Resuscitation 111 (2017) 41–47

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

A hemodynamic-directed approach to pediatric cardiopulmonary resuscitation (HD-CPR) improves survival☆

Ryan W. Morgan*, Todd J. Kilbaugh, Wesley Shoap, George Bratinov, Yuxi Lin, Ting-Chang Hsieh, Vinay M. Nadkarni, Robert A. Berg[1], Robert M. Sutton[1], on behalf of the Pediatric Cardiac Arrest Survival Outcomes PiCASO Laboratory Investigators[2]

The Children's Hospital of Philadelphia, Department of Anesthesiology and Critical Care Medicine, 34th Street & Civic Center Boulevard, Philadelphia, PA 19104, United States

ARTICLE INFO

Article history:
Received 7 June 2016
Received in revised form 1 September 2016
Accepted 22 November 2016

Keywords:
Pediatric cardiac arrest
Cardiopulmonary resuscitation
Coronary perfusion pressure
Blood pressure

ABSTRACT

Aim: Most pediatric in-hospital cardiac arrests (IHCAs) occur in ICUs where invasive hemodynamic monitoring is frequently available. Titrating cardiopulmonary resuscitation (CPR) to the hemodynamic response of the individual improves survival in preclinical models of adult cardiac arrest. The objective of this study was to determine if titrating CPR to systolic blood pressure (SBP) and coronary perfusion pressure (CoPP) in a pediatric porcine model of asphyxia-associated ventricular fibrillation (VF) IHCA would improve survival as compared to traditional CPR.

Methods: After 7 min of asphyxia followed by VF, 4-week-old piglets received either hemodynamic-directed CPR (HD-CPR; compression depth titrated to SBP of 90 mmHg and vasopressor administration to maintain CoPP ≥20 mmHg); or Standard Care (compression depth 1/3 of the anterior–posterior chest diameter and epinephrine every 4 min). All animals received CPR for 10 min prior to the first defibrillation attempt. CPR was continued for a maximum of 20 min. Protocolized intensive care was provided to all surviving animals for 4 h. The primary outcome was 4-h survival.

Results: Survival rate was greater with HD-CPR (12/12) than Standard Care (6/10; $p = 0.03$). CoPP during HD-CPR was higher compared to Standard Care (point estimate +8.1 mmHg, CI_{95}: 0.5–15.8 mmHg; $p = 0.04$). Chest compression depth was lower with HD-CPR than Standard Care (point estimate −14.0 mm, CI95: −9.6 to −18.4 mm; $p < 0.01$). Prior to the first defibrillation attempt, more vasopressor doses were administered with HD-CPR vs. Standard Care (median 5 vs. 2; $p < 0.01$).

Conclusions: Hemodynamic-directed CPR improves short-term survival compared to standard depth-targeted CPR in a porcine model of pediatric asphyxia-associated VF IHCA.

Introduction

Approximately 6000 children receive (CPR) for in-hospital cardiac arrest (IHCA) annually in the United States.[1] These events occur primarily in intensive care units (ICUs), where 1.4–6% of patients suffer an IHCA.[2–5] Despite considerable improvements in outcomes in recent decades, only 39–52% of children survive to hospital discharge.[5–10]

Standard CPR includes absolute depth and rate targets with time-based epinephrine dosing.[11–14] However, greater than 90% of pediatric IHCA events occur in an ICU setting, where CPR is generally provided by individuals with advanced training and where patient-specific physiologic monitoring (e.g., indwelling arterial catheters, end tidal carbon dioxide [$ETCO_2$] monitoring) is often available.[2] Therefore, it is reasonable for clinical teams to adjust resuscitation efforts based on an individual patient's hemodynamics during CPR. Notably, "personalized" hemodynamic-directed CPR has improved survival outcomes in pre-clinical adult models of IHCA,[15–17] but remains understudied in pediatric models.

The primary objective of this study was to determine if actively titrating CPR to hemodynamics (i.e., invasive arterial blood pressure [BP]) in a porcine model of pediatric asphyxia-associated ventric-

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2016.11.018.

* Corresponding author at: The Children's Hospital of Philadelphia, 34th Street & Civic Center Boulevard, Suite 8566, Philadelphia, PA 19104, United States. Fax: +1 267 426 5574.
E-mail address: morganr1@email.chop.edu (R.W. Morgan).

[1] Denotes co-senior authorship.

[2] PiCASO Laboratory Investigators include Thomas W. Conlon, MD; Andrew J. Lautz, MD; Maryam Y. Naim, MD; and Heather Wolfe, MD.

