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[Intervention Review]

Air versus saline in the loss of resistance technique for identification of the epidural space

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ABSTRACT

Background

The success of epidural anaesthesia depends on correct identification of the epidural space. For several decades, the decision of whether to use air or physiological saline during the loss of resistance technique for identification of the epidural space has been governed by the personal experience of the anaesthesiologist. Epidural block remains one of the main regional anaesthesia techniques. It is used for surgical anaesthesia, obstetrical analgesia, postoperative analgesia and treatment of chronic pain and as a complement to general anaesthesia. The sensation felt by the anaesthesiologist from the syringe plunger with loss of resistance is different when air is compared with saline (fluid). Frequently fluid allows a rapid change from resistance to non-resistance and increased movement of the plunger. However, the ideal technique for identification of the epidural space remains unclear.

Objectives

- To evaluate the efficacy and safety of both air and saline in the loss of resistance technique for identification of the epidural space.
- To evaluate complications related to the air or saline injected.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 9), MEDLINE, EMBASE and the Latin American and Caribbean Health Science Information Database (LILACS) (from inception to September 2013). We applied no language restrictions. The date of the most recent search was 7 September 2013.

Selection criteria

We included randomized controlled trials (RCTs) and quasi-randomized controlled trials (quasi-RCTs) on air and saline in the loss of resistance technique for identification of the epidural space.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data.

Main results

We included in the review seven studies with a total of 852 participants. The methodological quality of the included studies was generally ranked as showing low risk of bias in most domains, with the exception of one study, which did not mask participants. We were able to include data from 838 participants in the meta-analysis. We found no statistically significant differences between participants receiving air and those given saline in any of the outcomes evaluated: inability to locate the epidural space (three trials, 619 participants) (risk ratio (RR) 0.88, 95% confidence interval (CI) 0.33 to 2.31, low-quality evidence); accidental intravascular catheter placement (two trials, 223 participants) (RR 0.90, 95% CI 0.33 to 2.45, low-quality evidence); accidental subarachnoid catheter placement (four trials, 682 participants) (RR 2.95, 95% CI 0.12 to 71.90, low-quality evidence); combined spinal epidural failure (two trials, 400 participants) (RR 0.98, 95% CI 0.44 to 2.18, low-quality evidence); unblocked segments (five studies, 423 participants) (RR 1.66, 95% CI 0.72 to 3.85); and pain measured by VAS (two studies, 395 participants) (mean difference (MD) -0.09, 95% CI -0.37 to 0.18). With regard to adverse effects, we found no statistically significant differences between participants receiving air and those given saline in the occurrence of paraesthesias (three trials, 572 participants) (RR 0.89, 95% CI 0.69 to 1.15); difficulty in advancing the catheter (two trials, 227 participants) (RR 0.91, 95% CI 0.32 to 2.56); catheter replacement (two trials, 501 participants) (RR 0.69, 95% CI 0.26 to 1.83); and postdural puncture headache (one trial, 110 participants) (RR 0.83, 95% CI 0.12 to 5.71).

Authors' conclusions

Low-quality evidence shows that results do not differ between air and saline in terms of the loss of resistance technique for identification of the epidural space and reduction of complications. Applicability might be compromised, as most of the results described in this review were obtained from parturient patients. This review underlines the need to conduct well-designed trials in this field.

PLAIN LANGUAGE SUMMARY

Air versus saline in the loss of resistance technique for identification of the epidural space

Review question

Which technique, air or saline, is more efficacious and safe in reducing complications during the loss of resistance technique (sudden loss of pressure on the plunger of the syringe, making the plunger slide smoothly) for identification of the epidural space, and what guidance can be provided to clinicians in their clinical practice? (The epidural space surrounds the spinal cord and its covering layers, through which the spinal nerves pass as they connect to other nerves leading to and from all parts of the body.)

Background

A survey of anaesthesiologists showed that 53% of those who replied used loss of resistance technique (LOR) with saline, 37% used LOR with air and 6% LOR with both air and saline; 3% used a different technique with or without one of the above LOR approaches. The methods used for identification of the epidural space are important for good quality of anaesthesia and for avoidance of complications such as epidural haematoma (i.e. accumulation of blood between the skull and the dura mater) and occasional low back pain.

Study characteristics

Adults (18 years of age and older) undergoing surgical procedures, pregnant women in obstetrical labour and patients receiving postoperative pain relief. The evidence is current to September 2013. We found seven studies with a total of 852 participants. The maximum time that a participant was followed by the doctor was 24 hours after giving birth. The quality of the included studies was considered reasonable.

Key results

The following results were examined: inability to locate the epidural space; accidental catheter placement (mis-insertion of the catheter); combined spinal epidural failure (cases of failed regional anaesthetic technique, which combines the benefits of spinal and epidural anaesthesia); unblocked segments (patchy block); and pain. We found no convincing evidence that results differed when air or saline was used.

Quality of the evidence

Because conducted studies were only reasonably well conducted (results very similar across studies; minor issues with study design; and not enough data), we ranked the overall quality of the evidence as low. The applicability of findings might be compromised, as most of the results described in this review were obtained from parturient patients.

Conclusion and future research

Low-quality evidence shows that results do not differ between air and saline in using loss of resistance technique for identification of the epidural space and in reducing complications.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Air versus saline in the loss of resistance technique for identification of the epidural space

Patient or population: adults classified as ASA grades 1 to 3 undergoing surgical procedures, pregnant women in obstetrical labour and patients receiving postoperative analgesia

Intervention: air

Comparison: saline

Outcomes	Assumed risk (air)	Corresponding risk (saline)	Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
Inability to locate the epidural space Follow-up: 15 minutes after last dose of local anaesthetic (Beilin 2000); 4 hours of analgesia initiation (Grondin 2009); and not reported (Vigfússon 1995) ^a	27%	26%	RR 0.88 (0.33 to 2.31)	619 (3)	⊕⊕⊕⊕ low ^{b,d}
Accidental intravascular catheter placement Follow-up: 15 minutes after last dose of local anaesthetic (Beilin 2000) and 24 hours after delivery (Sarna 1990) ^a	6%	7%	RR 0.90 (0.33 to 2.45)	223 (2)	⊕⊕⊕⊕ low ^{b,d}
Accidental subarachnoid catheter placement Follow-up: 15 minutes after last dose of local anaesthetic (Beilin 2000); 4 hours of analgesia initiation (Grondin 2009); and 24 hours after delivery (Sarna 1990) ^e	0.2%	0%	RR 2.95 (0.12 to 71.90)	682 (4)	⊕⊕⊕⊕ low ^{b,c,d}
Unsuccessful combined spinal epidural Follow-up: 4 hours of analgesia initiation (Grondin 2009) and not reported (van den Berg 2010) ^e	5%	5%	RR 0.98 (0.44 to 2.18)	400 (2)	⊕⊕⊕⊕ low ^{b,d}

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) 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.

^aParturient individuals (with the exception of [Vigfússon 1995](#), which did not report the inclusion criteria; [van den Berg 2010](#), which considered any patients requesting or submitted for epidural labour analgesia and [Sarna 1990](#), which also considered other obstetrical procedures), so the applicability of findings might be compromised.

