Resuscitation 82 (2011) 313–318

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Two-year survival and neurodevelopmental outcomes after cardiopulmonary resuscitation in neonatal patients after complex cardiac surgery☆

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ARTICLE INFO

Article history:
Received 20 September 2010
Accepted 17 October 2010

Keywords:
Cardiopulmonary resuscitation
Neonate
Outcomes
Congenital heart disease

ABSTRACT

Aim: To examine survival and neurodevelopmental outcomes in neonates having post-operative cardiopulmonary resuscitation (CPR).
Methods: This inception cohort study included all neonates (6 weeks old or less) who received post-operative CPR (Group 1) after cardiac surgery from 1996 to 2005, matched for heart defect, year of surgery, chromosomal abnormality, and socioeconomic status to two neonates who did not receive post-operative CPR (Group 2). Two-year neurodevelopment was prospectively assessed with Bayley Scales of Infant Development II and Adaptive Behavior Assessment System II. Pre-, intra-, and post-operative variables were collected prospectively. Cardiac arrest variables were collected retrospectively. Predictors of mortality were analyzed by univariate analysis and conditional multiple logistic regression.
Results: There were 29 patients in Group 1, and 58 patients in Group 2. In survivors, there were no significant differences between Groups 1 and 2 in outcomes [mean (SD)] of mental developmental index [84.5 (12.2) vs. 81.0 (18.9)], psychomotor developmental index [82.8 (13.8) vs. 80.1 (21.9)], General Adaptive Composite [84.6 (15.3) vs. 84.3 (19.2)], Motor scale [8.4 (3.2) vs. 8.0 (3.8)], or delay on any of these scales. Two-year mortality [58.6% Group 1; 8.6% Group 2], was associated on conditional multiple logistic regression with CPR (OR 26.6; 95% CI, 5.4, 129.5). In Group 1, on multiple logistic regression, 2-year mortality was associated with minutes of chest compressions (OR 1.04, 95% CI, 1.01, 1.08).
Conclusions: Among neonates having cardiac surgery, CPR is associated with greater mortality. There is no evidence that CPR survivors have different 2-year neurodevelopmental outcomes than those neonates not having CPR.

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1. Introduction

Complex cardiac surgery for congenital heart lesions in the neonate is associated with adverse neurodevelopmental and behavioral sequelae.[1–4] Postoperatively, the developing brain may be especially vulnerable to hemodynamic, ventilatory, and oxygenation abnormalities.[4] On occasion, these complications necessitate the initiation of cardiopulmonary resuscitation (CPR), which may further exacerbate hypoxia and/or ischemia-reperfusion within the central nervous system.

Few studies have examined the effects of CPR in children with congenital heart lesions. Several groups however, have reported pediatric CPR outcomes in pediatric intensive care unit (PICU)[5–7] or in out/inpatients.[8–11] One-year survival from PICU resuscitations that included in part a wide age range of cardiac patients varied from 23%[5] to 54%,[8] with mild to no change in long term functional and neurologic status.[5,6,8] Comparatively, 1-year survival in out/inpatients having CPR has been reported at 33%,[11] with one study documenting that the majority of children demonstrated low adaptive behavior, achievement and neuropsychologic measures.[10]

Although complex cardiac surgery in the neonate is not uncommon, little is known about how significant postoperative

Abbreviations: ABAS, Adaptive Behavior Assessment System; BSID, Bayley Scales of Infant Development; CPB, cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; GAC, General Adaptive Composite score on the ABAS; MDI, mental developmental index; PDI, psychomotor developmental index; PICU, pediatric intensive care unit; SES, socioeconomic status.

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at doi:10.1016/j.resuscitation.2010.10.017.

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doi:10.1016/j.resuscitation.2010.10.017

complications affect the susceptible brain. Therefore, we sought to examine neurodevelopmental and survival outcomes in neonates (≤6 weeks old) requiring postoperative CPR.

2. Methods

This was a case-comparison within-cohort study utilizing data obtained from an inter-provincial inception cohort outcomes study. As previously described, from September 1996 to August 2005, neonates ≤6 weeks of age were identified at the time of cardiac surgery.[1,12] All surgeries were conducted at the Stollery Children's Hospital, Edmonton, Alberta, Canada.

2.1. Subjects

All patients that required postoperative CPR over the 9 years were identified (Group 1). A comparison group of patients who did not require CPR (Group 2) were matched for cardiac lesion, year of surgery, and socioeconomic status (SES) at a ratio of 2:1. The inclusion criteria were: (a) cardiac surgery with employment of cardiopulmonary bypass (CPB) at the Stollery Children's Hospital between September 1996 to August 2005, and (b) cardiac surgery performed at ≤6 weeks of age. The exclusion criteria were: cardiac surgery not requiring CPB, and patients having CPR preoperatively or in the operating room. All survivors were assessed in follow-up multidisciplinary neurodevelopmental clinics at their tertiary site of origin: Edmonton and Calgary, Alberta; Vancouver, British Columbia; Saskatoon and Regina, Saskatchewan; and Winnipeg, Manitoba. Each site obtained ethics board approvals. All parents or legal guardians provided signed informed consent forms.

