Lung recruitment manoeuvres for reducing respiratory morbidity in mechanically ventilated neonates (Protocol)

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[Intervention Protocol]

Lung recruitment manoeuvres for reducing respiratory morbidity in mechanically ventilated neonates

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To determine the evidence supporting the use of recruitment manoeuvres in mechanically ventilated neonates and identify the optimal method of lung recruitment. To determine the effects of lung recruitment manoeuvres in neonates receiving ventilatory support on neonatal mortality and development of chronic lung disease when compared to no recruitment.

If data are available, subgroup analyses will include:

chronological age, gestational age, lung pathophysiology and pre-existing lung disease, mode and length of ventilation, timing and frequency of recruitment techniques.

BACKGROUND

Description of the condition

Critically ill neonates commonly require intubation and mechanical ventilation. While this therapy is lifesaving, it is not without inherent problems (Dahlem 2003). Mechanical ventilation leads to lung injury and has been shown to aggravate proteinaceous lung oedema causing epithelial disruption and resulting in marked changes in lung perfusion (Nilsson 1978; Berry 1991; Hedenstierna 2005). Lung injury leads to reduced compliance, deteriorating shunt fraction and an inflammatory response that results from high transpulmonary pressures at end inspiration and inadequate end expiratory lung volume at end expiration (Artigas 1998; The ARDS Network 2000; Dyhr 2003; Schibler 2006). High levels of inspired oxygen also contribute to lung injury (Marraro 2005; Theil 2005; Sinclair 2004).

Lung injury induced by the ventilator is termed ventilator associated lung injury (VALI), also known as ventilator induced lung injury (VILI) (Frank 2002; Dyhr 2003). It can lead to acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), increased length of ventilation and length of stay, and can lead to chronic pulmonary impairment (Villagra 2002). In the preterm infant, secondary lung injury resulting from mechanical ventilation is considered one of the major precipitating factors for the development of chronic lung disease (CLD) (Clark 2001). The sequelae of CLD do not differ markedly from those caused by VALI in that infants with CLD have both reduced compliance and reactive airways disease (Donn 2003). Neonates with VALI and CLD have significant morbidity requiring prolonged respiratory support and oxygen therapy, an increased hospital stay and are a leading cause of late mortality (Clark 2001; Dahlem 2003; Hanson 2006; Halbertsma 2007).

Lung Protective Ventilation Strategies (LPVS) developed by the ARDS Network were devised to minimise the detrimental effects of ventilation in adults. They have largely been extrapolated to paediatric and neonatal populations (Arnold 2002). LPVS demands low tidal volumes ($\leq$ 6 ml/kg), adequate positive end expiratory pressure (PEEP) and clinician tolerance of relative hypoxia and hypercapnia (Woodgate 2001; Hanson 2006; Von Ungern-Sternberg 2007; Meade 2008). LPVS minimise high peak inspiratory pressures and inadequate functional residual capacity (FRC) by minimising tidal volumes and maintaining PEEP at a level that maintains alveolar patency (Dyhr 2003; Von Ungern-Sternberg 2007). Chronic de-recruitment of distal and dependant alveoli is possible with LPVS (Hanson 2006; Hinz 2007; Wolf 2007). Additionally, a rapid, profound and inhomogeneous de-recruitment of alveoli occurs with each disconnection of the endotracheal tube from the circuit and this is exacerbated by the application of suction (Cunha-Goncalves 2007; Lindgren 2007; Heinze 2008). Suctioning of the endotracheal tube to extricate secretions occurs regularly and routinely in intubated neonates.

Lung recruitment manoeuvres are postulated to be a means of reducing lung injury in intubated and mechanically ventilated neonates (Rimensberger 2000; Marcus 2002; Villagra 2002; Duff 2007; Halbertsma 2007; Jauncey-Cooke 2010).

Description of the intervention

Lung recruitment describes the process in which a deliberate technique is applied to transiently elevate airway pressures in the ventilated patient in order to maximise the number of alveoli participating in gas exchange (Arnold 2002; Dyhr 2003).