^bAll studies presented an overall low risk of bias; no inconsistency was noted across studies (i.e. $I^2 = 0\%$), and a reasonable overlap in confidence intervals was seen, as well as small sample sizes and small numbers of events with small (but not very narrow) confidence intervals.

^cThe latter is an exception for the outcome of accidental subarachnoid catheter placement, which presents a wider CI.

^dIt was not possible to verify publication bias, as fewer than 10 studies were included in the meta-analysis; however, the search strategy was comprehensive, and no language restriction was applied.

^eParturient individuals, so the applicability of findings might be compromised.

BACKGROUND

The success of epidural anaesthesia depends on correct identification of the epidural space. For several decades, the choice between using air or physiological saline during the loss of resistance technique for identification of the epidural space has been governed by the personal experience of the anaesthesiologist (Scott 1997).

In 1921 and 1933, Pagés and Dogliotti (Dogliotti 1933; Pagés 1991) described use of the loss of resistance technique (LOR) for identification of the epidural space. Nowadays, LOR appears to be the most frequently used method for identification of the epidural space (Cowan 2001; Howell 1998). A survey of anaesthesiologists, performed in 1998, showed that 53% of respondents used LOR with saline, 37% used LOR with air and 6% LOR with both air and saline; 3% used a different technique with or without one of the above LOR approaches (Howell 1998). Another more recent survey conducted among Canadian anaesthesiologists showed that LOR was the method of choice for 95.4% of them (Ames 2005). Furthermore, a variety of techniques have been described over the years (Baraka 2001; Evans 1982; Gutierrez 1932; Macintosh 1953; Sawada 2012; Tielens 2013). However the literature shows continued conflict as to which medium is the most appropriate method for placement of epidural catheters in patients undergoing surgical procedures, pregnant women in obstetrical labour and patients receiving postoperative analgesia.

Saberski et al suggested that air should not be used to detect loss of resistance, as it can cause neurological sequelae for the following reasons. Injected air can act as a space-occupying lesion and can exert pressure on the nervous structures within the spinal canal (Saberski 1997); air may reach the cranium and cause pneumocephalus; air may reach the tissue spaces at the upper end of the spine, or the retroperitoneal space; and nitrous oxide given during surgery can increase the volume of gas.

Description of the condition

Epidural block remains one of the main regional anaesthesia techniques. It is used for surgical anaesthesia, obstetrical analgesia, postoperative analgesia, treatment of chronic pain and as a complement to general anaesthesia.

The epidural space (also known as the extradural space or the peridural space) is the outermost part of the spinal canal. It is the space within the canal (formed by the surrounding vertebrae) lying outside the dura mater. The epidural space extends from the foramen magnum to the sacrococcygeal membrane. The epidural space contains semi liquid fat, blood vessels, lymphatic vessels and spinal nerves. The pressure in the epidural space is significantly higher in the prone position than in the sitting position (Moon 2010). Epidural pressure (EP) is lower, and the incidence of subatmospheric EP is higher in the midthoracic epidural space than in the low-thoracic epidural space (Shah 1994; Visser 2006). Negative pressure is created in the epidural space as the result of initial bulging of the ligamentum flavum in front of the advancing needle, followed by a rapid return to the resting position once the needle has perforated the ligament (Zarzur 1984).

The sensation felt by the anaesthesiologist from the syringe plunger with loss of resistance is different when air is compared with saline (fluid). Frequently fluid allows a rapid change from resistance

to non-resistance and increased movement of the plunger (Scott 1997).

Description of the intervention

Epidural anaesthesia is a central neuraxial block technique with many applications. Epidural anaesthesia can be used as the sole anaesthetic for procedures involving the lower limbs, pelvis, perineum and lower abdomen. Specific uses of epidural anaesthesia and/or analgesia include hip and knee surgery, vascular reconstruction of the lower limbs, amputation, labour analgesia (van den Berg 2010), postoperative analgesia for several kinds of surgical procedures and thoracic trauma with fracture of ribs or the sternum (Visser 2001).

The methods used in identification of the epidural space are extremely important for good quality of anaesthesia and for avoidance of complications such as perforation of the dura mater, epidural haematoma (due to lesions of vessels from the needle and catheter), patchy block, occasional low back pain and air venous embolism (Ash 1991; Carter 1984; Gonzalez-Carrasco 1993; Hiromi 1999; Nay 1993; Stride 1993).

A recent literature review concluded that use of a small volume of saline for loss of resistance is better than using air, not only because of increased effectiveness of analgesia but also because of associated decreased morbidity (Shenouda 2003).

With regard to recent clinical trials, studies show some advantages of either technique (saline or air), and each study author has demonstrated a preference concerning the loss of resistance technique (Aida 1998; Beilin 2000; Evron 2004; Sarna 1990; Valentine 1991). However the ideal technique for identification of the epidural space remains unclear.

How the intervention might work

The epidural space is identified by using the loss of resistance technique (LOR). This technique is based on the perception of loss of resistance as the advancing needle passes through the ligamentum flavum into the epidural space during compression of the plunger of the syringe (Beilin 2000).

Why it is important to do this review

We aim first to determine which technique (air or saline) is more efficacious and safe in reducing complications, and then to guide clinicians in their clinical practice.

OBJECTIVES

- To evaluate the efficacy and safety of both air and saline in the loss of resistance technique for identification of the epidural space.
- To evaluate complications related to the air or saline injected.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized controlled trials (RCTs) and quasi-randomized controlled trials (quasi-RCTs).

Types of participants

We included adults (> 18 years old) classified as American Society of Anesthesiologists (ASA) grades 1 to 3 undergoing surgical procedures, pregnant women in obstetrical labour and patients receiving postoperative analgesia.

We excluded patients with severe haemorrhage or shock or coagulation abnormalities, and patients using anticoagulants or with previous laminectomy; local puncture infection; or pre-eclampsia.

Types of interventions

- Intervention of interest: air.
- Control intervention: saline (fluid).

Types of outcome measures

We planned to include the following outcomes.

Primary outcomes

- Inability to locate the epidural space, defined as inability to identify the epidural space and/or unintentional dural puncture by epidural needle.
- Accidental intravascular catheter placement* and/or accidental subarachnoid catheter placement*.
- Combined spinal epidural failure* (i.e. inability to reach subarachnoid space and/or no fluid return by spinal needle puncture and/or spinal analgesia failure).

*Added post hoc (see [Differences between protocol and review](#)).

Secondary outcomes

- Morbidities (pneumonia, poor oxygenation, myocardial infarction, etc).
- Unblocked segments.
- Inadvertent dural puncture.
- Adverse events (defined as headache or migraine; neck pain; subcutaneous emphysema; difficulty in advancing the catheter; hypotension; paraesthesia; dysaesthesia; and catheter replacement and/or reposition).
- Pain relief* (however defined by the included studies).
- Participant satisfaction.

*Added post hoc (see [Differences between protocol and review](#)).

