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기관지 폐 이형성증과 폐 고혈압을 동반한 초미숙아의 신경학적 발달과 성장에 관한 고찰

Developmental Outcome of Preterm Infants with Bronchopulmonary Dysplasia associated Pulmonary Hypertension

2018년 2월

서울대학교 대학원
의학과 소아과학

최 의 경

A thesis of the Master's degree

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February 2018

The Department of Pediatrics,
Seoul National University
College of Medicine
Eui Kyung Choi

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지도교수 김 이 경

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위 원 장 김 한 석 (인)

부 위 원 장 박 찬 욱 (인)

위 원 김 이 경 (인)

Developmental Outcome of Preterm Infants with Bronchopulmonary Dysplasia associated Pulmonary Hypertension

by

Eui Kyung Choi

A thesis submitted to the Department of Pediatrics in partial fulfillment of the requirements for the Degree of Master of Science in Medicine at Seoul National University College of Medicine

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Approved by Thesis Committee:

Professor _____Chairman

Professor _____Vice chairman

Professor _____

Abstract

Developmental Outcome of Preterm Infants with Bronchopulmonary Dysplasia associated Pulmonary Hypertension

Eui Kyung Choi
Dept. Medicine
The Graduate School
Seoul National University

Background: Despite bronchopulmonary dysplasia (BPD) associated pulmonary hypertension (PH) is becoming a growing concern in preterm infants, there is only a few studies have focused on neurodevelopmental outcome.

Objectives: To identify the significance of PH on growth and neurodevelopmental outcome at 18 months of corrected age in preterm infants with BPD.

Methods: This study was conducted as a retrospective study, including 394 infants (< 28 weeks of gestation) who were admitted to the neonatal intensive care unit at Seoul National University Children's Hospital between 2005 and 2014. One hundred and forty-four infants (36.6%) had complete data regarding the growth assessment and the Bayley scales of infant and toddler development, third edition (Bayley-III) at 18 months of corrected age (CA). Of these, 81 infants (56.2%) were defined BPD. Baseline characteristics and outcomes were compared between the infants who developed BPD associated PH (n = 20) and infants who did not (n = 61). To control for BPD severity, the outcomes were compared between

the infants with and without PH among the infants diagnosed with severe BPD (n = 40) only.

Results: Infants with PH in BPD showed significantly lower in cognitive (85 vs. 95, p=0.004), language (81 vs. 89, p=0.040) and motor score (88 vs. 94, p=0.010) in Bayley-III at 18-month CA than infants without PH. The cognitive delay was more prevalent in the BPD with PH group and the adjusted odds ratio for cognitive delay in PH group was 4.2 (95% confidence interval, 1.1 - 15.5), compared to non- PH group. They had lower z-score of body weight (−1.4 ± 1.3 vs. −0.6 ± 1.1, p = 0.011) and head circumference (−1.2 ± 1.8 vs. −0.5 ± 1.0, p = 0.035) at 18 months of CA than only BPD infants. When controlling for BPD severity, the mean z-score of weight (−1.7 ± 1.2 vs. −0.7 ± 1.3, p = 0.016) and cognitive scores (85 vs. 95, p=0.048) were still significantly lesser in infants with PH.

Conclusion: We found an association between PH and a non-optimal growth and neurodevelopmental outcome at 18 months of CA. These results suggest that PH infants have additional risks for developmental delay caused by postnatal and post discharge growth restriction . Therefore, particular attentions for PH infants is needed to promote catch-up growth and to prevent negative consequences of neurodevelopment

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keywords : Preterm infant, Bronchopulmonary dysplasia, Pulmonary hypertension, Neurodevelopment, Growth, Bayley scale, Catch-up growth.

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1. Contents

List of tables and figures

Introduction

Improvement of critical care management for premature infants leads to increase in survivors with bronchopulmonary dysplasia (BPD) which is leading cause of late respiratory morbidity of preterm infants [1]. Early injury to the developing lung impairs angiogenesis and alveolarization, which contributes to the development of BPD and BPD associated pulmonary hypertension (PH). PH is a significant cardiovascular complication in BPD infants associated with increased morbidity and mortality, including longer hospitalization and oxygen therapy [2-4]. Recent efforts to identify PH in BPD infants by echocardiography may provide an opportunity for implementation of preventative or treatment strategies to improve long-term outcomes [5]. Despite the increased concern for PH, long-term outcomes of BPD associated PH infants remain uncertain. Recently, several studies have reported cardiovascular outcome of PH in preterm infants, there is no large longitudinal study reported on long-term pulmonary or neurodevelopmental outcomes [6, 7].

