

**Cochrane** Database of Systematic Reviews

# Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review)

Bruschettini M, O'Donnell CPF, Davis PG, Morley CJ, Moja L, Zappettini S, Calevo MG

Bruschettini M, O'Donnell CPF, Davis PG, Morley CJ, Moja L, Zappettini S, Calevo MG. Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD004953. DOI: 10.1002/14651858.CD004953.pub3.

# www.cochranelibrary.com

Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review)

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



# [Intervention Review]

# Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes

Matteo Bruschettini<sup>1,2</sup>, Colm PF O'Donnell<sup>3</sup>, Peter G Davis<sup>4,5,6</sup>, Colin J Morley<sup>7</sup>, Lorenzo Moja<sup>8,9</sup>, Simona Zappettini<sup>10</sup>, Maria Grazia Calevo<sup>11</sup>

<sup>1</sup>Department of Paediatrics, Lund University, Skåne University Hospital, Lund, Sweden. <sup>2</sup>Research & Development, Section for HTA Analysis, Skåne University Hospital, Lund, Sweden. <sup>3</sup>Department of Neonatology, National Maternity Hospital, Dublin 2, Ireland. <sup>4</sup>The University of Melbourne, Melbourne, Australia. <sup>5</sup>Murdoch Childrens Research Institute, Melbourne, Australia. <sup>6</sup>The Royal Women's Hospital, Parkville, Australia. <sup>7</sup>Department of Obstetrics and Gynecology, University of Cambridge, Cambridge, UK. <sup>8</sup>Department of Biomedical Sciences for Health, University of Milan, Milan, Italy. <sup>9</sup>Unit of Clinical Epidemiology, IRCCS Galeazzi Orthopaedic Institute, Milan, Italy. <sup>10</sup>Regional Health Agency of the Liguria Region, Genoa, Italy. <sup>11</sup>Epidemiology, Biostatistics and Committees Unit, Istituto Giannina Gaslini, Genoa, Italy

**Contact address:** Matteo Bruschettini, Department of Paediatrics, Lund University, Skåne University Hospital, Lund, Sweden. matteo.bruschettini@med.lu.se, matbrus@gmail.com.

# Editorial group: Cochrane Neonatal Group.

Publication status and date: Edited (no change to conclusions), published in Issue 7, 2017.

**Citation:** Bruschettini M, O'Donnell CPF, Davis PG, Morley CJ, Moja L, Zappettini S, Calevo MG. Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes. *Cochrane Database of Systematic Reviews* 2017, Issue 7. Art. No.: CD004953. DOI: 10.1002/14651858.CD004953.pub3.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

# ABSTRACT

# Background

At birth, infants' lungs are fluid-filled. For newborns to have a successful transition, this fluid must be replaced by air to enable effective breathing. Some infants are judged to have inadequate breathing at birth and are resuscitated with positive pressure ventilation (PPV). Giving prolonged (sustained) inflations at the start of PPV may help clear lung fluid and establish gas volume within the lungs.

# Objectives

To assess the efficacy of an initial sustained (> 1 second duration) lung inflation versus standard inflations (≤ 1 second) in newly born infants receiving resuscitation with intermittent PPV.

# Search methods

We used the standard search strategy of the Cochrane Neonatal Review Group to search the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 1), MEDLINE via PubMed (1966 to 17 February 2017), Embase (1980 to 17 February 2017), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1982 to 17 February 2017). We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles to identify randomised controlled trials and quasi-randomised trials.

# **Selection criteria**

Randomised controlled trials (RCTs) and quasi-RCTs comparing initial sustained lung inflation (SLI) versus standard inflations given to infants receiving resuscitation with PPV at birth.

# Data collection and analysis

We assessed the methodological quality of included trials using Cochrane Effective Practice and Organisation of Care Group (EPOC) criteria (assessing randomisation, blinding, loss to follow-up, and handling of outcome data). We evaluated treatment effects using a fixed-effect model with risk ratio (RR) for categorical data and mean, standard deviation (SD), and weighted mean difference (WMD) for continuous

Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review) Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



data. We assessed the quality of evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

