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Experimental paper

Effects of different durations of sustained inflation during cardiopulmonary resuscitation on return of spontaneous circulation and hemodynamic recovery in severely asphyxiated piglets☆

J. Mustofa[a,b], P.-Y. Cheung[b,c], S. Patel[b,c], T.F. Lee[b], M. Lu[b], M.P. Pasquin[b], M. O'Reilly[b,c], G.M. Schmölzer[b,c,*]

[a] Faculty of Science, University of Alberta, Edmonton, Alberta, Canada
[b] Centre for the Studies of Asphyxia and Resuscitation, Neonatal Research Unit, Royal Alexandra Hospital, Edmonton, Alberta, Canada
[c] Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada

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ABSTRACT

Objective: We previously demonstrated that sustained inflation (SI) during chest compression (CC) significantly reduces time to return of spontaneous circulation (ROSC) when compared to 3:1 compression:ventilation (C:V) ratio during neonatal resuscitation. However, the optimal length of SI during CC to improve ROSC and hemodynamic recovery in severely asphyxiated piglets is unknown.

Aim: To examine if different lengths of SI will improve ROSC and hemodynamic recovery in severely asphyxiated piglets.

Intervention and measurements: Thirty newborn piglets (1–3 days) were anesthetized, intubated, instrumented and exposed to 30-min normocapnic hypoxia followed by asphyxia. Piglets were randomized into four groups: 3:1 C:V (n = 8), CC with an SI duration of either 20 s (CC + SI 20) (n = 8) or 60 s (CC + SI 60) (n = 8), and a sham group (n = 6). Cardiac function, carotid blood flow, cerebral and renal oxygenation as well as respiratory parameters were continuously recorded throughout the experiment.

Main results: When compared with 3:1 group, both CC + SI 20 and CC + SI 60 groups had significantly shorter ROSC time (p = 0.002). All three intervention groups had similar hemodynamic recovery by the end of 4 h observation period. There was no difference in lung injury markers among all experimental groups. However, when compared to the sham group, the concentrations of IL-6 (thalamus) and IL-6 + IL-8 (frontoparietal cortex) of the 3:1 C:V group were significantly higher, respectively.

Conclusions: Even though relatively less animals achieved ROSC, CC during SI significantly improved ROSC time compared to 3:1 C:V in asphyxiated newborn piglets. However, there was no difference in ROSC characteristics and hemodynamic recovery between two CC + SI groups.

Introduction

The majority of newborn infants successfully make the transition from fetal to neonatal life [1]. Unfortunately, an estimated 10% of newborns need assistance to establish effective ventilation [2], which remains the most critical step of neonatal resuscitation. Fortunately, the need for chest compressions (CC) or medications in the delivery room is rare (approximately 0.1% of term infants and 15% of preterm infants) [3–9]. Birth asphyxia will result in approximately 1 million newborn deaths annually worldwide. A recent review of newborns who received prolonged CC and epinephrine without signs of life at 10 min following birth noted 83% mortality, with 93% of survivors suffering moderate-to-severe disability [10]. The poor prognosis associated with receiving CC alone or with medication in the delivery room raises questions as to whether improved cardiopulmonary resuscitation (CPR) methods specifically tailored to newborns could improve outcomes.

Abbreviations: CC, chest compression; CPR, cardiopulmonary resuscitation; CC + SI, chest compression during sustained inflation; ROSC, return of spontaneous circulation; 3:1 C:V, 3:1 compression:ventilation ratio; CC + SI 20, chest compression during sustained inflation with a 20 s sustained inflation; CC + SI 60, Chest compression during sustained inflation with a 60 s sustained inflation; V_T, tidal volume; $ETCO_2$, end-tidal CO_2; $crSO_2$, cerebral oxygenation

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* Corresponding author at: Centre for the Studies of Asphyxia and Resuscitation, Neonatal Research Unit, Royal Alexandra Hospital, 10240 Kingsway Avenue NW, T5H 3V9, Edmonton, Alberta, Canada.

E-mail address: georg.schmoelzer@me.com (G.M. Schmölzer).

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Despite extensive studies during the last decade, the most effective method of delivering CC remains controversial. Although the advantage for using sustained inflation (SI) for lung aeration in the delivery room remains unknown [11,12], animal studies have reported that SI provide rapid establishment of functional residual capacity (FRC) during initial resuscitation [13]. Further, it has been shown to dramatically increase carotid blood flow during CPR, and increase antegrade blood flow [14]. We have previously demonstrated that combining CC during SI (CC + SI) significantly improves ROSC and survival in newborn piglets [15–17]. Also different CC rates (90 vs. 120/min) during CC + SI have similar ROSC [17]. A single prolonged 30 s SI, but not a series of five 3 s SI, improved circulatory recovery in asphyxiated near-term lamb [18,19]. Furthermore, it has been demonstrated that FRC increased proportionally with prolonged SI times in both preterm sheep and rabbits [13,18]. Therefore, the duration of SI may be essential for achieving optimal ventilation. Our aim was to determine whether increasing the SI duration up to 60 s will further improve hemodynamics and resuscitation outcomes in newborn piglets with asphyxia-induced asystole. Furthermore, we also aimed to examine whether CC + SI will cause undesired side-effects on brain or lung injuries by measuring injury markers (brain and lung) in these asphyxia-resuscitated animals. We hypothesized that using CC + SI with either a SI duration of 20 s (CC + SI 20 s) or 60 s (CC + SI 60 s) significantly improves ROSC compared to 3:1 C:V CPR.

