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ABSTRACTS

SATURDAY, NOVEMBER 24, 2018

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STABILIZATION OF HIGH RISK INFANTS, RESPIRATORY CARE AND PULMONARY DISEASES

1
HIGH-FIDELITY SIMULATION VERSUS TRADITIONAL LOW-FIDELITY IN NEONATAL RESUSCITATION

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Background. High-fidelity simulation represents a useful teaching-learning strategy to enhance confidence and competence in neonatal practice, especially for residents in small hospital. At the University Hospital of Messina, neonatal advances life support (NALS) trainings for residents are performed with the use of a hi-fi simulation mannequin since 2012, while a standard plastic mannequin was used prior to 2012.
Objective. We compared the degree of education and performances of residents achieved with the use of a hi-fi simulation mannequin and with a standard plastic mannequin.
Methods. The primary outcome of this study was to retrospectively compare the degree of either knowledge or skill assessment scores for NRP certification, among 210 residents trained, by the same instructors, with the use of a traditional plastic mannequin in the period of 2009-2011, in comparison to 230 residents trained with the hi-fi mannequin in the period of 2012-2014. Currently the recommended passing standards for NRP certification is set as >80% on the knowledge assessment and >85% on the megacode assessment PLUS completion of 5 critical tasks. Knowledge was analyzed by using the standard written examination taken from the NRP instructor's manual. Skills were analyzed by using the megacode assessment form provided in the NRP instructor's manual.
Results. Compared with those trained with the traditional plastic mannequin, residents who were trained whit the hi-fi mannequin reached a greater mean score either in the knowledge assessment (90% ± 5% versus 92% ± 8%; P = 0.0020) and in the performances at the megacode assessment (90% ± 7% versus 92% ± 6%; P = 0.0015).
Conclusion. In our experience, the use of a hi-fi mannequin in neonatal resuscitation training was well-received by the residents and significantly improved the degree of knowledge and performance when compared with the traditional plastic mannequin.

2
TRENDS OF THE PREVALENCE AND THE MORTALITY OF CONGENITAL ANOMALIES IN KOREA, 2009-2016

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Background. Major congenital anomalies are important because they are the leading cause of fetal and infant death. Recent researches have reported that the prevalence rate of congenital anomalies in Korea is increasing every year, but they did not include fetal mortality due to congenital anomalies. Here, we report the prevalence rate of congenital anomalies including fetal death in Korea, and the annual changes in prevalence and infant mortality.
Methods. Data from Health Insurance Review and Assessment Service and annual birth, fetal death and infant death data of Korean National Statistical Office from 2009 to 2016 were used. Fetal and infant mortality as well as the prevalence rate due to congenital anomalies within one year of birth were studied.
Results. Prevalence rate of major congenital anomaly was high in cardiovascular (246.3 per 10,000 livebirths), musculoskeletal (143.6 per 10,000 livebirths) and urinary system (62.8 per 10,000 livebirths), and fetal mortality of major congenital anomaly was highest in chromosome disorder (3.0 per 10,000 livebirths and fetal deaths) followed by the nervous system (1.4 per 10,000 livebirths and fetal deaths). The prevalence rates of congenital anomaly showed an increase from 2009 – 2016 and mild defects, which are the majority in each system, mainly increased. Fetal mortality of congenital anomalies showed slight variations from year to year, with decreasing tendency.
Conclusions. The prevalence of congenital anomalies including fetal death rate showed a yearly increase related to a large number of mild defects, which takes up for most of the congenital anomalies.

3
A SURVEY ON THE CURRENT KNOWLEDGE AND PRACTICE OF UMBILICAL CORD CLAMPING AFTER BIRTH IN CHINA

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Objective. To investigate current knowledge and practices in healthcare professionals on the umbilical cord clamping in China.
Methods. Two to three provinces were selected at random in South, North, East, Central, Northwest, Southwest and Northeast of China, yielding 16 in total. In these provinces, we randomly selected one or two tertiary comprehensive hospitals and maternity-infant hospitals, and secondary comprehensive hospitals and maternity-infant hospitals, according the hospital level on the website of the National Health Commission of China. An extensive survey was conducted by online questionnaire.
Results. There were 5,672 participants who completed the questionnaire; the response rate was 71.8%, 84.0% of responders were aware of the concept and procedure of delayed cord clamping. Obstetricians, midwives and neonatal doctors accounted for 88.0%, 92.5% and 67.2%, respectively (p=0.000). The knowledge of delayed cord clamping mainly came from literature search (37.2%), expert lectures (58.8%) and international guidelines (35.1%) (p=0.0035). In practice, 30.9% regarded delayed umbilical cord clamping until the umbilical cord pulse has ceased, while the rest had set times. The main reason for delayed cord clamping was to increase blood volume and to stabilize the circulation (94.0%).
50.5%, 62.4% and 48.8% of obstetricians, midwives and neonatologists were aware of umbilical cord milking (p=0.001). The clinical application rate of complete umbilical cord milking was 1.11%.
Conclusion. Although there is a large amount of evidence supporting delayed cord clamping, there is no clear definition of it in policies and practice by care givers from the surveyed hospitals in China. While the majority of obstetricians and midwives participated in this study had a positive perception toward delayed cord clamping, this did not translate into their daily practice completely. Further studies are warranted to confirm these findings.

4
EVALUATION OF NEWBORNS WITH CONGENITAL PULMONARY AIRWAY MALFORMATION: A SINGLE CENTER EXPERIENCE

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Background. Congenital pulmonary airway malformation (CPAM) is a rare developmental anomaly affecting the lower respiratory tract in newborns. This study aimed to evaluate clinical, imaging, and surgical findings of newborns with CPAM.
Methods. The medical records of prenatally diagnosed CPAM patients born in the Severance Children's Hospital between January 2005 and July 2017 were reviewed. A total of 66 patients were enrolled. The pre- and postnatal data were collected and analyzed.
Results. 33 boys and 33 girls with a median gestational age of 38.8 weeks and a birthweight of 3050g were enrolled. 15 cases showed regression of cystic lesions in prenatal ultrasound before birth. However, 7 cases revealed inconsistent findings by postnatal lung ultrasound(U/S) or chest computed tomography (CT). In contrast, chest x-rays revealed no lesions in 22 cases. 16 cases with negative chest x-ray findings were diagnosed as having mass-like lesions by lung U/S and/or chest CT. 25 cases were symptomatic at birth, including pneumothorax and ventilator care. Respiratory symptoms during infancy were noted in 12 cases. Surgery was performed in 22 cases at a mean age of 23.4 month by video-assisted thoracoscopy. Pathology was compatible with previous image findings including CPAM type 1~3 and pulmonary sequestration. The type of CPAM was not significantly associated with respiratory symptoms at birth or respiratory morbidity during infancy.
Conclusion. We have provided a comprehensive picture of CPAM in a children's hospital; however, factors to predict respiratory symptoms at birth and during infancy are not well defined. Antenatal and postnatal U/S and neonatal chest x-ray were not consistent and appeared to be unreliable in the diagnoses of CPAM. Thus, chest CT combined with close monitoring of clinical symptoms in CPAM patients by regular follow up at outpatient clinics is important to guide the correct timing of elective surgery.

5
PHYSICAL ACTIVITY BUT NOT EXERCISE CAPACITY IS REDUCED IN SCHOOL-AGE CHILDREN BORN PREMATURELY WITH BRONCHOPULMONARY DYSPLASIA

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Background. Recent advances in neonatal care have improved survival rates in children born extremely preterm. Extreme prematurity is related to a higher incidence of bronchopulmonary dysplasia (BPD), not only affecting neonates but continuing to impact health during childhood and adolescence.
Objective. This study analyzes the impact of BPD on physical activity and exercise capacity at school-age.
Methods. 22 school-aged children (9 with BPD (PRE+BPD) 13 without BPD (=PRE)) born with a gestational age <32 weeks and a birthweight <1500 g as well as 15 healthy term-born controls (CON) were included in the study. Physical activity was measured by accelerometry, lung function and exercise capacity by spirometry and an incremental exercise test.
Results. PRE+BPD showed lower values in spirometry and diffusion capacity but an equal oxygen uptake during maximal exercise. However, PRE+BPD achieved a lower work load at maximal exercise. As to physical activity, PRE+BPD and PRE spent significantly more time in sedentary behavior and less in moderate and vigorous physical activity. In our cohort, prematurity is related to less engagement in physical activity and a preference for sedentary behavior at school-age. Although children with BPD showed a slight impairment of lung function, their oxygen uptake at maximum exercise did not differ from CON or PRE.
Conclusions. Inactivity and a reduced exercise capacity predispose for cardiovascular risk factors such as high blood pressure and are related to lower bone mineral density and impaired glucose tolerance. Counseling for regular exercise should be done in former preterm children, especially if they already show an impairment of lung function.

6
NEONATAL RESPIRATORY FAILURE ASSOCIATED WITH GENETIC SURFACTANT DYSFUNCTION DUE TO A MUTATION IN THE SURFACTANT PROTEIN – C GENE: A CASE REPORT.

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Background. Genetic surfactant dysfunction accounts for nearly 10% of all causes of interstitial lung disease in infants younger than 2 years of age. Surfactant protein C deficiency in neonates is associated with various clinical manifestations ranging from respiratory distress to lethal lung disease.
Objective. To study the clinical characteristics and treatment of interstitial lung disease associated with genetic surfactant dysfunction due to a mutation in the SFTPC gene.
Method. A case study and a literature review of cases of neonatal respiratory failure associated with genetic surfactant dysfunction was performed.
Results. We describe a 4-day-old newborn infant with progressive fatal respiratory symptoms that was associated with mutation c.563C>T (p.Leu188Pro) in exon 5 of the SFTPC gene. The histology of lung autopsy showed a diffuse proliferation of type II alveolar cells and interstitial fibroblasts. The patient did not responded to respiratory support and antibiotic treatment. A literature review shows a variety of clinical characteristics and a wide range of treatments, including lung lavage, surfactant replacement therapy, immunosuppressive therapy, and lung transplantation.
Conclusions. We recommended that this disorder should be confirmed as soon as possible in the infants with the suggested factors: interstitial lung disease on X-ray, familial history of respiratory diseases and non-response to antibiotic treatment.

7
THE PATTERN AND OUTCOMES OF USE OF INHALED NITRIC OXIDE IN PRETERM INFANTS IN PRACTICE, A 5 YEAR REVIEW

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Background. The use of inhaled nitric oxide (iNO) in preterm infants was not well supported by the current evidence. Recent epidemiological studies reported an increasing trend of its use. The clinical application of iNO in preterm infants is controversial.
Objective. Our study aimed at describing the pattern of clinical use of iNO in preterm infants in a tertiary neonatal intensive care unit in Hong Kong. The short-term outcomes of preterm infants received iNO and the characteristics associated with survival were also studied.
Methods. A retrospective case review were conducted on preterm infants, born at </= 34 weeks gestation, admitted to the neonatal intensive care unit (NICU) of Queen Elizabeth Hospital in Hong Kong and exposed to inhaled nitric oxide from January 2013 to December 2017. In the unit, iNO was used as a rescue therapy for infants with oxygenation failure and clinical diagnosis or suspicion of pulmonary hypertension. Baseline neonatal demographic data, antenatal and perinatal risk factors and ventilation variable related to iNO use were collected. Short-term outcomes including improvement in oxygenation and mortality were evaluated.
Results. A total of 47 infants received iNO therapy in the unit during the 5 year period. Twenty-one (45%) were preterm infants </= 34 weeks. Within the cohort, 18 infants received iNO within the first 28 days of life. The mean gestational age was 28.4 +/- 3.4 weeks and the mean birth weight was 1230+/- 633g. The majority were started on iNO with the first 3 days (83%) and put on high frequency ventilation (88.9%) when iNO was started. The mean oxygen index was 39.98 +/-31.59. Echocardiographic evidence of pulmonary hypertension was present in 77.8% of the infants. We found that 33% of infants showing improvement in oxygenation with FiO2 reduction after 1 hour of treatment . The mortality during their NICU stay was 55%. The infants who survived were of higher gestational age and larger birth weight, though not reaching significance. Premature prolonged rupture of membrane, oligohydramnios and sepsis were not shown to be associated with better survival.
Conclusion. In our clinical practice, iNO was mainly used as an early rescue therapy in preterm infants with oxygenation failure and clinical diagnosis of pulmonary hypertension. Only a small proportion of infants responded to iNO and the mortality was relatively high, which may be explained by the complexity and heterogeneity of the underlying aetiology of their respiratory conditions.