It has been already well established that severity of BPD is related to adverse neurodevelopmental outcomes, because of the complex mechanisms of hypoxemia, postnatal steroid exposure and altered environmental stimulation [8, 9]. In the setting of diverse interactions between prenatal and postnatal factors, influences of PH in BPD on growth and neurodevelopmental outcome is not well identified [4, 10-12]. In a current retrospective study by Nakanishi et al, it was found that BPD with PH is one of the independent perinatal risk factors for neurodevelopmental impairment (NDI) at 3 years of age [13].

The aim of the present study is to identify somatic growth and developmental outcomes in BPD associated PH survivors at 18 months of age, highlighting differences from BPD.

Methods

We retrospectively reviewed the medical records of 394 preterm infants who were born at <28 weeks' gestational age and admitted to the neonatal intensive care unit (NICU) in Seoul National University Children's Hospital between January 2005 and December 2014. Infants with major congenital anomaly, chromosomal abnormalities and incomplete medical records were excluded. Additional exclusion criteria included preterm infants with missing neurodevelopmental assessment and growth data at 18 to 24 months corrected gestational age and severe neurological injury. This study was approved by the Institutional Research Ethics Committee at Seoul National University Hospital (Seoul, South Korea).

The clinical data of the infants were collected included birth weight, gestational age, small for gestational age (SGA; birth weight $<10^{th}$ percentile for age), prenatal steroids (administration of any dose of corticosteroids during the concurrent pregnancy), histological chorioamnionitis (HCAM; histopathologic evidence of the presence of acute inflammatory changes on a membrane roll and the placental chorionicplate),and oligohydramnios (amniotic fluid index <5cm by ultrasound performed just before delivery). Comorbidities of preterm infants were assessed, including respiratory distress syndrome (RDS; the presence of respiratory distress, increased oxygen requirement and a radiological finding consistent with RDS), patent ductus arteriosus (PDA),intraventricular hemorrhage (IVH; grading according to Palile's classification [14]), culture-proven sepsis (at least a single blood culture and clinical signs of infection), retinopathy of prematurity (ROP) and necrotizing enterocolitis (NEC; according to modified Bell's criteria [15]). BPD was defined by using the National Institute of Health consensus definition for BPD and graded as mild, moderate, or severe according to the fraction of inspired oxygen (FiO2) or positive pressure ventilation

(PPV)[16].Mild BPD was defined as breathing room air, moderate BPD was defined as a FiO2 <0.30, and severe BPD was defined as a FiO2≥ 0.30 or PPV at 36weeks' post menstrual age (PMA). Factors for estimating short-term respiratory prognosis included postnatal steroid use, duration of mechanical ventilation, home oxygen therapy and total amount of oxygen supplementation until 36 weeks' post menstrual age were calculated as supplemented extra oxygen concentration(%)(fraction of inspired oxygen- 21) x duration (h) [17]. Episodes of hypoxemia (defined as a single value or consecutive values of SpO_2<80%)and bradycardia(pulse rate<80/min)were reviewed in severe BPD infants [18].

Pulmonary hypertension

Serial echocardiographic data for all preterm infants with BPD were reviewed, including evaluation with 2-dimensional, M-mode, and color-coded Doppler by a pediatric cardiologist at Seoul National University Children's Hospital. Infants were diagnosed with PH if an echocardiogram performed at >2 months of age demonstrated elevated pulmonary artery pressure based on the presence of at least one of the following criteria: 1) velocity of tricuspid valve regurgitation (TR) ≥ 3 m/s in the absence of pulmonary stenosis or 2) flat or left-deviated interventricular septal configuration and right ventricular hypertrophy with chamber dilation [19].