Methods

Thirty newborn mixed breed piglets (1–3 days of age, weighing 2.0 kg (± 0.13 kg)) were obtained on the day of experimentation from the University Swine Research Technology Centre. All experiments were conducted in accordance with the guidelines and approval of the Animal Care and Use Committee (Health Sciences), University of Alberta and presented according to the ARRIVE guidelines [20]. A graphical display of the study protocol is presented in Fig. 1.

Randomization

Piglets were randomly allocated to control (sham-operated) or intervention (SI or 3:1 C:V) groups. Allocation was block randomized with variable sized blocks (2–4) using a computer-generated randomization program (http://www.randomizer.org). Sequentially numbered, sealed, opaque envelopes containing the allocation were opened during the experiment (Fig. 1).

Animal preparation

Piglets were instrumented as previously described with modifications [15,21,22]. Following the induction of anaesthesia using isoflurane, piglets were intubated via a tracheostomy, and pressure-controlled ventilation (Acutronic Fabian HFO; Hirzel, Switzerland) was commenced at a respiratory rate of 16–20 breaths/min and pressure of 20/5 cmH_2O. Oxygen saturation was kept within 90–100%, glucose level and hydration was maintained with an intravenous infusion of 5% dextrose at 10 mL/kg/h. During the experiment anaesthesia was maintained with intravenous propofol 5–10 mg/kg/h and morphine 0.1 mg/kg/h. Additional doses of propofol (1–2 mg/kg) and morphine (0.05–0.1 mg/kg) were also given as needed. The piglet's body temperature was maintained at 38.5–39.5 °C using an overhead warmer and a heating pad.

Hemodynamic parameters

A 5-French Argyle® (Klein-Baker Medical Inc. San Antonio, TX) double-lumen catheter was inserted via the right femoral vein for administration of fluids and medications. A 5-French Argyle® single-lumen catheter was inserted above the right renal artery via the femoral artery for continuous arterial blood pressure monitoring in addition to arterial blood gas measurements. The right common carotid artery was also exposed and encircled with a real-time ultrasonic flow probe (2 mm; Transonic Systems Inc., Ithica, NY) to measure cerebral blood flow.

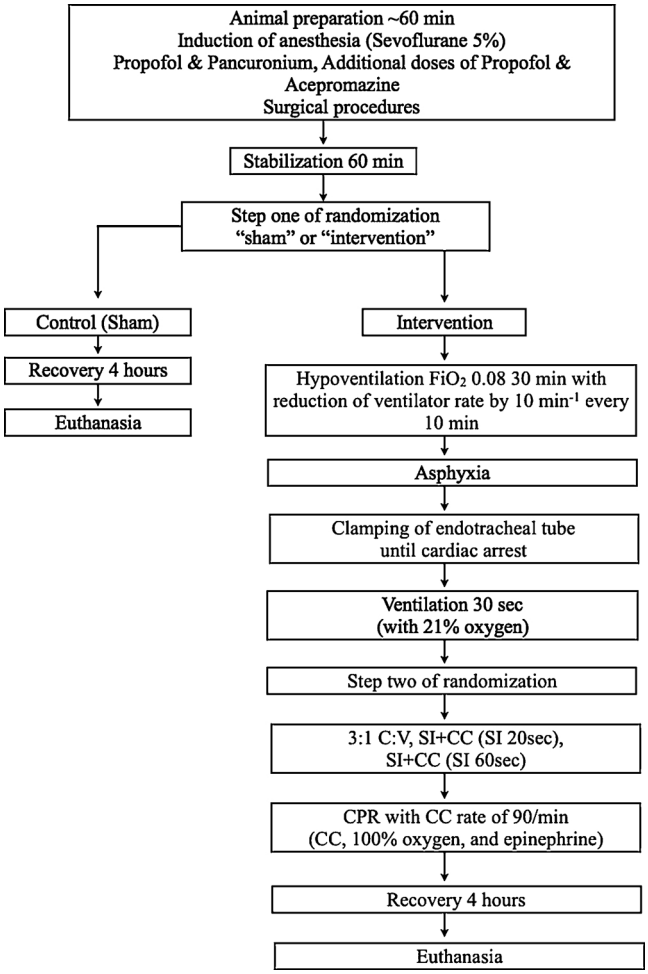

Fig. 1. Study flow chart.

Piglets were placed in supine position and allowed to recover from surgical instrumentation until baseline hemodynamic measures were stable (minimum of one hour). Ventilator rate was adjusted to keep the partial arterial CO_2 between 35–45 mmHg as determined by periodic arterial blood gas analysis. Mean systemic arterial pressure, systemic systolic arterial pressure, heart rate, and percutaneous oxygen saturation were continuously measured and recorded throughout the experiment with a Hewlett Packard 78833B monitor (Hewlett Packard Co., Palo Alto, CA).

Respiratory parameters

A respiratory function monitor (NM3, Respironics, Philips, Andover, MA) was used to continuously measure tidal volume (V_T), airway pressures, gas flow, and end-tidal CO_2 ($ETCO_2$). The combined gas flow and $ETCO_2$ sensor was placed between the endotracheal tube and the ventilation device. V_T was calculated by integrating the flow signal [23]. $ETCO_2$ was measured using non-dispersive infrared absorption technique. The accuracy for gas flow is ± 0.125 L/min, $ETCO_2$ ± 2 mmHg [24].