#### **Main results**

Eight trials enrolling 941 infants met our inclusion criteria. Investigators in seven trials (932 infants) administered sustained inflation with no chest compressions. Use of sustained inflation had no impact on the primary outcomes of this review - mortality in the delivery room (typical RR 2.66, 95% confidence interval (CI) 0.11 to 63.40; participants = 479; studies = 5; I<sup>2</sup> not applicable) and mortality during hospitalisation (typical RR 1.01, 95% CI 0.67 to 1.51; participants = 932; studies = 7; I<sup>2</sup> = 19%); the quality of the evidence was low for death in the delivery room (limitations in study design and imprecision of estimates) and was moderate for death before discharge (limitations in study design of most included trials). Amongst secondary outcomes, duration of mechanical ventilation was shorter in the SLI group (mean difference (MD) -5.37 days, 95% CI -6.31 to -4.43; participants = 524; studies = 5; I<sup>2</sup> = 95%; low-quality evidence). Heterogeneity, statistical significance, and magnitude of effects of this outcome are largely influenced by a single study: When this study was removed from the analysis, the effect was largely reduced (MD -1.71 days, 95% CI -3.04 to -0.39, I<sup>2</sup> = 0%). Results revealed no differences in any of the other secondary outcomes (e.g. rate of endotracheal intubation outside the delivery room by 72 hours of age (typical RR 0.93, 95% CI 0.79 to 1.09; participants = 811; studies = 5;  $l^2 = 0\%$ ); need for surfactant administration during hospital admission (typical RR 0.97, 95% CI 0.86 to 1.10; participants = 932; studies = 7; l<sup>2</sup> = 0%); rate of chronic lung disease (typical RR 0.95, 95% CI 0.74 to 1.22; participants = 683; studies = 5;  $l^2 = 47\%$ ); pneumothorax (typical RR 1.44, 95% Cl 0.76 to 2.72; studies = 6, 851 infants;  $l^2 = 26\%$ ); or rate of patent ductus arteriosus requiring pharmacological treatment (typical RR 1.08, 95% CI 0.90 to 1.30; studies = 6, 745 infants; I<sup>2</sup> = 36%). The quality of evidence for these secondary outcomes was moderate (limitations in study design of most included trials - GRADE) except for pneumothorax (low quality: limitations in study design and imprecision of estimates - GRADE).

#### **Authors' conclusions**

Sustained inflation was not better than intermittent ventilation for reducing mortality in the delivery room and during hospitalisation. The number of events across trials was limited, so differences cannot be excluded. When considering secondary outcomes, such as need for intubation, need for or duration of respiratory support, or bronchopulmonary dysplasia, we found no evidence of relevant benefit for sustained inflation over intermittent ventilation. The duration of mechanical ventilation was shortened in the SLI group. This result should be interpreted cautiously, as it can be influenced by study characteristics other than the intervention. Future RCTs should aim to enrol infants who are at higher risk of morbidity and mortality, should stratify participants by gestational age, and should provide more detailed monitoring of the procedure, including measurements of lung volume and presence of apnoea before or during the SLI.

# PLAIN LANGUAGE SUMMARY

# Prolonged lung inflation for neonatal resuscitation

#### **Review question**

Does the use of prolonged (or sustained, > 1 second duration) lung inflation rather than standard inflations (≤ 1 second) improve survival and other important outcomes among newly born babies receiving resuscitation at birth?

# Background

At birth, the lungs are filled with fluid, which must be replaced by air for babies to breathe properly. Some babies have difficulty establishing effective breathing at birth, and 1 in every 20 to 30 babies receives help to do so. A variety of devices are used to help babies begin normal breathing. Some of these devices allow caregivers to give long (or sustained) inflations. These sustained inflations may help inflate the lungs and may keep the lungs inflated better than if they are not used.

#### Study characteristics

We collected and analysed all relevant studies to answer the review question and found eight studies enrolling 941 infants. In all studies, babies were born before the due date (from 23 to 36 weeks of gestational age). The sustained inflation lasted between 15 and 20 seconds at pressure between 20 and 30 cmH<sub>2</sub>O. Most studies provided one or more additional sustained inflations in cases of poor clinical response, for example, persistent low heart rate. We analysed one study (which included only nine babies) separately because researchers combined use of sustained or standard inflations with chest compressions.

#### **Key results**

The included studies showed no important differences among babies who received sustained versus standard inflations in terms of mortality, need for intubation during the first three days of life, or chronic lung disease. Babies receiving sustained inflation at birth may spend fewer days on mechanical ventilation. Several ongoing studies might help us to clarify whether differences between the two techniques may occur, as now we cannot exclude that small to moderate differences exist.

# **Quality of evidence**

Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review) Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



The quality of evidence is low to moderate because overall only a small number of studies have looked at this intervention; few babies were included in these studies; and some studies could have been better designed.

#### How up-to-date is this review?

We searched for studies that had been published up to February 2017.

Sustained versus standard inflations during neonatal resuscitation to prevent mortality and improve respiratory outcomes (Review) Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.