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Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn (Review)

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TABLE OF CONTENTS

[Intervention Review]

Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

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ABSTRACT

Background

Pneumothorax occurs more frequently in the neonatal period than at any other time of life and is associated with increased mortality and morbidity. It may be treated with either needle aspiration or insertion of a chest tube. The former consists of aspiration of air with a syringe through a needle or an angiocatheter, usually through the second or third intercostal space in the midclavicular line. The chest tube is usually placed in the anterior pleural space passing through the sixth intercostal space into the pleural opening, turned anteriorly and directed to the location of the pneumothorax, and then connected to a Heimlich valve or an underwater seal with continuous suction.

Objectives

To compare the efficacy and safety of needle aspiration and intercostal tube drainage in the management of neonatal pneumothorax.

Search methods

We used the standard search strategy of the Cochrane Neonatal Review group to search the Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 11), MEDLINE via PubMed (1966 to 30 November 2015), EMBASE (1980 to 30 November 2015), and CINAHL (1982 to 30 November 2015). We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomised controlled trials and quasi-randomised trials.

Selection criteria

Randomised controlled trials, quasi-randomised controlled trials and cluster trials comparing needle aspiration (either with the needle or angiocatheter left in situ or removed immediately after aspiration) to intercostal tube drainage in newborn infants with pneumothorax.

Data collection and analysis

For each of the included trial, two authors independently extracted data (e.g. number of participants, birth weight, gestational age, kind of needle and chest tube, choice of intercostal space, pressure and device for drainage) and assessed the risk of bias (e.g. adequacy of randomisation, blinding, completeness of follow-up). The primary outcomes considered in this review are mortality during the neonatal period and during hospitalisation.

Main results

One randomised controlled trial (72 infants) met the inclusion criteria of this review. We found no differences in the rates of mortality (risk ratio (RR) 1.50, 95% confidence interval (CI) 0.27 to 8.45) or complications related to the procedure. After needle aspiration, the angiocatheter was left in situ (mean 27.1 hours) and not removed immediately after the aspiration. The angiocatheter was in place for a shorter duration than the intercostal tube (mean difference (MD) −11.20 hours, 95% CI −15.51 to −6.89). None of the 36 newborns treated with needle aspiration with the angiocatheter left in situ required the placement of an intercostal tube drainage. Overall, the quality of the evidence supporting this finding is low.

Authors' conclusions

At present there is insufficient evidence to determine the efficacy and safety of needle aspiration versus intercostal tube drainage in the management of neonatal pneumothorax. Randomised controlled trials comparing the two techniques are warranted.

PLAIN LANGUAGE SUMMARY

The aspiration of pneumothorax in the newborn with a small needle compared to a larger tube placed through the intercostal space

Review question: Does the use of a needle to aspirate pneumothorax compared to an intercostal tube reduce mortality in newborns?

Background: Pneumothorax is the presence of air in the pleural space (the space between the lung and the chest wall). It is a serious condition in the newborn and may be treated by needle aspiration or chest tube placement. The former is less invasive and might avoid the need for the insertion of a chest tube, thus reducing the duration of hospital stay. However the failure of needle aspiration might subsequently lead to the need for chest tube insertion, an additional invasive procedure. This systematic review evaluates the available evidence on the effectiveness of these two techniques in treating pneumothorax in neonates.

Study characteristics: We included one trial enrolling 72 newborn infants that compared needle aspiration with the angiocatheter left in situ to chest tube placement for the treatment of pneumothorax.

Results: The use of needle aspiration with the angiocatheter left in situ compared to chest tube placement does not reduce mortality or any complications related to the procedure. Infants with pneumothorax who were assigned to the less invasive technique (needle aspiration with the angiocatheter left in place) never required the placement of an intercostal tube and had a shorter duration of tube placement.

Conclusions: The one small trial identified does not provide sufficient information to determine which of the two techniques is better to treat pneumothorax in neonates.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Needle aspiration (left in situ) compared to intercostal tube drainage for pneumothorax in the newborn

Patient or population: patients with pneumothorax in the newborn
Intervention: Needle aspiration (left in situ)
Comparison: intercostal tube drainage

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk intercostal tube drainage	Corresponding risk Needle aspiration (left in situ)				
Mortality during hospitalisation	Study population 56 per 1000	84 per 1000 (15 to 473)	RR 1.5 (0.27 to 8.45)	72 (1 study)	⊕○○○ very low[1,2]	
Need for intercostal tube drainage	Study population 1000 per 1000	10 per 1000 (0 to 210)	RR 0.01 (0 to 0.21)	72 (1 study)	⊕○○○ very low[1,2]	
Successful evacuation of extra-pleural air	Study population 944 per 1000	944 per 1000 (840 to 1000)	RR 1 (0.89 to 1.12)	72 (1 study)	⊕○○○ very low[1,2]	
Bleeding from incision	Study population 28 per 1000	9 per 1000 (0 to 222)	RR 0.33 (0.01 to 7.92)	72 (1 study)	⊕○○○ very low[1,2]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

The assumed risk is the risk of the control arm.
[1] limitations in study design: high risk for performance bias (unblinded intervention)
[2] imprecision: 1 study, few events

BACKGROUND

Description of the condition

Pulmonary air leak is caused by overdistension and rupture of the alveolar wall with air subsequently leaking from the intra-alveolar space to different anatomic locations. The most frequent neonatal forms of air leak include pulmonary interstitial emphysema, pneumomediastinum, pneumopericardium and pneumothorax (PTX). Pneumothorax is the most common air leak and occurs when air accumulates between the parietal and visceral pleura (in the pleural space). PTX occurs more frequently in the neonatal period than at any other time of life and is most often seen in the first three days of life (Irving 1990; Kottmeier 1986). It occurs in 3% to 9% of very low birth weight (VLBW) infants and is associated with increased mortality and morbidity (Bhatia 2011; Walker 2002). A large-tension PTX may increase intrathoracic pressure, which may cause increased central venous pressure and decreased venous return leading to decreased cardiac output (Fernandes 2014), hypotension, bradycardia, and an increased risk for germinal matrix-intraventricular haemorrhage (GM-IVH; Pishva 2012).

Description of the intervention

Neonatal PTX may be managed with a variety of approaches, including observation ('watchful waiting'), simple needle aspiration (thoracentesis), or insertion of a chest tube (thoracostomy and chest tube placement). Giving 100% oxygen has been used in order to induce 'nitrogen washout', though studies in term infants have reported that this treatment is not associated with faster resolution of PTX and may result in exposure to unnecessary oxygen treatment (Clark 2014; Shaireen 2014).

