Resuscitation 85 (2014) 238–243

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Neonatal outcomes following extensive cardiopulmonary resuscitation in the delivery room for infants born at less than 33 weeks gestational age☆

Amuchou Singh Soraisham[a,*], Abhay Kumar Lodha[a], Nalini Singhal[a], Khalid Aziz[b], Junmin Yang[c], Shoo K. Lee[c], Prakesh S. Shah[c], on behalf of the Canadian Neonatal Network

[a] Department of Paediatrics, University of Calgary, Alberta Children's Hospital Research Institute for Child and Maternal Health, Foothills Medical Centre, 1403, 29th Street NW, Calgary, AB T2N 2T9, Canada
[b] Department of Paediatrics, University of Alberta, Royal Alexandra Hospital, 10240 Kingsway, Edmonton, AB T5H 3V9, Canada
[c] Department of Paediatrics, University of Toronto, Mount Sinai Hospital, 600 University Avenue, Toronto, Ontario M5G 1X5, Canada

ARTICLE INFO

Article history:
Received 6 August 2013
Received in revised form 8 October 2013
Accepted 15 October 2013

Keywords:
Adrenaline
Cardiopulmonary resuscitation
Epinephrine
Neonatal outcome
Premature

ABSTRACT

Aim: To examine the neonatal mortality and morbidity of infants born at <33 weeks gestational age (GA) who received extensive delivery room cardiopulmonary resuscitation (DR-CPR) immediately after birth.
Design/methods: In this retrospective cohort study, we performed secondary analyses of data from infants born at <33 weeks GA and admitted to participating NICUs in the Canadian Neonatal Network between January 2010 and December 2011. Infants were divided into two groups based on birth weight (<1000 g and ≥1000 g) and neonatal morbidity and mortality compared using bivariate and multivariate analyses.
Results: Of the 8033 eligible infants, 419 (5.2%) received DR-CPR. For infants weighing <1000 g at birth, 10.9% (outborn: 21.6%, inborn: 7.6%) received DR-CPR, whereas 3.4% (outborn: 9.6%, inborn: 2.2%) of those weighing ≥1000 g received DR-CPR. If infants received DR-CPR there was increased risk of mortality, bronchopulmonary dysplasia (BPD) and severe brain injury. Logistic regression analysis showed DR-CPR was associated with increased mortality (adjusted odds ratio [aOR]: 2.09, 95% CI [1.39, 3.14]) in infants born weighing <1000 g. Among infants born weighing ≥1000 g, DR-CPR was associated with increased mortality (aOR: 7.16, 95% CI [3.88, 13.2]), severe brain injury (aOR: 3.08, 95% CI [1.82, 5.22]), BPD (aOR: 2.14, 95% CI [1.25, 3.65]), pneumothorax (aOR: 3.11, 95% CI [1.53, 6.31]) and intestinal perforation (aOR: 3.47, 95% CI [1.46, 8.24]).
Conclusions: DR-CPR is associated with increased risk of mortality and morbidity especially in preterm infants born weighing ≥1000 g. Long-term neurodevelopmental follow up is warranted for these infants.

1. Introduction

The birth of an infant is associated with cessation of the feto-maternal circulation and subsequent rapid physiologic changes involving both the cardiac and respiratory systems. Failure of this adaptation results in cardiopulmonary compromise and the need for resuscitation. Approximately 5–10% of all newborns need some assistance to establish normal breathing at birth.[1] Stimulation and respiratory support alone may be sufficient to facilitate this transition. However, in less than 1% of newborns additional resuscitation measures are required, either because of an underlying condition or because of inadequate respiratory support.[1,2] As a consequence, cardiopulmonary resuscitation (CPR) with chest compressions and/or adrenaline is recommended when respiratory support alone does not establish circulatory transition within

Abbreviations: aOR, adjusted odds ratio; BPD, bronchopulmonary dysplasia; CNN, Canadian Neonatal Network; DR-CPR, delivery room cardiopulmonary resuscitation; ELBW, extremely low birth weight; GA, gestational age; IQR, interquartile range; IVH, intraventricular haemorrhage; NEC, necrotizing enterocolitis; OR, odds ratio; PDA, patent ductus arteriosus; PVL, periventricular leukomalacia; RDS, respiratory distress syndrome; ROP, retinopathy of prematurity; SD, standard deviation; SGA, small for gestational age; SNAP-II, Score for Neonatal Acute Physiology, version II.

☆ A Spanish translated version of the summary of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2013.10.016.

* Corresponding author at: Foothills Medical Centre, Room C-211, 1403, 29th Street NW, Calgary, AB T2N 2T9, Canada.
E-mail addresses: asoraish@ucalgary.ca, amuchou.soraisham@albertahealthservices.ca (A.S. Soraisham).

0300-9572/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.resuscitation.2013.10.016

minutes of birth. As such, 'extensive delivery room CPR' (DR-CPR) is defined as chest compressions with or without the use of adrenaline during delivery room resuscitation.