8
COMPARISON BETWEEN THE ANIMAL-DERIVED SURFACTANTS KELISU® AND CUROSURF®: IN VITRO BIOPHYSICAL PROPERTIES AND PULMONARY OUTCOMES IN VENTILATED PRETERM RABBITS WITH SEVERE SURFACTANT DEFICIENCY

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Background. Curosurf® and Kelisu® are two widely used surfactant preparations in China for the treatment of respiratory distress syndrome in preterm neonates with primary surfactant deficiency. The former preparation is extracted from pig lungs, with neutral lipids depleted, and licensed to be administered at doses of 100 and 200 mg/kg, whereas the latter preparation is from bovine (calf lung) origin and delivered at 70 mg/kg. A comparison of these surfactants addressing the *in vitro* performance as well as the *in vivo* pulmonary efficacy is not available yet.
Objective. To compare the biophysical properties and the pulmonary efficacy of the two surfactant preparations.
Methods. Biophysical properties and ultrastructure of both surfactants were investigated by Langmuir-Blodgett Trough (LBT) and Atomic Force Microscopy (AFM). The lipid composition was determined by liquid-chromatography mass-spectrometry. A head-to-head comparison of the clinical doses of Curosurf® (100 and 200 mg/kg) and Kelisu® (70 mg/kg) was performed in preterm rabbits (delivered d27, term d30-31). Two additional groups received 100 and 200 mg/kg of Kelisu® to match the clinical dose of Curosurf®. After randomization, pups underwent 3 hours of mechanical ventilation (MV, tidal volume 4-6 mL and positive end-expiratory pressure 2-3 cmH_2O). Dynamic compliance of respiratory system (C_{dyn}) and mortality were assessed during MV. *Post mortem*, lung injury scores and alveolar expansion (V_v) were determined.
Results. AFM revealed overlapping lipid bilayers in Curosurf®, which were absent in Kelisu®, most probably due to substantial differences in lipidic composition, i.e., the absence of cholesterol in Cursourf but the presence in Kelisu. This might lead to a longer plateau region of the isotherm and lower film compressibility of Kelisu® as determined by LBT. Curosurf® delivered at 200 mg/kg showed the highest C_{dyn} and V_v, and the lowest injury scores, and reduced mortality significantly compared to other groups. The remaining groups showed intermediate benefits, which were dose-dependent.
Conclusions. At the recommended initial therapeutic dose Curosurf® was more effective than Kelisu® in terms of alveolar expansion, protection of lung parenchyma for better animal survivals, which may be associated with composition properties.
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9
SPONTANEOUS BREATHING TRIAL TO FACILITATE EXTUBATION IN A TERTIARY NEONATAL INTENSIVE CARE UNIT

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Background. There are limited tools available to assess extubation readiness and predict extubation success of intubated neonates. Spontaneous breathing trial (SBT) is a well-known method used in adult and pediatric intensive care to assess extubation readiness. Studies using SBT in neonatal intensive care are limited.
Objective. The objective of this study is to evaluate the impact of implementing an SBT protocol on extubation failure (EF) and duration of mechanical ventilation at a tertiary level neonatal unit.
Method. This is a retrospective chart review study. Our NICU implemented an SBT protocol in 2013. This 10 minute trial is conducted in two stages: three minutes ETT CPAP (no change in PEEP), followed by seven minutes of CPAP with pressure support (PS). If patients meet pre-defined criteria they are considered ready for extubation. The charts of all intubated infants admitted to the NICU one year before (group 1) and one year after the SBT protocol implementation (group 2) were reviewed.
Results. A total of 820 charts were reviewed; 397 in group 1 and 423 in group 2. A total of 231 patients were excluded for predefined criteria, leaving 294 in group 1 and 295 in group 2 who were included in the analysis. There was a significant reduction of > 50 % in EF rate after SBT protocol implementation, as 29 out of 294 (9.86%) failed extubation in group 1 compared to 12 out of 295 (4.07%) in group 2, (P 0.006). The overall duration of intubation (DOI) prior to extubation attempt remained stable.
Conclusions. Implementation of SBT protocol in our NICU has significantly reduced extubation failure rate with no significant change in the duration of intubation. Our results suggest that an SBT protocol may be safely implemented in NICUs with a similar patients' population and may assist clinicians in assessing extubation readiness and reduce extubation failure.

10
HYPEROXIA EXPOSURE CAUSES EPITHELIAL MITOCHONDRIAL DYSFUNCTION AND CHANGES OF LUNG FUNCTION IN NEWBORN RATS

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Objective. We sought to examine the change of newborn rat pups lung function and mitochondrial function, mitophagy and apoptosis proteins, and lung development in different times of oxygen exposure in newborn rats and ATII cells.
Methods. We studied changes in lung injury and lung function in newborn rats as well as changes in mitochondrial function and protein expression in ATII cells from newborn rats after high oxygen(85%)exposure for different durations.
Results. In vivo, after 6 d of hyperoxia exposure, newborn rat pups exhibited significant weight loss, noticeable pulmonary inflammation, delayed alveolar development, and pulmonary fibrosis. Compared with normoxic rats, hyperoxic rats exhibited appreciable increases in basal pulmonary airway resistance (Rn), tissue damping (G) and tissue elastance (H); moreover, Rn, G, and H increased further in hyperoxic rats in response to increasing doses of a bronchoconstrictor. In vitro, ATII cells exhibited appreciably damaged mitochondrial function, reduced mitochondrial membrane potential, and the overproduction of both total cellular reactive oxygen species (ROS) and mitochondrial ROS after 24 h of hyperoxia exposure. The expression of mitochondrial autophagy and apoptotic proteins in lungs and ATII cells was significantly altered in a time-dependent manner. Noticeable autophagosomes appeared in ATII cells.
Conclusion. These results indicate that hyperoxia exposure activated mitochondrial autophagy and apoptosis in ATII cells, thereby affecting mitochondrial function and causing pulmonary epithelial cell death as well as delaying lung development and inducing changes in lung function in newborn rats.

11
THE EFFECT AND SAFETY OF MINIMALLY INVASIVE SURFACTANT THERAPY IN VERY PRETERM NEONATES WITH RESPIRATORY DISTRESS SYNDROME

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Objective. To explore the effect and security of minimally invasive surfactant therapy (MIST) in treatment of preterm neonates with respiratory distress syndrome (RDS).
Methods. Patients in 30-36 weeks of gestation with RDS were randomly divided into MIST (n=23) and intubation-surfactant-extubation-continuous positive airway pressure ventilation (INSURE, n=25). The MIST group was treated by nCPAP and a thin vascular catheter was inserted through the vocal cords under direct vision with laryngoscope, then pulmonary surfactant (PS) was infused into the lungs. INSURE group was first treated with nCPAP to stabilize, and then disconnected, endotracheal intubated and PS infused into the lungs, followed by bagging with positive airway pressure, then extubated to nCPAP again. The prevalences of adverse events related to the two strategies of surfactant application and major complications were recorded.
Results. There were no significant differences between the two groups in desaturation (26.1 vs. 36.0%), bradycardia (13.0 vs. 24.0%), repeated doses of PS (8.7 vs. 4.0%), and reintubation within 72 h. There was no significant difference in the noninvasive ventilation time (8 vs. 7 d), total oxygen intake and length (12 vs. 10 d), length of hospital stay (34.2±16.1 vs. 30.9±14.3 d), pneumothorax (0 vs. 4%), bronchopulmonary dysplasia (21.7 vs. 16.%), retinopathy of prematurity (21.7 vs. 12.0%), necrotizing enterocolitis (21.7 vs. 12.0%), and no intraventricular hemorrhage or mortality.
Conclusion. We achieved a safe and effective use of surfactant by either MIST or INSURE in very preterm infants with RDS, suggesting these methods of surfactant delivery could be beneficial in daily practice to minimize adverse events related to intratracheal intubation and mechanical ventilation.

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PROGNOSIS OF 141 PRETERM INFANTS WITH NEONATAL RESPIRATORY DISTRESS SYNDROME

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Objective. To explore morbidity, risk factors, prognosis of neonatal respiratory distress syndrome (RDS), we retrospectively analyzed the clinical data of neonatal RDS in our NICU for the past 4 years. The early preterm infants were divided into groups to analyze the prognostic risk factors.
Methods. Inborn preterm infants with RDS who were admitted to our NICU from January 2013 to December 2016 were recruited and their clinical data were analyzed. In 77 cases of neonatal RDS, those with GA < 32 weeks were divided into better or poor prognostic group according to the conditions at the time of discharge, and we then analyzed the risk factors affecting the prognosis.
Results. 141 cases of neonatal RDS were collected corresponding to an annual prevalence of major morbidity in the 4 years of 0.76%, 1.05%, 1.02% and 1.58%, respectively. The prevalence rates of RDS among GA < 32, 32-33, 34-36 and ≥37 were 58.2%, 24.8%, 12.8% and 4.2%, respectively. Common comorbidities and major complications were pneumonia (55.3%), PVH-IVH (49.6%), sepsis (30.5%), ROP (29.6%), BPD (17%), PDA (12.8%), pulmonary hemorrhage (6.4%), PPHN (2.8%), pneumothorax (2.8%), NEC (2.1%). Antenatal glucocorticoid use in RDS with GA < 34 weeks was 36.8%; surfactant use 81.6%, a success rate of nasal CPAP or oxygen was 34%, and 66% of cases required intratracheal ventilation. 116 preterm infants with RDS improved and were discharged from our hospital. The survival rate for each year was 68.2%, 90.6%, 80.6% and 83.9%. Twenty cases died or where withdrawn from treatment. Through analysis the neonatal RDS with GA < 32 weeks, we found that GA and BW of the poor prognostic group were lower compared to infants who had a better prognosis.
Conclusion. The trend of the prevalence of RDS suggests that preterm infants with GA < 32 weeks have a high risk of pulmonary morbidities and poor outcome.

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ANALYSIS OF RISK FACTORS AFFECTING POOR PROGNOSIS OF ACUTE BILIRUBIN ENCEPHALOPATHY IN NEONATES

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Objective. To investigate the risk factors affecting the poor prognosis of acute bilirubin encephalopathy (ABE) in neonates.
Methods. The clinical data of all newborns with ABE and a gestational age ≥35 weeks were retrospectively collected and analyzed for risk factors between Jan. 2015 and Dec. 2017. According to the follow-up results, these patients were divided into a better prognostic group and a poor prognostic group (including death, sequelae, etc.). Bilirubin-induced neurologic dysfunction (BIND) scores, peak values of total serum bilirubin (TSB), serum albumin (SA) levels, TSB/SA (B/A) ratios, early cranial MRI changes, and brainstem auditory evoked potential (BAEP) examinations were compared between the two groups.
Results. The study consisted of 92 participants, incomplete cases were excluded, resulting in 73 patients who were analyzed. 39 patients ended up with a good prognosis and 34 patients ended up with a poor prognosis. The BIND score, peak value of TSB, early change of cranial MRI and BAEP examination in the poor prognostic group yielded significantly higher values than those of the good prognosis group (t/X^2 = -4.99, -2.46, 16.68, 20.35, respectively, all $P \leq 0.001$). Concurrently, multivariate regression analysis indicated the following odds ratio (OR) and confidence interval (95% CI) for BIND (OR: 1.91, CI: 1.08-3.52), total bilirubin peak (OR: 1.94, CI: 1.28-3.19), and BAEP (OR: 1.25, CI: 1.08-2.96), all $P \leq 0.005$.
Conclusion. BIND score, TSB, and BAEP are important factors that severely affect the poor prognosis of ABE in neonates.

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CORRELATION ANALYSIS OF MULTIPLE CLINICAL INDICATORS OF NEONATAL BILIRUBIN ENCEPHALOPATHY: A MULTICENTER STUDY

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Objective. To analyze the clinical data of children with neonatal bilirubin encephalopathy (BA) and evaluate the value of bilirubin-induced neurological dysfunction (BIND) score, serum total bilirubin (TSB) and serum bilirubin/albumin ratio (B/A) value in judging severity and prognosis of this disease.
Methods. The clinical data and prognosis of children with BA with GA ≥ 35 weeks admitted to the four hospitals from January 2015 to December 2017 were retrospectively reviewed. BIND score, TSB, B/A, and brainstem auditory induction potential (BAEP), head MR, and prognosis were compared.
Results. (1) The incidence of BA was 0.23%, the mortality rate was 22.8%, and the sequela rate was 54.9%. (2) Comparison with domestic multicenter epidemiological data in 2012: The basic data were generally similar. The proportion of multiple concomitant diseases in this study was higher, but the two most common concomitant diseases were consistent. In this study, the peak level of TSB and hearing abnormality rate were higher, and the B/A level and MR abnormal rate were similar. The treatment was mainly phototherapy, followed by albumin infusion and blood transfusion. (3) BIND score and BAEP (r=0.41, P=0.023), MR (r=0.57, P=0.005), prognosis (r=0.666, P=0.000) were positively correlated; TSB was positively correlated with B/A (r=0.839, P=0.000); B/A level was negatively correlated with albumin (r = -0.316, P=0.022). BAEP was positively correlated with MR (r=0771, P=0.000) and prognosis (r=0.626, P=0.000). MR was positively correlated with prognosis (r=0.528, P=0.012).
Conclusions. (1) TSB or B/A alone have limited predictive effect on the occurrence and prognosis of acute BA; (2) BIND score, BAEP, MR results are related with prognosis obviously;(3) BIND score is significantly correlated with BAEP, MR, and prognosis. It also has a certain predictive effect on short-term prognosis while reflecting the severity of acute BA.

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THE COMPOSITION OF GUT MICROBIOTA IN NEONATES WITH SEVERE HYPERBILIRUBINEMIA AND ITS EFFECT ON BILIRUBIN-INDUCED BRAIN INJURY

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Objective. To investigate the composition of gut microbiota in neonates with severe hyperbilirubinemia and its association with bilirubin-induced brain injury.
Methods. A prospective study was conducted. The neonates with serum total bilirubin > 342 μmol/L were enrolled and were divided into brain injury (n = 26) and non-brain injury (n = 28) groups based on their brain MRI, brainstem auditory evoked potentials and clinical manifestations. The composition of gut microbiota in these neonates at admission was detected using 16S rDNA sequence analysis, which were compared between the two groups, along with bilirubin levels in serum and cerebrospinal fluid.
Results. The levels of unconjugated bilirubin in the cerebrospinal fluid were (9.53 ± 2.68) μmol/L in the brain injury group and (6.94 ± 2.31) μmol/L in the non-brain injury group (P = 0.0003). However, in both groups, the levels of unconjugated bilirubin in the cerebrospinal fluid and serum showed no correlation (r = 0.137, 0.081, p > 0.05). The abundance of gut microbiota in the brain injury group was significantly lower than that in the non-brain injury group, especially manifested the following five kinds: Fusobacterium, Catabacter, Succinivibrio, Clostridium and Bacteroides (all P < 0.05).
Conclusion. The level of bilirubin in the cerebrospinal fluid is the direct factor triggering bilirubin-induced brain injury in neonates who exhibited gut microbiota diversity as compared to those with no brain injury. The level of bilirubin in the cerebrospinal fluid of neonates with hyperbilirubinemia may be related to the difference in bilirubin blood-brain barrier permeability caused by different compositions of gut microbiota.