Search methods for identification of studies

We conducted systematic searches for RCTs. We applied no language, publication year or publication status restrictions. The date of the last search was September 2013.

Electronic searches

We searched the current issue of the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 9); MEDLINE via Ovid (1966 to September 2013); Ovid EMBASE (1980 to September 2013); the Latin American and Caribbean Health Science Information Database (LILACS) (1982 to September 2013); the Institute for Scientific Information (ISI) Web of Science (1945 to September 2013); the Cumulative Index to Nursing and Allied Health Literature (CINAHL) via Elton B. Stephens Company (EBSCO) (to September

2013); and [Metaregister for ongoing trials](#). The date of the most recent search was 7 September 2013.

The search strategy was composed only of terms for the intervention group (air), the control group (saline) and the condition to maximize sensitivity. As we searched both subject headings and free-text words, we expected that all relevant studies were identified.

The following exhaustive list of synonyms was identified.

(Air **OR** (injection*s and air) **OR** (Na Sodium Chloride) **OR** (NaCl Sodium Chloride)**OR** (Saline Solution)) **AND** ((Epidural analgesia) **OR** (epidural anaesthesia) **OR** (Peridural Anesthesia) **OR** (Extradural Anesthesia) **OR** (Epidural Spaces) **OR** (Epidural Space)).

Our detailed search strategies for the electronic databases can be found in the appendices: MEDLINE: [Appendix 1](#) ([Higgins 2011](#)); EMBASE: [Appendix 2](#); CENTRAL: [Appendix 3](#); CINAHL: [Appendix 4](#); Web of Science: [Appendix 5](#); and LILACS: [Appendix 6](#).

Searching other resources

We searched the reference lists of identified relevant studies to look for additional citations; we contacted specialists in the field and authors of the included trials to request unpublished data, and we contacted pharmaceutical manufacturers to verify the data and obtain additional unpublished data.

Data collection and analysis

Selection of studies

Two review authors (PA and RED) independently screened trials identified by the literature search, extracted the data, assessed trial quality and analysed the results. If consensus was not reached, we did not include the data from the trials in question unless and until the authors of those trials were able to resolve the contentious issues.

Data extraction and management

Two review authors (PA and RED) independently extracted data. We resolved discrepancies by discussion. We used a standard data extraction form based on recommendations of the Cochrane Anaesthesia Review Group (CARG) ([Appendix 7](#)) to extract the following information: characteristics of the study (design, methods of randomization); participants; interventions; and outcomes (types of outcome measures, adverse events).

Assessment of risk of bias in included studies

We used the new risk of bias approach for Cochrane reviews to assess study quality ([Higgins 2011](#)). We resolved discrepancies by discussion and used the following criteria.

Random sequence generation

Was the allocation sequence adequately generated, for example, with random number tables, computer-generated? We recorded this as 'low risk of bias,' 'high risk of bias' or 'unclear risk of bias.'

Allocation concealment

Was allocation adequately concealed in a way that would not allow the investigators or the participants to know or influence allocation

to an intervention group before an eligible participant was entered into the study (e.g. by using central randomization or sequentially numbered, opaque, sealed envelopes held by a third party)? We recorded this as 'low risk,' 'high risk' or 'unclear risk.'

Blinding

Were the study participants blinded from knowledge of which intervention a participant received? We noted where partial blinding had been performed (e.g. when it was not possible to blind participants but outcome assessment was carried out without knowledge of group assignment). We recorded this as 'low risk,' 'high risk' or 'unclear risk.' We did not consider blinding for the anaesthesiologist (i.e. personnel) who delivered the technique (i.e. air or saline), as this would not be feasible.

Incomplete outcome data

Were incomplete outcome data adequately addressed? Incomplete outcome data essentially include attrition, exclusions and missing data. If withdrawals occurred, were they described and reported by the treatment group with reasons given? We recorded whether clear explanations were provided for withdrawals and dropouts in the treatment groups. One adequate method of addressing incomplete outcome data is the use of an intention-to-treat analysis (ITT). This item was recorded as 'low risk,' 'high risk' or 'unclear risk.'

Selective reporting

Were reports of the study free from any suggestion of selective outcome reporting? This was interpreted as no evidence that statistically non-significant results might have been selectively withheld from publication, for example, selective underreporting of data or selective reporting of a subset of data. We recorded this as 'low risk,' 'high risk' or 'unclear risk.'

Other bias (e.g. conflict of interest)

Was the study apparently free of other problems that could put it at high risk of bias? We recorded this as 'low risk,' 'high risk' or 'unclear risk.'

We copied into an assessment table information relevant to making a judgement on a criterion from the original publication. If additional information was provided by study authors, we entered this information into the table, along with an indication that this is unpublished information. At least two review authors independently made a judgement as to whether the risk of bias for each criterion was considered to be 'low,' 'high' or 'unclear.' We resolved disagreements by discussion.

We considered that trials categorized as 'low risk' for all six criteria were trials with low risk of bias.

Measures of treatment effect

Binary outcomes

For dichotomous data, we used the risk ratio (RR) as the effect measure with 95% confidence intervals (CIs).

Continuous outcomes

For continuous data, we presented the results as mean differences (MDs) with 95% CIs. When pooling data across studies, we

estimated the MD if outcomes were measured in the same way between trials. We planned to use the standardized mean difference (SMD) to combine trials that used different methods to measure the same outcome.

Unit of analysis issues

We analysed data using participants with one or more events as the unit of analysis. If no events were reported in control or experimental groups, we planned to use the Peto odds ratio to avoid use of the continuity correction.

Dealing with missing data

An intention-to-treat analysis (ITT) is one in which all participants in a trial are analysed according to the intervention to which they were allocated, whether or not they received the intervention. We assumed that participants who dropped out are non-responders. For each trial, we reported whether the investigators stated if the analysis was performed according to the ITT principle. If participants were excluded after allocation, we reported in full any details provided.

Assessment of heterogeneity

We intended to quantify inconsistency among pooled estimates by using the I^2 statistic. This illustrates the percentage of variability in effect estimates that results from heterogeneity rather than from sampling error (Higgins 2003; Higgins 2011). We intended to examine forest plots for CI overlap and to calculate the χ^2 test for homogeneity with a 10% level of significance. We used I^2 statistical values to categorize heterogeneity: less than 25%; 26% to 50%; 51% to 75%; and greater than 75%.

Assessment of reporting biases

We planned to perform a funnel plot to assess publication bias (trial effect vs trial size).

Data synthesis

We planned to use the fixed-effect model to analyse data. If I^2 was greater than 50%, we intended to use random-effects models. We planned to undertake quantitative analyses of outcomes on an ITT basis. If a meta-analysis was not possible or appropriate, the results from clinically comparable trials were described qualitatively in the text.