Thoracentesis may be the only intervention needed in an infant who is not mechanically ventilated and may be a temporising measure in an infant who requires ventilation (Katar 2006; Litmanovitz 2008). Thoracentesis consists of aspiration of air with a 10 to 20 ml syringe through a needle (usually 23 or 25 gauge) or an angiocatheter (18 to 24 gauge). The needle is inserted into the second or third intercostal space in the midclavicular line, passing just above the top of the rib in order to reduce the risk of lacerating the intercostal artery. Flow of air into the syringe confirms that the PTX has been reached by the needle, which should not be inserted further to avoid lung damage. If using an angiocatheter, the plastic catheter can be left in situ (Cloherty 2011).

Thoracostomy is performed by placement of a chest tube (10 or 12 French size), usually in the anterior pleural space. The overlying skin is prepared with an antiseptic solution, the subcutaneous tissues are infiltrated with a local anaesthetic (such as lidocaine solution) and analgesia is administered. A small incision is made through the skin in the midaxillary line in the sixth intercostal space, the subcutaneous tissue is dissected, and a subcutaneous track to the intercostal space is made. A trochar might be used to facilitate the penetration of the tube, though this technique may be associated with an increased risk of lung perforation (Fraser 1988). The chest tube is passed into the pleural opening, turned anteriorly and directed to the location of the PTX, and then connected to a Heimlich valve or an underwater seal with continuous suction at a pressure of 10 to 20 cmH_2O. A less traumatic approach consists of the use of pigtail catheters, which are usually smaller (8 or 10 French) and possibly more suitable for preterm infants. Pigtail catheters are placed with a Seldinger technique, whereby the guide wire is inserted through the catheter, which is then removed and replaced by the pigtail catheter (Cloherty 2011).

The literature does not clearly define which option is best for the treatment of PTX, especially in haemodynamically stable infants with obvious signs of PTX on chest radiograph (such as mediastinal shift). In these cases, the most common treatment is thoracostomy and chest tube placement, a procedure associated with substantial complications (Kitsommart 2012; Troug 2005).

How the intervention might work

As noted above, symptomatic PTX may be treated by needle aspiration or thoracostomy and chest tube placement. The former might avoid or reduce the need for the insertion of a chest tube, a more invasive approach, and thus reduce the duration of respiratory support and hospital stay. On the other hand, the failure of needle aspiration might subsequently imply the need for chest tube insertion, an additional invasive procedure. We planned to evaluate both single and repeated aspiration procedures.

Why it is important to do this review

Newborns with PTX are at high risk of mortality, which may exceed 40% in extremely preterm infants (Bhatia 2011). It is therefore crucial to determine the best strategy for treatment. Interestingly, a Cochrane review has been published on PTX management, but it focuses on the adult population only (Wakai 2007). No systematic reviews are available on neonatal PTX treatment.

OBJECTIVES

To compare the efficacy and safety of needle aspiration and intercostal tube drainage in the management of neonatal pneumothorax (PTX).

We planned subgroup analyses regarding gestational age, birth weight, intubated versus not intubated, unilateral versus bilateral PTX, and single versus repeated aspirations (see Subgroup analysis and investigation of heterogeneity).

METHODS

Criteria for considering studies for this review

Types of studies

We included prospective randomised clinical controlled trials and quasi-randomised trials. We planned to include cluster randomised controlled trials if the definition of participants and clusters was sufficiently clear.

Cross-over trials were not included because the intervention might have a lasting effect that compromises entry to subsequent periods of the trial.

Types of participants

Newborn infants with PTX, any gestational age and birth weight, ventilated and non-ventilated.

Types of interventions

We compared needle aspiration to intercostal tube drainage in newborns with PTX.

Two separate comparisons were planned:

1. the needle (or angiocatheter) was left in situ;
2. the needle was removed immediately after aspiration

Aspirations could be repeated and could be performed on one or both sides of the chest. However, the condition had to be untreated prior to randomisation. Treatment with supplemental oxygen was not an exclusion criterion.

We excluded trials in which 'invasive management' (i.e. needle aspiration or intercostal tube drainage) and 'expectant management' (i.e. watchful waiting) were compared.

Types of outcome measures

Primary outcomes

1. Mortality: neonatal (first 28 days of life) or during hospitalisation.

Secondary outcomes

1. Need for intercostal tube drainage (yes/no). It should be noted that failure of needle aspiration may require intercostal tube drainage; however 100% of infants in the 'intercostal tube drainage' comparison group would have a drain placed.
2. Successful evacuation of extra-pleural air (as defined by the studies' authors).
3. Bleeding from incision for the insertion of the needle or the tube (any bleeding; yes/no).
4. Subcutaneous emphysema diagnosed by imaging (yes/no).
5. Haemothorax diagnosed by imaging (yes/no).
6. Duration of chest drain (days).
7. Number of chest drain insertions.
8. Duration of mechanical ventilation (MV; days).
9. Duration of MV post intervention (days).
10. Duration of respiratory support (MV or CPAP; days).
11. Duration of oxygen therapy (days).
12. Duration of hospital stay (days).
13. Sedation/agitation/pain scale during the insertion of needle or tube. This would be assessed by neonatal scales such as the Premature Infant Pain Profile (PIPP, Stevens 1996); PIPP-revised (Gibbins 2014); Neonatal Infant Pain Scale (NIPS, Lawrence 1993); CRIES score (Krechel 1995); and Neonatal Pain, Agitation and Sedation Scale (N-PASS, Hummel 2008).
14. Sedation/agitation/pain scale average daily score. This would be assessed by neonatal scales such as those mentioned for the previous outcome.
15. Germinal matrix-intraventricular haemorrhage (GM-IVH): any grade, severe IVH (grade 3 and 4) according to Papile classification (yes/no; Papile 1978).
16. Bronchopulmonary dysplasia (BPD)/chronic lung disease (CLD) defined as:
    - respiratory support or oxygen, or both, at 28 days of life (NIH 1979);
    - respiratory support or oxygen, or both, at 36 weeks of postmenstrual age (PMA; Jobe 2001);
    - physiological definition (Walsh 2004).

Search methods for identification of studies

See: Cochrane Neonatal Review Group (CNRG) search strategy.

Electronic searches

We used the criteria and standard methods of Cochrane and the Cochrane Neonatal Group (see: the Cochrane Neonatal Group search strategy for specialized register).

The full search strategies for each database are included in Appendix 1.

Search term: 'Pneumothorax' (limiting the search to newborn and clinical trial).

We undertook a comprehensive search including:

- The Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*;
- MEDLINE (from January 1996 to 30 November 2015);
- EMBASE (from January 1980 to 30 November 2015);
- CINAHL (from 1982 to 30 November 2015);
- Perinatal Society of Australia and New Zealand (PSANZ) from 2005;
- The abstracts of the Pediatric Academic Societies (PAS) from 2000 to current.

No language restrictions were applied. We searched the reference lists of any cited articles.