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PREDICTIVE VALUE OF PLASMA S100B AND TAU PROTEIN AND NSE LEVEL IN BILIRUBIN INDUCED-NEURONAL DAMAGE IN LATE PRETERM INFANTS

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Objective. To investigate the predictive value of plasma S100B, Tau protein and NSE level in bilirubin induced-nerve damage in late preterm infants.
Methods. We enrolled 190 late preterm infants admitted to NICU from May 2016 to December 2017. They were divided into an observation group with hyperbilirubinemia and a control group without hyperbilirubinemia. According to total serum bilirubin (TSB) level, the observation group was divided into three subgroups: mild, moderate and severe elevation. On the first day after birth, changes of venous plasma S100B, Tau protein and NSE levels were measured by ELISA, and TSB level were measured by DIAZO method. Neural development based on a neonatal behavioral neurological assessment (NBNA) score was detected 7 days after birth. Brainstem auditory evoked potential (BAEP) was measured, and brain magnetic resonance imaging (MRI) was performed 10 days after birth in the observation group.
Results. Levels of NSE, S100B and Tau protein in the observation were higher than those in the control group, especially in the moderate and severe hyperbilirubinemic subgroups ($P<0.05$), and the level of plasma S100B, Tau and protein NSE in the observation group was higher than that in the control ($P<0.05$), and those protein levels of the gestational age (GA) 34W group were higher than those in the GA35W and GA36W subgroups ($P<0.05$). The NBNA score of GA34W was significantly lower than that of the other two GA subgroups ($P<0.05$), and the hyperintensity on T1WI by MRI in the observation group (moderate and severe hyperbilirubinemic subgroups), especially in the severe hyperbilirubinemic group was significantly higher than that in the mild subgroup and the control ($P<0.05$).
Conclusion. Early detection of plasma S100B, Tau protein and NSE level combined with NBNA, BAEP and MRI was helpful in the identification of bilirubin neuronal damage in late preterm infants, and was of important clinical significance in the prevention of bilirubin encephalopathy.

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EARLY SCREENING OF WORKING MEMORY VIA EYE-TRACKING IN PREMATURE INFANTS

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Background: The testing of visuocognitive development in preterm infants shows strong interactions between perinatal characteristics and cognition in infants. The assessment of anticipatory gaze data of object-location bindings via eye-tracking can predict the neurodevelopment of preterm infants at the age of 3 years; little is known, however, on the early cognitive function during the first year of life.
Objective. The current study presents data from a novel assessment tool that employs the standardized LEA symbols of similar processing complexity in black and white. A Delayed Match Retrieval paradigm via eye-tracking was used to measure visual working memory skills with the aim to identify neurodevelopmental delays within the first year of life and early intervention is introduced.
Methods. A total of 37 infants participated in the present research with 8 eliminated from analysis due to limited attention during the procedure. 20 preterm infants (GA: 34.1weeks±2.03, 29-35w, CA:6.6months±1.3) and 9 healthy full-term infants (GA:40weeks±0, ChroA:6.8months±1.7) conducted the eye-tracking task measuring the ability to actively localize objects and to make predictions of object-location bindings (task duration: 4 minutes) and the Bayley III test.
Results. The analysis of the Bayley scores showed no significant difference between the two groups (Preterm: Cognitive M=96.75, Language M=104.6, Motor M=98.95; Full-term: Cognitive M=96.25, Language M=108.62, Motor M=95.75) while the eye-tracking data showed a significant group effect for gaze time on the object ($p<.001$), but not for object-location bindings. Overall preterm infants' performance (M=20.711±15.1) was significantly lower than full-term's (M=45.624, ±15.2).
Conclusions. Eye-tracking could prove a valid tool for the early screening of cognitive development successfully identifying at the early age of 7 months cognition difficulties due to prematurity so that early intervention is introduced.

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NEURODEVELOPMENTAL OUTCOME OF EXTREMELY PRETERM CHILDREN AT SCHOOL AGE: ASSOCIATED PERINATAL RISK FACTORS

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Background. Extreme prematurity is associated with negative neurodevelopmental outcome. Factors such as infection, head scan abnormalies, ART techniques considered to add an extra risk factor. At school age a high percentage will have Specific Learning Difficulties (SLDs) with Attention Deficit Hyperactivity Disorder (ADHD) co-morbidity and behavioral immaturities. Autist Spectrum Disorder (ASD) is of increased incidence possibly due to other factors such as ART techniques and cognitive delay. Motor disorders are mainly related to immaturity and discoordination compared to major anomalies such as cerebral palsy. Non favorable outcome associated risk factors such as head scan anomalies and infection reported in children with neurodevelopmental abnormalities as well as in children with typical outcome. Assisted Reproductive Techniques (ART) data are never or rarely complete to permit a clear association with outcome. Aims To analyze neurodevelopmental outcome and the type of associated neurodevelopmental disorder in a group of extremely preterm children up to school age stratified by GA, and to detect associations with factors such as infection, head scan anomalies, multiple birth and ART techniques.
Methods. We retrospectively analyzed medical records of extremely preterm children, <=29 weeks up to 24 weeks GA, from the data base system of our preterm follow up program from private and NHS NICUs. Analysis was focused on pre-school to school age outcome and associated perinatal factors. Results were stratified by GA.
Results. Sixty-six extremely preterm children with GA <=29 wks were included in the study. Stratified by GA at 24 wks were 4.54%, at 25 and at 26 wks 13, 63%, at 27 and at 28 wks 24.24% and at 29 wks 19.69%. Mean age at evaluation was 70.85 months (SD 38.656 months). ART pregnancy had 30.3% and twins were 46.9%. Autistic Spectrum Disorder was diagnosed in 15.15%, ADHD in 53% and Specific Learning Difficulties/immaturities in 34.84%. Infection reported in 37.83% of ADHD and SLDs cases, as well as in 38.46% of cases with no neurodevelopmental disorder. ART history had 4/6 (66.7%) children with typical ASD or Asperger. Head scan anomalies of any severity had 50% of cases of which 60% were subtle lesions. Children with ADHD, SLDs, behavioral disorders and motor immaturities had normal scan in 54.05% while on the other hand 45% of cases with subtle scan anomalies had ADHD and SLDs.
Conclusions. At school age 87.84% of extremely preterm children will have a degree of ADHD and/ or SLDs. Extremely preterm children with ADHD and SLDs have an history of perinatal infection in equal percentage with children with no abnormality. ART techniques are strongly associated with extremely preterm children with typical autism. Half children with ADHD and SLDs had normal head scan while almost half cases with subtle scan anomalies had ADHD and SLDs. Factors influencing outcome in extremely preterm children remain obscure.

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EFFECT OF NEONATAL TRANSITIONAL HYPOGLYCEMIA ON NEURODEVELOPMENTAL OUTCOMES AT 18 MONTHS OF AGE

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Objective. To investigate the impact of neonatal transitional hypoglycemia in the hospital on neurodevelopmental outcomes at 18-months age.
Methods. 58 hospitalized infants with hypoglycemia were enrolled within 48 hours after birth. They were given standardized management, aEEG detections, MRI scan, follow-up and assessed by using the Bayley Infant Development Scale(BSID) at 18 months after discharge.
Results. 1.The median of hypoglycemia occurrence time was 3.86 (0.5-44) h after birth, duration was 2.03±0.67 h and venous blood glucose concentrations was 1.62±0.37mmol/l. 2.The first aEEG results: Sleep-awake cycles disappeared in 2 cases, immature EEG in 7 cases; convulsions in 2 cases. The second aEEG results: 2 cases of immature sleep-wake cycle, the others were normal. 3. 45 cases of brain MRI scans, 7 cases of abnormalities. 4. BSID assessment results at 18 months of age: MDI and PDI were 93.9±6.3, 95.9±7.3, respectively; Spearman correlation analysis between blood glucose, and MDI, PDI, *r* were 0.061 and 0.656 (*P>0.05)*, the difference was not statistically significant and showed no correlation. The scatter diagram of each point presented mess disorder.
Conclusions. Neurodevelopmental outcomes for neonatal transitional hypoglycemia were normal at 18 months age through standardized blood glucose monitoring, and after appropriate intervention after birth. There was no association between blood glucose levels and neurodevelopmental outcome in our small study.

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THE EFFICACY AND SAFETY OF OROPHARYNGEALLY ADMINISTERED COLOSTRUM AND EXPRESSED BREAST MILK ON LATE ONSET SEPSIS OF PRETERM LOW BIRTH WEIGHT NEONATES

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Rationale. Preterm colostrum can provide protection against infection to the premature neonate during the 1st week of life. However, multiple factors associated with prematurity precludes feeding during this time. Oropharyngeal administration of colostrum is a possible alternative when enteral feeding is contraindicated.
Objectives. To determine the efficacy and safety of oropharyngeal administration of colostrum in the prevention of late onset sepsis among low birthweight preterm.
Study design. Prospective, blinded, randomized, controlled study.
Methods. Low birthweight preterm neonates on nil per os or nothing per orem (NPO) and requiring respiratory support were randomized into 2 groups. The treatment group received 0.2 ml colostrum or expressed breast milk and the placebo group received sterile water. The protocol and tools used for this study was reviewed and approved by the University of the Philippines Manila Research Ethics Board (UPMREB).
Measure. Complete blood count, blood culture and chest X-ray were obtained on admission and repeated on the 7th day of life.
Results. 98 preterm infants were enrolled and randomly allocated to the 2 trial arms. The incidences of necrotizing enterocolitis (NEC), late onset sepsis, and healthcare associated pneumonia were greater in sterile water group (45%, 41%, and 22%) compared to the colostrum group (12%, 29%, and 14%), but only the difference in the incidence of NEC (22 in sterile water vs 6 in colostrum) was statistically significance (p=.001). Time to reach feeding of 100mL/kg/day was longer in the control group (median 5 days vs. 4 days, p=.08). The mortality rate among the groups was not significant.
Conclusions. Oropharyngeal administration of mother's own milk to preterm infants was safe and feasible. However, in the incidence of late onset sepsis was not reduced following oropharyngeal administration of colostrum. We speculate that this strategy may have an protective effect on NEC.

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CONGENITAL SYPHILITIC PULMONARY CAVITATION

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Background. A 2880 g full term baby girl presented with multiple syphilitic pulmonary cavitating lesions. It is likely to be the first reported case of congenital syphilitic pulmonary cavitation in the English literature. Her mother had a non-reactive VDRL and HIV antibody tests in second trimester and was asymptomatic for sexually transmitted diseases throughout pregnancy. The newborn was asymptomatic at birth but was admitted on day 28 for skin rashes, tachypnoea and subcostal retractions.Oxygen saturation was 93 % in room air. There was also gross hepatosplenomegaly. Chest X-rays showed opacity at the right upper lung and multiple lucent lesions over both lungs. Contrast CT thorax showed multiple cavitating lesions without air fluid level. Blood for VDRL was 1:1024, FTA-ABS +++, TPPA ++ while her mother's blood for VDRL was 1:64 and FTA-ABS +++. Thus, congenital syphilis complicated by multiple pulmonary cavitating lesions and pneumonia was diagnosed. Other microbiological tests causing possible pulmonary cavitation were negative.
Results. She was treated with Penicillin G (4 weeks intravenously and 2 weeks orally) with clinical and radiological improvement. Serial serum VDRL assays showed falling titres. Within two months, chest X-rays and CT thorax showed resolution of pulmonary cavitation.
Conclusions. 1. Congenital syphilis presenting with pulmonary cavitating lesions is rarely reported in the literature. 2.Congenital syphilitic pulmonary cavitation can be cured with Penicillin G treatment. 3. A negative routine antenatal VDRL screening test does not exclude the diagnosis of congenital syphilis. 4. Blood for VDRL should be included in the evaluation of infants presenting with congenital syphilis symptomatology such as rashes and hepatosplenomegaly. 5. Blood for VDRL is advisable at time of delivery for all pregnant women or high risk women.

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STAPHYLOCOCCUS EPIDERMIDIS-DRIVEN INFLAMMATORY RESPONSES IN HUMAN LUNG EPITHELIAL CELLS: ARE THERE STRAIN SPECIFIC DIFFERENCES?

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Background. Staphylococcus epidermidis is the predominant pathogen of neonatal late-onset sepsis. Growing evidence implicates a strong association between S. epidermidis sepsis and neonatal inflammatory disorders like bronchopulmonary dysplasia. Nosocomial S. epidermidis strains are characterized by biofilm formation, but the interplay between bacterial phenotype and the host remains poorly understood.
Objective. To investigate the underlying mechanisms of S. epidermidis-driven inflammatory lung injuries, with a focus on the role of biofilm phenotype in the host-bacteria interaction.
Methods. A human alveolar epithelial cell line (A549) was incubated with nosocomial S. epidermidis RP62A (biofilm-positive) and noninfectious ATCC 12228 (biofilm-negative) strain for 24 h. Cell viability was assessed using methylthiazolyldiphenyl-tetrazolium bromide. The mRNA and protein expression of tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-8, IL-10, monocyte chemoattractant protein (MCP)-1, intercellular adhesion molecule 1 (ICAM-1), as well as Toll-like receptor (TLR)-2 were measured.
Results. Both S. epidermidis strains stimulated the release of pro-inflammatory cytokines (TNF-α, IL-6 and IL-8) and chemoattractants (MCP-1, ICAM-1) while hardly inducing anti-inflammatory IL-10 in alveolar epithelial cells, pushing the state towards pro-inflammation and cell death. The interaction between bacteria and cells was strain-dependent, with the biofilm-positive strain showing a more prominent pro-inflammatory and cytotoxic effect than the biofilm-negative strain ($p<0.05$). The expression of TLR2 was up-regulated in cells upon stimulation with S. epidermidis ($p<0.05$).
Conclusions. Our results challenge the conventional view that S. epidermidis are harmless commensals. S. epidermidis may trigger imbalanced inflammatory responses in alveolar epithelial cells. Biofilm-forming S. epidermidis strains seem to be more potent inducers of a pro-inflammatory host response.