Summary of findings tables

In our review, we used the principles of the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) system (Guyatt 2008) to assess the quality of the body of evidence associated with specific outcomes (inability to locate the epidural space; accidental intravascular catheter placement and/or accidental subarachnoid catheter placement; and combined spinal epidural failure) and constructed a summary of findings (SoF) table using GRADE software. The GRADE approach appraises the quality of a body of evidence according to the extent to which one can be confident that an estimate of effect or association reflects the item being assessed. Assessment of the quality of a body of evidence considers within-study risk of bias (methodological quality), directness of the evidence, heterogeneity of the data, precision of effect estimates and risk of publication bias. The quality of the evidence for a specific outcome will be altered by

a level according to the performance of studies against these five factors.

High-quality evidence: Findings are consistent among at least 75% of RCTs with low risk of bias; data are consistent, direct and precise, and no publication biases are known or suspected. Further research is unlikely to change the estimate or our confidence in the results.

Moderate-quality evidence: One of the domains is not met. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low-quality evidence: Two of the domains are not met. 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 evidence: Three of the domains are not met. We are very uncertain about the results.

No evidence: No RCTs that addressed this outcome were identified.

Subgroup analysis and investigation of heterogeneity

Subgroup analyses are secondary analyses in which participants are divided into groups according to shared characteristics, and outcome analyses are conducted to determine whether any significant treatment effect occurs according to that characteristic. In this review, subgroup analyses will be performed for the following.

- Different types of ASA grades (e.g. ASA 1 vs ASA 3).
- Different types of body mass index.
- Age (≥ 18 to 60 years old vs > 60 years old).
- Residents versus professional anaesthesiologists*.

*Added post hoc (see [Differences between protocol and review](#)).

However, the planned analyses could not be carried out because relevant data were lacking in the included studies.

Sensitivity analysis

We planned to perform the following sensitivity analyses.

- Trials with low risk of bias versus those with high risk of bias.
- Rates of withdrawal for each outcome ($< 20\%$ vs greater than and/or equal to 20%).

However, the planned analyses could not be carried out because relevant data were lacking in the included studies.

RESULTS

Description of studies

See the [Characteristics of included studies](#) table.

Results of the search

We identified a total of 2884 citations through database searches for the original review (see [Figure 1](#) for search results). After screening by title and then by abstract, we obtained full-paper copies for 13 citations that were potentially eligible for inclusion in the review. We excluded four studies ([Evron 2004](#); [Okutomi 1999](#); [Siddik-Sayyid 2006](#); [Wantman 2006](#)) for the reasons described in the [Characteristics of excluded studies](#) table. Two secondary publications of the [Evron 2004](#) and [Okutomi 1999](#) studies were identified. The remaining seven studies ([Beilin 2000](#); [Grondin 2009](#); [Norman 2006](#); [Sarna 1990](#); [Valentine 1991](#); [van den Berg 2010](#); [Vigfússon 1995](#)), with a total of 852 participants, met the minimal methodological requirements and were included in this review.

Figure 1. Study flow diagram.

Figure 1. (Continued)

Included studies

We included in this review seven studies with a total of 852 participants (Beilin 2000; Grondin 2009; Norman 2006; Sarna 1990; Valentine 1991; van den Berg 2010; Vigfússon 1995).

Design of the studies

All included studies (Beilin 2000; Grondin 2009; Norman 2006; Sarna 1990; Valentine 1991; van den Berg 2010; Vigfússon 1995) claimed to be RCTs.

Types of study participants

Beilin 2000 evaluated 160 participants with active labour who were having contractions at least once every five minutes, and who requested epidural analgesia, with mean age of 33 and 32 years in air and saline groups, respectively.

Grondin 2009 analysed 360 randomly assigned participants and 345 analysed with active labour and requesting neuraxial labour analgesia, or with cervical dilation of no more than 8 cm, a verbal rating score for pain of at least six of 10 maximum, vertex singleton pregnancy and no medical/obstetrical contraindications for combined spinal epidural anaesthesia (CSE) placement. Mean age of participants in the air and saline groups was 28 and 27 years, respectively.

Norman 2006 studied 50 parturient participants admitted for active labour, of any age, who were planning to have a vaginal birth and wanted epidural analgesia. Mean age for those in the air and saline groups was 24.9 and 24.2 years, respectively.

Sarna 1990 assessed 67 women who required the insertion of a lumbar epidural catheter for relief of pain in labour, caesarean section or other obstetrical procedure. Mean age for participants in the air and saline groups was 25.2 and 23.4 years, respectively.

Valentine 1991 randomly assigned 50 primiparous participants in early labour who had requested epidural analgesia to receive air (mean age, 25.3 years) or saline (mean age, 24.7 years).

van den Berg 2010 randomly assigned 55 participants requesting or submitted for epidural labour analgesia to receive air (mean age, 26.3 years) or saline (mean age, 24.4 years).

Vigfússon 1995 assessed 110 participants. No reports of mean age, gender or follow-up were provided.

Types of interventions and follow-up

All included studies (Beilin 2000; Grondin 2009; Norman 2006; Sarna 1990; Valentine 1991; van den Berg 2010; Vigfússon 1995) evaluated air compared with saline with a maximum follow-up of 24 hours after delivery (Sarna 1990) and a minimum of 15 minutes after the last dose of local anaesthetic had been administered (Beilin 2000).

The amount of air and saline injected ranged from 2 mL of air and 2 mL of 0.9% saline (Beilin 2000) to 3 mL of air and 3 mL of saline (Grondin 2009; Norman 2006), 4 mL of air and 4 mL of 0.9% saline (Valentine 1991), 5 mL of air and 5 mL of saline (van den Berg 2010) and 10 mL of air and also saline (Sarna 1990). The Vigfússon 1995 study did not report this.

Types of outcome measures

Beilin 2000 measured the incidence of paraesthesia; failed epidural; and analgesia requiring additional medication, as well as pain scores and catheter replacement.

Grondin 2009 evaluated the success of spinal labour analgesia defined by a verbal pain score no greater than three at 15 minutes after spinal dose administration; spontaneous fluid return and fluid return upon preinjection and postinjection aspiration; epidural catheter replacement rate; and average hourly total quantities of epidural medications required within four hours of initial epidural catheter insertion.

Norman 2006 measured pain using the visual analogue scale (VAS); a dermatome (vertebral level of anaesthesia); adverse events; and patchy blocks.

Sarna 1990 assessed the occurrence of paraesthesia; complications such as vascular puncture; difficulty in passing the epidural

catheter; quality of pain relief; and occurrence of unblocked segment.

[Valentine 1991](#) evaluated unblocked segments and participant satisfaction.

[van den Berg 2010](#) assessed both subjective and objective responses to dural puncture; grimacing and involuntary movement; and occurrence of paraesthesia, dysaesthesia and/or neurological deficit.

[Vigfússon 1995](#) measured the ability to locate the epidural space.

Excluded studies

We excluded four studies ([Evron 2004](#); [Okutomi 1999](#); [Siddik-Sayyid 2006](#); [Wantman 2006](#)) for the reasons described in the [Characteristics of excluded studies](#) table. Two secondary publications of the [Evron 2004](#) and [Okutomi 1999](#) studies were identified.

Studies awaiting assessment

No study is awaiting assessment.

Risk of bias in included studies

See [Figure 2](#) and [Figure 3](#).