Growth and Neurodevelopmental assessment

Preterm infants who discharged to home were evaluated at 18 to 24 months' corrected gestational age by one neonatologist in the neonatology outpatient clinic. Assessments included composite scores on the *Bayley Scales of Infant Development*, third edition (Bayley-III) [20] and growth parameters (body weight, head circumference and length) were recorded. Cognitive, language and motor delay was defined as a composite score of

less than 85 (1 SD below the mean of 100) on the Bayley-III. Growth data were presented as z-scores because infants were assessed at different gestational ages at birth and approximations of 18 months corrected age (CA). Fenton preterm growth charts provide reference values from 22 to 50 gestational weeks and the World Health Organization (WHO) Anthro program from term age onwards. According to the WHO growth definition, underweight was defined as z score < -2.0.

Statistical analysis

All data analysis was performed using SPSS 20.0 for Windows (SPSS Inc, Chicago, IL). Continuous variables were analyzed using either the t-test or the Mann-Whitney U test for normal or skewed distributions, respectively. Proportions were tested by chi-square test and Fisher's exact test. P values of < 0.05 were considered significant. The significant variables identified by univariate analysis were further assessed by a multivariable logistic regression analysis. Data are presented as the mean ± SD, median and range, or rate.

Results

Of the total 394 preterm infants born before 28 weeks of gestation, 72 died before discharge and an additional 6 were excluded due to major congenital malformation and chromosomal anomaly. The most common reasons for exclusion were incomplete neurodevelopmental or growth assessment data at 18 months of CA. Therefore, 144 infants (36.6%) were eligible for this study. Among them, 21 infants with a grade III or IV IVH, PVL, cerebral infarction, or hypoxic ischemic encephalomalacia diagnosed by cranial ultrasound or brain MRI were excluded because of controlling for neurologic complications. The remaining 123 preterm infants, 81 (66%) were classified as having moderate (41/81) or severe BPD (40/81). Among these 81 infants with moderate to severe BPD, 21 (26%) met criteria for PH. PH was complicated in 43% (17/40) of infants with severe BPD, 7% (3/41) in moderate BPD and not diagnosed in infants with mild BPD. A flow chart showing the study design is presented in figure 1.

Clinical characteristics and short-term morbidities of infants with and without PH are compared in Table 1. The analysis showed a statistically significant difference ($p < 0.05$) in four variables: multiple births, BPD severity, sepsis and length of hospital days. Severe BPD was more prevalent in the BPD with PH group than in the non-PH group (85% vs, 15%, $p < 0.001$). The median duration of hospitalization was longer in the PH group when compared to the non-PH group ($p = 0.044$). Table 2 shows the growth and developmental outcomes of infants with or without PH in BPD at 18 months CA. Mean z-score of weight (-1.4 ± 1.3 vs. -0.6 ± 1.1; $p = 0.011$) and head circumference (HC) (-1.2 ± 1.8 vs. 0.53 ± 1.0; $p = 0.035$) were significantly lesser in infants with PH. In addition, the infants in the PH group obtained a significantly lower scores on cognitive (85 vs. 95; $p = 0.004$), language (81 vs. 89; $p = 0.040$) and motor (88 vs. 94; $p = 0.010$) areas of the Bayley-III. There was a

significant difference among groups in the prevalence of cognitive delay (P < 0.001), which was more prevalent in the BPD with PH group than in the BPD group. Multivariate analysis was performed to investigate the risk factors for cognitive delay (table 2). The results after adjusting for variables that were significant in the univariate analysis; severe BPD, PH and NEC operation revealed that the significant risk factors for cognitive delay were PH (adjusted OR: 4.2; 95% CI, 1.1 - 15.5; p = 0.031) and severe BPD (adjusted OR: 5.6; 95% CI, 1.1 - 29.6; p = 0.040) (table 3).

Table 4 shows the comparison according to the presence or absence of PH in severe BPD infants only; it enabled to clarify of the effect of PH. When controlling for BPD severity, the comparison of clinical characteristics showed a statistically significant difference in one variables: multiple births (17.6% vs. 60.9%, respectively, p = 0.010). The duration of mechanical ventilation (p = 0.090), the rate of infants who received dexamethasone rescue therapy (p=1.000), the total amount of oxygen supplementation until 36 weeks' postmenstrual age (p=0.434) and the episodes of hypoxemic or bradycardia (p = 0.254 and p = 0.734, respectively) were not significantly different between the two groups. Table 5 shows the growth and developmental outcome of infants in severe BPD with and without PH. At hospital discharge, there was no difference between the two groups in z-scores of the body weight and HC. However, at 18 months CA, mean z-score of weight was significantly lesser in infants with PH (−1.7 ± 1.2 vs. −0.7 ± 1.3, p = 0.016). Compared with infants without PH, those with PH had lower Bayley III cognitive scores (85 vs. 95; p = 0.048) only, but PH was not a significant risk factor for cognitive delay (p = 0.091).

