ORIGINAL ARTICLE
Pediatrics

JKMS

http://dx.doi.org/10.3346/jkms.2015.30.S1.S45 • J Korean Med Sci 2015; 30: S45-51

Initial Resuscitation at Delivery and Short Term Neonatal Outcomes in Very-Low-Birth-Weight Infants

Su Jin Cho,[1] Jeonghee Shin,[2] and Ran Namgung[3]

[1]Department of Pediatrics, School of Medicine, Ewha Womans University, Seoul; [2]Department of Pediatrics, College of Medicine, Korea University, Seoul; [3]Department of Pediatrics, College of Medicine, Yonsei University, Seoul, Korea

Received: 14 April 2015
Accepted: 30 July 2015

Address for Correspondence:
Ran Namgung, MD
Department of Pediatrics, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82.2-2228-2058, Fax: +82.2-393-9118
E-mail: ranng@yuhs.ac

Funding: This work was supported by the Research Program funded by the Korean Centers for Disease Control and Prevention (2013-E63008-01).

Survival of very-low-birth-weight infants (VLBWI) depends on professional perinatal management that begins at delivery. Korean Neonatal Network data on neonatal resuscitation management and initial care of VLBWI of less than 33 weeks gestation born from January 2013 to June 2014 were reviewed to investigate the current practice of neonatal resuscitation in Korea. Antenatal data, perinatal data, and short-term morbidities were analyzed. Out of 2,132 neonates, 91.7% needed resuscitation at birth, chest compression was performed on only 104 infants (5.4%) and epinephrine was administered to 80 infants (4.1%). Infants who received cardiac compression and/or epinephrine administration at birth (DR-CPR) were significantly more acidotic ($P < 0.001$) and hypothermic ($P < 0.001$) than those who only needed positive pressure ventilation (PPV). On logistic regression, DR-CPR resulted in greater early mortality of less than 7 days (OR, 5.64; 95% CI 3.25-9.77) increased intraventricular hemorrhage ≥ grade 3 (OR, 2.71; 95% CI 1.57-4.68), periventricular leukomalacia (OR, 2.94; 95% CI 1.72-5.01), and necrotizing enterocolitis (OR, 2.12; 95% CI 1.15-3.91) compared with those infants who needed only PPV. Meticulous and aggressive management of infants who needed DR-CPR at birth and quality improvement of the delivery room management will result in reduced morbidities and early death for the vulnerable VLBWI.

Keywords: Infant, Very-Low-Birth-Weight; Cardiopulmonary Resuscitation; Infant, Premature; Apgar Score

INTRODUCTION

Despite the improvement in survival and outcomes of very-low-birth-weight infants (VLBWI) (birth weight less than 1,500 g), survivors are at high risk of neonatal mortality, short-term and long-term morbidities that result in life-long health problems (1). The survival of VLBWI is dependent on professional perinatal management (2) that begins at delivery. For successful delivery room management, various aspects of the postnatal adaption process need to be considered such as the support of the thermal adaptation, airway management, breathing, circulation and metabolism for this vulnerable population. Approximately 10% of all newborns require assistance to establish normal breathing at birth. In less than 1% of newborns additional resuscitation measures are performed when they do not respond to stimulation and respiratory support because of an underlying condition or inadequate respiratory support (3).

When VLBWI lack establishment of a functional residual capacity (4) or undergo placental gas exchange impairment resulting in fetal acidemia (5), cardiovascular collapse requiring cardiopulmonary resuscitation occurs. Delivery room cardiopulmonary resuscitation (DR-CPR) defined as chest compression and/or epinephrine administration was associated with early mortality increasing by a factor of 3.69 and neurodevelopmental impairment increasing by a factor of 1.23 in a study by the National Institute of Child Health and & Development (NICHD) Neonatal Research Network (NRN) (6). A recent prospective study by the California Perinatal Quality Care Collaborative (CPQCC) investigated the association between DR-CPR and outcomes at 22 weeks to 27 weeks and 6 days, and reported that premature infants receiving DR-CPR had worse outcomes, with variations in mortality and morbidity by gestational age groups (7). Other studies have reported no significant differences in the mortality and morbidity in infants who received DR-CPR (8,9). A meta-analysis by Shah of studies on DR-CPR of extremely low birth weight infants (ELBWI) and VLBWI reported a significantly increased odds ratio of 2.83 in mortality and 2.27 in severe neurological injury but similar rates of bronchopulmonary dysplasia (BPD) and severe retinopathy of prematurity (ROP) (10).