Searching other resources

We searched clinical trials registries for ongoing or recently completed trials (clinicaltrials.gov; the World Health Organization's International Clinical Trials Registry Platform http://www.who.int/ictrp/en/; and controlled-trials.com).

Data collection and analysis

We used the standard methods of the Cochrane Neonatal Review Group. We assessed methodology regarding blinding of randomisation, intervention and outcome measurements, as well as completeness of follow-up (i.e. > 80%). Where necessary, the investigators of each trial were asked to provide unpublished outcome data. We used Cochrane's standardised statistical methods. For categorical data the risk ratio (RR), absolute risk difference (RD), number needed to treat for an additional beneficial outcome (NNTB), and the number needed to treat for an additional harmful outcome (NNTH) were calculated. For continuous data the mean difference (MD) was calculated. Ninety-five per cent confidence intervals (CI) were used.

Selection of studies

Two review authors (OR, MB) independently searched and identified eligible trials that met the inclusion criteria. The review authors screened the titles and abstracts to identify potentially relevant citations. The review authors retrieved the full texts of all potentially relevant articles and independently assessed the eligibility of the studies by filling out eligibility forms designed in accordance with the specified inclusion criteria. We reviewed studies for relevance based on study design, types of participants, interventions and outcome measures. We resolved any disagreements by discussion and, if necessary, by consulting a third review author (MGC). We had planned to cite studies excluded from the review in the 'Characteristics of excluded studies' table along with the reasons for exclusion. We planned to contact the trial authors if the details of the primary trials were not clear.

Data extraction and management

Two reviewers (MB, OR) undertook data abstraction independently using a data extraction form developed ad hoc and integrated with a modified version of the Cochrane Effective Practice and Organisation of Care (EPOC) Group data collection checklist.

We extracted the following characteristics from each included trial:

- Administrative details: author(s); published or unpublished; year of publication; year in which trial was conducted; details of other relevant papers cited.
- Details of the trial: study design; type, duration and completeness of follow-up (i.e. > 80%); country and location of study informed consent and ethics approval.
- Details of participants: birth weight, gestational age, and number of participants.
- Details of intervention: kind of needle and chest tube, choice of intercostal space, pressure and device for drainage.
- Details of outcomes, as listed above.

Any disagreement was resolved by discussion between the reviewers. We described the details of ongoing studies where available, including the primary author, research question(s), methods, outcome measures, and an estimate of the reporting date. Where any queries might arise or where additional data might be required, we planned to contact the authors.

MGC entered all data into Review Manager 5 software (RevMan 2014).

Assessment of risk of bias in included studies

Two review authors (SZ, MB) independently assessed the methodological quality of all included studies. We assessed the risk of bias using Cochrane's 'Risk of bias' tool (Higgins 2011).

The items included for appraisal were:

1. Sequence generation and allocation sequence concealment (selection bias)

For each included trial, we categorised the risk of selection bias as:

- Sequence generation:
  - Low risk - adequate (any truly random process e.g. random number table, computer random number generator);
  - High risk - inadequate (any non-random process e.g. odd or even date of birth, hospital or clinic record number);
  - Unclear risk - no or unclear information provided.
- **Allocation sequence concealment**

For each included trial, we categorised the risk of bias regarding allocation concealment as:

- Low risk - adequate (e.g. telephone or central randomisation, consecutively numbered sealed opaque envelopes);
- High risk - inadequate (open random allocation, unsealed or non-opaque envelopes, alternation, date of birth);
- Unclear risk - no or unclear information provided.

2. Blinding (performance bias)

Care providers cannot be blinded to the intervention. Individuals involved in longer term follow-up could potentially be 'blinded' to the intervention.

3. Blinding (detection bias)

For each included trial, we categorised the methods used to blind outcome assessors from knowledge of which intervention a participant received.
We assessed blinding separately for different outcomes or classes of outcomes.

4. Incomplete outcome data (attrition bias)

For each included trial and for each outcome, we described the completeness of data, considering attrition and exclusions from the analysis. We noted whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data are balanced across groups or are likely to be related to outcomes. In order to reduce bias from trials with high loss to follow-up, we performed a sensitivity analysis including only trials that reported follow-up data for at least 80% of participants.

5. Selective outcome reporting (reporting bias)

For each included trial, we described how we investigated the risk of selective outcome reporting bias and what we found. We assessed the methods as:

- Low risk - adequate (where it is clear that all of the trial's pre-specified outcomes and all expected outcomes of interest to us have been reported);
- High risk - inadequate (where not all of the trial's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; trial failed to include results of a key outcome that would have been expected to have been reported);
- Unclear risk - no or unclear information provided (the study protocol was not available).

6. Other potential sources of bias (other bias)

For each included trial, we described any important concerns we had about other possible sources of bias (for example, whether there was a potential source of bias related to the specific study design or whether the trial was stopped early due to some data-dependent process). We assessed whether each trial was free of other problems that could put it at risk of bias as:

- Low risk: no concerns of other bias raised;
- High risk: the trial has at least one important risk of bias (e.g. the trial had a potential source of bias related to the specific study design used or has been claimed to have been fraudulent or had some other problem);
- Unclear risk: there may be a risk of bias, but there is either insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem would introduce bias.

Risk of bias was summarised for the primary outcomes within and across studies.
A 'Risk of bias' graph was used to illustrate risk across studies.
Any disagreements were resolved by consensus and, if necessary, by adjudication by a third review author (MGC).

Quality of evidence

Although this was not planned in the review protocol (see Differences between protocol and review), we summarised the evidence of this review in a 'Summary of findings' table. We used the control arm data to calculate the 'assumed risk' values and select mortality during hospitalisation.
We assessed the quality of evidence for the main comparison at the outcome level using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Guyatt 2011a). This methodological approach considers evidence from randomised controlled trials as high quality that may be downgraded based on consideration of any of five areas: design (risk of bias), consistency across studies, directness of the evidence, precision of estimates, and presence of publication bias (Guyatt 2011a). The GRADE approach results in an assessment of the quality of a body of evidence in one of four grades: 1) High: We are very confident that the true effect lies close to that of the estimate of the effect; 2) Moderate: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; 3) Low: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect; 4) Very Low: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect (Schünemann 2013).

The review authors independently assessed the quality of the evidence found for outcomes identified as critical or important for clinical decision making. Critical outcomes include neonatal mortality and mortality during hospitalisation; important outcomes: need for intercostal tube drainage, successful evacuation of extrapleural air, bleeding from incision for the insertion of the needle or the tube, haemothorax.
In cases where we considered the risk of bias arising from inadequate concealment of allocation, randomised assignment, complete follow-up or blinded outcome assessment to reduce our confidence in the effect estimates, we downgraded the quality of evidence accordingly (Guyatt 2011b). We evaluated consistency by similarity of point estimates, extent of overlap of confidence intervals and statistical criteria including measurement of heterogeneity (I^2). We downgraded the quality of evidence when large and unexplained inconsistency across studies' results was present (i.e. some studies suggest important benefit and others no effect

or harm without a clinical explanation) (Guyatt 2011d). We assessed precision with 95% confidence intervals (CI) around the pooled estimation (Guyatt 2011c). When trials were conducted in populations other than the target population, we downgraded the quality of evidence because of indirectness (Guyatt 2011e).