Figure 1. Flow chart of the study.

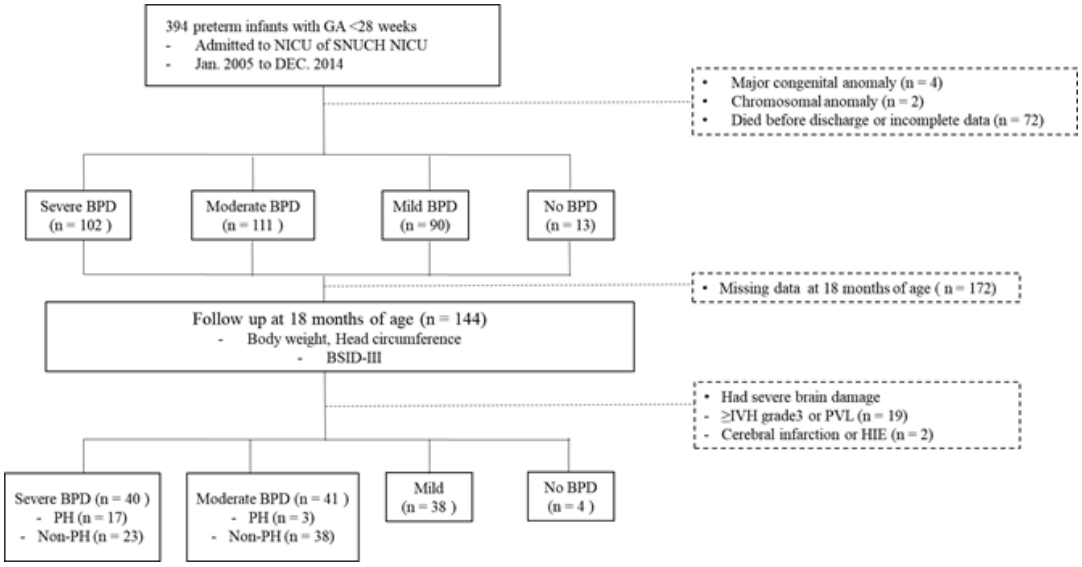

Table 1. Clinical characteristics of subjects with and without pulmonary hypertension.

	PH (n = 20)	Non-PH (n = 61)	P values
Gestational age, weeks	25.3 ± 1.4	25.8 ± 1.1	0.126
Birth weight, g	710.1 ± 183.6	758.6 ± 159.1	0.257
Birth weight <10thpercentile for age, n(%)	5 (25.0)	9 (14.8)	0.317
Multiple birth, n (%)	3 (15.0)	35 (57.4)	0.002
Cesarean section, n (%)	13 (65.0)	35 (57.4)	0.608
Perinatal steroids administration, n (%)	15 (75.0)	42 (68.9)	0.601
Chorioamnionitis ,n (%)	12 (60.0)	25 (41.0)	0.138
Oligohydramnios ,n (%)	4 (20.0)	3 (5.1)	0.059
RDS, n (%)	16 (80.0)	45 (73.8)	0.767
Treated PDA, n (%)	16 (80.0)	47 (77.0)	1.000
BPD, n (%)			
Moderate/Severe	3/17 (15.0/85.0)	38/23 (62.3/37.7)	<0.001
Culture proven sepsis, n (%)	11 (55.0)	15 (24.6)	0.011
ROP operation, n (%)	7 (35.0)	34 (55.7)	0.128
NEC operation, n (%)	6 (30.0)	6 (9.8)	0.063
BPD steroid, n (%)	5 (25.0)	6 (9.8)	0.128
Length of stay, days	111 (82-268)	103 (71-163)	0.044

Data are presented as mean ± SD, median and range, or rate. RDS: respiratory distress syndrome, PDA: patent ductus arteriosus, BPD: bronchopulmonary dysplasia, ROP: retinopathy of prematurity, NEC: necrotizing enterocolitis.