Faced with a decline in birth rate, an increase in elderly primigravidas and a rapid increase of high-risk infants such as preterm infants, neonatologists in Korea came together to address this issue. To improve the survival rate and to reduce the incidence of major morbidities of high risk infants, the Korean Neonatal Network (KNN) was established by the Korean Society of

pISSN 1011-8934
eISSN 1598-6357

Neonatology with support from Korea Centers for Disease Control & Prevention. It began its official operation with a launch declaration on April 15th, 2013. KNN would be an infrastructure for active and productive multi-center research for quality improvement of neonatal intensive care units (NICU) and the development of Korean-style guidelines or strategy for NICU management (11).

The Neonatal Resuscitation Program (NRP) by the American Academy of Pediatrics (AAP) and the American Heart Association (AHA) has been followed in Korea since 2002. Initial resuscitation practices at delivery and short-term outcomes vary across NICUs and have not been reported as a multicenter study in Korea. The objective of this study was to assess the current practice of neonatal resuscitation performed for a cohort of VLBWI in Korea based on KNN data from 2013 and early 2014 and to compare it with data from other countries. The impact of DR-CPR on neonatal status upon admission to the NICU, early mortality and short-term morbidities in VLBWI born at less than 33 weeks gestational age were investigated, to provide a basis for quality improvement in delivery room management of the VLBWI which will lead to improved outcome for this most vulnerable population.

MATERIALS AND METHODS

Data collection from the Korean Neonatal Network Database

VLBWI born in or transferred within 28 days of birth to the 55 participating NICUs between January 2013 and June 2014 were included in the study. During that period, 2,386 VLBWI were registered in the KNN registry. Out of those infants, 2,132 VLBWI of less than 33 weeks gestation were selected as the study population. Clinical parameters were entered in accordance with the KNN manual of operation (http://www.knn.or.kr/index.jsp). Gestational age was expressed as completed age as determined by obstetric examination with ultrasonography early during the pregnancy or, if an early ultrasound was unavailable, via obstetric history based on the mother's last menstrual period.

Data analysis

A subgroup analysis was performed for each gestational age group: group I, 21-23 weeks; group II, 24-28 weeks; and group III, 29-32 weeks. The resuscitation steps were analyzed by birth weights: up to 500 g, 501-999 g, and 1,000 g and over. Antenatal data such as maternal condition, delivery method, resuscitation, and short-term outcomes were analyzed. Positive pressure ventilation (PPV) was defined as positive pressure provided via self-inflating bag, flow-inflating bag, or T-piece for any time duration. The method and duration of PPV was not noted in the network database. DR-CPR was defined as chest compressions and/or administration of epinephrine in the delivery room as a binary variable. The duration of chest compressions and the route and volume of epinephrine administered, was not taken into account. Hypothermia was defined as body temperature of less than 36°C upon admission to the NICU. Short-term outcomes were defined as per standardized data collection for KNN. The initial status such as body temperature, pH, and base excess upon admission to the NICU and short-term outcomes such as mortality within seven days of life, intraventricular hemorrhage (IVH) ≥ grade 3, periventricular leukomalacia (PVL), sepsis, and necrotizing enterocolitis (NEC) was compared between VLBWI who received PPV and those who received DR-CPR with a logistic regression model with adjustment for gestational age, maternal hypertension, antenatal steroid, and chorioamnionitis.

Statistical analyses

Maternal and neonatal characteristics were compared between the gestational age groups. Categorical variables were analyzed using the chi-square test. Continuous variables were compared using ANOVA. Scheffe post hoc tests were performed if overall comparison was significant. Logistic regression was used to estimate the odds ratios (OR) with 95% confidence intervals (CI) with adjustment for gestational age. A *P* value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 21 (IBM Corp., Chicago, IL, USA).

Ethics statement

The KNN registry was approved by the institutional review board at each participating hospital and informed consent to use the clinical data and outcome of the VLBWI was obtained from the parents at enrollment by the NICUs participating in KNN.

RESULTS

A total of 2,386 VLBWI were enrolled in the KNN database during the study period. Of these infants, 2,132 VLBWI of less than 33 weeks gestational age were included in the analysis. The infants were divided into three gestational age groups depending on the level of lung maturity: 21-23 weeks, 24-28 weeks, and 29-32 weeks. The number of VLBWI in each group was 116, 1,106, and 910. The mean birth weight of each group was as follows; 586 ± 129 g, 933 ± 232 g, and 1,236 ± 208 g. The percentage of male infants was not different between the groups.