There are various methods of recruiting alveoli and a consensus is yet to be achieved as to which is the most effective at reducing respiratory morbidity (Gattinoni 1993; Dyhr 2003; Maggiore 2003; Lim 2004a; Borges 2006; Halter 2007; Morrow 2007; Syring 2007; Wolf 2007; Gattinoni 2008; Hodgson 2009). Lung recruitment is most commonly achieved by either manipulating end expiratory lung volume with positive end expiratory pressure (PEEP) or end inspiratory lung volume by using inspiratory holds or sustained inflation. The sustained inflation manoeuvre (SI) consists of applying a high pressure to the lung that is sustained for a short period (30 sec) before returning to previous mean airway pressures (Kolton 1982; Walsh 1988). This volume recruitment strategy has been shown to be as protective as high-frequency oscillation at similar lung volumes (Rimensberger 2000). Theoretically, a combined peak inspiratory pressure (PIP) and PEEP elevation is the most effective manoeuvre as recruitment and de-recruitment are continuous processes throughout the ventilatory cycle, during which PIP recruits alveoli and PEEP maintains alveolar patency (Halter 2003; Barbas 2005). With isolated PIP increases (manual recruitment manoeuvres) there is a risk of alveolar overdistension and increased shear stress forces in non-stabilised alveoli and it has been suggested that the increases should only be used when there is a need to rapidly recruit collapsed alveoli, such as with endotracheal suctioning (Maggiore 2003). Sustained elevation of PEEP is thought to be less injurious and lead to increases in pulmonary aeration (Dreyfuss 1988).

There is the potential that recruitment manoeuvres may result in adverse effects (Claesson 2003; Lim 2004b; Nunes 2004; Toth 2007). Increasing intrathoracic pressure may reduce cardiac output, impacting on perfusion and may increase intracranial pressure as a consequence of the returning pressure differential, which may impact on the incidence and severity of intracranial ventricular haemorrhage (IVH) (Graham 2006; Nielsen 2006; Duff 2007). Lung recruitment manoeuvres may increase the incidence of air leak, especially pneumothorax and pulmonary interstitial emphysema (Odenstedt 2005). The association between neonatal chronic lung disease (CLD) and bronchopulmonary dysplasia (BPD) and lung recruitment is unknown.

How the intervention might work

Despite the potential that recruitment manoeuvres may result in adverse events of the cardiovascular system, it is thought that they will minimise adverse events associated with suction and disconnection from the ventilator and therefore reduce the incidence of lung injury. It is proposed that lung recruitment manoeuvres may restore end expiratory lung volume (EELV) resulting in more stable alveoli. This may then minimise shearing injury to the alveoli associated with cyclic opening and closing.

Why it is important to do this review

It is known that lung recruitment in adults post-suctioning is effective (Lapinsky 1999; Dyhr 2003; Maggiore 2003; Almgren 2004), however the use of lung recruitment procedures has seldom been reported in infants and children (Sargent 2002; Morrow 2007; Jobe 2009). There is no consensus of opinion as to whether lung recruitment in neonates is appropriate or that it minimises the incidence of lung injury. The intent of this review is to establish what evidence exists for the use of recruitment manoeuvres in ventilated neonates and thus to inform clinical practice.

OBJECTIVES

To determine the evidence supporting the use of recruitment manoeuvres in mechanically ventilated neonates and identify the optimal method of lung recruitment. To determine the effects of lung recruitment manoeuvres in neonates receiving ventilatory support on neonatal mortality and development of chronic lung disease when compared to no recruitment.

If data are available, subgroup analyses will include:

chronological age, gestational age, lung pathophysiology and pre-existing lung disease, mode and length of ventilation, timing and frequency of recruitment techniques.

METHODS

Criteria for considering studies for this review

Types of studies

We will include prospective, randomised controlled trials (RCTs) that compare ventilation management with recruitment manoeuvres to ventilation with no recruitment manoeuvres in neonatal patients. We will include all RCTs and quasi-randomised controlled trials (that is, trials in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) evaluating the effect of recruitment manoeuvres administered to mechanically ventilated neonates. We will also include randomised cross-over studies.

