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Neonatology

O-NEO-001

Minimally invasive surfactant therapy using gastric tube in preterm infants with respiratory distress syndrome

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Abstract

Background For many years, preterm infants with respiratory distress syndrome (RDS) have been managed with intubation and mechanically ventilated for surfactant therapy. Mechanical ventilation (MV) can lead to lung injury and ultimately to bronchopulmonary dysplasia (BPD). Minimally invasive surfactant therapy (MIST) allows surfactant to be administered to a spontaneously breathing infant who then remains on continuous positive airway pressure (CPAP). The MIST have shown good results reducing the need of MV, BPD and improving oxygenation.

Objective To describe the feasibility of MIST using gastric tube in preterm infants with RDS.

Methods In this prospective cohort study, preterm infants with gestational age ≤ 32 weeks, requiring a fraction of inspired oxygen (FiO_2) ≥ 0.30 during nasal CPAP pressure of ≥ 7 cmH_2O were eligible for MIST. Surfactant (100 mg/kg body weight) was instilled in less than 6 hours after birth, using a sterile gastric tube 5 F. The need for intubation in 72 hours, duration of oxygen supplementation and neonatal outcome were recorded.

Results There were 12 infants included. Reduction of FiO_2 was observed in all cases after surfactant administration. Intubation in 72 hours was conducted in 1 infant. Average duration of oxygen supplementation was 6.1 (SD 4.8) days. Incidence of BPD found in 2 patients, who also had necrotizing enterocolitis and septicemia. There were no other outcomes found such as intraventricular hemorrhage, periventricular leucomalacia, and ROP requiring treatment.

Conclusion The MIST using gastric tube in spontaneously breathing infants on nasal CPAP is feasible and deserves further studies.

Keywords: surfactant, RDS, MIST, gastric tube

O-NEO-002

Cranial ultrasound screening in preterm infants and its correlation with perinatal risk factors

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Abstract

Background Preterm birth is associated with variable degree of brain injury and medical complication. Cranial ultrasonography (cUS) is most widely used and routine procedure in NICU.

Objective To perform cranial ultrasound screening in preterm infant and determine risk factors of abnormal cUS.

Methods A cross-sectional study, in March to May 2016 of preterm infant in NICU Dr. Soetomo Hospital, using am3 ultrasound transportable machine with curved and linier tranducers, frequency of 5-10 MHz. Statistical analysis used Chi-square and logistic regression multivariate analysis for risk factor of cUS abnormality.

Results One-hundred-twelve infants were enrolled, 57 (50.9%) were males, mean age was 3.1 (SD 3.03) days. Mean gestasional age of abnormal cUS were 30.1 (SD 2.75) weeks whereas in normal cUS were 32.1 (SD 1.93) weeks. Twenty three infant (20.5%) were abnormal cUS, consist of intraventricular hemorrhage (IVH) 16 (14.3%), three infants (2.7%) were periventricular leucomalacia, and four infants (3.6%) were ventricular dilatation. The univariate analysis of birth weight (OR 8.72, 95%CI 2.93 to 25.97), gestational age (OR 3.21, 95%CI 1.09 to 9.42), asphyxia (OR 10.96, 95%CI 3.87 to 31.02), duration of oxygenation (OR 6.07, 95%CI 2.11 to 17.44), and resuscitation (OR 5.35; 95%CI 1.95 to 14.67; P<0.05) predicted abnormal cUS. Multivariate analysis of birth weight and asphyxia was predicting abnormal cUS with AUC 84.5% (95%CI 75.1 to 93.8%).

Conclusion The most common cUS abnormality is IVH. Birth weight under 1500g and asphyxia are important risk factors of cUS abnormality in preterm infant.

Keywords: *preterm, screening, cranial ultrasound*

Cranial ultrasound screening in preterm infant and correlation with perinatal risk factors

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ABSTRACT

Background: Preterm birth is associated with variable degree of brain injury and medical complication. Cranial ultrasonography (cUS) is most widely used and routine procedure in NICU.

Objective: To perform cranial ultrasound screening in preterm infant and determine risk factors of abnormal cUS.

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Conclusion: The most common cUS abnormality was IVH. Birth weight under 1500g and asphyxia are important risk factor of cUS abnormality in preterm infant.