Group I and group III each had more multiple births compared with group II. Cesarean section was more frequently performed in group III than in group I and group II, and more in group II than in group I. Antenatal steroids were given to the mother more frequently in groups II and III than in group I. Chorioamnionitis was more common in groups I and II than in group III. Maternal pregnancy induced hypertension was statistically more frequent in group III than in group II and group I.

Surfactant was given in the majority of the VLBWI. The rates

http://dx.doi.org/10.3346/jkms.2015.30.S1.S45

of surfactant administration per gestational age group were 99.1%, 97.4%, and 72.0% respectively, and the rates of prophylactic surfactant administration were 91.3%, 79.8%, and 54.5%, respectively (Table 1). One-minute and five-minute Apgar scores (AS) and resuscitation performance were compared across gestational age groups. The overall one-minute and five-minute AS were 4 and 7, respectively. The one-minute and five-minute AS increased with the increase in gestational age groups to a statistically significant degree: 2, 4, 5 and 5, 7, 7.

Each step of resuscitation performances including supplemental oxygen, PPV, intubation, chest compression, and epinephrine administration were analyzed. 91.7% of the VLBWI needed supplemental oxygen at birth. The percentage was not dependent on maturity per se. PPV was performed in 88.3% of the VLBWI and 77.7% were intubated at delivery. Those of less than 29 weeks gestation received more PPV than those above 29 weeks. More intubations were performed in those less than 29 weeks gestation. Chest compression and epinephrine administration was rarely performed in any of the gestational groups; chest compression in 14.7%, 11.2%, and 3% respectively and epinephrine administration in 4.8%, 3%, and 2.1%, respectively (Table 2). The rate of DR-CPR was 5.9% for the study population. A similar trend was demonstrated when the VLBWI were sorted into three groups depending on their birth weight: up to 500 g, 501-999 g, and 1,000 g and over (Table 3). Infant groups in earlier gestations and with lower birth weights needed more extensive resuscitative effort.

The initial status of the VLBWI after resuscitation was assessed by the body temperature, initial pH and initial base excess obtained within one hour of admission to the NICU. The prevalence of hypothermia was dependent on the gestational age. Less mature VLBWI had more frequent occurrences of hypothermia. The initial pH and initial base excess were lower in VLBWI of less than 23 weeks gestation (Table 4). This data was re-analyzed by gestational age group depending on the need for DR-CPR. Those needing DR-CPR had worse status, with more acidosis (Table 5).

Short-term mortality and morbidities were compared between those who received only PPV and those who needed DR-CPR. In a logistic regression analysis with adjustment for gestational age, maternal hypertension, antenatal steroids, and cho-

Table 1. Demographic characteristics of the very-low-birth-weight infants according to gestational age groups

Demographic	Group I 21-23 weeks (n = 116)	Group II 24-28 weeks (n = 1,106)	Group III 29-32 weeks (n = 910)
Gestational age (week)	23.2 ± 0.59	26.8 ± 1.4*	30.5 ± 1.06*,†
Birth weight (g)	586 ± 129	933 ± 232*	1,236 ± 208*,†
Male	68 (58.6%)	569 (51.4%)	439 (48.2%)
Multiple births	50 (43.1%)	345 (31.2%)*	358 (39.3%)†
C/S	45 (38.8%)	785 (71.0%)*	742 (81.5%)*,†
Antenatal steroid	74 (65.5%)	872 (80.8%)*	695 (78.2%)*
Chorioamnionitis	59 (57.3%)	400 (42.9%)	190 (24.9%)*,†
PIH	2 (1.7%)	116 (10.5%)*	219 (24.1%)*,†
Surfactant	115 (99.1%)	1,077 (97.4%)	655 (72.0%)*,†
Prophylactic	105 (91.3%)	859 (79.8%)*	357 (54.5%)*,†

Data as absolute numbers; percentages in parentheses. *Scheffe-adjusted $P < 0.05$ for multiple comparisons (reference: group I); †Scheffe-adjusted $P < 0.05$ for multiple comparisons (reference: group II). C/S, Cesarean Section; PIH, pregnancy induced hypertension.