Table 2. Growth and developmental outcomes of infants with or without PH in BPD.

	PH (n = 20)	Non-PH (n = 61)	P values
Outcome at 18 months			
Body weight, kg	9.5 ± 1.5	10.2 ± 1.3	0.051
z score	−1.4 ± 1.3	−0.6 ± 1.1	0.011
Head circumference, cm	44.9 ± 1.9	46.4 ± 1.5	0.001
z score	−1.2 ± 1.8	−0.53 ± 1.0	0.035
Bayley III			
Cognitive score	85 (65-105)	95 (55-125)	0.004
score <85	9 (45.0)	6 (9.8)	<0.001
Language score	81 (47-100)	89 (53-118)	0.040
score <85	10 (50.0)	20 (32.8)	0.167
Motor score	88 (52-107)	94 (46-115)	0.010
score <85	8 (40.0)	12 (20.3)	0.081

Table 3. Influence of pulmonary hypertension on cognitive delay in regression models.

	Unadjusted OR (95% CI)	P values	Adjusted OR (95% CI)	P values
Severe BPD	9.4 (2.0 – 45.0)	0.001	5.6 (1.1 – 29.6)	0.040
Pulmonary hypertension	7.5 (2.2 – 25.4)	<0.001	4.2 (1.1 – 15.5)	0.031

Table 4. Clinical characteristics according to the presence or absence of PH in severe BPD

	Severe BPD		P values
	PH (n = 17)	Non-PH (n = 23)	
Gestational age, weeks	25.3 ± 1.4	25.5 ± 1.0	0.470
Birth weight, g	709.5 ± 195.5	744.0 ± 158.6	0.543
Birth weight <10thpercentileforage,n(%)	5 (29.4)	4 (17.4)	0.456
Multiple birth, n (%)	3 (17.6)	14 (60.9)	0.010
Cesarean section, n (%)	12 (70.6)	13 (56.5)	0.512
Perinatal steroids administration, n (%)	13 (76.5)	17 (77.3)	1.000
Chorioamnionitis ,n (%)	9 (52.9)	11 (47.8)	0.749
Oligohydramnios ,n (%)	4 (23.5)	2 (8.7)	0.373
RDS, n (%)	14 (82.4)	19 (82.6)	1.000
Treated PDA, n (%)	14 (82.4)	18 (78.3)	0.616
Culture proven sepsis, n (%)	9 (52.9)	8 (34.8)	0.251
ROP operation, n (%)	6 (35.3)	14 (60.9)	0.110
NEC operation, n (%)	5 (31.2)	3 (13.0)	0.235
Length of stay, days	115 (94-268)	113 (77-163)	0.448
Respiratory management			
Duration of CV or HFV, days	72(0-199)	40 (6-148)	0.090
BPD steroid, n (%)	5 (29.4)	6 (26.1)	1.000
Dexamethasone cumulative dose (mg/kg)	1.80 (1.10-3.23)	1.10 (0.42-3.04)	0.416
Discharge on oxygen, n (%)	12 (70.6)	15 (65.2)	0.720
Total extra O2 supplementation*	25,199(1,428-71,095)	20,325(11,417-46,362)	0.434
Episodes of hypoxia†	338 (172-1,205)	258 (57-696)	0.254
Episodes of bradycardia‡	40 (8-216)	56 (4-169)	0.734

Data are presented as mean ± SD, median and range, or rate. RDS: respiratory distress syndrome, PDA: patent ductus arteriosus, ROP: retinopathy of prematurity, NEC: necrotizing enterocolitis. CV: conventional ventilation, HFV: high-frequency ventilation. * Supplemented extra O_2concentration(%)(fractionofinspiredO_2- 21). †Single value or consecutive values of SpO2 <80% until 36 weeks' postmenstrual age. ‡ Single value or consecutive values of pulse rate <80/min until 36 weeks' postmenstrual age.

Table 5. Growth and developmental outcome of infants with or without PH in severe BPD.