We entered data (i.e. pooled estimates of the effects and corresponding 95% CI) and explicit judgements for each of the above-mentioned assessed aspects into the Guideline Development Tool, the software used to create 'Summary of findings' tables (GRADEpro 2008). We explained all judgements involving the assessment of the study characteristics described above in footnotes or comments in the 'Summary of findings' table.

Measures of treatment effect

Categorical data were extracted for each intervention group, and risk ratio (RR) or absolute risk difference (RD) were calculated. Mean and standard deviation were obtained for continuous data and analysis performed using the mean difference (MD). For each measure of effect the 95% CI were given. NNTB and NNTH were presented when the RD was statistically significant.

Unit of analysis issues

In cluster trials, groups of individuals are randomly allocated to study arms; outcomes are then measured based on the individual cluster members. Under such circumstances, it is necessary to adjust the results to account for the fact that the randomisation was performed on the clusters rather than the individuals. As many cluster-randomised trials fail to report appropriate analysis, corrections for clustering are needed before they are included in a meta-analysis.

To calculate adjusted (inflated) CIs that account for the clustering, we planned to conduct an approximate analysis as suggested by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We would multiply the standard error of the effect estimate (from an analysis ignoring clustering) by the square root of the design effect. The design effect would be calculated from the average cluster size and the intra-cluster correlation coefficient. Intra-cluster correlation coefficient(s) would be borrowed from similar studies. If this correction was not possible, we planned to include the cluster trials in the review but would not include them in the meta-analyses.

Dealing with missing data

We planned to determine the drop-out rate for each trial (and each trial outcome). A drop-out rate that is equal to or greater than the event rate of the control group would have been considered significant. We planned to perform a sensitivity analysis to evaluate the overall results with and without the inclusion of studies with significant drop-out rates. If a trial reported outcomes only for participants completing the trial or only for participants who followed the protocol, we planned to contact author(s) and ask them to provide additional information to facilitate an intention-to-treat analysis. No assumptions were planned regarding the outcome of infants lost to follow-up. We planned to calculate and report the percentage lost to follow-up if there was a discrepancy in the number randomised and the numbers analysed in each treatment group. Moreover we planned to request additional data from the author(s) of each trial if data on outcomes was missing or unclear.

Assessment of heterogeneity

We planned to assess clinical heterogeneity by comparing the distribution of important participant factors between trials (for example, age) and trial factors (randomisation concealment, blinding of outcome assessment, losses to follow-up, treatment type, co-interventions). We would assess statistical heterogeneity by examining the I^2 statistic (Higgins 2011), a quantity that describes the proportion of variation in point estimates that is due to variability across studies rather than sampling error. We would interpret the I^2 statistic as described by Higgins 2003:

- < 25% no heterogeneity;
- 25 to 49% low heterogeneity;
- 50 to 74% moderate heterogeneity; and
- ≥ 75 high heterogeneity.

In addition, we planned to employ a Chi^2 test of homogeneity to determine the strength of evidence that heterogeneity is genuine.

Assessment of reporting biases

We planned to assess publication bias using funnel plots if at least 10 clinical trials met our inclusion criteria (Egger 1997; Higgins 2011).

Data synthesis

Data were summarised using Review Manager 5 (RevMan 2014). We used the standard methods of the Cochrane Neonatal Review Group to synthesize data using RR, RD, NNTB, NNTH, weighted mean differences (WMDs) and 95% CIs. Our preference was for a fixed-effect model to perform meta-analyses. However, in case of moderate or high heterogeneity among the studies, we planned to conduct and report meta-analyses using a random-effects model.

Subgroup analysis and investigation of heterogeneity

1. Gestational age (with three subgroups: < 32 weeks versus 32 to 36 weeks versus ≥ 37 weeks).
2. Birth weight (with three subgroups: < 1500 grams versus 1500 to 2500 grams versus ≥ 2500 grams).
3. Intubated versus not intubated.

4. Unilateral versus bilateral PTX.
5. Single versus repeated aspirations.

Sensitivity analysis

We planned to conduct sensitivity analyses to explore the effect of the methodological quality of the trials, checking to ascertain if studies with a high risk of bias overestimate the effect of treatment.

