.

Successful treatment of intractable hyperinsulinic hypoglycemia by diazoxide in a neonate with trisomy 13

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Background:

Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoglycemia in neonates and infants. Immediate evaluation and early diagnosis of CHI are important for initiating the appropriate treatment. Trisomy 13 (T13) is one of the most common numerical chromosomal disorder with poor mortality and morbidity. There has been no report regarding a relationship between CHI and T13 although genes regarding insulin resistance are involved in chromosome 13. Here, we describe a Japanese male infant with T13 who developed intractable CHI.

Case presentation:

A Japanese male infant was born at 31 weeks of gestation via emergent Caesarean section due to deterioration of maternal pregnancy-induced hypertension. His birth weight and Apgar scores were 1,298 g and 2-6, respectively. Upon admission, he was suspected to have chromosomal disorder owing to low birth weight, partial scalp defect, cleft lip and palate, binaural hypoplasia, polydactyly, rocker-bottom feet, and atrial septal defect; T13 was confirmed by G-banding on the day of life (DOL) 22. Soon after birth, he showed hypoglycemia despite receiving continuous intravenous infusion of 10% dextrose in water. Glucose infusion rate (GIR) was increased, but hypoglycemia persisted. On DOL 28 he showed hypoglycemia of 39 mg/dL concomitant with hyperinsulinemia of 47.5 μ U/mL (rr: <1). GIR was increased up to 10 mg/kg/min to maintain normal blood glucose level. He was diagnosed with CHI, and 5 mg/kg/day of diazoxide was administered orally on DOL 35. After starting diazoxide, he got prompt resolution of hypoglycemia and intravenous infusion of dextrose was discontinued on DOL 48. No serious complications regarding diazoxide were seen.

Conclusion:

CHI is rare condition in T13 but may lead to serious condition due to severe hypoglycemia. Diazoxide may be a beneficial and feasible option for intractable CHI even in patients with chromosomal disorder including T13.

Effects of fish oil-containing lipid emulsions on retinopathy of prematurity in very low birth weight infants

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Background:

The aim of the study was to assess the impact of different types of lipid emulsions on retinopathy of prematurity (ROP) in very low birth weight (VLBW, birth body weight <1500 g) infants by comparing fish oil-containing and soy-based parenteral emulsions.

Methods:

Data of preterm infants with body weights below 1500 gm at birth and receiving total parenteral nutrition (TPN) for a minimum of 7 days during the period between January 2009 and November 2017 were analyzed in this retrospective study. We compared clinical outcomes in two epochs using different lipid emulsions: epoch 1 (soybean-based lipid emulsions, January 2009-February 2014) versus epoch 2 (fish oil-containing lipid emulsions, January 2015-November 2017). The primary outcomes measured were the incidence of ROP and the number of ROP cases requiring bevacizumab therapy.

Results:

A total of 396 infants were enrolled in this study (203 in epoch 1 and 193 in epoch 2). A lower incidence of any stage ROP (24.1 versus 11.4%, $p < 0.001$) and lower requirement of bevacizumab therapy (12.8 versus 5.2%, $p = 0.001$) were observed in epoch 2. Gestational age; glutamic-pyruvic transaminase, total bilirubin, and alkaline phosphatase levels; and type of lipid emulsion in TPN were associated with higher ROP incidence. Multivariate logistic regression analysis revealed that parenteral nutrition in the form of lipid emulsions containing fish oil was associated with a lower risk of development of ROP [Odds Ratio: 0.178, 95% confidence interval (CI): 0.095-0.330, $p < 0.001$].

Conclusions:

Compared with soybean-based lipid solutions, the use of fish oil-containing lipid solutions may be associated with a lower incidence of ROP and decreased need for bevacizumab treatment in preterm infants.

Thioredoxin-1 ameliorates oxygen-induced retinopathy in newborn mice

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Introduction:

Oxygen-induced retinopathy (OIR) is a model for human retinopathy of prematurity, which is one of the leading cause of blindness in children. In mice with OIR, avascular region and neovascularization were observed in the retina. Thioredoxin-1 (TRX) is a small redox protein which has cytoprotective and anti-inflammatory effects against various oxidative stresses. In the present study, we evaluated the role of TRX on OIR in newborn mice.

Method:

C57BL/6 wild-type (WT) and TRX transgenic (TRX-Tg) mice were exposed to either 21% or 75% oxygen from postnatal day 7 to 12. Some mice were allowed to recover in room air to postnatal day 17. Avascular and neovascular regions of the retinas were analyzed using fluorescence immunostaining of whole-mount retinas with anti-CD31 antibody. Total RNA was extracted from retinal tissues for quantitative PCR.

Result:

In air, the WT developed well-organized retinas. In contrast, exposure of WT newborn mice to 5-day hyperoxia impaired retinal development, resulting in increased avascular and neovascular areas of the retinas on day 12 and 17, respectively. After hyperoxic exposure, TRX-Tg had improved avascularization in the retina compared with WT. Furthermore, during recovery from 5-day hyperoxia, TRX-Tg suppressed retinal neovascularization (abnormally tortuous and dilated retinal vessels) compared with WT, indicating that TRX-Tg mitigated the effect of hyperoxia on retinal development.

Conclusion:

We conclude that TRX ameliorates OIR in newborn mice. Further studies are needed to understand the mechanism of this beneficial effects of TRX on modulating neonatal retinal development.

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