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

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Beilin 2000	+	+	?	?	+	+	+
Grondin 2009	+	+	+	+	+	+	+
Norman 2006	+	?	-	?	+	+	+
Sarna 1990	?	?	+	+	?	+	+
Valentine 1991	?	?	?	+	+	+	+
van den Berg 2010	+	?	?	?	+	+	+
Vigfússon 1995	?	?	?	?	?	+	+

Allocation

Two studies (Beilin 2000; Grondin 2009) described in an adequate manner the methods used for generation of allocation sequence (computer-generated numbers) and allocation concealment (sealed opaque envelopes and without knowledge of previous or future participant group assignment, respectively). Therefore, using the criteria of the *Cochrane Handbook for Systematic Reviews*

of Interventions (Higgins 2011), we graded these studies as having low risk of bias.

Two studies (Norman 2006; van den Berg 2010) adequately described the methods used for generation of allocation sequence as a computerized table of random numbers and a pre-prepared block randomization list, respectively. Therefore, they were ranked

as having low risk of bias for generation of allocation sequence and unclear risk of bias (not reported) for allocation concealment.

Three studies (Sarna 1990; Valentine 1991; Vigfússon 1995) did not report how allocation was generated or how allocation was concealed; therefore, we ranked them as having unclear risk of bias.

Blinding

Beilin 2000; van den Berg 2010; and Vigfússon 1995 did not report whether blinding for participants or outcome assessors was performed. We ranked these studies as having unclear risk of bias for this domain.

Grondin 2009 and Sarna 1990 described that both participants and data collectors were blinded to treatment allocation. We ranked these studies as having low risk of bias for this domain.

In Norman 2006, the study authors mentioned that no blinding assessment was provided for participants. This study was ranked as having high risk of bias for this domain, although no mention was made of blinding of outcome assessment (unclear risk of bias).

Valentine 1991 did not report whether participants were blinded to treatment allocation (unclear risk of bias), but the data collector who assessed the onset of sensory loss and dermatomal spread was blinded (low risk of bias).

Incomplete outcome data

No withdrawals or dropouts were reported in three studies (Beilin 2000; van den Berg 2010; Sarna 1990), which were therefore ranked as having low risk of bias.

Three studies reported withdrawals (Grondin 2009; Norman 2006; Valentine 1991); withdrawals for all were less than 20% of the total participants in each study. These studies were ranked as having low risk of bias for this domain.

Vigfússon 1995 did not report the withdrawals or the dropouts; therefore we ranked this study as having unclear risk of bias.

Selective reporting

No evidence of selective reporting was noted in any of the included studies (Beilin 2000; Grondin 2009; Norman 2006; Sarna 1990; Valentine 1991; van den Berg 2010; Vigfússon 1995); therefore all were ranked as having low risk of bias for this domain.

Other potential sources of bias

No evidence of other biases was found in any of the included studies (Beilin 2000; Grondin 2009; Norman 2006; Sarna 1990; Valentine 1991; van den Berg 2010; Vigfússon 1995); therefore all were ranked as having low risk of bias.

Effects of interventions

See: [Summary of findings for the main comparison](#)

See [Summary of findings for the main comparison](#).

Outcome: inability to locate the epidural space (Analysis 1.1)

We found no statistically significant differences between participants receiving air and those given saline in the meta-analysis of three studies (Beilin 2000; Grondin 2009; Vigfússon 1995;

619 participants). The risk ratio (RR) was 0.88 (95% confidence interval (CI) 0.33 to 2.31) for inability to locate the epidural space.

Outcome: accidental catheter placement (Analysis 1.2) and/or accidental subarachnoid catheter placement (Analysis 1.3)

We found no statistically significant differences between participants receiving air and those given saline in the meta-analysis of two studies (Beilin 2000; Sarna 1990; 223 participants) (RR 0.90, 95% CI 0.33 to 2.45).

We found no statistically significant differences between participants receiving air and those given saline in the meta-analysis of four studies (Beilin 2000; Grondin 2009; Sarna 1990; Vigfússon 1995; 682 participants) (RR 2.95, 95% CI 0.12 to 71.90).

Outcome: combined spinal epidural failure (Analysis 1.4)

We found no statistically significant differences between participants receiving air and those given saline in the meta-analysis of two studies (Grondin 2009; van den Berg 2010; 400 participants) (RR 0.98, 95% CI 0.44 to 2.18).

Outcome: unblocked segments (Analysis 1.5)

In Beilin 2000, participants for whom the catheter could not be threaded into the epidural space and those for whom the catheter was threaded into the intravascular space were excluded from the analysis of adequate analgesia. A total of 74 participants remained in the air group and 72 in the saline group.

We found no statistically significant differences between participants receiving air and those given saline in the meta-analysis of five studies (Beilin 2000; Norman 2006; Sarna 1990; Valentine 1991; Vigfússon 1995; 423 participants) (RR 1.66, 95% CI 0.72, 3.85).

Outcome: adverse events (i.e. neck pain; subcutaneous emphysema; difficulty in advancing the catheter; hypotension; paraesthesia; dysaesthesia; and catheter replacement and/or reposition) (Analysis 1.6)

We found no statistically significant differences between participants receiving air and those given saline in the occurrence of paraesthesia (RR 0.89, 95% CI 0.69 to 1.15; three studies, Beilin 2000; Grondin 2009; Sarna 1990); difficulty in advancing the catheter (RR 0.91, 95% CI 0.32 to 2.56; two studies, Beilin 2000; Sarna 1990); catheter replacement (RR 0.69, 95% CI 0.26 to 1.83; two studies, Beilin 2000; Grondin 2009); and postdural puncture headache (RR 0.83, 95% CI 0.12 to 5.71; one study, Vigfússon 1995). Data on paraesthesias from the Grondin 2009 study were related to spinal needle puncture, but those from Beilin 2000 and Sarna 1990 were related to catheter placement.

Outcome: pain relief (Analysis 1.7)

We found no statistically significant differences between participants receiving air and those given saline in the meta-analysis of two studies (Grondin 2009; Norman 2006; 395 participants) regarding pain relief measured by visual analogue scale. The mean difference (MD) was -0.09 (95% CI -0.37 to 0.18) for inability to locate the epidural space.

DISCUSSION

Summary of main results

We aimed to identify the best available clinical evidence to answer our question, "Which technique (air or saline) is more efficacious and safe in reducing complications during the loss of resistance technique for identifying the epidural space and guiding clinicians in their clinical practice?" We performed an extensive search of the literature and found low-quality evidence showing that results do not differ between air and saline in use of the loss of resistance technique to locate the epidural space and in reduction of complications.

To appropriately identify the epidural space, it is necessary to have good knowledge of the relevant anatomy and of contents of the space. Use of air or saline has been controversial amongst anaesthesiologists. However, it is essential to determine which technique is more effective for avoiding unnecessary complications such as paraesthesia, air venous embolism, neurological complications, accidental puncture of the dura mater, total subarachnoid block, epidural haematoma due to blood vessel lesions, epilepsy and pneumoencephalo. Furthermore, inability to locate the epidural space (defined as inability to identify the epidural space and/or unintentional dural puncture by the epidural needle) appears to be dependent on the amount of training the anaesthesiologist has undergone.