Previous studies on delivery room resuscitation have drawn conflicting conclusions with respect to the neonatal outcomes of DR-CPR among preterm infants.[3–10] Many studies have reported that preterm infants who require extensive DR-CPR immediately after birth are at increased risk for one or more of neonatal mortality,[3–8] intraventricular haemorrhage (IVH),[5,6] bronchopulmonary dysplasia (BPD)[8] and neurodevelopmental morbidity including cerebral palsy and cognitive delays.[8] In contrast, some studies have reported no significant differences in the mortality or neurologic morbidity in infants who received extensive DR-CPR, especially in extremely low birth weight (ELBW, <1000 g) infants.[9,10]

Most of these studies are from single centres, retrospective, and of small sample size, which limits the ability to generalize the results.[3,5–7,9,10] A few multicentre studies on the outcomes of DR-CPR have been performed but these are also conflicting.[4,8] For example, a study of centres enrolled in the Vermont Oxford Network reported only a limited effect of DR-CPR on outcomes,[4] while results from the National Institute of Child Health and Development Neonatal Research Network (NICHD-NRN), a network of University-affiliated neonatal centres, showed significant adverse outcomes in association with DR-CPR.[8] Finally, in a meta-analysis of studies of ELBW and very low birth weight (VLBW, <1500 g) infants who received DR-CPR, which included many of the studies just described, Shah reported significantly increased risks for mortality and severe brain injury, but similar rates of BPD and severe ROP.[11] In an attempt to resolve the previously conflicting data, the objective of this study was to examine the impact of extensive DR-CPR on neonatal mortality and morbidity in preterm infants born at <33 weeks gestational age (GA) who were admitted to participating neonatal intensive care units (NICUs) in the Canadian Neonatal Network™ (CNN), a Canada-wide, population-based network. The secondary objective was to compare neonatal outcomes among those who received extensive DR-CPR and those who did not according to whether infants were born weighing <1000 g or ≥1000 g.

2. Methods

2.1. Study population

The study cohort consisted of all preterm infants who were born at <33 weeks GA and admitted to one of 30 tertiary NICUs participating in the CNN between January 1st, 2010 and December 31st, 2011. All level III NICUs in Canada are members of the CNN. All infants are resuscitated by health personnel (residents, fellows, respiratory therapists and/or staff neonatologists for all inborn neonates; and transport team members, registered nurses or paediatricians for outborn neonates) who have completed the Neonatal Resuscitation Programme course.[12] Infants with major congenital anomalies and those who were considered for palliative care prior to birth were excluded.

2.2. Data collection

Trained data abstractors collected neonatal data from the participating sites and submitted it to be stored centrally in the CNN database. Details of data collection and data management for CNN have been published elsewhere.[13] Data collection at each site was approved by either research ethics board or quality improvement and data management committees. Retrospective evaluation of de-identified data was approved by the CNN Steering Committee.

2.3. Definitions

Indices of neonatal outcome were defined according to the CNN Data Abstractor's Manual.[14] For this study, extensive DR-CPR was defined as chest compressions for ≥30 s with or without adrenaline administration in the immediate period after birth. Outcomes were defined as per standardized data collection for the network. Diagnosis and severity of IVH was based on the criteria of Papile.[15] Severe brain injury was defined as radiological evidence of parenchymal brain injury or ventriculomegaly with or without intraventricular haemorrhage (i.e. ≥grade 3 IVH and/or periventricular leukomalacia). Seizure was defined as "presence of abnormal movements along with electroencephalographic (EEG) or amplitude integrated EEG diagnosis of seizure activity" or clinical observation of seizure like movement coupled with administration of anticonvulsant (phenobarbitone). Necrotizing enterocolitis (NEC) was defined according to modified Bell's criteria (≥stage 2).[16] Patent ductus arteriosus (PDA) was defined as clinical diagnosis plus treatment with indomethacin/Ibuprofen, surgical ligation, or both. BPD was defined as requirement for oxygen at 36 weeks postmenstrual age[17] or at discharge from the participating unit. ROP was diagnosed according to the International Classification of Retinopathy of Prematurity.[18] Severity of illness was measured using the Score for Neonatal Acute Physiology, version II (SNAP-II) as described by Richardson et al.[19] Small for gestational age (SGA) was defined as birth weight less than the 10th percentile for the given GA and "outborn" status was assigned if the infant was born at a hospital different from the one in which the participating NICU was located. Major congenital anomalies were identified from a defined list within the CNN database. Survival without major morbidity was defined as survival without severe brain injury, BPD, NEC ≥ stage 2 or ROP ≥ stage 3.

2.4. Data analyses

The eligible infants were divided into 2 groups based on birth weight: (a) birth weight < 1000 g (ELBW group) and (b) birth weight ≥ 1000 g (non-ELBW group). In each group we compared the neonatal outcomes between infants who received extensive DR-CPR and those who did not. Categorical variables were analyzed using the chi-square and Fisher's exact test. Continuous variables were analyzed using comparisons of means, except when the data were not normally distributed and/or when the variances were significantly different, in which case the Mann–Whitney *U* test or median test was used. In multivariate analysis, we controlled for potential confounders that might influence neonatal outcomes. These included antenatal steroid use, maternal chorioamnionitis, GA, sex, SGA, mode of delivery, multiple births and outborn status. A p value of <0.05 was considered statistically significant. Odds ratios (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI) were computed for various outcomes. Odds ratios were adjusted using the confounders listed above. Statistical analyses were performed using the SAS version 9.2 (SAS Institute, Inc., Cary, NC) software package.

3. Results

A total of 8419 preterm infants (<33 weeks GA) were admitted to the 30 NICUs during the study period. Of these 386 infants were excluded. Fig. 1 shows the study population profile. Of the 8033 eligible infants, 419 (5.2%) received DR-CPR. Of the 419 infants, 264