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SOURCES OF INFECTION IN A TERTIARY CARE NEONATAL UNIT AND ROLE OF FUMIGATION AND DISINFECTION

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Background. Environmental contamination is a major concern for nosocomial infections in neonatal units. Contamination with pathogens occurs during routine medical care. Coagulase negative Staphylococcus is a common nosocomial pathogen followed by Klebsiella and Pseudomonas species. Cleaning of medical equipment and fumigation of neonatal units have some role in reducing hospital acquired infections.
Objectives. The study was designed to find out the potential sources of infection and role of various methods in its eradication. The study was conducted in the Neonatology Department of the Children's Hospital & the Institute of Child Health, Lahore, Pakistan.
Methods. It was a cross sectional study conducted from March 2007-October 2012. We obtained samples for cultures from the potential sources of infection like environmental air, patients' beds, incubators, warmers and hands of health care workers. Fumigation was done by formalin solution and carbolic acid after environmental cleaning. Samples were taken before and after doing the fumigation. The data was entered on a proforma and then analyzed in SPSS v16. P-value < 0.05 was taken as significant.
Results. Total 556 cultures were taken from environmental sources. In the pre fumigation and disinfection stage 227 out of 288 cultures were positive while only 94 isolates were detected from 268 samples after fumigation and disinfection ($P<0.05$). Staphylococcus epidermidis was most common followed by Bacillus- and Klebsiella-species, Staphylococcus aureus and Pseudomonas species. All cultures taken from the environmental air before and after fumigation and disinfection were positive.
Conclusion. Microorganisms were isolated from various sources of neonatal ward and are potential reservoirs for nosocomial infections. Environmental disinfection along with fumigation is effective in reducing the burden of pathogenic microorganisms. However, we did not find fumigation as a successful tool for disinfecting our neonatal ICU's environmental air.

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COMPARISON OF DIFFERENT SCREENING APPROACHES FOR EARLY ONSET SEPSIS IN TERM AND LATE PRETERM NEONATES

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Background. Severe early onset sepsis (EOS) in term and late preterm infants is an important cause of neonatal morbidity and mortality. Early diagnosis and treatment are important to improve outcomes. Over the years, our centre has used three different algorithms for EOS screening. It is unclear whether changes in screening algorithms have led to improved neonatal outcomes.
Objective. To compare different screening approaches for EOS in term and late preterm neonates admitted to Prince of Wales Hospital in Hong Kong.
Methods. We identified three time periods during which different EOS screening algorithms were used. Phase 1 (31/12/2004 to 31/12/2009): all newborns with infection risk, except for isolated PROM, were admitted to neonatal unit for sepsis screening. Phase 2 (1/1/2010 to 31/12/2010): infants were categorized to high/medium/low EOS risk categories, and only cases with medium/high risk were admitted to neonatal unit. Phase 3 (27/2/2012 to 29/2/2016): universal GBS screening was implemented, and we adapted the local GBS screening guideline. We recruited all cases who were admitted to our hospital and had blood taken for sepsis evaluation within the first 3 days of life. We collected relevant data from the medical records and compared the three approaches.
Results. 19385 cases were evaluated. 17151 cases were term infants, and 2234 cases were late preterm. Algorithm 1 had the highest admission rate (65.90%), average frequency of blood taken (2.32 per case), rate of antibiotic use (43.83%) and average length of stay (LOS, 7.94 days). Algorithm 3 had the lowest admission rate (31.21%), average frequency of blood taken (1.95 per case), rate of antibiotic use (31.71%), average LOS (6.81 days) and mortality rate (0.16%). The change of average LOS in late preterm infants was not significant.
Conclusions. The implementation of GBS screening significantly improved the outcome of term and late preterm infants with EOS risk.

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CORRELATION OF MATERNAL SERUM NEUTROPHIL-TO-LYMPHOCYTE RATIO WITH ADVERSE PERINATAL OUTCOMES OF PRETERM BIRTH

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Background. Maternal serum neutrophil to lymphocyte ratio (NLR) has been reported as a predictive marker to reflect maternal-fetal inflammation status.
Objective. The purpose of this study is to investigate the relationship NLR with adverse perinatal outcomes in preterm birth pregnancies, focusing on the delivery latency and neonatal outcomes.
Methods. This retrospective study was conducted on a total of 100 pregnancies with preterm birth from 24+0 weeks to 36+6 weeks of gestation. Values of complete blood count (CBC), NLR, platelet-to-lymphocyte ratio (PLR), C-reactive protein (CRP) were estimated at admission day and 24 hours before delivery. These values were analyzed according to delivery latency and associated composite neonatal complications including respiratory, cerebral, gastro-enteral, infectious and ophthalmic disease. The statistical differences were analyzed by using two-tailed test and Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Covariance variables were adjusted by logistic regression analysis.
Results. Gestational age, parity and body mass index (BMI) before and after pregnancy had statistical differences with delivery latency at 3 days. Values of admission day (WBC, neutrophil, NLR and CRP) were significantly higher within 3 days of latency ($P < 0.05$) but these parameters had no clinical correlations with neonatal complications. Values of these markers at delivery day were also statistically higher at less than 3 days of latency and in the group with neonatal complications.
Conclusions. NLR at delivery day could be a useful marker to predict delivery latency and neonatal outcomes. In particular, NLR at admission was more correlated with delivery latency, and its value at the day of delivery was more relevant with neonatal outcomes.

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DURATION OF PRETERM PREMATURE RUPTURE OF MEMBRANES AS PREDICTOR OF HISTOLOGIC CHORIOAMNIONITIS AND EARLY ONSET NEONATAL SEPSIS; A PROSPECTIVE COHORT STUDY

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Background. Preterm premature rupture of membranes (PPROM) has important implications in pregnancy and its outcome.
Objective. To determine the duration of PPROM that can predict histologic chorioamnionitis and early onset sepsis.
Methodology. A prospective cohort study done at a tertiary referral center. Mothers less than 37 weeks age of gestation by last menstrual period or early ultrasound with spontaneous rupture of membranes of various duration were recruited. After delivery, placentas were sent for histologic chorioamnionitis examination. Neonates were monitored for development of early onset neonatal sepsis, following WHO definition of culture proven sepsis within the first 3 days of life and other neonatal outcomes. Characteristics of mothers and neonates, including the latency of PPROM were obtained and their association with histologic chorioamnionitis (HCA) and early onset neonatal sepsis (EONS) was determined using Receiver Operating Curve (ROC) analysis and tests of association.
Results. 569 mother-neonate dyads at a tertiary referral center were recruited. The duration of preterm premature rupture of membranes is a fair predictor of HCA based on Receiver Operating Characteristic curve (ROC) (area under the curve [AUC] of 0.753 [95% CI: 0.695, 0.821]). There is a significant association between histologic chorioamnionitis and longer latency with a cut-off of 31.5 hours having higher accuracy and stronger association compared with the standard cut-off of 18.0 hours (OR of 4.56 and 2.86, both p-values <0.0001). PPROM latency could not predict early onset neonatal sepsis based on ROC (AUC of 0.519 [95%CI: 0.463, 0.576]) and is not associated with it at either the 31.5 or 18.0 hour cut off values (both p>0.05).
Conclusion. Longer PPROM is associated with histologic chorioamnionitis.In this research, 31.5 hours or more is the optimal cut off. PPROM latency could not predict early onset neonatal sepsis.

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REDUCING IN HOSPITAL AQUIRED INFECTION IN THE NICU

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Background. In 2003 as part of an internal audit the infection rate among VLBW newborns (equal or less than 1500gms) were reviewed at our unit and it was found to be high. A committee was formed of NICU physicians, nurses, clerks and housekeeping to plan and implement processes to decrease infection rate among NICU admissions. Indicators to be monitored: NICU infection rates= infection episodes /1000 patients days, infections % in = < 1500 grams. Total number of episodes and causative organisms. NICU mortalities secondary to infection intervention: Using QI tools 4 strategies were implemented:
1. Hand hygiene using the new recommendation published by the CDC. A. Written Policy. B. Monthly in-service for all health care provider in the NICU starting from October 2004 to March 2005, then 3 times per year. C. The distribution of alcohol hand rubs for each bed. D. Educational materials were posted at entrance and above sinks.
2. Isolation: All babies infected with gram negative organisms were isolated.
3. Cover gowns: Consistent with CDC,AAP and OSHA recommendations. Gowns for mothers were designed to be culturally compatible.
4. Antibiotic usage in the NICU: A. Written policy for the empiric use of antibiotics to Penicillin and Gentamicin for early on-set sepsis, Flucloxacillin and Gentamicin for late on-set sepsis. B. Vancomycin reduction protocol implemented (level B-II). C. Discontinuing antibiotics after 48 hours negative cultures (C1). D. Oral Nystatine prophylaxis for the VLBW newborn (starting at 3rd day of life till they attain the weight of 1250gms) (A-II).
Results: NICU infection rate per 1000 patient days decreased from 12.4/1000 in 2004 to 3.3/1000 in 2017. Infection rate in babies less or equal to 1500 grams decreased from 97% in 2004 to 15% in 2017. Overall, infection episodes decreased and mortality secondary to sepsis decreased from 2.3% to 0.3%.

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THE EFFECT OF SURFACTANT ON BACTERIAL PROLIFERATION AND PULMONARY INFLAMMATION IN VENTILATED NEAR-TERM NEWBORN RABBITS WITH GROUP B STREPTOCOCCAL PNEUMONIA

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Background. Benefits of exogenous surfactants in neonatal bacterial pneumonia are controversial. We aim to investigate the anti-bacterial and anti-inflammatory effects of surfactant on near-term newborn rabbit lungs with group B streptococcal (GBS) infection.
Methods. After cesarean delivery and tracheostomy, rabbit fetuses at gestational age 30 days (term 30-31 days) were administrated intratracheally with 5 ml/kg of human-derived GBS (10^9 colony forming units/ml) or 0.9% NaCl, and then ventilated in a ventilator-multi-body-plethysmograph system with standardized tidal volume (4-6 mL/kg) and 100% oxygen. After 1 hour, surfactant (100 mg/kg or 200 mg/kg) or 2.5 ml/kg NaCl were administrated via airway. The survival time and dynamic compliance of respiratory system (Cdyn) were recorded. Animals surviving beyond 6 hours of ventilation were sacrificed for blood and lung bacterial culture, lung histopathological and ultrastructural examination. The mRNA expression of inflammatory mediators in lung tissues were assessed with PCR techniques.
Results. Surfactant exerted no significant effect on the survival rate and Cdyn in GBS-infected groups. However, blood and lung bacterial counts were significantly decreased in the high-dose surfactant group vs non-treated GBS group. Histopathologically, surfactant was associated with lower lung injury score, better alveolar expansion, and mitigated leukocyte infiltration and edema, with improved alveolar ultrastructure. Surfactant suppressed the mRNA expression of tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6 and IL-8, as well as nuclear factor-kappa B (NF-κB) and toll-like receptor (TLR)-2 vs. non-treated GBS group, with a dose-dependent effect.
Conclusion. In the ventilated newborn rabbit model of lung GBS infection, surfactant markedly inhibited bacterial proliferation and translocation, ameliorated pulmonary inflammation through the transcription of inflammatory mediators, but failed to improve animal survival and lung mechanics.
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NEONATAL VERTICAL TRANSMITTED TUBERCULOSIS IN PRETERM TWINS

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Background. Tuberculosis remains an unresolved health global problem. Genital tuberculosis of both male and female, represents one of the main causes of infertility. Congenital infection by vertical transmission is a rare complication which has been reported in only 358 cases until 1995 and in 18 cases from 2001 to 2005. This form is responsible for a high mortality and morbidity in the neonatal period. Infection in the foetus can be transmitted from the maternal circulation through the placenta or by aspiration and swallowing of infected amniotic fluid prenatally or during birth. Clinical findings in the newborn often are non specific including distress and sepsis-related aspects. Tuberculosis in pregnancy is responsible of recurrent abortions, stillbirths, PROM and preterm labour.
Objective. Guidelines for management of newborns from infected mothers are still a controversial issue.
Method. Key points in diagnosis making are Cantwell’s criteria and detection of Mycobacteria by examination of the placenta.
Results. We present 27 weeks’ of gestation preterm twins (birth weight 950 gr and 980 gr) from a mother affected by miliary tuberculosis. Mother’s history revealed infertility which ended whit a medical induced pregnancy needing steroid therapy before and during gestational period. At birth the preterm infants presented with severe RDS needing mechanical ventilation and surfactant replacement. Fluids, inotropes, amoxicillin/clavulanate were the first pharmacological approaches, extended by isoniazid on second day of life. In the following days we could isolate Mycobacterium tuberculosis by gastric aspirate in only one infant. Cerebrospinal fluid specimens were negative. After informed parental consent we initiated a specific therapy (isoniazid, rifampicin, ethambutol and pyrazinamide) in the first week which is currently continued.
Conclusions. Congenital tuberculosis as vertical infection remains a rare diagnosis which, however, requires rapid diagnosis and appropriate treatment.

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A MULTICENTER EPIDEMIOLOGICAL STUDY OF NEONATAL BACTERIAL MENINGITIS IN NICU FROM GUANGDONG AND GUANGXI

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Objective. To analyze the epidemiological characteristics of neonatal bacterial meningitis in Guangdong Province and Guangxi Zhuang Autonomous Region.
Methods. A retrospective epidemiological study was carried out in neonatal infants with bacterial meningitis admitted to 12 NICU of collaborative hospitals from Jan 2011 to Dec 2016. Clinical data on pathogen strains, year prevalence, clinical features and outcomes were analyzed.
Results. A total of 838 cases met the criteria of neonatal bacterial meningitis; 249 neonates (29.7%) had positive bacterial cultures, with Streptococcus agalactiae (GBS), Escherichia coli, Coagulase negative staphylococcus and Klebsiella pneumoniae as the most common strains. The prevalence of positive rate was 29.6% (47/159), 33.6% (85/253) and 27.5% (117/426) in 2011-2012, 2013-2014 and 2015-2016, respectively, with no significant difference between each epochs. In the culture positive cases, there was no significant difference between the Gram-negative bacilli and Gram-positive cocci proportion in the three different periods. The positive rates of cerebrospinal fluid (CSF) culture and blood culture were 33.0% (64/194) and 28.7% (185/644) in early-onset and late-onset bacterial meningitis infants, with the most common bacteria being GBS. The positive rates of CSF culture and blood culture were 26.9% (57/212) and 30.7% (192/626) in preterm and term infants, respectively. The differences of Gram-negative bacilli and Gram-positive cocci proportion in the two groups were significant; the bacteria of preterm infants were mainly Gram-negative bacilli, with E. coli being the most common microorganism whereas in term infants, GBS, were the prominent Gram-positive cocci. There were 45 cases (5.4%) whose CSF WBC counts were <20/mm^3, in which 5 were bacterial positive. There were 728 cases (91.7%) of CSF WBC <20/mm^3 at discharge. The positive rate of blood culture and CSF culture declined by 8.2% and 5.3% when antibiotic use was $\geq$24 or <24 h, respectively ($p<0.05$). Fever was the most common manifestation (633, 75.5%) and hydrocephalus was the most common complication (167, 20%). Gram-negative bacilli were more common than Gram-positive cocci. There were 801 infants (801/838, 95.6%) who were cured, however, 13 (1.6%) died. The single antibiotic use was mainly meropenem (83.67%) and third-generation cephalosporins; the combined ones mainly meropenem, penicillin, or vancomycin, plus third-generation cephalosporin. There was no significant difference between single one and combined usages on the treatment efficacy in those infants with culture positive findings.
Conclusion. The most common bacteria of neonatal bacterial meningitis were GBS, E. coli and coagulase negative Staphylococcus in the NICUs from municipal cities in Guangdong and Guangxi provinces.