RESULTS

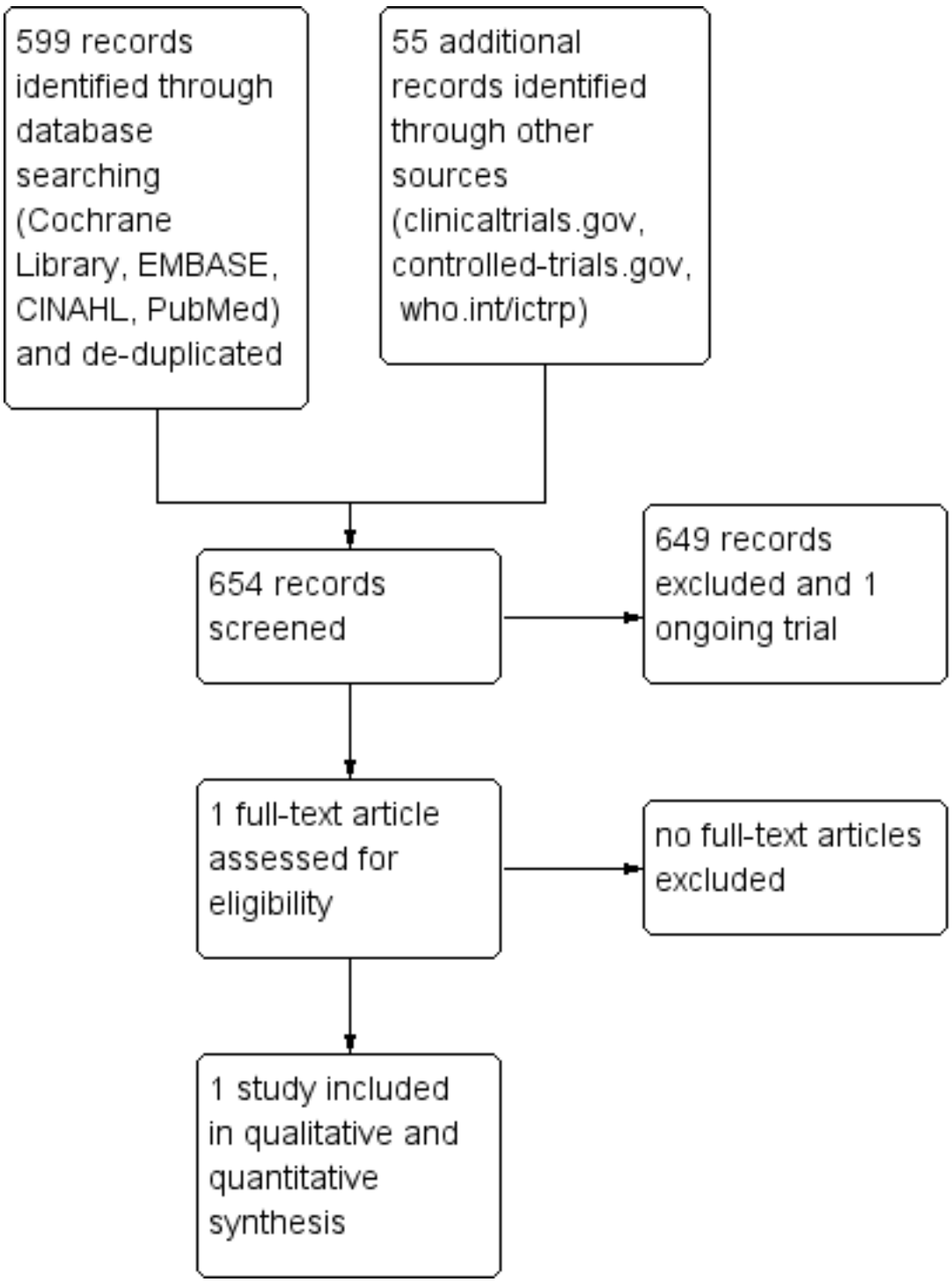
Description of studies

See Characteristics of included studies and Characteristics of ongoing studies.

Results of the search

The literature search run in June 2015 identified 635 references (Figure 1). After screening, we included only one randomised controlled trial (Arda 2002) and we identified one ongoing trial (ISRCTN65161530).

Figure 1. Study flow diagram.



Searches were updated in November 2015 and identified an additional 19 references, none of which were eligible for inclusion.

Included studies

One trial recruiting 72 infants met the inclusion criteria (Arda 2002) (see Characteristics of included studies). This unblinded randomised controlled trial was conducted in term and preterm newborns with PTX in two hospitals in Turkey and compared two different techniques to treat PTX, i.e. venous catheter versus intercostal tube. The mean birth weight (SD) was 2547.2 (± 448.1) grams in the needle group and 2690.2 (± 419.4) grams in the intercostal tube group; mean gestational age (SD) was 36.4 (± 2.6) weeks in the needle group and 35.8 (± 2.8) weeks in the intercostal tube group.

Criteria to drain PTX included persistent or increased air detected in serial lung X-rays, mediastinal shifting, respiratory difficulty with cyanosis and patients with PTX on ventilator. In the needle group, an 18-gauge 45 mm long venous catheter was introduced by the surgeon without local anaesthesia through the fourth or fifth intercostal space on the anterior axillary line and, after guide needle withdrawal, the catheter was directed toward the superior part of the thoracic cavity. Of note, the needle was taped to the skin with a dressing and left in situ (mean 27.1 hours), and not removed immediately after the aspiration. In the intercostal tube drainage group, the surgeon made an incision at the fifth or sixth intercostal space with local anaesthesia (Prilocaine hydrochloride), separated the intercostal muscle fibres, blunt-dissected a subcutaneous tunnel, pierced the pleura and inserted a 12-F standard chest tube catheter through the tunnel into the pleural space. In both groups, the chest tube or venous catheter were connected to an underwater drainage system and a chest X-ray was taken immediately after each procedure to check for the presence of residual air in the thoracic cavity. When the bubbling in the water-seal chamber stopped, the drainage system was clamped. The system was then kept closed for at least six hours. Once a final chest X-ray showed no residual air, the chest tube or venous catheter was removed. Main outcomes were duration of the procedure, duration of the tubes and catheters in place, and the rates of complications.

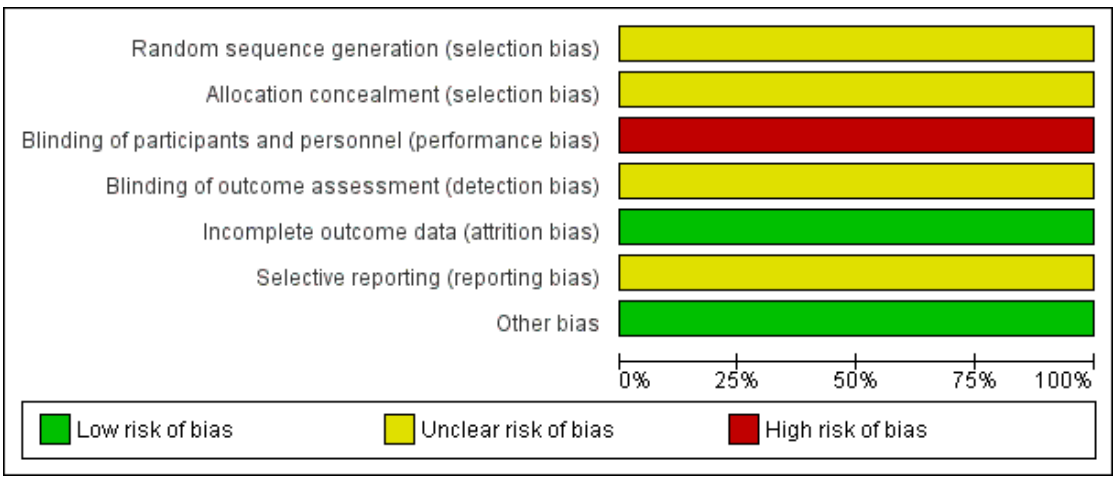
Excluded studies

We considered eligible none of the other 635 identified studies.

Risk of bias in included studies

Figure 2 summarises the risk of bias of the included trial.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

The included randomised trial did not provide clear information on allocation sequence generation.

Blinding

Both the intervention and the comparison were performed by the same investigator in a unblinded pattern. No information was

available regarding blinding of the outcome assessors.

Incomplete outcome data

We could not identify any missing outcome data.

Selective reporting

The risk of bias was assessed as unclear because no protocol was identified.

Other potential sources of bias

The trial appeared free of other biases.

Effects of interventions

See: **Summary of findings for the main comparison** Needle aspiration (left in situ) compared to intercostal tube drainage for pneumothorax in the newborn

Comparison 1: needle aspiration (needle or angiocatheter left in situ) versus intercostal tube drainage

We identified only one trial (Arda 2002), which included a total of 72 infants (see Characteristics of included studies and Summary of findings for the main comparison).

Tests for heterogeneity were not applicable for any of the analyses as only one study was included.