The literature indicates that unintentional dural puncture by the Tuohy needle increases the risk of chronic headache (Webb 2012). In an observational study (Webb 2012), 40 parturient participants who sustained unintentional dural puncture with a 17-gauge Tuohy needle were analysed and matched with 40 control participants. A higher incidence of chronic headache was reported in the study group, with a rate of 28% compared with 5% among matched controls. In another study, conducted in 100 obstetrical participants with accidental dural puncture with a Tuohy needle, study authors reported a headache rate of 81% (Banks 2001). One severe consequence when an unintentional dural puncture occurs is the injection of a large volume of local anaesthetic into the subarachnoid space. This might result in total spinal anaesthesia, causing apnoea, hypotension and bradycardia.

Our review shows that probably no difference exists between efficacy among the two studied techniques (air and saline) in locating the epidural space. This is so because no statistically significant differences were noted in any of the outcomes evaluated. However, this fact may be related to the experience of the anaesthesiologist who was performing the technique. Furthermore, as noted in Analysis 1.3, the occurrence of accidental subarachnoid catheter placement is a rare event and may not be relevant to the issues that we have discussed.

Another variable that might be independent of the technique used to locate the epidural space, and that should be investigated, is the correlation between volume of anaesthetic injected by the epidural needle and successful catheter passage afterwards. It seems that a large volume of local anaesthetics through the needle facilitates catheter placement, decreasing the chance of accidental intravascular or subarachnoid catheter placement (Cesur 2005; Mhyre 2009).

The most widely reported adverse event among the studies included in this review was the occurrence of paraesthesia during performance of the technique. This shows the possibility of no difference between air and saline solution.

Also, among the studies included in this review, no reports described severe morbidities such as pneumonia, poor oxygenation and myocardial infarction, which are unlikely to be correlated with the application of the two techniques.

We could not determine whether the included studies were equivalent in terms of types of catheters used (i.e. soft vs rigid and uni-orifice vs multi-orifice), as only two studies (Beilin 2000; Grondin 2009) reported this as per 20-gauge multi-orifice and per 19-gauge triport epidural catheter (Becton Dickinson and Company), respectively. However, theoretically, the rigid catheter may be associated with a higher rate of inadvertent intravascular catheter misplacement, although the multi-orifice type might not show differences when compared with the uni-orifice type, as the former also presents a distal orifice. In terms of position of the participant during performance of the technique, the Beilin 2000; Sarna 1990; and van den Berg 2010 studies used the sitting position, and Grondin 2009 and Valentine 1991 used the lateral position. The studies of Norman 2006 and Vigfússon 1995 did not report this information. However, no difference was seen in our statistical data, given the position variable, and further studies are needed to perform a subgroup analysis per type of position used (i.e. lateral or sitting).

Amounts injected in some studies ranged from 2 mL of air and 2 mL of 0.9% saline (Beilin 2000) to 3 mL of air and 3 mL of saline (Grondin 2009; Norman 2006), 4 mL of air and 4 mL of 0.9% saline (Valentine 1991), 5 mL of air and 5 mL of saline (van den Berg 2010) and 10 mL of air and of saline (Sarna 1990). In future studies, researchers should evaluate the optimal dosing of both air and saline to allow comparisons between them.

In terms of length of catheter insertion past the needle tip, also theoretically, the depth to which the catheter goes may have implications for the rates of inadvertent intravascular catheter misplacement. The most used length of catheter insertion was 5 cm (Beilin 2000; Grondin 2009; Norman 2006; van den Berg 2010). However, clinical trials should investigate this variable as well.

Furthermore, future clinical trials should address the implications of performing the technique from the perspective of a resident and of a professional anaesthesiologist with many years of experience. This might play an important role in the success of the technique under investigation. As previously stated, future research should focus on whether injection of different volumes of anaesthetic or saline solution after identification of the epidural space facilitates passage of the catheter, thereby reducing accidental intravascular and subarachnoid catheter placement.

Overall completeness and applicability of evidence

We developed a comprehensive search strategy, handsearched the reference lists of identified studies for additional citations and made contact with experts in the field. We are therefore confident that we have mapped all clinical trials comparing air versus saline in the loss of resistance technique for identification of the epidural space.

All included studies, with the exception of one (Vigfússon 1995), evaluated parturient individuals as their population of interest; therefore the applicability of the results of this review might be compromised for patients undergoing surgical procedures and for those receiving postoperative analgesia.

Quality of the evidence

The methodological quality of the included studies was generally ranked as showing low risk of bias in most domains (Beilin 2000; Grondin 2009; Sarna 1990; Valentine 1991; van den Berg 2010; Vigfússon 1995), with the exception of one study (Norman 2006), which showed a high risk of introducing bias related to inadequate blinding of participants. No inconsistency was noted across studies (i.e. $I^2 = 0\%$) and the overlap in confidence intervals was reasonable, but a small sample size was studied. The numbers of events presented small, but not very narrow, confidence intervals, with the exception of the outcome 'accidental subarachnoid catheter placement.' This outcome presented a wider confidence interval (RR 2.95, 95% CI 0.12 to 71.90), but it was not possible to verify publication bias, as fewer than 10 studies were included in this meta-analysis.

Potential biases in the review process

Although we included seven studies in this review, the overall sample size of the studies was small, because most of the studies that we assessed were classified as showing low risk of bias regarding their methodological quality. This would be reflected in any conclusions drawn from this review. Another area of concern was that the included studies have not yet standardized the outcomes, and this makes performance of a meta-analysis more difficult.

Agreements and disagreements with other studies or reviews

Saberski et al showed that use of saline to identify the epidural space may help to reduce the incidence of pneumocephalus, spinal cord and nerve root compression, retroperitoneal air, subcutaneous emphysema and venous air embolism (Saberski 1997). This review searched only the MEDLINE database and was limited to the years from 1966 to 1995.

Another narrative review concluded, through case reports, that air may be harmful or might impede the onset and quality of

epidural analgesia (Norman 2003). The review authors noted that results, in favouring air or saline, are contradictory throughout the literature; however they pointed out that use of saline may result in more rapid pain relief of satisfactory quality among parturient individuals (Norman 2003).

AUTHORS' CONCLUSIONS

Implications for practice

Low-quality evidence shows that results do not differ between air and saline when the loss of resistance technique is used to locate the epidural space and to reduce complications. The applicability of these findings might be compromised, as most of the results described in this review were obtained from parturient individuals. This review underlines the need to conduct well-designed trials in this field.