Keywords: *Preterm, screening, cranial ultrasound.*

BACKGROUND

Preterm infants defined as babies born less than 36 weeks of gestation. Being born prematurely is not a normal event despite its routine nature. The fetal or preterm infant brain is vulnerable to both hemorrhagic and ischemic injury during the late second and early third trimester.This is due to vascular, cellular and anatomical features of the developing brain, and the tendency for preterm infants to experience periods of physiological instability at a time when they have limited cerebral circulatory autoregulation. Even premature infants who have relatively uncomplicated neonatal causes are at substantial risk for developmental delays in cognition and motor skills. Although advances in neonatal care have greatly improved the survival and outcome of these vulnerable patients, brain injury still remains a major concern. Early diagnosis is important for prognostication, optimal treatment, and neurological outcome.[1,2]

Cranial ultrasonography (cUS) is the most widely used as a routine procedure technique for evaluating brain morphology and cerebral lesions in neonates in neonatal intensive care, and in particular in all the infants who are at risk for brain lesions. Serial ultrasound scans can identify not only the presence of lesions but also their type and extent. The major advantages of cUS are: it is relatively inexpensive and safe compared to other neuroimaging techniques, can be performed bedside with little manipulation of the infant. It can be repeated as often as necessary and thereby enables visualizations of ongoing brain maturation and the evaluation of brain lesion in addition to assessing the timing of brain damage. When cUS is used repeatedly, its sensitivity and specificity can be very high. Many studies have been performed in preterm infants and these have provided important information on the incidence and evolution of cerebral lesions and their relation with gestational age.[1,2,3]

Intraventricular hemorrhage (IVH), periventricular leukomalacia(PVL), and ventriculomegaly (VM) are major neuropathologicalcomplications occurring commonly in premature infantsdan can be evaluated using cranial ultrasonography, and are associated with high mortality and adverse neurodevelopmental outcome.[4,5]

We therefore decided to perform a hospital-based cranial ultrasonography screening program aiming to describe the pattern of cUS abnormalities in preterm infants and to define the potential need for cUS according to perinatal risk factors.

METHODS

A cUS screening of preterm infants was carried out between March to May 2016 in a single neonatal tertiarycare center (Neonatal Intensive Care Unit, NICU, RumahSakit Dr. Soetomo, Surabaya, Indonesia). All preterm infants (less than 36weeks gestational age) were considered eligible. Cranial ultrasonography wereperformed after 24 hours of life. Babies were excluded for parental refusal or when they had multiple congenital anomaly.

The following obstetrics and neonatal characteristics were collected: mode of delivery (vaginal delivery, vacuum extractor, elective or emergency caesarean section), gender, gestational age (GA), birth weight (BW), Apgar score at 1 and 5 min of life). Comorbidities were classified as: transient tachypnea (TT, defined as tachypnea > 60 breaths/min shortly after delivery that usually resolves within 72 h and doesn't require any assisted ventilation), respiratory distress syndrome (RDS, requiring either nasal continuous positive pressure, nCPAP, or invasive mechanical ventilation, congenital anomalies, necrotizing enterocolitis (NEC, requiring surgical treatment), sepsis (defined as increase in serum inflammatory markers and positive blood culture associated with clinical signs of infection). Morbidity at NICU admission was recorded and considered in the analysis. CUS scans were performed by radiology resident according to the clinical protocol of the unit and under the supervision. The radiologic resident were previously trained in performing cUS for at least 6 months.

Babies were scanned at bedside in supine position. Scans were performed with an IM3 machine using a convex transducer with frequency of 7.5 MHz.CUS report included the description of: ventricular system, midline structures, parenchymal echogenicity, posterior fossa structures. Ventricular dilatation was estimated according to the measurement of anterior horn width and of the thalamo-occipital distance. The parenchymal echogenicity in the periventricular areas was defined as periventricular hyperechogenicity (PHE) when isoechogenic/hyperechogenic to the choroid plexus.

Cranial ultrasonography findings were classified as: 1. normal; 2. mild abnormalities: asymmetric lateral ventricles, mild dilatation of the occipital horns (thalamo-occipital distance <95 percentiles), cysts of the chorioid plexus, frontal, temporal and caudothalamicpseudocysts, lenticulostriatevasculopathy; 3. PHE; 4.severe abnormalities: GHMIVH, defined according to the Papile's criteria, cPVL, venous/arterial stroke and malformations.