Comparison 2: needle aspiration (needle removed immediately after aspiration) versus intercostal tube drainage

No trials were identified within this comparison.

Primary outcomes

Death during hospitalisation (Outcome 1.1)

Five of the patients died, three in the needle group and two in the intercostal tube group (RR 1.50, 95% CI 0.27 to 8.45) (Analysis 1.1; Figure 3). It was not specified by the trial's authors whether data referred to neonatal mortality or during hospitalisation. Four patients died of sepsis and one due to congenital heart disease. None of the five deaths were linked to PTX or to its treatment.

Figure 3. Forest plot of comparison: 1 Needle aspiration vs intercostal tube drainage, outcome: 1.1 Mortality during hospitalisation.

Secondary outcomes

Need for intercostal tube drainage; (it should be noted that failure of needle aspiration may require intercostal tube drainage, however 100% of infants in the 'intercostal tube drainage' comparison group would have a drain placed) (Outcome 1.2)

None of the newborns treated with needle aspiration needed the placement of intercostal tube drainage (RR 0.01, 95% CI 0.00 to 0.21) (Analysis 1.2)

Successful evacuation of extra-pleural air (Outcome 1.3)

The authors of the included study did not define any successful PTX evacuation. However two newborns in each group required re-insertion of tube/catheter (RR 1.00, 95% CI 0.89 to 1.12) (Analysis 1.3).

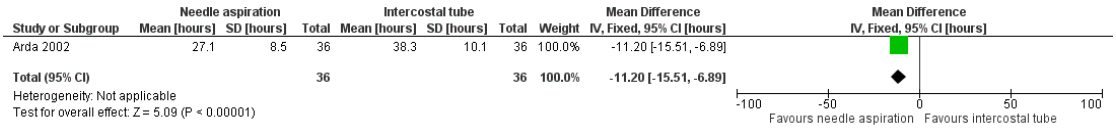
Bleeding from incision for the insertion of the needle or the tube (Outcome 1.4)

One event occurred in the intercostal tube group, none in the needle aspiration group (RR 0.33, 95% CI 0.01 to 7.92) (Analysis 1.4).

Duration of chest drain (Outcome 1.5)

Duration of needle in place was shorter than duration of intercostal tube (MD −11.20 hours, 95% CI −15.51 to −6.89) (Analysis 1.5; Figure 4).

Figure 4. Forest plot of comparison: 1 Needle aspiration vs intercostal tube drainage, outcome: 1.5 Duration of catheter/tube in place [hours].



Number of chest drain insertions (Outcome 1.6)

Infants in the needle aspiration group never required chest drain insertion, though the catheter had to be re-inserted in two cases. Infants in the intercostal tube group required re-insertion of the tube in two cases (RR 1.00, 95% CI 0.15 to 6.72) (Analysis 1.6).

No data were reported on the following outcomes:

- Subcutaneous emphysema diagnosed by imaging
- Haemothorax diagnosed by imaging
- Duration of mechanical ventilation
- Duration of MV post intervention
- Duration of respiratory support
- Duration of oxygen therapy
- Duration of hospital stay
- Sedation/agitation/pain scale during the insertion of needle or tube
- Sedation/agitation/pain scale average daily score
- Germinal matrix-intraventricular haemorrhage (GM-IVH)
- Bronchopulmonary dysplasia (BPD)/chronic lung disease (CLD).

Subgroup analysis

We were unable to conduct any subgroup analysis as we included only one trial.

DISCUSSION

Summary of main results

We evaluated the efficacy of needle aspiration compared to intercostal tube drainage in the treatment of pneumothorax in newborns. Only one trial enrolling 72 infants with a broad range of weight and gestational age met the inclusion criteria of this review (Arda 2002). There was insufficient evidence to determine the efficacy and safety of the two techniques. Mortality rate did not differ between the two groups. None of the 36 newborns treated with needle aspiration required the placement of an intercostal tube drainage. Duration of needle in place was shorter than duration of intercostal tube.

We identified one ongoing trial (ISRCTN65161530).

Overall completeness and applicability of evidence

The available evidence is insufficient to understand which is the more effective and safe intervention for treating neonatal pneumothorax. Only one randomised trial (72 newborns) assessed the study question. There were insufficient data available to assess the primary outcome of this review and other important outcomes which were identified a priori. Outcomes such as haemothorax, duration of respiratory support, intraventricular haemorrhage and bronchopulmonary dysplasia were not reported. Importantly, in Arda 2002 the investigators inserted the needle with the intention of leaving the angiocatheter in situ; whereas in clinical practice, most practitioners aspirate air until it stops coming and then remove the needle. This discrepancy might affect the generalisability of the study results and therefore of the present review. We could not perform a priori subgroup analysis (gestational age, birth weight, intubated versus not intubated, unilateral versus bilateral PTX, single versus repeated aspirations) to detect differential effects as there was only one included RCT. Other larger trials are required to draw any conclusion. One ongoing trial that we identified is currently recruiting newborns (ISRCTN65161530).

Quality of the evidence

The overall quality of the evidence was judged to be 'very low' due to the presence of multiple biases (see Summary of findings for the main comparison). The main limitation of the quality of evidence is linked to the imprecision of the estimate, due to the presence of only one trial that met the inclusion criteria. We downgraded the overall quality of evidence for the outcomes because of 1) limitations in the study design (unblinded intervention); and 2) the imprecision of results (only one trial included).

Potential biases in the review process

It is unlikely that the literature search applied to this review may have missed relevant trials, thus we are confident that this systematic review summarises all the presently available randomised trial evidence on treatment of neonatal pneumothorax. We did not exclude any potentially relevant trial. We did not succeed in obtaining additional information on the population and the outcomes included in the trial by Arda 2002. The included trial was unblinded due to the nature of the intervention.

Agreements and disagreements with other studies or reviews

We are not aware of other reviews that address the same clinical question. We described the characteristics of the only clinical trial that has been published.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence to establish the efficacy and safety of needle aspiration and intercostal tube drainage in the management of neonatal pneumothorax. The only included trial showed no differences in mortality. Limited or no evidence is available on other clinically relevant outcomes.

Implications for research

Randomised controlled trials of neonatal pneumothorax treatment are warranted. These trials should be stratified by gestational age, describe population characteristics (e.g. presence of ventilation, unilateral or bilateral pneumothorax) and details of the procedures (e.g. single versus repeated aspirations; needle removed immediately after aspiration versus left in situ), and report on clinically relevant outcomes such as intraventricular haemorrhage and bronchopulmonary dysplasia.