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VITAMIN D DEFICIENCY IN LOW BIRTH WEIGHT INFANTS

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Background. Vitamin D is an essential nutrient that plays an important role in calcium homeostasis and bone health. Vitamin D deficiency is defined as 25-hydroxyvitamin D3 (25-OHD3) levels lower than 20 ng/mL with levels lower than 10 ng/mL defined as severe deficiency. The adequate dose or duration of vitamin D supplementation in low birth weight infant (LBWI, with a birth weight less than 2,500 g) is not well understood.
Objective. Our aims were to investigate the prevalence of and characteristics associated with vitamin D deficiency in LBWIs at 2 weeks of age and evaluate the changes of serum 25-OHD3 and parathyroid hormone (PTH) concentration in response to three different doses of vitamin D supplementation.
Methods. A total of 194 LBWIs were enrolled. We analyzed the relationship between serum 25-OHD3 levels and clinical characteristics. Serum 25-OHD3 and PTH levels were assessed following either 200-599, 600-799, or more than 800 IU daily vitamin D supplementation at 4~6, 8~10 and 12~14 weeks of age.
Results. Mean 25-OHD3 concentrations were 12.93±6.4 ng/mL in enrolled infants and 13.1±6.7 ng/mL in LBWIs at more than 37 weeks' gestation. They were significantly lower in infants whose birth weight was lower (P=0.047) and those of multiple births (P=0.036). At 2 weeks of age, the incidence of vitamin D deficiency was 89.2%, and 40.7% of LBWIs were classified as having severe vitamin D deficiency. LBWIs with severe vitamin D deficiency showed lower GA (P=0.030), higher frequency of triplets (P=0.046). The mean concentration of 25-OHD3 was significantly lower (P=0.000) at 2 weeks of age in infants receiving more than 800 IU daily because we have specified the amount of Vit D supplementation given according to the concentration of 25-OHD3. Even after more than 10 weeks of higher-dosage Vit D supplementation, infants receiving more than 800 IU daily showed a lower trend of mean concentration of 25-OHD3 (P=0.088) and significantly higher mean level of PTH (*P*=0.033) compared to other two groups.
Conclusions. LBWIs including SGA term neonates need vitamin D supplementation. Our results support consideration of longer duration of vitamin D supplementation with a higher daily dose for LBW infants with severe vitamin D deficiency.

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IMPACT OF SUCROSE ANALGESIA ON PAIN REACTIVITY AND CORTISOL LEVELS IN PRETERM INFANTS

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Objective. To explore the impact of sucrose analgesia on pain reactivity and cortisol levels in preterm infants.
Methods. Preterm infants with gestational age <34 weeks, birth weight <2,000 g, admitted to NICU between Jan 2014 and Oct 2016, with length of hospital stay ≥14 d, were randomized to two groups: intervention group received 0.3-0.5 mL of 12% sucrose solution two minutes before every painful procedure, control group received no placebo. At term equivalent age and 8 months corrected age (CA), pain reactivity was measured and saliva samples were collected pre- and post- painful procedure, respectively. Saliva samples were stored at -20^{o}C until assay using ELISA to quantify cortisol.
Results. 1. Ninety-six infants were enrolled, of which 14 failed to follow-up, 82 infants were enrolled (42 in intervention, 40 in control group). 2. There were no significant differences between two groups in pain reactivity at both term equivalent age and 8 months CA. 3 Infants in intervention group had higher post-procedure cortisol levels compared to those in the control at both ages (10.0±8.9 vs. 7.5±6.9 ng/ml, 7.2±5.4 vs. 4.7±1.9 ng/ml, p=0.020 and 0.042, respectively), but no difference existed for pre-procedurel cortisol levels between two groups at both ages. 4. Multiple stepwise regressions analysis showed that post-procedure cortisol levels were negatively associated with cumulative number of painful procedures, and positively related to sucrose analgesia, at both ages, while pre-procedural cortisol levels had no significant association with either of the two factors.
Conclusion. Sucrose analgesia may mitigate the negative effect of repeated procedural pain on cortisol regulation in preterm infants, but has no influence on pain reactivity.

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FATTY ACIDS OF PRETERM BREAST MILK

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Objective. Triglyceride (TAG) is one of the most important nutrients in preterm milk, but its composition and structure are still unclear. This paper aims to elucidate the composition and positional distribution of fatty acids in preterm milk TAG.
Methods. We recruited lactating mothers who delivered preterm infants at Wuxi Maternal and Child Health Care Hospital between December 2016 and April 2017. Milk samples, including colostrum (4±3 days), transitional milk (11±3 days), 1-month (30±3 days), 2-month (60±3 days), and 3-month milk (90±3 days), all were collected postpartum. Fatty acids composition in milk was determined with gas chromatography, and to analyze maternal characteristics on fatty acids composition.
Results. 1) The main fatty acids were C16:0, C18:1n-9 and C18:2n-6, which accounted for 21.2%-29.7%, 20.2%-27.6% and 14.3%-18.8% of the total fatty acids, respectively. 2) Among 35 fatty acids, 5 showed stable positional selectivity in TAG. C14:0, C15:0, C16:0 and C22:6n-3 are mainly distributed in *sn*-2 position, whereas C20:3n-6 was mainly located at *sn*-3 position. 3) The content of C18:2n-6 and C20:4n-6 in total fatty acids, C18:2n-6, C18:3n-3, C20:4n-6 and C22:6n-3 in *sn*-2 position, as well as C20:4n-6 in *sn*-3 position changed significantly with the development of lactation. 4) The relative content of C18:3n-3 and C20:4n-6 in total fatty acids varied significantly depending on gestational age. 5) Concentrations of long chain saturated fatty acids (LCSFAs) and monounsaturated fatty acids (MUFAs) were much lower whereas medium chain fatty acids (MCSFAs) were much higher in colostrum compared to transitional milk. 6) Concentrations of MUFAs, LCSFAs, and n-6 family long chain polyunsaturated fatty acids (PUFAs) were higher in early preterm milk compared to moderate preterm and near term milk. 7) Levels of LCSFAs, C22:6n-3, and C18:2n-6 in *sn* -2 position were lower in colostrum from mother with pre-pregnancy body mass index higher than 24 kg/m^2. 8) Concentrations of PUFAs in *sn*-2 position were lower in preterm colostrum from women >30 years of age.
Conclusion. The main fatty acids were C16:0, C18:1n-9 and C18:2n-6, and fatty acids in human milk are mainly distributed in *sn*-2 position. Fatty acids compositions are markedly impacted by lactation, gestational age, maternal pre-pregnancy BMI, and maternal age.

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CHANGING PATTERNS OF NECROTIZING ENTEROCOLITIS IN NEWBORNS FROM GUANGDONG PROVINCE, 2005 - 2014

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Objective. To compare the outcome of term infants with moderate-to-severe necrotizing enterocolitis (NEC) in two periods in Guangdong province.
Methods. A retrospective study was carried out in term infants with Bell's stage ≥ II NEC in 6 collaborating hospitals in two periods (2005-2009 and 2010-2014). A reference group of NEC in preterm infants of the same periods was also included for comparison.
Results. A total of 365 newborns with NEC, (2005-2009: n=119; 2010-2014: n=246), and 455 preterm infants were enrolled. In 2010-2014, male proportion was significantly lower (59.3 vs. 76.5%); birth weight (3010±595 vs. 3155±495 g) and mortality were identical (5.3 vs. 5.3%). The most common causes of death were septic shock (65%) and neonatal sepsis (55%); the onset time occurred mainly within 7 days after birth (58.6%). The most commonly underlying disease in NEC of preterm infants was respiratory distress syndrome (31.0%); onset time: > 7 postnatal days (64.8%). Preterm infants most often had abdominal distention, vomiting and hematochezia, the incidence of feeding intolerance was significantly higher in the preterm infants compared to newborns (23.1 vs. 12.6%). The proportion of patients developed Bell's stage III in term NEC was compared with preterm infants (21.9 vs. 31.2%), and mortality was also significantly lower (9.0 vs. 15.4%) ($p<0.05$).
Conclusions. NEC is still an important cause of morbidity and mortality in preterm infants and newborns.

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CHANGES AND IMPLICATIONS OF BLOOD C-REACTIVE PROTEIN AND PROCALCITONIN IN NEONATES WITH NECROTIZING ENTEROCOLITIS

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Objective. To investigate changes in and clinical implications of blood C-reactive protein (CRP) and procalcitonin (PCT) levels in neonates with necrotizing enterocolitis (NEC).
Methods. A total of 142 neonates diagnosed as NEC were divided into 3 groups according to modified Bell's staging criteria: Bell I (40 cases), Bell II (72) and Bell III group (30). Conventional management was provided for 124 cases including 12 cases of Bell III; 18 cases underwent surgical ligation for Bell III. CRP and PCT were detected in each group at three time-points: pre-treatment, the first day post-treatment and the convalescence.
Results. The levels of blood CRP in Bell III group were significantly higher than those in other groups during different time-points ($p<0.05$). The levels of CRP in Bell III and Bell II group, and levels of PCT in Bell III group were significantly higher on the first day post-treatment than pre-treatment ($p<0.05$). Levels of CRP and PCT in the convalescence were significantly lower than those in other time-points during the same Bell stage in Bell II and III group ($p<0.05$). The incidence rate of respiratory failure and mechanical ventilation were significantly higher in Bell III than in other groups ($p<0.05$), and sepsis occurred more frequently in Bell III than in Bell II group ($p=0.010$). Gastrointestinal perforation (10 cases) and intestinal stenosis (8 cases) only occurred in NEC at Bell III. Predictive value for NEC at Bell III stage of CRP on the first day post-treatment, and predictive value for surgical NEC of CRP on pre-treatment and on the first day post-treatment achieved statistical significance ($p<0.05$).
Conclusion. The levels of CRP and PCT indexes and changes in its levels were helpful in early diagnosis of NEC at Bell II and III stage, CRP could be a potential auxiliary index for predicting the incidence of NEC at Bell III stage and surgical ligation.

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INFLUENCES OF ANTIBIOTICS AND PROBIOTICS ON INTESTINAL FIORA IN LATE PRETERM INFANTS

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Objective. The aim of this study was to investigate the influences of antibiotics and probiotics on the establishment of intestinal flora in late preterm infants by high-throughput sequencing.
Methods. Criteria were set for inclusion and exclusion of late preterm infants exposed to antibiotics from NICU admissions. A total of 10 dyads in which mothers and neonates received antibiotics were included. They were divided into two groups as either antibiotics or antibiotics plus probiotics group. The antibiotic group was defined as infants whose mothers received antenatal antibiotics one week before delivery and their newborns received antibiotics within 48 h postnatally (both with duration of treatment ≤7 days). The probiotic group received probiotics in day 3-10 postnatally in addition to the administration of antibiotics as in the antibiotic group. Control infants with similar gestational age and birthweight were matched from relatively healthy subjects not exposed to antibiotics or probiotics. Stool samples from each infant were collected at 3, 7 and 14 days of postnatal age. DNA was extracted from stool samples using the QiAamp Fast DNA Stool Mini Kit (Qiagen, Germany). The fecal bacterial composition and diversity were analyzed by sequencing V3-V4 region of 16S rRNA with Illumina Miseq platform.
Results. 116S rDNA sequence data were generated from a total of 15 preterm infants with 44 samples. The data yielded sequences belonging to 15 phyla, 28 classes, 62 orders, 103 families, 210 genera, 289 species and 345 OTUs. The rarefaction curves and Shannon curves showed a reasonable sequenced data, and a near-complete sampling of the community. In the control group, intestinal flora diversity increased gradually during the first 14 days of life. On the other hand, in the antibiotic group and probiotic group, the diversity index decreased from days 3 to 7, and then increased gradually in the following week. The diversity index on days 7 were significantly lower in the antibiotic group than in the control group and probiotic group (P<0.05). In control group, *Proteobacteria* dominated the intestinal flora day 3, followed by *Firmicutes*, *Bacteroidetes*, *Actinobacteria*. The control group had modest decrease in abundance of *Proteobacteria,* and increases in *Firmicutes*, *Bacteroidetes* and *Actinobacteria*. On day 14 *Firmicutes* became clearly the dominant population, followed by *Actinobacteria*, *Proteobacteria* and *Bacteroidetes*, in the control group. At genus levels, the intestinal flora in control group on days 3 was dominanted by facultative anaerobes including *Escherichia-Shigella* and *Enterobacter.* The facultative anaerobes such as *Escherichia-Shigella* and *Enterobacter* decreased gradually in control group, while the anaerobes including *Bifidobacterium* and *Clostridium* had a tendency of increase and dominated the intestinal flora on day 14. However, there was a trend toward increased abundance of facultative anaerobes such as *Streptococcus*, *Enterococcus,* and so forth. Furthermore, these facultative anaerobes still had a considerable proportion in control group on day 14. On the contrary, infants in the antibiotic group had modest increase in abundance of *Proteobacteria* (*Escherichia-Shigella*), and decrease in *Firmicutes* (*Enterococcus* and *Streptococcus*) and *Actinobacteria* (*Bifidobacterium*). Furthermore, the abundance of several phylum (i.e. *Bacteroidetes*, *Planctomycetes*, *Deinococcus-Thermus* and *Cyanobacteria*) was also significantly decreased and could not be detected after antibiotic exposure (p<0.05). There was no difference in the composition of intestinal flora on days 3 between antibiotic group and probiotic group. With chronological progression, there was a trend toward increased abundance of *Actinobacteria* (*Bifidobacterium*) during the first 14 days of life. On day 7, the abundance of *Actinobacteria* (*Bifidobacterium*) in probiotic group was significantly higher than those in antibiotic goup (p<0.05).
Conclusion. 1. The early dominance pattern of intestinal flora in late preterm infants within 14 postnatal days indicates that antenatal and early postnatal antibiotics exposure can significantly reduce the diversity of intestinal flora and affect bacterial colonization, and that probiotic supplement may alter the diversity of intestinal flora and strengthen the colonization of *Actinobacteria* (mainly *bifidobacterium*). Probiotic use in early postnatal life may minimize antibiotics-induced disruption of gut microbiota, thus promoting the recovery of intestinal microbiota.