Types of participants

We will include neonatal participants from birth, irrespective of gestational age (including term and preterm infants), up to four weeks of age or participants that authors define as neonates. Participants will be intubated and undergoing mechanical ventilation.
In this review mechanical ventilation is defined as any invasive method of positive pressure ventilation via either an endotracheal tube or tracheostomy.
In paediatric studies that may have included neonates, we will contact the authors to determine if the neonatal data can be isolated.

Types of interventions

We will define recruitment manoeuvres as a deliberate effort to elevate pulmonary pressures in order to increase the percentage of alveoli participating in alveolar ventilation. We will communicate with authors of studies to determine the precise method of lung recruitment.

Types of outcome measures

Primary outcomes

1. Mortality (death within 28 days of birth and mortality to discharge).
2. Prevalence of chronic lung disease (CLD):
   i) supplemental oxygen at 36 weeks post-menstrual age (PMA);
   ii) supplemental oxygen at 28 days of life;
   iii) requirement for home oxygen therapy.
3. Duration of supplemental oxygen after intervention (days).
4. Duration of ventilatory support: mechanical ventilation (MV) and continuous positive airway pressure (CPAP) (hours or days).
5. Duration of neonatal intensive care unit (NICU) stay (hours or days).
6. Duration of hospital stay (days).

Secondary outcomes

1. Incidence of air leak (e.g., pneumothorax and pulmonary interstitial emphysema).
2. Lung compliance as measured by respiratory mechanics monitor pre- and post-recruitment.
3. Oxygenation during intervention as reported in study:
   i) incidence of hypoxaemia (SaO_2 < 90% or PaO_2 < 50 mm Hg);

ii) Incidence of hyperoxaemia (SaO_2 > 94% or PaO_2 > 80 mm Hg);

iii) incidence of hypocarbia ($PaCO_2$ < 30 mm Hg);

iv) incidence of hypercarbia ($PaCO_2$ > 55 mm Hg).

4. Bradycardia (change in heart rate to < 30% of baseline or < 100 beats per minute) during intervention, as reported in study.

5. Blood pressure (change in baseline by 20%) during or post-intervention, as reported in study.

6. End expiratory lung volume as measured by computed tomography or electrical impedance tomography, or both, pre-, during and post-intervention.

7. Rates and types of intracranial lesions diagnosed by ultrasound scan:

i) intraventricular haemorrhage (IVH), any IVH, grade 3 and 4 (Papile 1978);

ii) periventricular leukomalacia (PVL).

8. Neurodevelopmental impairment: cerebral palsy, sensorineural hearing loss, visual impairment or developmental delay (e.g. Griffith's or Bayley Scales of Infant Development) assessed at 12 to 24 months corrected age, two years, or five years.

Search methods for identification of studies

We will obtain all relevant studies irrespective of language or publication status (published, unpublished, in press, and in progress) using the following methods. See the Appendix for the search strategy.

Electronic searches

We will search the current issue of the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*); MEDLINE via Ovid (January 1966 to present); EMBASE via Ovid (January 1980 to present); CiNAHL via EBSCO host (1982 to present); LILACS (1982 to present).

We will search the following electronic databases of higher degree theses for relevant unpublished trials: Index to Theses (1950 to date), Australian Digital Theses Program (1997 to date) and Proquest Digital Dissertations (1980 to date).

We will combine our MEDLINE search strategy with the Cochrane highly sensitive search strategy for identifying Randomised controlled trials (RCTs) as suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). We will adapt the search strategy for MEDLINE for searching in all other databases. See Appendices: CENTRAL, Appendix 1; MEDLINE, Appendix 2; EMBASE, Appendix 3; CINAHL, Appendix 4; LILACS, Appendix 5.

Searching other resources

We will handsearch citations.

We will not exclude studies on the basis of language.

We will contact authors known in the field to determine if unpublished work is available.