ACKNOWLEDGEMENTS

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Arda 2002

Methods	Two centre unblinded randomised controlled trial. Criteria to drain PTX included persistent or increased air detected in serial lung X-rays, mediastinal shifting, respiratory difficulty with cyanosis and patients with PTX on ventilator
Participants	72 newborns with PTX. The mean birth weight (SD) was 2547.2 (± 448.1) grams in the needle group and 2690.2 (± 419.4) grams in the intercostal tube group; mean gestational age (SD) was 36.4 (± 2.6) weeks in the needle group and 35.8 (± 2.8) weeks in the intercostal tube group Settings: two Turkish neonatal intensive care units, i.e. Social Security Children's Hospital and Baskent University Hospital
Interventions	In the needle group, an 18-gauge 45 mm long venous catheter was introduced by the surgeon without local anaesthesia through the fourth or fifth intercostal space on the anterior axillary line and after guide needle withdrawal the catheter was directed toward the superior part of the thoracic cavity In the intercostal tube drainage, the surgeon made an incision at the fifth or sixth intercostal space with local anaesthesia (Prilocaine hydrochloride), separated the intercostal muscle fibres, blunt-dissected a subcutaneous tunnel, pierced the pleura and inserted a 12-F standard chest tube catheter through the tunnel into the pleural space In both groups, the chest tube or venous catheter were connected to an underwater drainage system and a chest X-ray was taken immediately after each procedure to check for the presence of residual air in the thoracic cavity. When the bubbling in the water-seal chamber stopped, the drainage system was clamped. The system was then kept closed for at least 6 hours. Once a final chest X-ray showed no residual air, the chest tube or venous catheter was removed The same surgeon performed all procedures in both groups.
Outcomes	Main outcomes were duration of the procedure, duration of the tubes and catheters in place and the rates of major complications (tube accidentally dislodged, air leakage through the incision, iatrogenic pneumothorax) and minor complications (kinking of the chest tube, bleeding from the incision, evident pain causing respiratory difficulty, catheter breakage) Other outcomes included mortality (unspecified) and need for re-insertion of tube/catheter
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation sequence generation is not specified.

Arda 2002 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Allocation concealment is not specified.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded intervention.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All infants accounted for.
Selective reporting (reporting bias)	Unclear risk	We could not ascertain if there were deviations from the original protocol in the final publication (trial not registered, protocol not available)
Other bias	Low risk	Appeared free of other biases.

Characteristics of ongoing studies *[ordered by study ID]*

ISRCTN65161530

Trial name or title	The NORD trial: Needle aspiration or chest drain insertion for pneumothorax in newborns
Methods	Randomised controlled trial comparing two different techniques to treat neonatal PTX Study hypothesis: "In newborn infants with symptomatic pneumothoraces, aspirating air with a needle reduces the need for chest drain insertion" Follow-up until hospital discharge.
Participants	Sample size: 70 newborns (both term and preterm). Inclusion criteria: 1. PTX diagnosed on chest x-ray; 2. Need for respiratory support; 3. PTX judged as requiring treatment Exclusion criteria: 1. Absence of respiratory distress; 2. Significant pulmonary hypoplasia, e.g. Potter's sequence
Interventions	Aspiration with a 23 or 25 gauge 'butterfly' needle and 20 mL syringe versus chest drain insertion
Outcomes	Primary outcome measures: Chest drain insertion for management of PTX on chest x-ray within 6 hours of diagnosis Secondary outcome measures: 1. Duration of chest drain; 2. Number of chest drain insertions; 3. Duration of ventilation post intervention; 4. Duration of ventilation; 5. Duration of nasal continuous positive airway pressure; 6. Duration of supplemental oxygen; 7. Bronchopulmonary dysplasia - oxygen treatment at 28 days; 8. Chronic lung disease - oxygen treatment at 36 weeks postmenstrual age; 9. Nosocomial infections; 10. Pleural effusions; 11. Duration of hospital stay; 12. Death before discharge from hospital
Starting date	19 August 2013.

ISRCTN65161530 (*Continued*)

Contact information	Dr. Colm O'Donnell codonnell@nmh.ie
Notes	Trial's status: patients' enrolment (assessed on July 2015).

DATA AND ANALYSES

Comparison 1. Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality during hospitalisation	1	72	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.27, 8.45]
2 Need for intercostal tube drainage	1	72	Risk Ratio (M-H, Fixed, 95% CI)	0.01 [0.00, 0.21]
3 Successful evacuation of extra-pleural air	1	72	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.89, 1.12]
4 Bleeding from incision	1	72	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.92]
5 Duration of catheter/tube in place	1	72	Mean Difference (IV, Fixed, 95% CI)	-11.20 [-15.51, -6.89]
6 Number of chest drain insertions	1	72	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.15, 6.72]

Analysis 1.1. Comparison 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage, Outcome 1 Mortality during hospitalisation.

Review: Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

Comparison: 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome: 1 Mortality during hospitalisation

Study or subgroup	Needle aspiration n/N	Intercostal tube n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Arda 2002	3/36	2/36		100.0 %	1.50 [0.27, 8.45]
Total (95% CI)	**36**	**36**		**100.0 %**	**1.50 [0.27, 8.45]**
Total events: 3 (Needle aspiration), 2 (Intercostal tube)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.46 (P = 0.65)					
Test for subgroup differences: Not applicable					

Analysis 1.2. Comparison 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage, Outcome 2 Need for intercostal tube drainage.

Review: Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

Comparison: 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome: 2 Need for intercostal tube drainage

Study or subgroup	Favours needle aspiration n/N	Intercostal tube n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Arda 2002	0/36	36/36		100.0 %	0.01 [0.00, 0.21]
Total (95% CI)	**36**	**36**		**100.0 %**	**0.01 [0.00, 0.21]**
Total events: 0 (Favours needle aspiration), 36 (Intercostal tube)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.05 (P = 0.0023)					
Test for subgroup differences: Not applicable					

Analysis 1.3. Comparison 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage, Outcome 3 Successful evacuation of extra-pleural air.