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A COMPARISON OF TRANSCUTANEOUS AND INVASIVE METHODS FOR THE DETERMINATION OF BILIRUBINEMIA IN PREMATURE INFANTS

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Background. Currently there is not sufficient clinical data to recommend routine transcutaneous bilirubin measurement in preterm infants.
Objective. The purpose of this study was to compare transcutaneous and invasive methods for the determination of bilirubin in a group of premature infants with gestational ages of 28 to 34 weeks of gestation.
Methods. Bilirubin in venous and capillary blood was assessed using a biochemical analyzer (Dimension Rxl max), and a gas analyzer (ABL800); transcutaneous measurements were performed, with the device JM-105. Measurements were carried out in parallel, and in a time range of ± 30 min. The level of total bilirubin in blood serum was within the wide range of values (50 to 270 µmol/l). Levels of bilirubin above 270 µmol/l were excluded from the study because the sensitivity of the transcutaneous method sharply decreased for these values. The study included 44 preterm infants with gestational ages of 28 to 34 weeks, body weight at birth ranged from 980 to 2720 grams, age of analysis ranged from 2 to 14 days of life. Statistical analysis was performed by calculating the pairwise correlation coefficient (r).
Results & Conclusions. Bilirubin levels from 50 to 270 µmol/l correlated between invasive methods and TcB on the fore head (r=0,94), and on the chest JM-105 (r=0.95). The correlation coefficient between total bilirubin in capillary blood and JM105 was NO r = 0.89 on the fore head and the chest. In conclusion, the device JM-105 has demonstrated good efficiency, however, it requires further evaluation in larger number of preterm infants.

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EFFECT OF KANGAROO MOTHER CARE ON BREAST-FEEDING IN 6 MONTHS OLD PRETERM INFANTS - A META-ANALYSIS

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Background. WHO nutrition target for 2025 is to improve exclusive breastfeeding rate to 50%. Kangaroo mother care (KMC) can potentially increase breastfeeding rates especially in preterm and low birth weight (LBW) infants.
Objectives. To determine the effect of KMC on 6 months of exclusive breastfeeding among low birth weight infants (LBW).
Search methods. A comprehensive search of CENTRAL and MEDLINE was conducted for trials published until June 2018. Various search engines and local publications were also hand searched for relevant articles.
Selection criteria. All randomized controlled trials and prospective observational studies comparing KMC and conventional care among preterm infants and LBW infants were reviewed. The primary outcome was exclusive breastfeeding at six months of age.
Data collection and analysis. Two authors independently assesed trial quality and extracted data. Statistical analysis was done using Review Manager (RevMan) version 5.3
Results. Nine eligible trials involving 1,202 neonates were identified. All studies were high quality trials with low-moderate risks of bias. KMC significantly increased the rates of exclusive breastfeeding at 6 months (p=0.001)
Conclusion. KMC is an important intervention which can increase exclusive breastfeeding among preterm and LBW infants at an age of 6 months.

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EFFECTIVENESS OF REVERSE KANGAROO MOTHER CARE IN DECREASING ADVERSE PHYSIOLOGICAL EVENTS AND PAIN DURING RETINOPATHY OF PREMATURITY SCREENING PREMATURE NEONATES

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Background. Retinopathy of prematurity (ROP) screening is uncomfortable and even painful in preterm infants.
Objective. To determine the effectiveness of Reverse-Kangaroo Mother Care (R-KMC) compared with conventional care in decreasing adverse physiological events and pain during ROP screening.
Methodology. This was a parallel randomized controlled trial with two treatment arms – R-KMC and conventional care (control). A slight modification to the traditional KMC position (chest to chest) was made by placing the infant's back to the mother's chest (reverse KMC: R-KMC) to facilitate ROP screening in this study. The primary outcomes included increased oxygen saturation, decreases heart and respiratory rates and decreased pain intensity measured by Prematurity Infant Pain Profile (PIPP).
Results. There were 100 preterm infants recruited in the study. There was no difference in baseline characteristics, mean ROP screening duration, mean physiological parameters after the mydriatic application and during ROP screening between the 2 groups. The R-KMC group had a significantly lower mean PIPP score (6.5±2.06 vs. 8.8±2.80; $p<0.0001$) after mydriatic application and during ROP screening (7.6±2.05 vs. 9.8±2.90; $p<0.0001$) compared with the control. No apnea was observed after mydriatic application but there was 1 apneic episode in the control during ROP screening. Twenty-six percent of the ROP screeners recommended R-KMC position during ROP screening, while a majority (70%) was neutral.
Conclusion. R-KMC, a low-cost intervention, significantly reduces pain during ROP screening. It is recommended as a position of choice during ROP screening.

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THE EFFECTIVENESS OF KANGAROO CARE IN ALLEVIATING MATERNAL ANXIETY STATES AT THE NEONATAL ICU: A PROSPECTIVE COHORT STUDY

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Background. Kangaroo mother care is is a technique done in low birthweight newborns especially in preterm infants wherein the infant is held, skin to skin with an adult. Kangaroo care, named for the similiarity to how certain marsupials carry their young, was initially developed to care for preterm infants in areas where incubators are either unavailable or unreliable. This practice can also possibly alleviate maternal anxiety.
Objectives. To determine the effect of kangaroo care on the level of anxiety of mothers of low birthweight neonates during the immediate newborn period.
Study Design. Prospective cohort, tertiary hospital.
Methods. Eligible participants were the mothers of low birthweight infants (birthweight of less than or equal to 2500 grams) admitted at the neonatal intensive care unit of the Philippine General Hospital. This study included 138 post-partum mothers who were encouraged to do KMC one day post-partum and did kangaroo care < 6 hours, > 6 hours or did not do KMC (control group). The primary study outcome was to determine the effect of kanagaroo care in alleviating maternal anxiety and depression in the immediate post-partum period with the use of the Hospital Anxiety and Depression Scale-Pilipino (HADS-P).
Results. Compared to the control group, both KMC groups showed a decrease in anxiety scores ($\leq$ 6 hours, p= 0.001*; > 6 hours, p= 0.007*) from day 1 post-partum to discharge. In comparing anxiety scores from day 1 to day 7 post-partum, KMC for $\leq$ 6 hours (mean difference: 2.423; p value=0.009*) had a more significant decrease in anxiety scores in comparison to KMC for > 6 hours (mean difference: 1.524; p value=0.6116).
However, from day 1 post-partum to discharge, KMC for > 6 hours had a greater effect in lowering anxiety scores (mean difference: 5.095; p=0.005*) than $\leq$ 6 hours (mean difference: 2.538; p=0.0065*) though for both groups the decrease in anxiety scores are clinically significant.
Mothers who did KMC had a significant decrease in depression scores (p value=0.005*) versus mothers who did not do KMC (p value= 0.5243). There is also note of a significant difference in depression scores in both KMC groups from day 1 post-partum to discharge (mean difference: 5.095; p value= 0.005*) and a lesser but still significant effect from day 7 post-partum to discharge (mean difference: 3.571; p value=0.0144).
Conclusion. The Hospital Anxiety and Depression Scale-Pilipino (HADS-P) is a valid tool in assessing cases of anxiety and depression among mothers of low birth weight newborns in the immediate post-partum period. KMC for > 6 hours has a greater effect over-all on lowering maternal anxiety and depression if it is done from day 1 post-partum to discharge.

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INCIDENCE, SEVERITY AND RISK FACTORS OF RETINOPATHY OF PREMATURITY IN A TERTIARY CARE HOSPITAL IN BANGLADESH

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Background. Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the retina which is due to failure of normal progression of retinal vessels in preterm infants. It is an important and preventable cause of visual impairment in childhood.
Objective. To determine the prevalence and severity of ROP, identification of potential risk factors, and the treatment required.
Methods. Preterm infants with a birth weight of < 2500 gm and/or gestational age <35 weeks were screened for ROP from March 2013 to February 2018 in a Neonatal Intensive Care Unit (NICU), Apollo Hospitals, Dhaka, Bangladesh. The infants were followed up until maturation of retina or regression of the disease. Risk factors were analyzed by ANOVA and Chi –square test.
Results. Ninety-three infants were eligible with mean birth weight (± SD) of 1230 ± 279 g and mean gestational age (± SD) 30.65 ± 2 weeks. ROP was diagnosed in 46 infants (49%). Of these, severe ROP was found in 26 infants (28%), all of whom required LASER therapy. Risk factors associated with ROP were low gestational age, low birth weight, longer duration of oxygen therapy, longer duration of hospital stay, sepsis, PDA, ventilator requirement, PRBC transfusion and BPD.
Conclusion. Screening for ROP is a relatively new screening program in Bangladesh and is only limited to a few centers. The urgent need for a national screening program is substantiated by the remarkably high incidence and severity of ROP noted in our cohort. The recognition and treatment of ROP, a preventable cause of visual impairment in childhood is imperative. Furthermore, we have noted that the recognition of risk factors is essential to reduce the incidence and severity of ROP. Especially the uncontrolled use of oxygen has to be strictly avoided.

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TOWARDS LARGE, SIMPLE AND EFFICIENT NEONATAL RANDOMISED TRIALS USING ROUTINELY RECORDED ELECTRONIC PATIENT RECORD DATA: HARMONISATION OF CORE DATA ITEMS FOR THE NEOEPOCH PROJECT (NEONATAL ELECTRONIC POINT-OF-CARE TRIALS FOR HEALTH)

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Background. Many neonatal practices are not based on robust evidence, because such evidence does not exist. Routinely recorded Electronic Patient Record (EPR) data provides an opportunity to undertake simple and pragmatic clinical trials to address these uncertainties. Such trials can be termed “point-of-care” trials; harmonisation of data items is critical to such trials. In the United Kingdom, the National Neonatal Research Database (NNRD) holds EPR data on all neonatal admissions.
Objective. To identify core data items for pragmatic neonatal trials and demonstrate the effectiveness of routinely recorded EPR data held in the NNRD for such trials.
Methods. We identified core neonatal data items for trials through systematic reviews and developed a neonatal core outcome set using a Delphi consensus process. We tested the completeness of neonatal EPR data in the NNRD to determine suitability for clinical trials. We developed a pilot “point-of-care” trial: the WHEAT trial will randomise preterm infants to continued or withheld feeds around blood transfusions.
Results. 14 background data items were identified through a systematic review of trials; these are highly complete in the NNRD. 104 neonatal outcomes were identified from clinical trials and qualitative literature, 414 stakeholders from 25 countries identified 12 neonatal core outcomes: survival, sepsis, necrotising enterocolitis, brain injury, gross motor ability, cognitive ability, quality of life, adverse events, visual impairment, hearing impairment, retinopathy of prematurity, chronic lung disease. The WHEAT trial is recruiting preterm infants into a prospective “point-of-care” trial across 17 neonatal units.
Conclusions. A set of core data items has been identified for neonatal trials, these should facilitate common neonatal data sets internationally. Large, simple and efficient neonatal randomised controlled trials appear feasible within the current UK neonatal EPR system utilising data held in the NNRD.

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RANDOMIZED CONTROLLED TRIAL ON EFFECTIVENESS OF BREASTFEEDING IN CRADLE POSITION VERSUS CRADLE POSITION ALONE FOR PAIN REDUCTION DURING THE HEEL LANCE PROCEDURE FOR NEWBORN METABOLIC SCREENING AMONG TERM INFANTS

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Background. Pain reduction is a much-studied field in adults and older children. However, relatively little is known about pain and pain reduction in neonates.
Objective. The study objective was to compare the efficacy of breastfeeding while being held in the cradle position, versus being held in the cradle position alone, in reducing pain response during the heel lance procedure, as measured by Neonatal Infant Pain Scale (NIPS).
Methods. This was a randomized controlled, single blind, prospective study in a public tertiary hospital, the Philippine General Hospital. Twenty-six term neonates with gestational age 37-42 weeks with APGAR score ≥7 were included. Infants were randomly assigned using pre-drawn sealed envelopes to either Group A, which consisted of patients on breastfeeding while held in the cradle position (n=13), or Group B, which were patients held in the cradle position alone (n=13), during heel lance procedure. The primary outcome measures of the study were the behavioral responses, which were the components of the NIPS. These were facial expression, breathing patterns, state of arousal, and extremity response during heel lance procedure. The NIPS score was measured before and after the completion of the procedure. A p-value < 0.05 using the t-test was considered statistically significant.
Results. A total of 26 term neonates were included in the study. The mean total NIPS score were significantly lower in the breastfeeding group (4.15 ±0.80) compared to the control group (5.84 ±0.98) (p=0.0001).
Conclusion. This study suggests that it is breastfeeding itself and not just the “containment” that occurs in the breastfeeding position that affords pain relief during noxious procedures.