Table 2. Resuscitation of the very-low-birth-weight infants according to gestational age groups

Resuscitation/Intervention	Group I 21-23 weeks (n = 116)	Group II 24-28 weeks (n = 1,106)	Group III 29-32 weeks (n = 910)	*P* value	Total (n = 2,132)
1 min A/S (IQR)	2 (1, 4)	4 (2, 5)*	5 (4, 7)*,†	< 0.001	4 (3, 6)
5 min A/S (IQR)	5 (3, 6)	7 (5, 7)*	7 (6, 8)*,†	< 0.001	7 (6, 8)
Supplemental oxygen	105 (90.5%)	965 (91.1%)	709 (92.8%)	0.388	1,779 (91.7%)
Positive pressure ventilation	113 (97.4%)	1,003 (94.7%)	597 (78.1%)*,†	< 0.001	1,713 (88.3%)
Intubation	114 (98.3%)	961 (90.7%)	432 (56.5%)*,†	< 0.001	1,507 (77.7%)
Chest compression	17 (14.7%)	64 (6%)*	23 (3%)*	< 0.001	104 (5.4%)
Epinephrine administration	13 (11.2%)	51 (4.8%)*	16 (2.1%)*	< 0.001	80 (4.1%)

Data as absolute numbers; percentages in parentheses. 1 min A/S and 5 min A/S: median value with interquartile range. *Scheffe -adjusted $P < 0.05$ for multiple comparisons (reference: group I); †Scheffe -adjusted $P < 0.05$ for multiple comparisons (reference: group II). A/S, Apgar score.

Table 3. Resuscitation of the very-low-birth-weight infants according to birth weight

Intervention	< 500 g (n = 65)	501-999 g (n = 854)	> 1,000 g (n = 1,213)	*P* value
Supplemental oxygen	54 (83.1%)	751 (91.3%)	974 (92.7%)	0.007
Positive pressure ventilation	65 (100%)	783 (95.1%)	865 (82.3%)*,†	< 0.001
Intubation	62 (95.4%)	754 (91.6%)	691 (65.7%)*,†	< 0.001
Chest compression	8 (12.3%)	65 (7.9%)	31 (2.9%)*,†	< 0.001
Epinephrine administration	7 (10.8%)	50 (5.9%)	23 (2.2%)*,†	< 0.001

Data as absolute numbers; percentages in parentheses. *Scheffe -adjusted $P < 0.05$ for multiple comparisons (reference: group I); †Scheffe -adjusted $P < 0.05$ for multiple comparisons (reference: group II).

Table 4. Initial status of the very-low-birth-weight infants upon admission to the NICU according to gestational age groups

Parameters	Group I 21-23 weeks (n = 116)	Group II 24-28 weeks (n = 1,106)	Group III 29-32 weeks (n = 910)	*P* value	Total (n = 2,132)
BT (°C)	35.2 ± 1.04	36.0 ± 0.66*	36.1 ± 0.57*	< 0.001	36.0 ± 0.68
Hypothermia	101 (95.3%)	822 (79.7%)*	621 (71.90%)*,†	< 0.001	1,544 (77.1%)
Initial pH	7.22 ± 0.14	7.27 ± 0.12*	7.28 ± 0.11*	< 0.001	7.26 ± 0.12
Initial pH < 7.2	39 (41.1%)	183 (21%)*	135 (18.6%)*	< 0.001	357 (21.1%)
Initial BE (mEq/L)	-8.4 ± 4.8	-5.5 ± 3.9*	-4.9 ± 3.6*	< 0.001	-5.4 ± 4.0
Initial BE < -6 mEq/L	61 (64.2%)	305 (35.1%)*	195 (27%)*,†	< 0.001	561 (33.3%)

Data as absolute numbers; percentages in parentheses. *Scheffe-adjusted $P < 0.05$ for multiple comparisons (reference: group I); †Scheffe -adjusted $P < 0.05$ for multiple comparisons (reference: group II). BT, body temperature at admission to the NICU; BE, base excess.

rioamnionitis, VLBWI who needed DR-CPR had a significantly increased risk of mortality within seven days (OR, 5.64; 95% CI 3.25-9.77) increased IVH ≥ grade 3 (OR, 2.71; 95% CI 1.57-4.68), PVL (OR, 2.94; 95% CI 1.72-5.01), and NEC (OR, 2.12; 95% CI 1.15-3.91) compared to those who only needed PPV (Table 6). Subgroup analysis by gestational age group was performed to compare the short-term outcomes of the PPV-only group versus the DR-CPR group with a logistic regression model with adjustment for gestational age, maternal hypertension, antenatal steroids, and chorioamnionitis. With the increase in gestation, the percentage of VLBWI affected with a poor outcome decreased accordingly. The mortality and morbidities of the PPV only group in group III (29-32 weeks gestation) decreased markedly, resulting in a higher odds ratio of worse outcome in the DR-CPR group (Table 6).

DISCUSSION

This is the first report of initial resuscitation at delivery of VLBWI of less than 33 weeks gestational age from multiple NICUs in Korea. Most required supplemental oxygen and/or PPV but only a few received DR-CPR. Higher risk of early death and adverse outcomes was demonstrated for VLBWI who needed DR-CPR compared to those who only needed PPV.