Implications for research

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. Therefore well-conducted clinical trials should be carried out, including assessment of the following outcomes: inability to locate the epidural space; accidental intravascular and subarachnoid catheter placement; combined spinal epidural anaesthesia failure; and morbidities.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Beilin 2000

Methods	Design: RCT Multi-centre or single-centre: not reported Period of recruitment: not reported Sample size: justified (71 in each group is sufficient to provide 80% power to detect a difference between the 2 groups if 1 of the groups has a 10% incidence of inadequate analgesia and the other group has a 30% incidence. This is based on a 2-tailed test at the 5% level of significance) Follow-up: 15 minutes after the last dose of local anaesthetic had been administered with reassessment considered
Participants	N = 160 Sex (male/female): 0/160 Age (mean), years: air group, 33; saline group, 32 Setting: not reported Inclusion criteria: patients in active labour with contractions at least once every 5 minutes, who requested epidural analgesia Exclusion criteria: spinal column disorders, including scoliosis and herniated discs, and previous spine surgery
Interventions	Air 2 mL (n = 80) versus 2 mL of 0.9% saline (n = 80)
Outcomes	Incidence of paraesthesia; failed epidural; and analgesia requiring additional medication, as well as pain scores and catheter replacement
Notes	We contacted the first study author on 16 October 2013 to clarify whether researchers had evaluated any other outcomes predefined in our protocol and not described in their paper

Beilin 2000 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated restricted random number programme
Allocation concealment (selection bias)	Low risk	Sealed in opaque envelopes and opened sequentially by the anaesthesiologist after the participant requested labour analgesia
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: not reported. Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals and no dropouts were reported. However, the study authors did not consider an intention-to-treat analysis because participants for whom the catheter could not be threaded into the epidural space, or for whom the catheter was threaded into the intravascular space, were excluded from the analysis of adequate analgesia
Selective reporting (reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

Grondin 2009

Methods	Design: RCT Multi-centre Period of recruitment: not reported Sample size: justified (160 per group was needed to demonstrate the stated difference (90% vs 98%) between groups in the primary outcome variable to achieve a power of 0.8 and an alpha of 0.05. An estimated total of 360 participants was planned for enrolment, with the goal to obtain at least 320 participants) Follow-up: 4 hours of analgesia initiation
Participants	N = 360 randomly assigned but only 345 analysed Sex (male/female): 0/360 Age (mean),years: air group, 28; saline group, 27 Setting: not reported Inclusion criteria: patients in active labour and requesting neuraxial labour analgesia; those with cervical dilation of no more than 8 cm, verbal rating score for pain of at least 6 of 10 maximum, vertex singleton pregnancy and no medical/obstetrical contraindications for CSE placement

Grondin 2009 (Continued)

Exclusion criteria: American Society of Anesthesiologists physical status greater than 2, or weight greater than 114 kg

Interventions	Air (n = 173) versus saline (n = 172)
Outcomes	Success of spinal labour analgesia as defined by verbal pain score of no more than 3 at 15 minutes after spinal dose administration; spontaneous fluid return and fluid return upon preinjection and postinjection aspiration; epidural catheter replacement rate; and average hourly total quantities of epidural medications required within 4 hours of initial epidural catheter insertion
Notes	<ul style="list-style-type: none"> Anaesthesia residents with more than 2 months of successful obstetrical anaesthesia training experiences, obstetrical anaesthesia fellows and attending obstetrical anaesthesiologists, all of whom are comfortable with the CSE procedure using air or saline LORT, participated in placing the blocks. All trainees were supervised by an attending obstetrical anaesthesiologist We contacted the first study author on 16 October 2013 to clarify whether investigators had evaluated any other outcomes predefined in our protocol and not described in their paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization
Allocation concealment (selection bias)	Low risk	Without knowledge of previous or future participant group assignment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants: blinded. Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Data collector and interpreters were blinded to group assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	15 excluded patients (less than 20%)
Selective reporting (reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

Norman 2006

Methods	Design: RCT Single-centre Period of recruitment: not reported Sample size: justified but inadequate (power for analysis with VAS scores was calculated at 0.85 for this study)
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Norman 2006 (Continued)

Follow-up: 30 minutes after epidural placement. For epidural-related adverse events, follow-up involved removal of the epidural catheters and care provided several hours post partum and on the following day

Participants	<p>N = 50</p> <p>Sex (male/female): 0/50</p> <p>Age (mean), years: air group, 24.9; saline group, 24.2</p> <p>Setting: US military medical centre in the mid-Atlantic region</p> <p>Inclusion criteria: parturient individuals admitted for active labour, of any age, planning to have a vaginal birth and wanting epidural analgesia</p> <p>Exclusion criteria: conditions that contraindicate epidural analgesia or make it a poor choice for pain relief; coagulopathies associated with severe pre-eclampsia; previous lumbar spine surgery; severe scoliosis; receipt of magnesium sulfate; or any condition likely to require rapid preparation for a caesarean section</p>
Interventions	Air 3 mL (n = 25) versus 3 mL of saline (n = 25)
Outcomes	Pain relief by VAS; dermatome (vertebral level of anaesthesia); adverse events; and patchy blocks
Notes	We contacted the first study author on 16 October 2013 to clarify whether researchers had evaluated any other outcomes predefined in our protocol and not described in their paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerized table of random numbers
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants: not blinded (information was not shared with participants unless they requested the information). Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only one participant was unable to complete the study and was not included in the analysis
Selective reporting (reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

Sarna 1990

Methods	Design: RCT
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Air versus saline in the loss of resistance technique for identification of the epidural space (Review)

Sarna 1990 (Continued)

Multi-centre or single-centre: not reported

Period of recruitment: not reported

Sample size: not reported

Follow-up: 24 hours after delivery

Participants	<p>N = 67</p> <p>Sex (male/female): 0/67</p> <p>Age (mean), years: air group, 25.2; saline group, 23.4</p> <p>Setting: not reported</p> <p>Inclusion criteria: women who required insertion of a lumbar epidural catheter for relief of pain in labour, caesarean section or other obstetrical procedure</p> <p>Exclusion criteria: not reported</p>
Interventions	Air 10 mL (n = 32) versus 10 mL saline (n = 35)
Outcomes	Paraesthesia; complications such as vascular puncture; difficulty in passing the epidural catheter; quality of pain relief; occurrence of unblocked segment
Notes	We contacted the first study author on 16 October 2013 to clarify whether investigators had evaluated any other outcomes predefined in our protocol and not described in their paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants: blinded. Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The midwife, who was blind to the technique, ensured that the anaesthetist did not influence the participant's assessment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