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THE ACCURACY OF THE WINROP 2 ALGORITHM AS A SCREENING TOOL FOR CLINICALLY SIGNIFICANT RETINOPATHY OF PREMATURITY: A META-ANALYSIS

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Background. Retinopathy of prematurity continues to be a major cause of childhood blindness worldwide. The gold standard for its detection is indirect ophthalmoscopy, a painful and stressful procedure with a number of possible complications; hence, the need for other screening tools to minimize its use. One of the new predictive models used for ROP is the WINROP-2 (weight, insulin-like growth factor, neonatal ROP) algorithm. It is an online surveillance system based on weekly postnatal measurements of body weight to evaluate the risk of developing sight-threatening ROP.
Objective. This study aims to review and pool available data on the accuracy of WINROP 2 as a screening tool for clinically significant ROP in preterm infants <32 weeks
Methods. Articles reporting the accuracy of WINROP-2 were identified through an electronic search in PubMed, Cochrane Library, EMBASE and Google Scholar using the key words: WINROP, weight gain, retinopathy of prematurity and ROP. It is conducted in adherence to the PRISMA standards for selecting eligible studies for systematic reviews. Data on sensitivity, specificity and odds ratio were extracted from each included study and were analyzed using forest plots and SROC curves. Statistical analysis was facilitated using Metadisc version 1.4.
Results. A total of 121 studies were identified by literature search, with 18 articles meeting all the criteria for inclusion. The pooled sensitivity, specificity and diagnostic odds ratio are 90% (95% CI: 88%-92%), 54% (95% CI: 53%-56%) and 10.27 (95% CI: 5.47-19.27), respectively. I2 index, a measure of heterogeneity of study results, is 67.7%. The SROC curve shows an AUC of 0.80.
Conclusion. Evidence from this meta-analysis recommends the use of the WINROP-2 algorithm as a useful screening tool for ROP with values more suggestive for ruling in the disease.

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THE EFFECT OF FAMILY INTEGRATED CARE ON PRETERM INFANTS AFTER DISCHARGE: A FOLLOW-UP STUDY

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Objective. The transmission from a closed and non-parent model to a parent accompanying management mode in the Neonatal Intensive Care Unit (NICU) is a current trend in the development of neonatal medicine. In recent years, our research team initiated a multi-center clinical study focusing on the impact of Family Integrated Care (FICare) in NICU on the prognosis of preterm infants. The objective of this study is to investigate the effect of FICare on the physical and neurological development of preterm infants.
Methods. A total of 180 premature infants admitted to the NICU of the Third Xiangya Hospital of Central South University during September 2014 and January 2016 were included in the study. We divided these infants into FICare group (90 cases) and control group (90 cases) according to the nested control analysis. During the entire hospitalization period, in the FICare group, after trained by the nurses, parents were permitted to care for their infants together with nurses in NICU as long as the infants' condition allowed. In the control group, all nursing work was completed by nurses and parents almost had no chance to care for their infant until discharge of the infant. All patients were followed up until 18 months of age. We collected general clinical data, the corrected gestational age (CGA), length/weight/head circumference at 42weeks, 3 and 6 months of age, the breastfeeding rate at 1 month, the re-hospitalization rate within 30 days after discharge. In addition, Bayley scales of infant development at 18 months of age were performed. Data analysis was performed by using S*P*SS21.0 software.
Results. 1). There was no significant difference in both infants' and mothers' general condition between the FICare group and the control group. The gestational age of FICare and control group was 32.2±1.78 and 32.6±1.67 weeks. The birth weight of FICare and control group was 17.8.4±349.6 and 1800±383.9 grams. 2). At the CGA 42 weeks, 3 and 6 months, the lengths of infant in FICare and control groups were 50.8±1.93 vs 50.1±2.44, 59.55±1.83 vs 58.76±2.86, 66.42±1.67 vs 65.84±2.12, respectively (*P* values were 0.045, 0.028, and 0.044, respectively). The head circumferences of infant in FICare and control groups were 34.7±1.45 vs 34.2±1.82, 39.34±1.71 vs 38.84±1.67, and 43.01±0.84 vs 42±1.39 cm, respectively (*P* values were 0.043, 0.049, and 0.048, respectively). The weights of infants in the FICare and control groups were 3.61±0.44 vs 3.44±0.64, 5.96±0.55 vs 5.78±0.63, 7.68±0.51 vs 7.51±0.66 kg, respectively (*P* values were 0.037, 0.045, and 0.047, respectively). 3) At CGA1, 3, and 6 months, the breastfeeding rates of the FICare group and the control group were 98.89 vs 96.67, 95.56 vs 90, and 95.56 vs 70%, respectively (*P* values were 0.621, 0.15, and 0.005, respectively). At CGA18 months, the MDI scores of infants in FICare group and the control group were 88.2±5.7 and 84.3±6.1 (*P* =0.01). The PDI score was 84.2±3.4 vs 80.8±5.6 (*P* =0.000).
Conclusion. FICare model enables parents to join the caring team for preterm infants in NICU, and is beneficial to the physical and neurological development of preterm infants in China.

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EFFICACY OF SCREENING FOR CONGENITAL HEART DISEASES AT A TERTIARY CARE HOSPITAL IN SINGAPORE

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Background. Congenital heart disease (CHD) is a leading cause of infant mortality. The aim of our study was to evaluate the incidence and types of CHD over a decade. We hypothesized that the current screening program comprising antenatal ultrasonography and postnatal clinical examination did not detect a significant proportion of CHD.
Methods. A retrospective review of live-births with CHD from 2003 to 2012 was conducted. Babies diagnosed with arrhythmia, isolated patent ductus arteriosus, foramen ovale and persistent pulmonary hypertension were excluded. Prenatal and postnatal diagnosis was examined for all CHD, including 7 "critical" CHD selected for risk of adverse perinatal outcome if undetected. Sensitivity and specificity of the screening program was calculated for all CHD and for the 7 "critical" CHD.
Results. The incidence of CHD at birth was 9.8 per 1000 live-births with near-complete case ascertainment. The sensitivity of antenatal screening was 11.4% with wide difference in prenatal detection rates amongst various CHD. Only three of seven types of "critical" CHD were detected prenatally. Sensitivity and specificity of the screening program for any CHD was 64.9% and 99.7% respectively. Sensitivity and specificity of the 7 types of "critical" CHD was 100% and 99.1% respectively.
Conclusions. A screening program comprising antenatal ultrasonography and postnatal clinical examination without pulse oximetry, detected 64.9% of CHD.

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THE EFFICACY AND SAFETY OF ORAL PROPRANOLOL ADMINISTRATION IN THE PREVENTION AND TREATMENT OF RETINOPATHY OF PREMATURITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives. To check out the efficacy and safety of oral propranolol administration in the prevention and treatment of retinopathy of prematurity.
Methods. PubMed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, EMBASE, Web of Science, and clinical trial registration websites were searched through September 15, 2017. Randomized clinical trials about oral propranolol for retinopathy of prematurity were included. Data were independently extracted by 2 reviewers. The quality of the included studies was examined in accordance with the Cochrane guidelines. Data were pooled using a Mantel-Haenszel fixed-effects model.
Results. A total of 101 articles were screened. After intensive literature appraisal, 4 unique studies involving a total of 352 neonates with gestational age less than 32 weeks were enrolled. The incidence of additional treatment application in the propranolol group was 25 of 174 (14.37%) compared to 51 of 178 (28.65%) in the control group, with a Mantel-Haenszel fixed-effects risk ratio of 0.49 (95% CI, 0.33-0.74; heterogeneity, P = .95; I^2 = 0%; moderate QOE). The incidence of significant ROP progression in the propranolol group was lower than the control group, with a risk ratio of 0.39 (M-H fixed-effects, 95% CI, 0.21-0.72; heterogeneity, P =.30; I^2 = 17%; low QOE). Adverse events such as bradycardia and hypotension were reported in propranolol group.
Conclusions. This meta-analysis showed that propranolol administration might be potentially effective in the prevention and treatment of retinopathy of prematurity, without increasing the risk of complications based on current limited evidence. The safety of propranolol requires further carefully performed trials.

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PARENT´S PERCEPTIONS OF THE VERBAL AND WRITTEN INFORMATION GIVEN IN A NEONATAL CLINICAL TRIAL

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Background. Preterm birth is a burdening event for families. In earlier studies, parents expressed that information was one of the most important factors in managing their stress. In this study, we investigated how parents of extremely prematurely born children perceived the information they received in the informed consent process in connection to a clinical trial.
Methods. 102 infants were included at this interim analysis. Parents received a questionnaire from a study nurse at two time points, when the infants were 7 days and 40 weeks postmenstrual age. The questionnaire was available either on paper or electronically. Seven questions including the following topics were given: if the information was understandable, clear and correct and what influence the information had on parents' sense of security during the trial.
Results. The response rate was 55%. On the question "was the information clear enough to make a decision to participate?" 86% answered yes, 3% answered no, 2% answered don't know and 9% gave their own comments. 66% felt completely secure with the information and answers they received before the clinical trial, 16% secure, 0% insecure and 9% gave their own comments. Suggestions made by parents concerned the time-point, language and the situation in which the information was given.
Conclusions. The results show that most parents were satisfied and felt secure with the information. The informed consent process not only depends on well-formulated information, but also on time and situation when the information is given.

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COMPARING THE COMPLICATIONS OF THREE METHODS OF FUROSEMIDE ADMINISTERED TO PREMATURE NEONATES SUFFERING FROM PATENT DUCTUS ARTERIOSUS

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Background. Patent ductus arteriosus (PDA) needs treatment for cases whose ducts are not closed spontaneously. Furosemide reduces preload, but there is still controversy regarding the protocol of its administration between pediatricians and pediatric cardiologists. We aimed to compare renal complications and electrolyte imbalance of three protocols of administering furosemide.
Methods. In this prospective study, 127 preterm neonates with PDA were randomly assigned into three different groups, very slow infusion of Furosemide (2 mg/kg) was given intravenously to 47 neonates every other day (group A), 1 mg/kg of Furosemide was administered by very slow infusion to 39 neonates every day (group B), and bolus doses (0.5 mg/kg) were given twice a day to 41 neonates (group C) for about 14 days. All participants underwent kidney ultrasonography. Blood and urine samples were taken on day 3 and 17. Data were analyzed by SPSS software.
Results. Electrolyte imbalance included higher sodium and calcium on the third day in group A ($P<0.05$) with no difference in serum level of potassium, PH, and HCO3. The serum level of calcium and Ca/Cr ratio was higher in group A ($P<0.05$) and serum level of BUN was higher in group B ($P<0.05$). Also, higher serum level of calcium and Ca/Cr ratio was observed on the seventeenth day in group A. Nephrocalcinosis was observed in 8.7% of neonates on the seventeenth day after furosemide with normal level of creatinine ($P=0.896$).
Conclusion. Administering furosemide in two bolus doses is superior regarding electrolyte imbalance and BUN levels, but nephrocalcinosis was not found to be different in three protocols.

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TWO NEWBORNS WITH SEVERE THROMBOSIS TREATED SUCCESSUFFLY WITH LOW MOLECULAR WEIGHT HEPARIN

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Background. We report two newborns who suffered from necrosis of limbs due to thromboses which were treated with low molecular weight heparin. The first case was a 2-day-old premature female infant (32 weeks of GA) who developed a necrosis of the whole right upper limb caused by a thrombosis due to an accidental tightening. The other case was a 6-day-old term male newborn who developed a thrombosis on four limbs, as a consequence of a neonatal sepsis and disseminated intravascular coagulation caused by Klebsiella spp. None of the patients had hemophilia or congenital hypercoagulopathy, and both were treated with low molecular weight heparin for 5.5days and 22days, i.v. antibiotics and wound care. Both neonates had a rapid improvement and survived; the limbs recovered completely without severe complications.

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A CONTROLLED STUDY OF PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS TREATED WITH ACETAMINOPHEN AND PLATELET-RICH PLASMA

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Objective. To understand possible mechanisms, efficacy and safety of acetaminophen and platelet-rich plasma (PRP) on promoting the closing of ductus arteriosus in preterm infants.
Methods. Preterm infants with symptomatic patent ductus arteriosus (sPDA) admitted to the department of neonatology from Jan 2016 to May 2018 were enrolled. Oral acetaminophen was given at doses 15 mg/kg every 6 hours for three days. When there were any contraindications of oral acetaminophen or drug therapy failure, PRP transfusion was given at a single dose 20 ml/kg. Echocardiography, platelet-derived growth factors (PDGF) and urinary prostaglandin E2 (PGE2) were monitored before treatment and 72 hours after treatment. SPSS 20.0 software was used for data analysis.
Results. The treatment success rate of acetaminophen group [41/61 (67.2%)] was similar to that of PRP first-line treatment subgroup [6/9 (66.6%)] (χ^2 = 0.000, P = 1.000), and was significantly higher than that of PRP rescue treatment subgroup [6/17 (35.2%)] (χ^2= 5.565, P = 0.017). There were upper gastrointestinal hemorrhage (5 cases, 8.1%), positive fecal occult blood test (4 cases, 6.6%) and oliguria (3 cases, 4.9%) in acetaminophen group. There were no upper gastrointestinal hemorrhage and positive fecal occult blood test, but there was oliguria (1 case, 3.8%) in PRP group. There was one case III~IV level intraventricular hemorrhage and one case ≥II phase necrotizing enterocolitis in both groups. The urinary PGE2 level of post-treatment were lower than pre-treatment in acetaminophen group (t = 7.870, P = 0.000). The blood platelet count, plateletocrit and blood PDGF of post-treatment were higher than pre-treatment in PRP group (t = -3.460, -2.250, -3.480; P = 0.002, 0.034, 0.002).
Conclusion. The acetaminophen promotes the closing of ductus arteriosus in preterm infants by reducing PGE2 level, while the PRP promotes the closing of ductus arteriosus in preterm infants by supplying platelet and PDGF possibly. The efficacy was similar between two groups. The adverse reactions of PRP group was slightly fewer than acetaminophen group. When there were any contraindications of oral acetaminophen or drug therapy failure, PRP transfusion may be one of the candidate therapies of promoting the closing of ductus arteriosus in preterm infants.

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HIGH-DOSE IBUPROFEN FOR PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

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Background. Patent ductus arteriosus (PDA) is associated with various morbidities related to prematurity. PDA in preterm newborns can be treated effectively with intravenous ibuprofen. Recent studies have suggested that the failure of pharmacologic treatment of PDA may be due to the inadequacy of the standard-dose regimen.
Objective. The aim of this study was to compare the efficacy and possible adverse effects of high-dose intravenous ibuprofen regimen to that of standard regimen in closing PDA.
Methods. This is a single-center, retrospective study of 28 infants born at less than 35 weeks' gestational age from December 2015 to February 2018. Infants with echocardiographic evidence of significant PDA were randomized to receive either standard dose (10-5-5 mg/kg/day, group 1) or high-dose (20-10-10 mg/kg/day, group 2) course of ibuprofen. Both groups were compared. The rate of PDA closure and the incidence of side effects related to the use of ibuprofen were analyzed.
Results. A total of 28 infants were enrolled in the study and randomized into two groups: group 1 (n = 15) or group 2 (n = 13). We found no significant differences in obstetric risk factors and clinical characteristics between the two groups. After the first course of ibuprofen, 46.7% of the infants in the standard-dose regimen group had persistent PDA compared to 30.8% in the high-dose regimen group (P = 0.638). There were no significant differences in the level of serum blood urea nitrogen and creatinine and platelet counts before and after treatment. Neither the occurrence of bleeding tendency nor the incidence of NEC or gastrointestinal bleeding differed between the two groups.
Conclusions. High-dose ibuprofen regimen is not more effective in closing PDA nor does it increase the adverse effects compared with standard-dose regimen in preterm infants.