Through advances in neonatal medicine, the outcomes of VLBWI have improved significantly over the past years (2). Such advances begin with initial resuscitation at delivery during "the golden hour" when the VLBWI goes through the transition from intrauterine to extra-uterine life. The most recent guideline on neonatal resuscitation was updated in 2010 by the International Liaison Committee on Resuscitation (ILCOR) and AHA (12). Korean neonatologists have adopted the guideline and follow it without local adjustments.

At birth, cessation of the feto-maternal circulation and physiologic changes of the cardiac and respiratory system are necessary for a smooth transition into extra-uterine life. About 10% of all newborns need some help during this transition and in less than 1% of the newborns, cardiopulmonary resuscitation with chest compression and/or epinephrine administration is recommended at birth when respiratory support alone is inadequate (12).

The percentage of VLBWI given supplemental oxygen was 91.7% in our study. KNN data did not specify the FiO_2 given to these infants. This is comparable to the Vermont Oxford Network data from 2000 to 2009 which ranged from 89.3% to 92.1% for infants with a birth weight of 501-1,500 g (13). In the Italian Neonatal Network, 76.2% of the infants under 1,500 g received supplemental oxygen (14).

The rate of intubation of this study is 77.7%, which is greater than other neonatal networks. Soll et al. (13) reported a range of 54.5%-58.3% intubation rate for Vermont Oxford Network infants with a birth weight of 501-1,500 g. The Korean National Health Insurance has reimbursed prophylactic surfactant administration to premature infants of less than 30 weeks gestation at delivery since 2009, and many neonatologists tend to follow this guideline and administer surfactant after intubating the infant. Such practice is a confounding factor in analyzing the need for intubation for the most immature infants and thus increased elective intubation of premature infants of less than 30 weeks for surfactant administration would be a notable feature demonstrated in Korea. Prophylactic surfactant administration at delivery was performed in 91.3%, 79.8%, and 54.5% for each gestational age group, respectively. This is much greater than the Vermont Oxford Network from 2000 to 2009 which ranged from 19% to 35.9% (13) and the Italian Neonatal Network reported a lower rate of 16.8% for infants under 1,500 g (14).

Maternal characteristics such as chorioamnionitis or preeclampsia are high risk for adverse neonatal status at birth. Low pH and base excess in infants with a gestational age > 29 weeks who needed DR-CPR suggest that peripartum factors in addition to maturity per se plays an important role in the initial status of the VLBWI. The EPICure study reported that hypothermia was associated with increased mortality in infants of less than 26 weeks gestation (15). Hypothermia was twice as frequent in infants born at 23 weeks compared with infants born at 25 weeks in the EPICure study, reflecting the increased risk associated with immaturity. The overall rate of hypothermia was greater in our study population, and needs to be monitored and followed up for improved outcomes. Delivery room temperatures of at least 26°C for newborns at < 28 weeks' gestation in combi-

http://dx.doi.org/10.3346/jkms.2015.30.S1.S45

JKMS

Table 5. Initial status of the very-low-birth-weight infants upon admission to the NICU comparing those who only needed PPV to those who received DR-CPR at birth according to gestational age groups

Parameters	Group I 21-23 weeks (n = 116)			Group II 24-28 weeks (n = 1,106)			Group III 29-32 weeks (n = 910)			Total (n = 2,132)		
	PPV (+) (n = 98)	DR-CPR (n = 18)	*P* value	PPV (+) (n = 987)	DR-CPR (n = 72)	*P* value	PPV (+) (n = 740)	DR-CPR (n = 24)	*P* value	PPV (+) (n = 1,825)	DR-CPR (n = 114)	*P* value
BT (°C)	35.3 ± 1.01	34.9 ± 1.15	0.219	36.0 ± 0.62*	35.8 ± 0.99*	0.014	36.1 ± 0.54*,†	35.6 ± 1.28	< 0.001	36.0 ± 0.65	35.6 ± 1.12	< 0.001
Hypothermia	84 (94.4%)	17 (100%)	0.410	753 (80.3%)	46 (73.0%)	0.112	516 (72.9%)	12 (63.2%)	0.243	1,353 (78%)	75 (75.8%)	0.619
Initial pH	7.24 ± 0.13	7.11 ± 0.13	0.001	7.27 ± 0.11*	7.14 ± 0.19	< 0.001	7.28 ± 0.10*	6.99 ± 0.26†	< 0.001	7.28 ± 0.11	7.11 ± 0.21	< 0.001
Initial pH < 7.2	29 (35.8%)	10 (71.4%)	0.018	150 (18.8%)	30 (54.5%)	< 0.001	111 (19%)	11 (64.7%)	< 0.001	290 (19.8%)	51 (59.3%)	< 0.001
Initial BE (mEq/L)	-7.9 ± 4.6	-11.2 ± 5.4	0.005	-5.3 ± 3.7*	-9.8 ± 5.6	< 0.001	-4.8 ± 3.4*	-12.7 ± 7.8	< 0.001	-5.3 ± 3.7	-10.6 ± 6.1	0.051
Initial BE < -6 mEq/L	50 (61.7%)	11 (78.6%)	0.386	260 (32.8%)	40 (74.1%)	< 0.001	159 (27.3%)	13 (76.5%)	< 0.001	469 (32.2%)	64 (75.3%)	0.054