Data collection and analysis

Selection of studies

Eight authors (JJC, AS, FB, KG, JH, MD, CG and CE) will undertake the review. We will use the search strategy described to obtain titles and abstracts of studies that may be relevant to the review. Two authors (JJC and CG) will independently screen all titles and abstracts. We will discard studies that are not applicable, although initially we will retain studies and reviews that might include relevant data or information on trials. We (JJC, CG) will independently assess retrieved abstracts, and if necessary the full text of these studies, to determine which studies satisfy the inclusion criteria. We will describe our reasons for excluding studies in the table 'Characteristics of excluded studies'. We will resolve disagreement by discussion and in consultation with CE.

Data extraction and management

We will adapt the standardised Cochrane Neonatal Review Group data extraction form to capture relevant data specific to this review. We (JJC and CG) will use this form to extract data from relevant studies. We (JJC and CG) will independently perform data extraction and quality assessment of eligible trials. We will pilot the standardised form using a representative sample of trials to ensure consistency of reporting between the review authors. We will revise the tools if we find inconsistencies. We will translate studies reported in non-English language journals before assessment. Where more than one publication of one trial exists, we will only include the publication with the most complete data. Where relevant outcomes are only published in other versions, we will use this data. We will highlight any discrepancy between published versions. We will request any further information required from the original author by written correspondence and we will include any relevant information obtained in this manner in the review. We will resolve disagreements by consensus and in consultation with CE.

Assessment of risk of bias in included studies

We will appraise the methodological quality of each trial and will include assessment of bias (selection, performance, detection and attrition). We will grade the method of treatment allocation and concealment of the allocation by using the GRADE approach, as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). We will assess the levels of quality of a body of evidence using the GRADE approach. We will assess other aspects of methodological quality using a standardised checklist with each individual component recorded as: yes, no or unclear.

The primary author will enter the data into the Review Manager Software (RevMan 5.0) with verification of data entry conducted independently. For each study we will construct a risk of bias graph and risk of bias summary figure from the risk of bias table.

Measures of treatment effect

We will summarise trials that meet the inclusion criteria in tables to enable comparison of trial characteristics and individual components of the quality assessment. We will tabulate the bibliographic details of trials excluded from the review with the reasons for exclusion documented. We will discuss the level of agreement between review authors during the screening, data extraction and critical appraisal process in a narrative form. We will review the summary tables of included trials to identify substantial clinical heterogeneity amongst trials. If there are two or more randomised trials with comparable populations undergoing similar interventions, we will implement a meta-analysis using RevMan 5.0 software. If there is clear evidence of heterogeneity among trials or their populations, we will undertake a narrative summary of the findings.

We will quantitatively analyse outcomes from comparable trials to estimate each trial's treatment effect with 95% confidence intervals (CI). We will compare the results graphically within forest plots with risk ratio (RR) as the point estimate for dichotomous outcomes and mean difference (MD) for continuous outcomes. We will calculate standardised mean difference (SMD) if different scales are used to measure continuous outcomes across trials. We will conduct a meta-analysis of pooled data using RevMan 5.0 to provide a summary statistic of effect if the combined data have minimal statistical heterogeneity (Sutton 2008).

Unit of analysis issues

We will conduct a sensitivity analysis on data pooled within a meta-analysis. We will analyse individual components of the standardised quality assessment separately in order to examine their impact on the review's findings. It is not feasible to blind health professionals providing the lung recruitment; therefore we will not subject participant and caregiver blinding to sensitivity analysis. We will compare the results with or without trials by addressing adequate randomisation, adequate concealed allocation, outcome assessor blinding, standard management and co-interventions applied equally across groups, and loss to follow up of less than 20% with an intention-to-treat analysis. We will undertake a sensitivity analysis based on the choice of summary statistic and on the presence of outlying trials. In addition, we are aware that requests for missing data from trial authors may or may not be successful. We will consider assessment for publication bias through funnel plots if there are more than 10 included trials. A large number of trials are required to provide moderate power for detection of publication bias (Higgins 2008).