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HEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS MAY BE ASSOCIATED WITH VARIATIONS OF PLATELET COUNTS AND PLATELETOCRIT WITHIN 24 HOURS OF BIRTH

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Background. We investigated mechanism of hemodynamically significant patent ductus arteriosus (hsPDA) in preterm infants with special emphasis on levels of platelet counts (PLT) and plateletocrit within 24 hours of birth.
Methods. The clinical data was retrieved from November 2010 to October 2015. Based on the inclusion and exclusion criteria, 1,270 cases were enrolled for the blood platelet parameters in venous blood samples within 24 h of birth. Their values were analyzed in association with clinical factors related to PDA and echocardiographic findings on postnatal day (D) 4-7. A non-PDA group included 982 (77.3%), a non-hsPDA group with 178 (14.0%) and a hsPDA group with 110 cases (8.7%).
Results. We found that the difference in platelet distribution width, mean platelet volume and platelet-large contrast ratio within 24 h after birth was not statistically significant ($p>0.05$). The lower gestational age, lower birth weight, the lower PLT and plateletocrit within 24h after birth were associated with greater likelihood of PDA (P = 0.035, 0.000, 0.000, 0.000, respectively). The predicted area under the ROC curve of hsPDA on the preterm children by PLT and plateletocrit within 24 h after birth was 0.703 (95% CI 0.655-0.751) and 0.748 (95% CI 0.699-0.797); the best critical values were 241.5×109/L (sensitivity: 78.2%, specificity: 67.0%) and 0.245% (sensitivity: 68.2%, specificity: 74.2%). For the preterm infants with PLT $<241.5\times10^9$/L, $<150\times10^9$/L and $<100\times10^9$/L as well as plateletocrit <0.245% and 0.09% within 24 h after birth, the risks of hsPDA were 1.876, 2.169, 6.216, 1.749 and 5.407 times of PLT≥241.5×109/L, ≥150×109/L and ≥100×109/L as well as plateletocrit ≥0.245%, ≥0.09% and ≥0.09%, respectively. The logistic regression analysis showed that the gestational age and PLT within 24h after birth was not independently associated with the hsPDA of preterm infants (P =0.911 and 0.392). The birth weight and plateletocrit within 24 h after birth were independent risk factors for premature infants with hsPDA (P=0.000 and 0.000). The risk of the preterm infants with hsPDA was increased by 3.328 times (95% CI: 2.455-4.512) if the plateletocrit was decreased by 0.10%.
Conclusion. Decrease in plateletocrit rather than decrease in PLT of preterm infants within 24 hours of birth was an independent risk factor of hsPDA on D4-D7.

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ASSOCIATION OF ANTENATAL CORTICOSTEROIDS WITH PERINATAL-NEONATAL MORBIDITY AND MORTALITY IN PRETERM INFANTS: A BIRTH POPULATION-BASED SURVEY IN HUAI'AN IN 2015

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Objective. To explore the association between the use of antenatal corticosteroids and perinatal-neonatal outcomes of the preterm infants from a regional birth population study.
Methods. Data were collected prospectively in a birth population based study from all level I-III hospitals in Huai'an, Jiangsu in 2015. Perinatal-neonatal morbidity and mortality in relation to antenatal corticosteroids use were analyzed.
Results. In 59,424 total births, 2404 preterm births were recorded, with 844 (mean 36.6%) infants exposed to antenatal corticosteroids. Antenatal corticosteroids exposure rates for infants born at <32 and 32-36 weeks were 58.2% and 33.6%, respectively. Exposure rates for those born at <1500 g, 1500-2499 g, 2500-3999 g and 4000 g were 57.7%, 48.5%, 24.6% and 13.6%. In the hospitals of level I (85), II (16) and III (6), the coverage of antenatal corticosteroids was 17.3%, 31.0% and 39.9%, with average covering gestation being 34.7, 34.4 and 33.1 weeks of the preterm infants. The rates of death in the delivery room were 1% (9/844) for those received antenatal corticosteroids and 8.2% (128/1560) for those who did not (OR=0.12, 95%CI 0.06,0.23). The referral rate to neonatal unit on the first day after birth was 76.9% (649/844) for those exposed to antenatal corticosteroids vs. 48.8% (761/1560) for those who did not (OR=3.49, 95%CI 2.89, 4.22).
Conclusions. Our regional birth-population data in 2015 outlined a profile of the antenatal corticosteroid use in preterm births, and its relation with perinatal-neonatal outcomes under current perinatal health care settings.

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HIGH RISK PREGNANCY ASSOCIATED PERINATAL MORBIDITY AND MORTALITY: A SECOND BIRTH POPULATION-BASED SURVEY IN HUAI'AN IN 2015

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Background. Pregnancy-associated complications and delivery have an adverse impact on perinatal mortality. The objective of this study was to explore the association between pregnancy complications and perinatal outcome from a regional birth population. Additionally, comparison was made with the results of 2010 survey in the same region.
Methods. In this prospective survey of birth population from all level I-III hospitals in Huai'an in 2015, perinatal morbidity and mortality in relation to pregnancy complications and maternal and perinatal characteristics were analyzed using international definitions.
Results. Of 59,424 total births in the hospitals of level I (85), II (16) and III (6), delivery rate was 30.4%, 40.1% and 29.5%, and rates of pregnancy complications were 12.9%, 9.8% and 21.1% (average 14.1%), with antenatal corticosteroids rate in <37 gestational weeks being 17.3%, 31.0% and 39.9% (mean 36.6%), respectively. The preterm birth rate was 0.6%, 2.7% and 9.5% (mean 4.06%), and the composite rate of fetal death, stillbirth and death immediately after delivery was 0.1%, 0.4% and 0.6%, respectively. By multi-variate logistic regression analysis, congenital anomalies, low Apgar scores, multi-pregnancy and amniotic fluid contamination were risk factors of adverse perinatal outcomes. Despite a higher rate of pregnancy complications than in 2010 survey, a >30% reduction of perinatal mortality was found in 2015, in particular in the preterm infants. The high Cesarean Section rate in non-medically indicated cases remained a challenge.
Conclusions. Our regional birth-population data registry in 2015 revealed a robust and persistent improvement in the perinatal care and management of high risk pregnancy, providing further evidence for the validity and applicability of the study concept and protocol for vital statistics.
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DIAGNOSTIC AND PREDICTIVE VALUE OF RENAL RESISTIVE INDEX IN CASE OF NEONATAL ACUTE KIDNEY INJURY

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Background. The promising methods of investigation enabling to estimate objectively the condition of renal functions is ultrasonic examination, especially application of pulsed-wave Doppler examination. The objective was to determine diagnostic and predictive value of renal resistive index (RI) in case of acute kidney injury (AKI) in critically ill full-term newborns on first day of life.
Methods. A comprehensive ultrasound examination in 25 critically ill full-term newborns with AKI, and 24 ones without AKI was performed. Area under the receiver operating characteristic curves (ROCs) was used to deduce the diagnostic accuracies of RI. The 2×2 tables were constructed to derive sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and cut-off level of RI.
Results. The critically ill full-term neonates with AKI had significantly higher level of RI compared to neonates without AKI. Mean RI was 0.84 (95% CI 0.81; 0.88) and 0.77 (95% CI 0.72; 0.81) respectively ($p<0.05$) in the right main artery; mean RI was 0.85 (95% CI 0.81; 0.88) and 0.79 (95% CI 0.76; 0.83) respectively ($p<0.05$) in the left main artery. But analyses of ROC-curves didn't detect high level of diagnostic and predictive values of this index for indicate AKI. So, level of AUROC-index for right renal RI was 0.72 ($p=0.027$), Se – 84.0% (95% CI 63.9; 95.5), Sp – 58.3% (95% CI 36.6; 77.9), PPV – 67.7% (95% CI 48.6; 83.3), NPV – 77.8% (95% CI 52.4; 93.6), a cut-off level - higher than 0.79. The level of AUROC-index for left renal RI was 0.67 ($p=0.07$), Se – 36.0% (95% CI 17.9; 57.5), Sp – 95.8% (95% CI 78.8; 99.9), PPV – 90.0% (95% CI 55.5; 99.8), NPV – 58.9% (95% CI 42.1; 74.4), a cut-off level - higher than 0.89.
Conclusions. The analyses of ROC-curves did not detect high level of diagnostic and predictive values of RI for indicate of AKI in full-term newborns. A larger study cohort is needed to correlate between groups with and without AKI, and with different types of AKI.

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PERITONEAL DIALYSIS IN A VERY LOW BIRTH WEIGHT INFANT WITH ACUTE KIDNEY INJURY: A CASE REPORT AND LITERATURE REVIEW

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Objective. Experience of peritoneal dialysis in low birth weight (VLBW) infants is scarce in emerging NICU of Western region in China. We report our experience in management of a VLBW infant with acute kidney injury (AKI).
Method. A VLBW infant diagnosed with AKI was studied and the case history was compared with literature from Chinese and international literature: CNKI, Wan-Fang and Pubmed database by searching key words peritoneal dialysis (PD), low birth weight and preterm. A total of 11 papers were retrieved from Jan 2003 to Jan 2018.
Results. The case treated in this unit was a male newborn at 28 4/7 weeks gestation with birth weight of 1170 g. He had intrapartum asphyxia which was complicated by sepsis. On day 3 of postnatal life (D3), the patient developed AKI and PD was initiated and continued for 6 days. On D9 the patient was weaned from PD and discharged on D43. By comparing 11 literature reports in 79 cases with gestational age of 24-39 weeks and birth weight 264-2400 g, the main causes of AKI were asphyxia and sepsis. Complications associated with the PD were peritonitis (8, 10%), circuit leakage (16, 20%), circuit obstruction (2, 2.5%), perforation (1, 1.25%) and hernia (1, 1.25%). Survival rate was 47% (37).
Conclusion. We succeeded in rescuing a VLBW infant with AKI by PD. This limited experience should be encouraging to explore more suitable cases of VLBW with AKI.

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CLINICAL FEATURES OF LATE-ONSET CIRCULATORY COLLAPSE IN PRETERM INFANTS

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Background. Preterm infants may develop acute systemic hypotension that responds to glucocorticoid, but not to volume expanders or inotropics, during the postnatal period. This condition is termed late-onset circulatory collapse(LCC).
Objective. This study aims to describe the clinical features of LCC in preterm infants.
Methods. Medical records of infants (< 32 gestational weeks) who were admitted to NICU of Seoul National University Bundang Hospital from January 2014 to December 2017 were retrospectively reviewed. The LCC was defined as a refractory hypotension occurring after 7 days of life which responds to a glucocorticoid. The clinical characteristics of infants with LCC were compared to those of infants who developed hypotension with apparent causes after 7 days of life.
Results. Among 327 preterm infants enrolled, 65 infants developed circulatory collapse after 7 days of life. Among 65 infants, 35 (53.8%) infants met the definition of LCC. There were no significant differences in prenatal and perinatal characteristics between infants with LCC and infants with hypotension of other causes. In comparison to infants with hypotension from other causes, infants with LCC had significantly lower incidence of severe bronchopulmonary dysplasia or death (73.3% vs. 42.9%, P=0.013). The mean gestational age and birth weight of infants with LCC was 27+5±2+1 weeks and birth weight was 963±245 g. LCC occurred at a mean postnatal age of 20±2 days (30+3±0+3 postmenstrual weeks). The mean body weight at the time of LCC was 1,130±446 g. The incidence of LCC peaked in preterm infants with a gestational age of 25 weeks (31.3%) and in infants with birth weights between 1,000-1,250 g (34.3%). The mean serum cortisol level measured just before a glucocorticoid administration in infants with LCC was 12.3±5.4 ug/dL. Among preterm infants who developed hypotension after 7 days of life, nearly half of the infants had the diagnosis of LCC without apparent causes.
Conclusion. LCC was a relatively reversible condition when glucocorticoids were administered promptly.

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DIAGNOSTICAL VALUE OF PROCALCITONIN IN NEWBORNS WITH HYPERBILIRUBINEMIA

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Background. Disturbed adaptation of newborns in the early neonatal period may have great impact on the overall health of a child and his further development. This may also hold true for prolonged neonatal hyperbilirubinemia.
Methods. 100 newborns with prolonged neonatal hyperbilirubinemia which lasted more than 14 days were included in this study. Newborns with prolonged neonatal hyperbilirubinemia were divided into following groups: newborns with prolonged neonatal hyperbilirubinemia 31 (31%), 37 (37%) newborns with a history of perinatal infection of intrauterine origin were examined but bacteriologically not confirmed, 22 (22%), and newborns with cerebral ischemia and 10 (10%) newborns born from mothers with hypothyroidism.
Procalcitonin (PCT) in plasma or serum was analyzed by a immunochromatographical method (BRAHMS Diagnostica, Germany).
Results. Newborns with prolonged neonatal hyperbilirubinemia were 38,1 ± 1,07 weeks of gestational age in all studied groups. 50 out of 100 neonates had PCT levels less than 0,5 ng/ml which were not dependent on gestational, postnatal age and weigh.
In 4 newborns PCT levels at 14-18 days of life were 0,5 ng/ml. One newborn with a complicated maternal history (prolonged rupture of membranes, maternal fever) had a PCT-concentration of 2 ng/ml (<10) at day 4 which decreased to 0.5 mg/ml within 2 days.
Conclusion. A concentration of PCT in plasma or serum > 0.5 ng/ml may detect hidden inflammatory processes in children with prolonged neonatal hyperbilirubinemia.