Data as absolute numbers; percentages in parentheses. BT, body temperature at admission to the NICU; BE, base excess. *Scheffe-adjusted $P < 0.05$ for multiple comparisons (reference: group I); †Scheffe-adjusted $P < 0.05$ for multiple comparisons (reference: group II).

Table 6. Short-term outcomes of the VLBWI who survived for greater than 7 days, comparing those who only needed PPV to those who received DR-CPR at birth according to gestational age groups

Outcomes	Group I 21-23 weeks (n = 116)				Group II 24-28 weeks (n = 1,059)				Group III 29-32 weeks (n = 764)				Total (n = 2,132)			
	PPV (+) (n = 98)	DR-CPR (n = 18)	OR (95% CI)	*P* value	PPV (+) (n = 987)	DR-CPR (n = 72)	OR (95% CI)	*P* value	PPV (+) (n = 740)	DR-CPR (n = 24)	OR (95% CI)	*P* value	PPV (+) (n = 1,739)	DR-CPR (n = 83)	OR (95% CI)	*P* value
Mortality < 7 days (%)	26 (26.5)	11 (61.1)	5.31 (1.41-20.09)	0.014	52 (5.3)	13 (18.1)	3.87 (1.87-8.01)	< 0.001	6 (0.8)	6 (25)	34.59 (9.30-128.73)	< 0.001	84 (4.6)	30 (26.3)	5.64 (3.21-9.77)	< 0.001
IVH ≥ G 3 (%)	38 (44.2)	3 (27.3)	0.88 (0.18-4.43)	0.881	141 (14.7)	22 (33.3)	3.05 (1.65-5.65)	< 0.001	22 (3)	4 (20)	6.02 (1.49-24.31)	0.010	201 (11.3)	29 (29.9)	2.71 (1.57-4.68)	< 0.001
PVL (%)	14 (16.5)	0 (0)	NA	NA	112 (11.8)	17 (25.8)	2.61 (1.37-4.97)	0.003	46 (6.3)	8 (42.1)	10.85 (3.70-31.83)	< 0.001	172 (9.8)	25 (30.1)	2.94 (1.72-5.01)	< 0.001
Sepsis (%)	42 (42.9)	4 (22.2)	0.50 (0.12-2.03)	0.330	285 (28.9)	22 (30.6)	0.95 (0.52-1.71)	0.850	108 (14.6)	5 (20.8)	1.57 (0.51-4.88)	0.437	435 (25)	31 (37.3)	0.87 (0.53-1.42)	0.568
NEC (%)	21 (29.2)	3 (42.9)	0.83 (0.17-4.03)	0.819	94 (9.6)	13 (18.3)	1.76 (0.82-3.77)	0.149	18 (2.4)	4 (16.7)	18.11 (4.61-71.07)	< 0.001	133 (7.6)	20 (24.1)	2.12 (1.15-3.91)	0.016

Data as absolute numbers; percentages in parentheses. OR, odds ratio of the CC and or EPI group relative to the PPC only group in logistic regression model with adjustment for gestational age, maternal hypertension, antenatal steroid, and chorioamnionitis, missing values deleted listwise. PPV, positive pressure ventilation; DR-CPR, delivery room cardiopulmonary resuscitation; IVH ≥ G 3, intraventricular hemorrhage greater or equal to grade 3; PVL, periventricular leukomalacia, NEC: necrotizing enterocolitis.

http://dx.doi.org/10.3346/jkms.2015.30.S1.S45

nation with polythene wraps or bags are known to maintain temperatures most effectively (3) and such practices are commonly followed in Korea but data on practices to prevent hypothermia at each participating institution are not available. Those infants who required DR-CPR at birth were more acidotic and hypothermic compared to those infants who needed PPV only.