We will include cross-over trials and cluster randomised trials in the review. We will consider the wash-out period in each cross-over trial in determining whether any carry-over effect is possible on subsequent measurements (Higgins 2008). We will also confirm that the order of treatments have been randomised (Higgins 2008). We will attempt to access paired and unpaired data (Higgins 2008). We will consider cross-over studies only in reference to secondary outcomes.

Dealing with missing data

In the first instance we will contact the study authors to source missing data. If the study author either does not respond or it is not possible to find them, we will include the trial in question in the review but will analyse its inclusion and exclusion for overall effect on the results as part of the sensitivity analysis.

Assessment of heterogeneity

We will analyse heterogeneity using a Chi^2 test on N - 1 degrees of freedom, with an alpha of 0.1 used for statistical significance and with the I^2 test (Higgins 2008). I^2 values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity. We will test for homogeneity between trials for each outcome using the Cochran's Q statistic, with P less than or equal to 0.10. We will formally test for the impact of heterogeneity by using the I^2 test (Higgins 2008). We will set an I^2 threshold of greater than 50% to indicate that variation across trials due to heterogeneity is substantial. We will examine possible sources of substantial heterogeneity through a summary of trial characteristics and quality. We will use a fixed-effect model if we find insignificant heterogeneity between trials. We will use a random-effects model if significant heterogeneity exists among trials (Higgins 2008).

Clinical heterogeneity may exist due to the nature of the inclusion criteria. Clinical differences could include age at enrolment in the trials, gestation etc. Positive pressure breaths may alter the effects of lung recruitment compared to spontaneous, pressure supported breathing. Therefore, we will undertake subgroup analysis to examine possible clinical variability when the I^2 statistic is less than 50% but heterogeneity remains statistically significant. We will analyse outcome data from trial populations rather than individuals to explain possible sources of variability.

We will examine differences in populations based on age (corrected) and disease status, in particular pulmonary pathology.

Assessment of reporting biases

We will assess publication bias or a systematic difference between smaller and larger studies (small study effects) by preparing a funnel plot, assuming we source at least 10 studies.

Data synthesis

We will tabulate studies that meet the inclusion criteria to enable comparison of trial characteristics and individual components of the quality assessment. We will also tabulate the bibliographic details of trials excluded from the review with the reason for exclusion documented.

We will review the summary tables of included trials to identify clinical heterogeneity amongst trials. If there are two or more randomised trials with comparable populations undergoing similar interventions, we will implement a meta-analysis with a random-effects model using RevMan 5.0 software. If there is clear evidence of heterogeneity among trials, we will undertake a narrative summary of the findings (Sutton 2008).

We will quantitatively analyse outcomes from comparable trials to estimate each trial's treatment effect with 95% confidence intervals (CI). We will compare the results graphically within forest plots with risk ratio (RR) as the point estimate for dichotomous outcomes and mean difference (MD) for continuous outcomes. We will calculate standardised mean difference (SMD) if different scales are used to measure continuous outcomes across trials. We will conduct a meta-analysis of pooled data to provide a summary statistic of effect if the combined data have minimal statistical heterogeneity (Higgins 2008).

Subgroup analysis and investigation of heterogeneity

We will use subgroup analysis to explore possible sources of heterogeneity (for example participants, interventions). Heterogeneity among participants could be related to age, gestational age, lung pathophysiology and pre-existing lung disease. Heterogeneity in treatments could be related to mode and length of ventilation. We will determine heterogeneity in recruitment techniques, timing and frequency of recruitment via communication with authors where necessary. We will also explore the impact of differing modes of ventilation and recruitment methods with a subgroup analysis. We will tabulate and assess adverse effects with descriptive techniques as they are likely to be different for the various subgroups. Where possible, we will calculate the risk ratio with 95% CI for each adverse effect, either compared to no treatment or to a different method of lung recruitment.