Ethics, consent and permissions

All procedures performed in the study were in accordance with the ethical standards of the institutional research committee in RumahSakit Dr. Soetomo. Informed consent was obtained from the parents of participants included in the study.

Statistical analysis

Agreement between cUS scans over time was examined using Cohen's kappa statistics. We fitted univariate and multiple logistic regression models to calculate the odds ratio (OR) and 95 % confidence interval (CI). To evaluate the usefulness of cUS when added to other selected clinical variables, after the logistic models we estimated the receiver operating characteristic (ROC) curves and their area under the curve (AUC). Statistical analyses were performed with SPSS statistics 17.0

Results

there were 112 preterm infants were eligible. The characteristics of the study population are shown in Table 1.

Table 1 Characteristics of the study population

n	= 112
Gender	57 (50.9%)
Male	55 (49.1%)
Female	
Age (mean, SD) days	3.1 (SD 3.03)
Gestational Age (weeks)	
≤ 32	65(58%)
>32	47(42%)
Birth Weight (gram)	
≤ 1500	44 (39.3%)
>1500	68 (60.7%)
Apgar score in 5'	
<5	28 (25%)
≥5	84 (75%)
Resuscitation	
Yes	24 (21.4%)
No	88 (78.6%)
Duration of oxygenation (days)	
≤3	92 (82.1%)
>3	20 (17.9%)
Cranial ultrasound finding	
abnormal	23 (20.5%)
normal	89 (79.5%)

57 (50.9%) were males, mean age was 3.1 (SD 3.03) days. Mean gestasional age of abnormal cUS were 30.1 (SD 2.75) weeks whereas in normal cUS were 32.1 (SD 1.93) weeks. Twenty three infant (20.5%) were abnormal cUS, consist of intraventricular hemorrhage (IVH) 16 (14.3%), three infants (2.7%) were periventricular leucomalacia, and four infants (3.6%) were ventricular dilatation were shown by Table 2.

Table 2. Cranial ultrasound finding

Cranial ultrasound finding	N (%)
Normal	89 (79.5%)
Abnormal	23 (20.5%)
IVH	16(69.5%)
PVL	3 (13.1%)
Ventricular dilatation	4 (17.4%)

Table 3. Perinatal risk factor associated with abnormal cranial ultrasound

Risk factors	OR	95%CI
Birth weight ≤ 1500g	8.72	2.93-25.97
Gestational age ≤ 32 weeks	3.21	1.09-9.42
Asphyxia	10.96	3.87-31.02
>3 days of oxygenation	6.07	2.11-17.44
Resuscitation	5.35	1.95-14.67

P<0.05 , univariate analysis

The univariate regression (Table 3) was used to investigate the association between perinatal risk factors and abnormal cUS at 5 weeks. Birth weight ≤1500g (OR 8.72; 95%CI 2.93-25.97), gestational age ≤ 32 weeks (OR 3.21; 95%CI 1.09-9.42), Asphyxia (OR 10.96; 95%CI 3.87-31.02), more than 3 days of oxygenation (OR 6.07; 95%CI 2.11-17.44), need resuscitation (OR 5.35; 95%CI 1.95-14.67).

At the multivariate analysis (Table 4) the accuracy inpredicting unfavorable cUS, estimated by combinedbirth weight and asphyxia ROC curve, was AUC 84.5% (95%CI 75.1 to 93.8%)(Fig. 1).

Table 4. Perinatal risk factor associated with abnormal cranial ultrasound

Risk factors	OR	95%CI	p
Birth weight ≤ 1500g	12.09	2.87-50.93	0.01*
Gestational age ≤ 32 weeks	0.29	0.03-2.52	0.26
Asphyxia	5.90	1.69-20.55	0.005*
>3 days of oxygenation	3.65	0.98-13.60	0.053
Resuscitation	0.62	0.12-3.26	0.58