Most VLBWI needed resuscitation at birth with PPV: DR-CPR was needed in only a small percentage of VLBWI, 5.9%. The rate of DR-CPR varies according to the study populations. NICHD NRN reported a higher rate of 15% receiving DR-CPR (6). The CPQCC study reported a rate of 6.2% (7), similar to our study. The Canadian Neonatal Network (CNN) reported a DR-CPR rate of 10.9% in infants of under 1,000 g and a DR-CPR rate of 5.2% of all infants born at less than 33 weeks gestational age (16). The Vermont Oxford Network reported a large multicenter study and of 27,707 infants weighing 501-1,500 g, 6% needed DR-CPR which is similar to the findings of this study (17).

VLBWI who needed DR-CPR had worse outcomes on logistic regression analysis even after adjustment for gestational age, maternal hypertension, antenatal steroids, and chorioamnionitis. The need for DR-CPR decreased with maturity when comparing groups II and III against group I. The relative risk for adverse outcome was different according to gestational age groups. In group I (21-23 weeks gestation), mortality increased with DR-CPR (OR, 5.31; 95% CI 1.41-20.01). More than half of the infants in this subgroup died within seven days and such high mortality may have affected the timely assessment of short-term outcomes; IVH, PVL, sepsis, and NEC. In group II and III, 24-32 weeks gestation, mortality and short-term morbidities were increased with DR-CPR versus the PPV-only group.

With the increase in gestation, the percentage of VLBWI affected with a poor outcome decreased accordingly. Mature VLBWI who received DR-CPR still had a higher risk for adverse outcome compared with those who needed PPV only. However, the mortality and morbidities of the PPV only group in group III (29-32 weeks gestation) decreased markedly, resulting in a higher odds ratio of worse outcome in the DR-CPR group.

Increased IVH after DR-CPR (OR, 1.47; 95% CI 1.23-1.74) has been reported by the NICHD NRN (6). CNN reported an increase in severe brain injury, defined as radiological evidence of parenchymal brain injury or ventriculomegaly with or without IVHs (OR, 3.08; 95% CI 1.82-5.22) (16). Low blood pressure during asphyxia induced bradycardia, and rebound hypertension following epinephrine administration may contribute to IVH (6). Quality and depth of chest compression and/or the administration of epinephrine, a vasoactive drug causes rapid increase in blood pressure and vascular tone (18). Such fluctuations in blood pressure during resuscitation are known to increase IVH (7).

A single institution study from the US reported that 79% of the 19 ELBWI who needed DR-CPR were alive and well at hospital discharge (8). The Vermont Oxford Network data showed that survival of infants receiving DR-CPR was 23.9% for infants 401-500 g and 63.3% for infants of 501-1,500 g compared with 16.7% and 87.9% for infants in the same weight groups not receiving DR-CPR. Grade 3 or 4 IVH was seen in 15.3% of infants who received DR-CPR compared with 4.9% of those who did not (17).

Our study carries some limitations. The study population was limited to premature infants enrolled in the KNN. This covers up to 52% of the VLBWI and more than half of active NICU's in Korea but nevertheless the results cannot be generalized to represent Korea as a whole. A wide spectrum of aggressiveness in the management of periviable infants exists across hospitals and this may affect the data of group I (21-23 weeks gestation). A survey via email to the participating NICUs was conducted and 60% replied. More than half of those NICUs reported that neonatal resuscitation is performed for all babies greater than 23 weeks gestation and for those with a birth weight greater than 400 g. The rate of Cesarean section is lowest in group I which supports the finding that most VLBWI in group I were not offered aggressive care at delivery. DR-CPR was offered to those of less than 24 weeks gestation in concert with the NRP guidelines, which do not differ by gestational age. Group I was nevertheless included in analysis because it represents around 5% of the VLBWI enrolled in KNN. The VLBWI cohort of KNN began in 2013 and presently lacks the long-term follow-up data and data on neurodevelopmental impairments at 18 months of age could not be included for this analysis.

This is the first study to describe the current practice of neonatal resuscitation and short-term outcomes in Korean VLBWI of less than 33 weeks gestation. Our study may provide helpful information for medical personnel and families of VLBWI concerning mortality and short-term morbidity after delivery room resuscitation. Meticulous and aggressive management of infants who received DR-CPR is necessary to improve the initial status and short-term outcomes of VLBWI. Such efforts will contribute to the quality improvement of the delivery room management of VLBWI, thus leading to reduced morbidities and early death of the most vulnerable infants.