Sensitivity analysis

If there are adequate numbers of studies, we will perform a sensitivity analysis to explore the causes of heterogeneity and the robustness of the results. We will include the following factors in the sensitivity analysis by separating studies according to: quality of allocation concealment (adequate or unclear or inadequate); blinding (adequate or unclear or inadequate or not performed); analysis using both random-effects or fixed-effect models; and intention-to-treat analysis and available case analysis (only for dichotomous data) (Higgins 2008).

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Search strategy

1 CENTRAL search strategy

#1 MeSH descriptor Positive-Pressure Respiration explode all trees
#2 MeSH descriptor Continuous Positive Airway Pressure explode all trees
#3 MeSH descriptor Intermittent Positive-Pressure Breathing explode all trees
#4 MeSH descriptor Respiration, Artificial, this term only
#5 recruit* near (manoeuv* or manouev* or manuev* or techniq* or airway*)
#6 ((artificial* or mechanical*) near (respirat* or ventilat*)):ti,ab
#7 (Positive pressure or (sustained near inflation)):ti,ab
#8 (recruitment or derecruitment or PEEP or CPAP):ti,ab
#9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)
#10 MeSH descriptor Lung Injury explode all trees
#11 MeSH descriptor Acute Lung Injury explode all trees

#12 MeSH descriptor Lung, this term only
#13 MeSH descriptor Respiratory Insufficiency explode all trees
#14 MeSH descriptor Respiratory Distress Syndrome, Adult explode all trees
#15 MeSH descriptor Respiratory Distress Syndrome, Newborn explode all trees
#16 MeSH descriptor Pulmonary Atelectasis explode all trees
#17 lung and (injur* or collaps* or consolidat*)
#18 (respirator* near distress):ti,ab
#19 (hypox?emia or hypoxic or oxygenation):ti,ab
#20 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19)
#21 (#9 AND #20)
#22 neonat* or infant* or pre-term

Appendix 2. MEDLINE search strategy

1. exp Positive-Pressure Respiration/ or exp Continuous Positive Airway Pressure/ or exp Intermittent Positive-Pressure Breathing/ or Respiration, Artificial/ or ((recruit* adj5 (manoeuv* or manouev* or manuev* or techniq* or airway*)) or ((artificial* or mechanical*) adj5 (respirat* or ventilat*))).mp. or (Positive pressure or (sustained adj3 inflation) or (recruitment or derecruitment or PEEP or CPAP)).ti,ab.
2. exp Lung Injury/ or exp Acute Lung Injury/ or exp Lung/ or exp Respiratory Insufficiency/ or exp Respiratory Distress Syndrome, Newborn/ or exp Respiratory Distress Syndrome, Adult/ or exp Pulmonary Atelectasis/ or ((lung adj4 (injur* or collaps* or consolidat*)) or (respirator* adj3 distress)).mp. or (hypox?emia or hypoxic or oxygenation).ti,ab.
3. 1 and 2
4. exp Pediatrics/ or exp Children/ or exp Child/ or exp Infant/ or exp Pre-term/ or exp Child, Preschool/ or (p?ediatric or infant* or child* or neonat*).mp.
5. exp Adult/ or adult*.mp.
6. 5 not (4 and 5)
7. 3 not (6 or pre?term.mp.)
8. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.) not (animals not (humans and animals)).sh.
9. 8 and 7