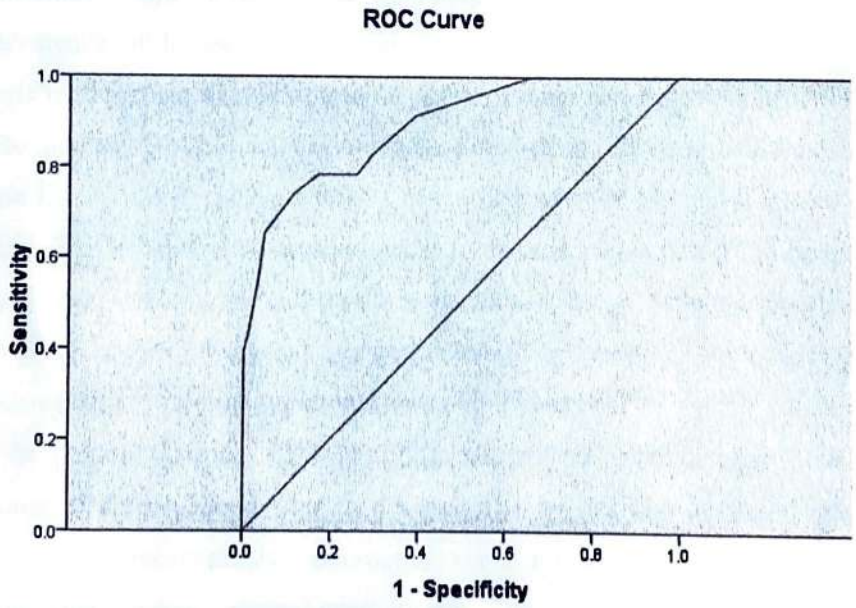

Figure 1.ROC curves for variables. The thin continuous line represents the reference model; the dashed line represents the model withbirth weight and asphyxia

Discussion

Our data support the hypothesis that birth weight and the occurrence of neonatal comorbidities arethe most important risk factors for detecting brainlesions in the preterm population.The combination of birth weight less than 1500g and the occurrence of asphyxia represents the strongest indicationto perform a cUS scan.[1,3,6]

GMH-IVH mostly occurs during the first 72 h of ageand a very early 1st scan (within the defined interval time1st–7th day of life) may have missed it. The problem of undetectedGMH-IVH may be further compounded by recentevidence showing that cUS sensitivity in detecting grade1–2 GMH- IVH is surprisingly low, compared to MRI. GMH-IVH is a rare although unusual event in lateprematurity. In addition, also minor form occurring inVLBW babies are associated with impaired neurologicaloutcome as very recent and robust studies demonstrated. Thus, we included also grade I-II GMH- IVH in theunfavorable cUS. These negative effects are consistent withgerminal matrix destruction and loss of astrocytic precursorcells or with periventricular white matter inflammationdue to astrocytes activation triggered by the longpersistence of haemosiderin along the ependymal.[7,8]Difficulties in performing an early diagnosis tend tooccur also with arterial stroke, a brain lesion developingwithin the first week, rarely beyond day 3 of life, but becomingmore obvious at cUS over the following few days.It is a common finding invery preterm infants in the first week of life and it ismore pronounced with declining GA. It can be eitherpathological (pre-cystic phase of cPVL) or transient(related to increased water content) and not resulting ina definite lesion. Scan is supported by the evidence thatcPVL still occurs among early preterm infants (28–35weeks) despite the dramatic decrease in its incidence atthe youngest gestational ages (24–27 weeks).[1,8,9]

In preterm infants, RDS requiring mechanical ventilationhas been associated with fluctuation of cerebralblood flow in the first days of life and increased risk of brain injury, mainly IVH. Cerebrovascular autoregulationand reactivity play a role in brain injury in prematurebabies and mechanical ventilation may interferewith these physiological mechanisms by affecting systemichaemodynamics and modulating arterial carbon dioxide tension. The causative association between comorbidities andsevere cUS abnormalities deserves further analysis asthey seem to act as a second "hit" triggering or aggravatingpathological processes in the developing brain ofpremature babies and affecting both the white matterand the involuting structures, such as the germinal matrix.[7,8,10]

The univariate analysis did not support the possiblerole of twin birth as risk factor for brain lesions.Twin pregnancies carry a higher risk of neonatal death,cerebral palsy and intrauterine death. However,increased neonatal morbidity appears to be related toprematurity rather than to twin birth itself althoughmonochorionicity seems to play a detrimental role, inparticular when complicated by twin-to-twin transfusionsyndrome.[2,8]

Conclusions

At the low birth weight, the intrinsic vulnerability of the developing brainincreases the risk of developing brain lesions in particularwhen extrinsic factors, such as comorbidities, coexist. Theindication to perform a cranial ultrasound scan in a preterm infant should be modulated according to birth weight and the comorbidities, in particularthe occurrence of respiratory distress syndrome or asphyxia

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