http://dx.doi.org/10.1016/j.resuscitation.2016.11.018
0300-9572/

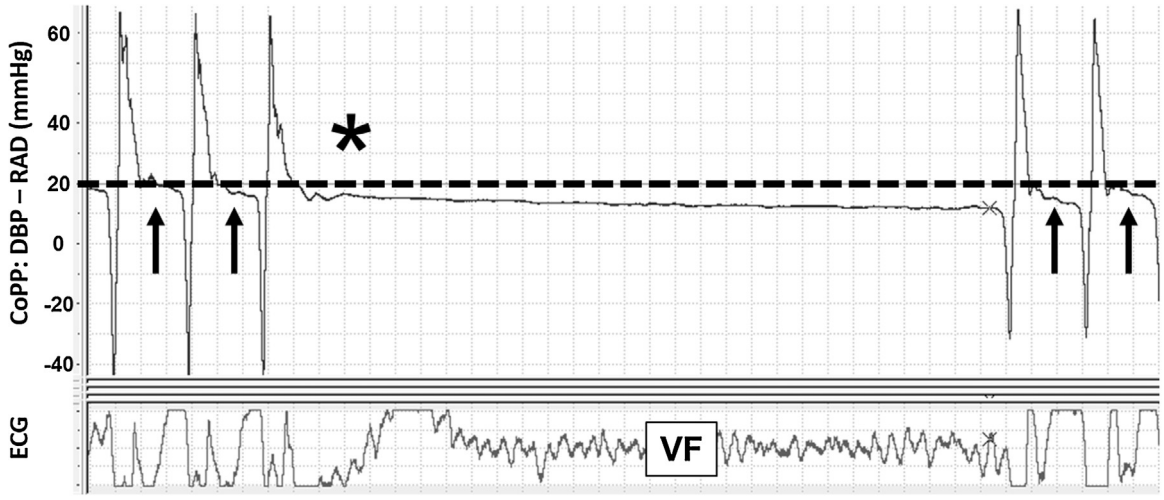

Fig. 1. Coronary perfusion pressure during cardiopulmonary resuscitation.
Representative sample during experimental protocol from PowerLab data acquisition system. Dotted line indicates coronary perfusion pressure of 20 mmHg, goal coronary perfusion pressure in the HD-CPR group. Arrows represent period of coronary perfusion pressure assessment in mid-diastole. *Pause in CPR as per resuscitation protocol. *Definitions of abbreviations:* ECG = electrocardiogram; CoPP = coronary perfusion pressure; DBP = aortic diastolic pressure; RAD = right atrial diastolic pressure; VF = ventricular fibrillation.

ular fibrillation (VF) IHCA would improve survival compared with optimized standard CPR. We hypothesized that rates of the return of spontaneous circulation (ROSC) and 4-h survival would be higher in animals treated with a method of hemodynamic-directed CPR (HD-CPR) compared with standard care. We further hypothesized that coronary perfusion pressure (CoPP) during HD-CPR would be higher compared to standard CPR, providing a potential physiologic mechanism for improved outcomes.

Methods

Animal preparation

The Children's Hospital of Philadelphia Institutional Animal Care and Use Committee approved this experimental protocol. Twenty-two healthy 1-month old female domestic piglets were utilized for the study. All piglets underwent an overnight fast and were then anesthetized and tracheally intubated. They were mechanically ventilated with an anesthesia machine (Modulus SE; Datex Ohmeda, Madison, WI) on a mixture of room air and titrated isoflurane (approximately 1%) to maintain anesthesia. Ventilator settings included tidal volumes of 10 mL/kg, positive end-expiratory pressure (PEEP) of 6 cm H_2O, and the titration of respiratory rates to maintain continuously monitored $ETCO_2$ values between 38 and 42 mmHg (NICO; Novametrix Medical Systems Inc., Wallingford, CT). Weights and anterior–posterior (AP) chest diameters were measured and recorded.

An external jugular vein, femoral artery, and bilateral femoral veins were cannulated with vascular introducer sheaths (Cordis Corp., Fremont, CA) under ultrasound guidance using percutaneous Seldinger technique. High fidelity, solid-state, micromanometer-tipped catheters (4.5–6F; Millar Instruments, Houston, TX) were advanced through the femoral artery and vein access sites to measure continuous aortic and right atrial pressures, respectively. A balloon-tipped pulmonary artery thermodilution catheter (Edwards Lifesciences, Irvine, CA) was advanced to the pulmonary artery via a femoral vein and a bipolar pacing wire (Edwards Lifesciences) was advanced into the right ventricle via the external jugular vein. All catheter positions were confirmed by fluoroscopy. Unfractionated heparin (200 U/kg) was administered to prevent catheter clotting. In an effort to replete intravascular volume to a euvolemic state after the overnight fast, 20 mL/kg of 0.9% sodium chloride solution was administered to all animals.

Measurements

Prior to and during the experimental protocol, the electrocardiograph, aortic blood pressure, right atrial pressure, pulse oximetry, and $ETCO_2$ waveforms were displayed and recorded (PowerLab; ADInstruments, Colorado Springs, CO). CoPP was calculated and displayed in real time by subtracting the mid-diastolic (release) right atrial pressure from the mid-diastolic aortic pressure[18,19] (Fig. 1). Arterial blood gas specimens were obtained from the thoracic aorta at baseline (prior to start of experimental protocol), 6.5 min into the asphyxial period, and 6 min into the resuscitation period.

A CPR recording defibrillator (Philips Heart Start MRx defibrillator with Q-CPR option [Philips Health Care, Andover, MA; and Laerdal Medical Corporation, Stavanger, Norway] or Zoll R Series Plus [Zoll Medical Corporation, Chelmsford, MA]) was utilized during CPR. These devices are validated to accurately measure chest compression depth within 1.6 mm[20] and 6 mm,[21] respectively. The defibrillator displayed and recorded chest compression depth (mm) and rate (min^{-1}).

Model justification

A porcine model was selected because of the similarity between swine and humans in relation to AP chest diameter and chest compression characteristics.[22] One-month old piglets are neurodevelopmentally similar to human toddlers,[23] who account for 42% of pediatric IHCAs.[6] Likewise, these animals are similar in body mass to children between 1 and 2 years of age.[24] The injury model utilized in this study was designed to simulate pediatric IHCA preceded by an asphyxial event, as 42–52% of pediatric IHCAs have an underlying respiratory etiology.[2,9,10,25,26] The duration of asphyxia (7 min) was intended to produce severe arterial hypoxemia and hypercarbia.[15,17] While induction of VF is somewhat artificial, it was induced in order to ensure that the cardiac arrest would be maintained for a uniform 10-min period to evaluate the effects CPR in both groups. Ten minutes is the median duration of CPR among pediatric survivors in the Get With The Guidelines-Resuscitation registry.[26] Additionally, as nearly 1/3 of pediatric IHCAs will have