	Severe BPD		P values
	Non-PH (n = 23)	PH (n = 17)	
Growth at hospital discharge			
Body weight, kg	2.9 ± 0.6	3.4 ± 1.0	0.098
z score	−2.1 ± 1.5	−2.2 ± 1.7	0.982
Head circumference, cm	33.3 ± 1.8	33.7 ± 2.8	0.663
z score	−1.8 ± 1.0	−2.3 ± 1.5	0.225
Growth at 18 months			
Body weight, kg	10.1 ± 1.3	9.2 ± 1.4	0.050
z score	−0.7 ± 1.3	−1.7 ± 1.2	0.016
Head circumference, cm	46.0 ± 1.4	44.7 ± 2.0	0.024
z score	−0.7 ± 1.1	−1.3 ± 1.9	0.243
Bayley III at 18 months			
Cognitive	95 (55-110)	85 (65-105)	0.048
Language	83 (53-115)	83 (47-100)	0.551
Motor	89 (46-110)	88 (52-97)	0.124

Discussion

This study found the BPD associated PH survivors showed significantly lower scores on cognitive, language and motor composite scores in the Bayley-III at 18 months of CA. In addition, the number of infants with cognitive delay was significantly higher in the PH group and BPD associated PH was the one of the risk factor for the cognitive delay. They had much lower body weight and head circumference than only BPD infants. And after adjustment of BPD severity, particularly cognitive scores and body weight are still lower in PH with severe BPD infants. Previous study by Nakanishi et al. [13] reported significantly delayed performance which is defined as a developmental quotient in all areas of < 70 using the developmental test of Neonatal Research Network in Japan was more prevalent at 3 years in the BPD with PH group. But there were no significant differences of scores in each domain; postural-motor, cognitive-adaptive, and language-social. They also identified the body weight at 3 years in the PH group was lower than the BPD without PH group. In present study, we demonstrated that PH was associated with neurodevelopmental delay, especially in cognitive area assessing by Bayley-III scales which is globally used in preterm infants.

BPD has been associated with poor neurodevelopmental outcome, the mechanism responsible for brain injury is not yet fully understood. It is probably multifactorial and the pathophysiology may include chronic, intermittent hypoxia associated with prolonged oxygen dependence leading to hypoxic-ischemic cerebral injury [21]. Our data confirms the poor neurodevelopmental outcome of the BPD with PH infants because severe BPD was more prevalent than BPD without PH infants. However, within the severe BPD only, despite PH infants had lower cognitive scores than non-PH infants, respiratory management such as total extra oxygen supplementation, intermittent hypoxemia and bradycardia events was not

different between two groups. These data suggest that although PH is a marker of more advanced BPD, there is not an absolute correlation between supplemental oxygen requirement and increased neurodevelopmental disability. Lodha et al.[22] reveled BPD with chronic dependency dose not predict adversely neurodevelopmental outcome than BPD only.

We suggest the potential explanations for neurodevelopmental disability in PH include prenatal and postnatal restricted growth. Placental insufficiency as manifested by small for gestational age (SGA) has been recognized as an important risk factor for BPD and PH [12]. Whether being SGA increases the risk of adverse neurodevelopmental outcome in premature infants remains controversial, some studies reported increased levels of cognitive and behavioral difficulties [23]. In present study, prevalence of SGA was not significantly different between two groups, but poorer weight gain after discharge in PH infants with severe BPD was identified than severe BPD only. There are several mechanisms of growth failure in infants with BPD: increased caloric expenditure in the work of breathing, restricted fluids, diuretic and postnatal steroid therapy, and comorbidities such as sepsis [24]. The association between postnatal growth failure and poorer neurodevelopmental outcomes in preterm infants has been well established in several large cohort studies [25, 26]. Therefore, our results suggest that catch-up growth may represent modifiable mechanisms to further improve the neurodevelopment of at-risk preterm infants.

Our study is limited by its retrospective design. The most important limitation of this study includes the small sample size. The follow-up rate was low, 63.4% of the study population did not have complete outcome data at the 18 months of age. In present study, the percentage of multiple births in the non-PH group seems high. Our institution characterized the large percentage of multiple births as the other studies mentioned previously, it might be also influenced by small sample size. But further

large study may be necessary about the impact of multiple births on the BPD and PH [10]. Although BPD associated PH infants showed significantly lower scores on motor composite scores in the Bayley-III, very small number of enrolled infants were diagnosed with CP (4/144) and any infant with PH were not diagnosed. This study demonstrated that post discharge growth restricted infants were more frequently seen in PH with severe BPD group, data on exact causes of feeding difficulties, composition of nutrition, details of caloric and protein intake, and timing of initiation of enteral feeds were not available.