Appendix 3. EMBASE search strategy

1. exp positive end expiratory pressure/ or artificial ventilation/ or exp positive end expiratory pressure/ or exp intermittent positive pressure ventilation/ or ((recruit* adj5 (manoeuv* or manouev* or manuev* or techniq* or airway*)) or ((artificial* or mechanical*) adj5 (respirat* or ventilat*))).mp. or (Positive pressure or (sustained adj3 inflation) or (recruitment or derecruitment or PEEP or CPAP)).ti,ab.
2. exp acute lung injury/ or exp lung injury/ or exp lung/ or exp lung collapse/ or exp respiratory failure/ or exp respiratory distress syndrome/ or exp atelectasis/ or piratory Distress Syndrome, Newborn/ or exp Respiratory Distress Syndrome, Adult/ or exp Pulmonary Atelectasis/ or ((lung adj4 (injur* or collaps* or consolidat*)) or (respirator* adj3 distress)).mp. or (hypox?emia or hypoxic or oxygenation).ti,ab.
3. 1 and 2
4. exp pediatrics/ or exp adult child/ or exp child/ or exp infant/ or exp adolescent/ or (p?ediatric or infant* or child* or adoles* or teenage* or neonat*).mp.
5. exp adult/ or adult*.mp.
6. 5 not (4 and 5)
7. 3 not (6 or pre?term.mp.)
8. (placebo.sh. or controlled study.ab. or random*.ti,ab. or trial*.ti,ab.) not (animals not (humans and animals)).sh.
9. 7 and 8

Appendix 4. CINAHL search strategy

S1 (MM "Positive-Pressure Respiration, Intrinsic") or (MH "Positive Pressure Ventilation+") or (MM "Continuous Positive Airway Pressure") or (MH "Intermittent Positive Pressure Breathing") or (MM "Intermittent Positive Pressure Ventilation") or (MM "Positive End-Expiratory Pressure")
S2 TX recruit* and (manoeuv* or manouev* or manuev* or techniq* or airway*)
S3 TX (artificial* or mechanical*) and (respirat* or ventilat*)
S4 S1 or S2 or S3
S5 (MM "Atelectasis") or (MH "Respiratory Distress Syndrome+") or (MH "Respiratory Failure+") or (MH "Lung+")
S6 TX lung and (injur* or collaps* or consolidat*)
S7 TX (respirator* and distress)
S8 TI (hypox?emia or hypoxic or oxygenation) or AB (hypox?emia or hypoxic or oxygenation)
S9 S5 or S6 or S7 or S8
S10 S4 and S9
S11 TX p?ediatric or infant* or child* or adoles* or teenage* or neonat*
S12 S10 and S11
S13 TX random* or trial*
S14 (MH "Random Assignment") or (MH "Clinical Trials+") or (MM "Double-Blind Studies") or (MM "Single-Blind Studies") or (MM "Triple-Blind Studies") or (MM "Placebos") or (MM "Multicenter Studies")
S15 S13 or S14
S16 S12 and S15

Appendix 5. LILACS search strategy

((‘recruit$ or derecruit$" or "respiration, artificial" or "positive pressure ventil$")) and ("oxygenation" or "hypoxic" or "hypoxemia") or "atelecta$" or "alveoli$ collapse" or "alveolar consoled$" or "lung injury" or "respiratory distress syndrome" and ("paediatric" or "pediatric" or "child$" or pre-term$")

HISTORY

Protocol first published: Issue 7, 2012

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Conceiving the review:

Co-ordinating the review: Jacqueline Jauncey-Cooke (JJC)

Undertaking manual searches: JJC

Screening search results: JJC and Caroline Grant (CG)

Organizing retrieval of papers: JJC

Screening retrieved papers against inclusion criteria: JJC, CG

Appraising quality of papers: JJC, CG, Andreas Schibler (AS), CE

Abstracting data from papers: JJC and CG

Writing to authors of papers for additional information: JJC

Providing additional data about papers: JJC

Obtaining and screening data on unpublished studies: JJC

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Other statistical analysis not using RevMan 5.0: KG

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Interpretation of data: JJC, FB, JH, CE

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Writing the review: JJC

Securing funding for the review: N/A

Performing previous work that was the foundation of the present study:

Guarantor for the review (one author): CE

Person responsible for reading and checking review before submission:CE, MD, FB

DECLARATIONS OF INTEREST

Jacqueline Jauncey-Cooke, Christine E East, Fiona Bogossian, Caroline A Grant and Andreas Schibler: we are conducting an RCT exploring the manipulation of PEEP in mechanically ventilated children to restore end expiratory lung volume. This study may be eligible for inclusion in future revisions of this review.

Kristen Gibbons: none known.

Mark Davies: none known.

Judith Hough: none known.

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