Review: Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

Comparison: 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome: 3 Successful evacuation of extra-pleural air

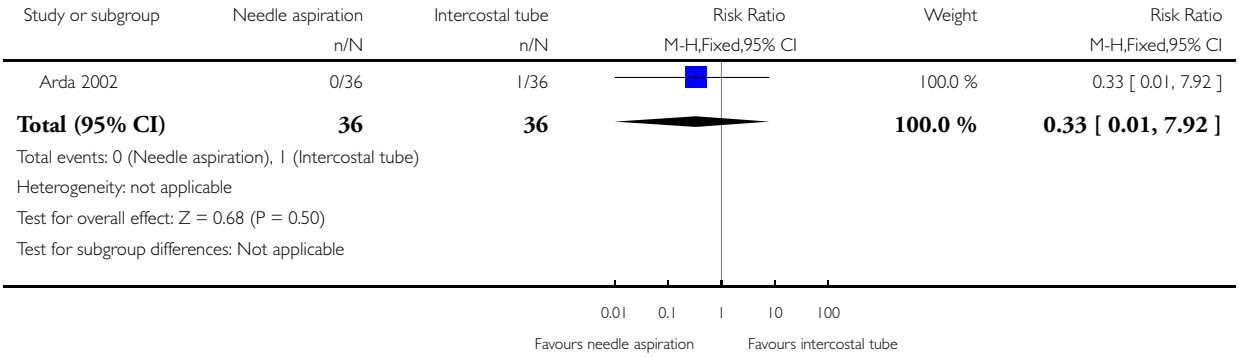
Study or subgroup	Needle aspiration n/N	Intercostal tube n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Arda 2002	34/36	34/36		100.0 %	1.00 [0.89, 1.12]
Total (95% CI)	**36**	**36**		**100.0 %**	**1.00 [0.89, 1.12]**
Total events: 34 (Needle aspiration), 34 (Intercostal tube)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.0 (P = 1.0)					
Test for subgroup differences: Not applicable					

Analysis 1.4. Comparison 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage, Outcome 4 Bleeding from incision.

Review: Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

Comparison: 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome: 4 Bleeding from incision

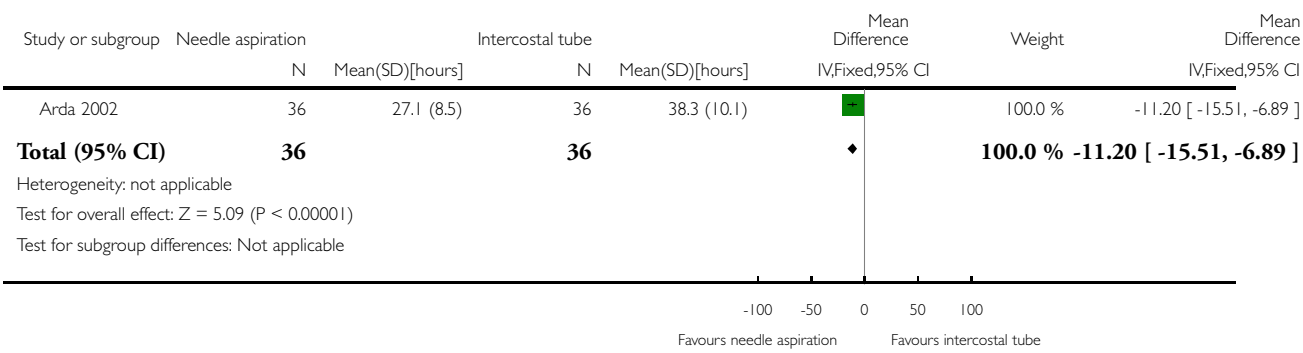


Analysis 1.5. Comparison 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage, Outcome 5 Duration of catheter/tube in place.

Review: Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

Comparison: 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome: 5 Duration of catheter/tube in place

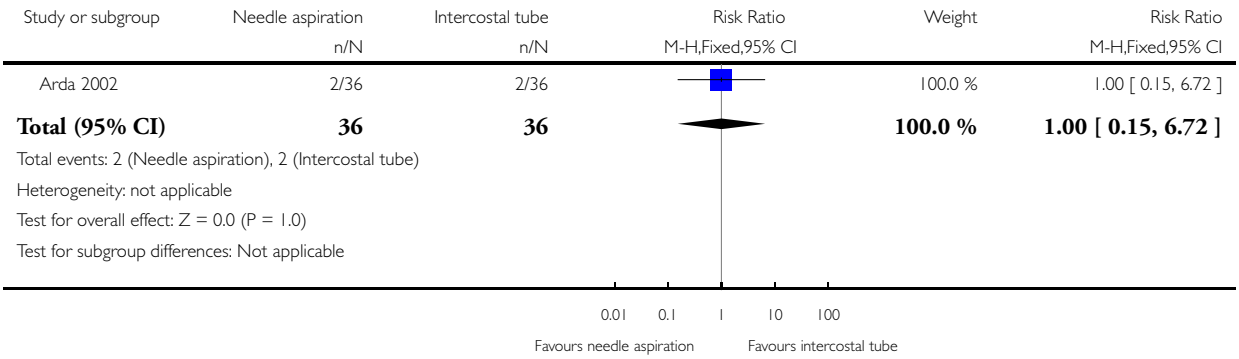


Analysis 1.6. Comparison 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage, Outcome 6 Number of chest drain insertions.

Review: Needle aspiration versus intercostal tube drainage for pneumothorax in the newborn

Comparison: 1 Needle aspiration (needle or angiocatheter left in situ) vs. intercostal tube drainage

Outcome: 6 Number of chest drain insertions



APPENDICES

Appendix 1. Search strategy

- *The Cochrane Library*: Search Terms: pneumothorax AND (infant or newborn or neonate or neonatal or premature or very low birth weight or low birth weight or VLBW or LBW)
- MEDLINE: pneumothorax AND ((infant, newborn[MeSH] OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or infan* or neonat*) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR Clinical Trial[ptyp] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh]))
- EMBASE: pneumothorax and (infant, newborn or newborn or neonate or neonatal or premature or very low birth weight or low birth weight or VLBW or LBW or Newborn or infan* or neonat*) and (human not animal) and (randomized controlled trial or controlled clinical trial or randomized or placebo or clinical trials as topic or randomly or trial or clinical trial)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
- CINAHL: pneumothorax AND (infant, newborn OR newborn OR neonate OR neonatal OR premature OR low birth weight OR VLBW OR LBW or Newborn or infan* or neonat*) AND (randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR clinical trials as topic OR randomly OR trial OR PT clinical trial)
- abstractsonline of the Pediatric Academic Societies (PAS) from 2000 to 2015: pneumothorax AND infant
- clinicaltrials.gov and controlled-trials.com: pneumothorax AND infant

CONTRIBUTIONS OF AUTHORS

MB and OR reviewed the literature and wrote the review.

SZ and MGC assisted in the review of literature and in writing of the review.

COD and LAR commented on the review.

DECLARATIONS OF INTEREST

MB, OR, LAR, SZ, COD and MGC declare having no competing financial conflict of interest.

SOURCES OF SUPPORT

Internal sources

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MB and OR are employed by this organisation

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added the methodology and plan for 'Summary of findings' tables and GRADE recommendations, which were not included in the original protocol (see Summary of findings for the main comparison).

We have specified two separate comparisons (the needle or angiocatheter is left in situ*;* the needle is removed immediately after aspiration).

INDEX TERMS

Medical Subject Headings (MeSH)

*Chest Tubes; Pneumothorax [mortality; *therapy]; Randomized Controlled Trials as Topic; Risk; Suction [instrumentation; methods]; Thoracentesis [instrumentation; *methods]; Thoracostomy [methods]

MeSH check words

Humans; Infant, Newborn