Resuscitation 111 (2017) 68–73

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Randomised controlled trial of sustained lung inflation for resuscitation of preterm infants in the delivery room[☆,☆☆]

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ARTICLE INFO

Article history:
Received 4 August 2016
Received in revised form 4 November 2016
Accepted 1 December 2016

Keywords:
Preterm infant
Resuscitation
Sustained lung inflation

ABSTRACT

Aim: To compare the effects of sustained lung inflation (SLI) vs. standard resuscitation on physiologic responses of preterm infants during resuscitation.
Methods: Preterm infants (25–32 weeks gestational age) requiring positive-pressure ventilation or continuous positive airway pressure were randomly assigned to either the SLI group (SLI at 25 cmH_2O for 15 s) or Non-SLI group (standard resuscitation alone). The heart rate (HR), oxygen saturation (SpO_2), oxygen requirement, and intubation rate in the delivery room were evaluated.
Results: Eighty-one infants were enrolled (SLI group, 43; Non-SLI group, 38). The use of SLI effectively reduced the oxygen requirement. The mean fraction of inspired oxygen 10 min after birth was 0.28 (95% CI, 0.26–0.30) in the SLI group and 0.47 (95% CI, 0.43–0.52) in the Non-SLI group ($p < 0.001$). During the first 5 min, infants in the SLI group trended towards a higher HR and SpO_2 than those in the Non-SLI group. The intubation rate in the delivery room was not different between the two groups; however, among infants ≤28 weeks gestational age, the intubation rate was lower in the SLI than Non-SLI group (5 of 17 [29%] vs. 10 of 16 [63%], respectively; $p = 0.05$). The duration of respiratory support, survival without bronchopulmonary dysplasia, and the occurrence of pneumothorax were not different between the groups.
Conclusion: SLI in infants who require respiratory support appears to be effective in facilitating postnatal transition as determined by HR and SpO_2 responses, resulting in less oxygen supplementation. Further studies are needed to confirm the benefits of SLI.

Introduction

Replacement of lung fluid by air to establish a gaseous functional residual capacity (FRC) is indispensable for successful transition after birth. Clinical and laboratory observations have indicated that application of continuous positive airway pressure (CPAP) helps to establish a gaseous FRC and improves gas exchange.[1,2] Application of sustained lung inflation (SLI) for 10–20 s further enhances movement of lung fluid into the distal airways, resulting in an increased FRC and more uniform lung aeration than CPAP alone.[3,4]

Very preterm infants generally have difficulty getting through this transitional period because of poor respiratory effort, immature lungs, inadequate surfactant, and high chest wall compliance.[5] Appropriate respiratory support is therefore needed immediately after birth to maintain respiratory function. The American Heart Association currently recommends the use of CPAP in spontaneously breathing premature infants with respiratory distress and, because of insufficient evidence, careful consideration of the use of SLI in certain individual clinical circumstances or in the research setting.[6]

In term infants, the first few breaths differ from other breaths with respect to a prolonged inspiratory phase, high positive intrathoracic pressure, and interspersion of brief inspiratory components.[7–10] The phase of high positive pressure is postulated to facilitate the distribution of air within the lungs and assist formation of the FRC.[10,11] Therefore, lung protection strategies could be initiated in the delivery room from the first few breaths.

Abbreviations: CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen; FRC, functional residual capacity; GA, gestational age; HR, heart rate; MV, mechanical ventilation; PPV, positive-pressure ventilation; ROP, retinopathy of prematurity; SLI, sustained lung inflation; SpO_2, oxygen saturation.

☆ 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.2016.12.003.

☆☆ Thai Clinical Trial Registration number: TCTR20140418001.

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http://dx.doi.org/10.1016/j.resuscitation.2016.12.003
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Clinical evidence shows that effective resuscitation, especially during the first 1–2 min after birth, is the key to successful resuscitation.[12] Effective resuscitation results in immediate improvement in the oxygen saturation (SpO_2) and heart rate (HR) and reduces the oxygen requirement during resuscitation.[13,14]

Performance of the SLI manoeuvre through delivery of a brief period of peak pressure (20–30 cmH_2O) to the airways via a nasopharyngeal tube or mask may permit lung recruitment immediately after birth.[15–17] This has been shown to be an effective method to establish an FRC in animal models.[3,18–20] However, a meta-analysis of clinical studies using SLI for resuscitation of infants in delivery rooms showed contradictory results.[21] Some studies[22–27] have revealed that early performance of the SLI procedure effectively decreases the need for mechanical ventilation (MV) and improves respiratory outcomes in preterm infants, but other studies[28,29] have demonstrated no benefit.

Information regarding the immediate effects of SLI on physiologic responses (i.e., oxygen requirement, SpO_2, and HR) during resuscitation in the delivery room is very limited.[30] Therefore, we compared the effects of SLI vs. standard resuscitation on physiologic responses during the transitional period after birth. We hypothesised that use of the SLI manoeuvre to resuscitate preterm infants at risk of respiratory distress is safe and effective in facilitating smooth transitional adaptation.