2.2. Neurodevelopmental assessment

Early childhood assessments were conducted at a planned age of 21 ± 3 months. Physical parameters at follow up including height, weight, and head circumference were charted as previously described.[1,12] Socioeconomic status was ascertained by the Blishen Index, which scores occupations on income and educational characteristics.[13] As previously described, pediatricians with experience in neurodevelopment assessed for cerebral palsy and visual impairments, certified pediatric audiologists evaluated hearing impairments, and pediatric psychologists and psychometrists administered the Bayley Scales of Infant Development II (BSID-II).[1,12,14,15] Visual or hearing impairment were established if the corrected visual acuity in the better eye was <20/60, and binaural/bilateral sensorineural hearing loss >40 dB at any frequency from 250 to 4000 Hz.[1,12] Developmental indices of <70 (2 SD below the population mean) in either the mental (MDI) or psychomotor (PDI) developmental index indicated mental or motor delay.[1,12] The General Adaptive Composite (GAC) Score and Motor Score of the Adaptive Behavioral Assessment System parent questionnaire were also determined.[16]

2.3. Variables

Previously agreed upon demographic and perioperative variables were recorded prospectively in the database.[1,12] Demographic variables included birth weight, gender, SES, prenatal diagnosis, race, year of surgery, gestational age, home location, guardianship, and out of region referral. Preoperative variables included cardiac diagnoses, seizure, lowest pH and PaO2, and highest plasma lactate. Intra-operative variables included CPB time, aortic cross-clamp time, deep hypothermic circulatory arrest use and time, and need for re-CPB in the operating room. Post-operative variables included seizure, extra-corporeal life support (ECLS), highest plasma lactate on day 1, duration of post-operative ventilation, and overall duration of ventilation and hospitalization. Post-operative CPR variables were collected by retrospective chart review and entered into the database. These CPR variables included initial rhythm, minutes of chest compressions, defibrillation, number of doses of epinephrine and bicarbonate, time to return of spontaneous circulation, number of cardiac arrests, and highest lactate in the 24 h after CPR.

2.4. Statistics

The primary outcomes were 2-year neurodevelopmental indices and disability. Disability was defined as visual impairment, sensorineural hearing loss, and/or cerebral palsy. The secondary outcomes included both mortality and morbidity. Morbidity was defined by growth variables of weight, height, and head circumference, and need for gastrostomy tube feeding.

For univariate unmatched comparisons of group characteristics, difference in means or proportions and their 95% confidence intervals (CI) were calculated. Continuous neurodevelopmental outcomes were available for survivors only and hence the intended matching in a 2:1 ratio was lost and crude two sample *t*-test was used for comparison. A secondary analysis of these was done using mixed effects modeling to account for cluster effect, taking the heart and chromosomal abnormality as strata (cluster). These supported the crude *t*-test comparison that there is no evidence of a difference due to CPR (the results of the cluster analysis are not presented). For mortality at 2 years conditional multiple logistic regression was used, to account for the matching strata, and variables a priori chosen because of their potential clinical influence were included as possible predictors. Within the CPR group, multiple logistic regression was used, with CPR variables, for death by 2 years of age. The Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL) version 12.0 for Windows and The R Project for Statistical Computing were used for analysis. Significance level was set at 0.05.

3. Results

3.1. Description of cohort

There were 29 patients in Group 1 and 58 patients in comparison Group 2. Timing of CPR in Group 1 was on the day postoperatively in 17 (59%), between days 2 and 7 postoperatively in 6 (21%), and more than 1 week postoperatively in 6 (21%). Over the time period of the study there were 343 neonatal cardiac surgery procedures performed, with postoperative CPR performed in 29 (8%).

Table 1
Congenital heart defects in a group of 29 postoperative cardiopulmonary resuscitation infants (Group 1) and 58 matched comparison patients (Group 2).

Heart defect	Group 1	Group 2
Single ventricle anatomy	15	30
Transposition of the great arteries without ventricular septal defect	1	2
Transposition of the great arteries, complex	3	6
Hypoplastic left heart syndrome	12	24
Total anomalous pulmonary venous connection	4	8
Truncus arteriosis	2	4
Atrioventricular septal defect (Trisomy 21)	1	2
Tetralogy of Fallot	1	2
Aortic atresia	1	2
Hypoplastic aortic arch with atrioventricular septal defect	1	2
Single ventricle with pulmonary artery dysplasia	1	2
Interrupted aortic arch with chromosome deletion 22q11.2	1	2
Interrupted aortic arch without chromosomal abnormality	1	2

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