DISCLOSURE

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conception and design of the study: all authors. Acquisition of data: Cho SJ. Statistical Analysis: Cho SJ. First draft of the manuscript: Cho SJ, Namgung R. Revision and critical review of the manuscript: all authors. Manuscript approval: all authors.

http://dx.doi.org/10.3346/jkms.2015.30.S1.S45

ORCID

Su Jin Cho *http://orcid.org/0000-0002-3851-9073*
Jeonghee Shin *http://orcid.org/0000-0003-3718-968X*
Ran Namgung *http://orcid.org/0000-0001-7182-9535*

REFERENCES

1. Tyson JE, Parikh NA, Langer J, Green C, Higgins RD; National Institute of Child Health and Human Development Neonatal Research Network. *Intensive care for extreme prematurity--moving beyond gestational age. N Engl J Med 2008; 358: 1672-81.*
2. Fanaroff AA, Stoll BJ, Wright LL, Carlo WA, Ehrenkranz RA, Stark AR, Bauer CR, Donovan EF, Korones SB, Laptook AR, et al.; NICHD Neonatal Research Network. *Trends in neonatal morbidity and mortality for very low birthweight infants. Am J Obstet Gynecol 2007; 196: 147.e1-8.*
3. Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, Hazinski MF, Halamek LP, Kumar P, Little G, et al.; American Heart Association. *Neonatal resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Pediatrics 2010; 126: e1400-13.*
4. Vyas H, Field D, Milner AD, Hopkin IE. *Determinants of the first inspiratory volume and functional residual capacity at birth. Pediatr Pulmonol 1986; 2: 189-93.*
5. ACOG Committee on Obstetric Practice. *ACOG Committee Opinion No. 348, November 2006: umbilical cord blood gas and acid-base analysis. Obstet Gynecol 2006; 108: 1319-22.*
6. Wyckoff MH, Salhab WA, Heyne RJ, Kendrick DE, Stoll BJ, Laptook AR; National Institute of Child Health and Human Development Neonatal Research Network. *Outcome of extremely low birth weight infants who received delivery room cardiopulmonary resuscitation. J Pediatr 2012; 160: 239-44.e2.*
7. Handley SC, Sun Y, Wyckoff MH, Lee HC. *Outcomes of extremely preterm infants after delivery room cardiopulmonary resuscitation in a population-based cohort. J Perinatol 2015; 35: 379-83.*
8. Finer NN, Tarin T, Vaucher YE, Barrington K, Bejar R. *Intact survival in extremely low birth weight infants after delivery room resuscitation. Pediatrics 1999; 104: e40.*
9. Jankov RP, Asztalos EV, Skidmore MB. *Favourable neurological outcomes following delivery room cardiopulmonary resuscitation of infants < or = 750 g at birth. J Paediatr Child Health 2000; 36: 19-22.*
10. Shah PS. *Extensive cardiopulmonary resuscitation for VLBW and ELBW infants: a systematic review and meta-analyses. J Perinatol 2009; 29: 655-61.*
11. Chang YS, Ahn SY, Park WS. *Committee on program and planning and advisory committee of Korean Neonatal Network. Neonatal Med 2013; 20: 169-78.*
12. Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, Hazinski MF, Halamek LP, Kumar P, Little G, et al. *Part 15: neonatal resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010; 122: S909-19.*
13. Soll RF, Edwards EM, Badger GJ, Kenny MJ, Morrow KA, Buzas JS, Horbar JD. *Obstetric and neonatal care practices for infants 501 to 1500 g from 2000 to 2009. Pediatrics 2013; 132: 222-8.*
14. Bellu R, Gagliardi L, Tagliabue P, Corchia C, Vendettuoli V, Mosca F, Zanini R; Italian Neonatal Network. *Survey of neonatal respiratory care and surfactant administration in very preterm infants in the Italian Neonatal Network. Acta Biomed 2013; 84: 7-11.*
15. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. *The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. Pediatrics 2000; 106: 659-71.*
16. Soraisham AS, Lodha AK, Singhal N, Aziz K, Yang J, Lee SK, Shah PS; Canadian Neonatal Network. *Neonatal outcomes following extensive cardiopulmonary resuscitation in the delivery room for infants born at less than 33 weeks gestational age. Resuscitation 2014; 85: 238-43.*
17. Finer NN, Horbar JD, Carpenter JH. *Cardiopulmonary resuscitation in the very low birth weight infant: the Vermont Oxford Network experience. Pediatrics 1999; 104: 428-34.*
18. Sims DG, Heal CA, Bartle SM. *Use of adrenaline and atropine in neonatal resuscitation. Arch Dis Child Fetal Neonatal Ed 1994; 70: F3-9; discussion F-10.*