In summary, BPD associated PH is associated with significantly lower scores on cognitive, language and motor areas in the Bayley-III at 18 months CA. And PH is the one of the risk factor for the cognitive delay. After controlling for BPD severity, particularly cognitive score is still lower in PH infants. Infants with PH in severe BPD are more likely to persist growth restriction after discharge than infants with severe BPD only. Therefore, it is necessary to monitor postdischarge growth in PH infants at risk of poor neurodevelopment. Additional prospective and large studies are needed to confirm our results and improve the long term outcomes of preterm infants with PH.

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국 문 초 록

기관지 폐 이형성증과 폐 고혈압을 동반한
초 미숙아의 신경학적 발달과 성장에 관한 고찰

기관지 폐 이형성증의 합병증인 폐 고혈압은 최근 미숙아의 생존율이 향상되면서 증가 추세에 있다. 그러나 폐 고혈압이 합병된 미숙아의 신경학적 예후에 대해서는 아직 알려진 바가 없다. 이에 이번 연구는 기관지 폐 이형성증에 이환 된 미숙아에서 폐 고혈압이 합병되었을 때 장기적인 성장과 뇌신경 발달에 폐 고혈압이 미치는 영향에 대해 알아보고자 하였다. 2005년부터 2014년까지 서울대학교 어린이병원 신생아 중환자실에 입원한 394명의 재태 주수 28주 미만의 미숙아의 후향적인 챠트 리뷰를 통해 연구가 시행되었다. 교정 연령 18개월에 측정한 성장과 Bayley 발달 검사 III 결과가 있는 144(144/394, 36.5%)명 중에서 81(56.2%)명이 기관지 폐 이형성증으로 진단되었다. 이 중 폐 고혈압이 합병된 기관지 폐 이형성증 환아 (20명)와 없는 환아 (61명)의 비교를 하였고 기관지 폐 이형성증의 중증도가 미칠 수 있는 영향을 배제하기 위하여 중증 기관지 폐 이형성증이 있는 환아(40명)에서 다시 폐 고혈압의 유무에 따라 비교 하였다.

결과: 폐 고혈압이 합병된 기관지 폐 이형성증 환아에서 교정 연령 18개월의 인지 (85 vs. 95, p=0.004), 언어 (81 vs. 89, p=0.040), 운동 (88 vs. 94, p=0.010) 영역의 Bayley 발달 검사 점수와 체중(−1.4 ± 1.3 vs. −0.6 ± 1.1, p = 0.011)과 머리 둘레의 평균 z-score(−1.2 ± 1.8 vs. −0.5 ± 1.0, p = 0.035)가 폐 고혈압이 합병되지 않은 환아 보다 유의하게 낮았다. 인지 발달 지연의 빈도는 폐 고혈압 군에서 높게 나타났으며 폐 고혈압이 없는 군에 대한 교정된 오즈 비는 4.2 (95% 신뢰 구간, 1.1 - 15.5)로 나타났다. 기관지 폐 이형성증의 중증 도를 보정 한 후에는 폐 고혈압군의 교정 18개월의 체중의 평균 z-score (−1.7 ± 1.2 vs. −0.7 ± 1.3, p = 0.016)와 인지 점수 (85 vs. 95, p=0.048)가 유의하게 낮음을 알 수 있었다.

결론적으로 초 미숙아의 기관지 폐 이형성증에 합병된 폐 고혈압은 교정 연령 18개월의 성장 부진과 나쁜 뇌 신경 발달과 의미 있는 관계가 있었다. 이러한 결과는 폐 고혈압이 있는 환아에게 부적당한 성장으로 인한 뇌 신경 발달 지연의 위험이 있음을 시사한다. 따라서 장기적인 뇌신경발달 저하의 위험이 있는 폐 고혈압 환아에서는 퇴원 후 따라 잡기 성장에 대한 특별한 관심을 요한다.

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주요어 : 미숙아, 기관지 폐 이형성증, 폐 고혈압, 뇌신경발달, 성장, 베일리 발달 검사, 따라잡기 성장.

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