Methods

This randomised controlled trial was conducted from November 2013 to March 2015 in the delivery room of the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. The study protocol (***ID** 01-57-14*) was approved by the Institutional Ethics Committee. Written informed consent was obtained from the parents of all infants before delivery of admitted pregnant women who were expected to have an inevitably preterm delivery. We included newly born infants with a gestational age (GA) of 25–32 weeks who required respiratory support soon after birth by either positive-pressure ventilation (PPV) or CPAP in the delivery room. We excluded infants with major congenital anomalies, hydrops foetalis, a prenatal diagnosis of upper airway obstruction, or meconium-stained amniotic fluid. The study was registered in the Thai Clinical Trials Registry (TCTR20140418001).

Randomisation

The infants were randomly assigned to receive either SLI (SLI group) or standard newborn resuscitation (Non-SLI group) under a block of 4 randomisation stratified by GA (25–28 weeks and 29–32 weeks). The sequence numbers were kept in opaque sealed envelopes that were opened just before birth in the delivery room by a person not involved in resuscitation of the infants. Infants of multiple gestations were enrolled in the same intervention group. The assigned intervention could not be blinded to the resuscitation team because of the obvious differences in the intervention manoeuvres.

Study intervention

All enrolled infants underwent initial standard resuscitation according to the American Heart Association 2010 Guidelines.[31] Immediately after birth, while the infant was still covered with a polyethylene plastic bag to prevent hypothermia, an oximeter probe was placed on the right hand or wrist and connected to a pulse oximeter. After oropharyngeal and nasal suctioning, infants requiring PPV or CPAP were enrolled into the assigned groups.

In the SLI group, the infants underwent pressure-controlled (25 cmH_2O) inflation that was sustained for 15 s using a properly sized neonatal mask via a T-piece resuscitator (Neopuff Infant T-Piece Resuscitator; Fisher & Paykel, Auckland, New Zealand) followed by delivery of CPAP at 6 cmH_2O via a face mask for 5–10 s. Their cardiorespiratory status was then re-evaluated. The next steps of resuscitation were as follows. (1) If the HR was ≥100 beats/min and respiratory effort was improved, CPAP via the face mask was continued. (2) If the HR was ≤60 beats/min, PPV was initiated. (3) If the HR was 60–100 beats/min and/or the respiratory effort was poor, a second SLI manoeuvre was initiated similar to the first SLI manoeuvre. If the HR was ≤100 beats/min or gasping/apnoea was present during the second SLI manoeuvre, PPV was initiated and further resuscitation steps were performed according to the Neonatal Resuscitation Program 2010 Guidelines[31]; otherwise, if the HR was ≥100 beats/min and no apnoea/gasping was present during the second SLI manoeuvre, CPAP was performed via a face mask. A flow chart of the resuscitation protocol in the SLI group is shown in Fig. 1. The physicians comprising the research team had been trained to perform the SLI technique before starting the study and were the only persons responsible for performing SLI during resuscitation.

In the Non-SLI group, PPV was given via a T-piece resuscitator with a peak inspiratory pressure of 15–20 cmH_2O and positive end-expiratory pressure of 5 cmH_2O for 30 s, and the next step of resuscitation was performed according to the guidelines.[31] Infants were placed on CPAP at 6 cmH_2O via a face mask if they still had laboured breathing.

All enrolled infants were resuscitated with an initial fraction of inspired oxygen (FiO_2) of 0.3, which was adjusted by 0.1 every 30 s to achieve the target SpO_2 specified in the guidelines.[31] An FiO_2 of 1.0 was applied when one of the following occurred: (1) chest compressions were begun or (2) the target SpO_2 was not reached by 5 min after birth. The criteria for intubation included one of the following: remaining apnoea after PPV, HR of <100 beats/min after effective ventilation via a face mask for >30 s before starting chest compressions, or an SpO_2 of <80% despite CPAP via a mask with an FiO_2 of 1.0 for 5–10 min.

During resuscitation, the pulse oximeter (Radical-7; Masimo Corporation, Irvine, CA) was set at the maximum sensitivity to monitor the HR and SpO_2. The HR and SpO_2 data were recorded continuously and displayed on a Microsoft Excel spreadsheet for further analysis, as in our previous study.[32]

Outcome measures and data collection

The primary outcomes were changes in the oxygen requirement, HR, and SpO_2 during resuscitation; the proportion of infants on room air during the first 10 min after birth; and the need for intubation in the delivery room. The secondary outcomes were survival at discharge, duration of hospitalisation, proportion of infants on MV within the first 72 h of life, duration of MV, duration of oxygen supplementation, need for surfactant, need for postnatal steroids, pneumothorax within the first 48 h after neonatal intensive care unit admission, and moderate to severe bronchopulmonary dysplasia as defined by Jobe and Bancalari.[33] Other data recorded for each infant included GA, birth weight, sex, Apgar score at 5 min, use of completed course of antenatal steroids, occurrence of pneumothorax, patent ductus arteriosus and need of surgical closure, grade 3 to 4 intraventricular haemorrhage, cystic periventricular leukomalacia, stage >2 retinopathy of prematurity (ROP), and ROP requiring treatment.

Statistical analysis

The chi-squared test and Fisher's exact test were used for categorical variables, whereas Student's *t* test or the Mann–Whitney *U* test (if data were not normally distributed) was used for continuous