Valentine 1991

Methods	Design: RCT Multi-centre or single-centre: not reported Period of recruitment: not reported Sample size: not reported Follow-up: 30-minute duration of the study
Participants	N = 50 Sex (male/female): 0/50 Age (mean), years: air group, 25.3; saline group, 24.7 Setting: not reported Inclusion criteria: primiparous individuals in early labour who had requested extradural analgesia Exclusion criteria: patients who had previously experienced an extradural or spinal procedure, patients in whom urgent delivery was anticipated and those who had a contraindication to extradural analgesia
Interventions	4 mL of air (n = 25) versus 4 mL of 0.9% saline (n = 25)
Outcomes	Unblocked segments and participant satisfaction with insertion
Notes	<ul style="list-style-type: none"> The blocks were undertaken by a group of 5 anaesthetists, including investigators, all of whom had more than 3 years of experience with the extradural technique We contacted the first study author on 16 October 2013 to clarify whether researchers had evaluated any other outcomes predefined in our protocol and not described in their paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: not reported. Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Low risk	An investigator who had no knowledge of the medium used to identify the extradural space assessed onset of sensory loss and dermatomal spread, using sterile 21-gauge needles to test pinprick at 5-minute intervals up to 30 minutes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals
Selective reporting (reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

van den Berg 2010

Methods	<p>Design: RCT</p> <p>Multi-centre or single-centre: not reported</p> <p>Period of recruitment: not reported</p> <p>Sample size: justified (25 participants per group using the formula for a 2-sided comparison, with confidence limits of 95% and 80% power, on the basis that a 40% difference in incidence of any subjective or objective response would be a significant outcome)</p> <p>Follow-up: not reported</p>
Participants	<p>N = 55</p> <p>Sex (male/female): 0/55</p> <p>Age (mean), years: air group, 26.3; saline group, 24.4</p> <p>Setting: not reported</p> <p>Inclusion criteria: patients requesting and those submitted for epidural labour analgesia</p> <p>Exclusion criteria: contraindication to neuraxial block or pertinent drug allergy</p>
Interventions	Air (n = 27) versus saline (n = 28)
Outcomes	Subjective and objective responses to dural puncture; grimacing and involuntary movement; occurrence of paraesthesia, dysaesthesia and/or neurological deficit
Notes	<ul style="list-style-type: none"> One participant was excluded because of present combined spinal epidural failure, and another participant was enrolled. However, we considered the excluded participant in the air group for the outcome of combined spinal epidural failure (i.e. n = 28 for air group) We contacted the first study author on 16 October 2013 to clarify whether researchers had evaluated any other outcomes predefined in our protocol and not described in their paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Pre-prepared block randomization list (sequential groups of 5 participants)
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: not reported. Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals and no dropouts were reported

van den Berg 2010 (Continued)

Selective reporting (re-reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

Vigfússon 1995

Methods	Design: RCT Multi-centre or single-centre: not reported Period of recruitment: not reported Sample size: not reported Follow-up: not reported
Participants	N = 110 Sex (male/female): not reported Age (mean), years: not reported Setting: not reported Inclusion criteria: not reported Exclusion criteria: not reported
Interventions	Air (n = 60) versus saline (n = 50)
Outcomes	Ability to locate the epidural space: easy, relatively easy, difficult or impossible
Notes	<ul style="list-style-type: none"> Study available only in abstract We contacted the first study author on 16 October 2013 to clarify whether researchers had evaluated any other outcomes predefined in our protocol and not described in their paper, as well as to ask for a possible full-text article. The study author replied on 16 November 2013 with information related to outcomes data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants: not reported. Personnel: not applicable
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported

Vigfússon 1995 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	Not detectable
Other bias	Low risk	Not detectable

CSE = combined spinal epidural anaesthesia.

LORT = loss of resistance technique.

mL = millilitre.

RCT = randomized controlled trial.

US = United States.

VAS = visual analogue scale.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Evron 2004	Randomized controlled trial (RCT), however evaluated air versus lidocaine
Okutomi 1999	Randomized controlled trial (RCT), however evaluated 1, 5 or 10 mL of saline solution
Siddik-Sayyid 2006	Randomized controlled trial (RCT), however evaluated 2 versus 10 mL of saline solution
Wantman 2006	Systematic survey to assess method preferred (air vs saline) by anaesthesiologists

DATA AND ANALYSES
Comparison 1. Air versus saline

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Inability to locate the epidural space	3	619	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.33, 2.31]
2 Accidental intravascular catheter placement	2	223	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.33, 2.45]
3 Accidental subarachnoid catheter placement	4	682	Risk Ratio (M-H, Random, 95% CI)	2.95 [0.12, 71.90]
4 Combined spinal epidural failure	2	400	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.44, 2.18]
5 Unblocked segments	5	423	Risk Ratio (M-H, Random, 95% CI)	1.66 [0.72, 3.85]
6 Adverse events	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Air versus saline in the loss of resistance technique for identification of the epidural space (Review)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Paraesthesias	3	572	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.69, 1.15]
6.2 Difficulty in advancing the catheter	2	227	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.32, 2.56]
6.3 Catheter replacement and/or reposition	2	501	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.26, 1.83]
6.4 Postdural puncture headache	1	110	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.12, 5.71]
7 Pain relief	2	395	Mean Difference (IV, Random, 95% CI)	-0.09 [-0.37, 0.18]

Analysis 1.1. Comparison 1 Air versus saline, Outcome 1 Inability to locate the epidural space.

Analysis 1.2. Comparison 1 Air versus saline, Outcome 2 Accidental intravascular catheter placement.

Analysis 1.3. Comparison 1 Air versus saline, Outcome 3 Accidental subarachnoid catheter placement.

Analysis 1.4. Comparison 1 Air versus saline, Outcome 4 Combined spinal epidural failure.

Analysis 1.5. Comparison 1 Air versus saline, Outcome 5 Unblocked segments.

Analysis 1.6. Comparison 1 Air versus saline, Outcome 6 Adverse events.

Analysis 1.7. Comparison 1 Air versus saline, Outcome 7 Pain relief.

APPENDICES

Appendix 1. Search strategy for MEDLINE (Ovid SP)

1. exp Air/
2. exp Sodium Chloride/
3. air.mp.
4. (injection* adj3 air).mp.
5. Sodium Chloride.mp.
6. Saline Solution*.mp.
7. 6 or 3 or 4 or 1 or 2 or 5
8. exp Epidural Space/
9. exp Injections, Epidural/
10. resistance techniq*.mp.
11. exp Analgesia, Epidural/
12. exp Anesthesia, Epidural/
13. ((an?esthesia or analgesia) adj3 (Epidural or Peridural or Extradural)).mp.
14. Epidural Space*.mp.
15. 8 or 11 or 13 or 10 or 9 or 12 or 14
16. 7 and 15
17. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh.
18. 16 and 17

Appendix 2. Search strategy for EMBASE (Ovid SP)

1. exp Air/
2. exp Sodium Chloride/
3. air.mp.
4. (injection* adj3 air).mp.
5. Sodium Chloride.mp.
6. Saline Solution*.mp.
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp Epidural Space/
9. exp Epidural Drug Administration/
10. resistance techniq*.mp.
11. exp Epidural Anesthesia/
12. ((an?esthesia or analgesia) adj3 (Epidural or Peridural or Extradural)).mp.
13. Epidural Space*.mp.
14. 8 or 11 or 13 or 10 or 9 or 12
15. 7 and 14
16. (Randomized controlled trial/ or Controlled study/ or Randomization/ or Double blind procedure/ or Single blind procedure/ or Clinical trial/ or (clinical adj5 trial\$).ti,ab,hw. or ((doubl\$ or singl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).ti,ab,hw. or Placebo/ or Placebo \$.ti,ab,hw. or Random\$.ti,ab,hw. or Methodology.sh. or latin square.ti,ab,hw. or crossover.ti,ab,hw. or cross-over.ti,ab,hw. or Crossover Procedure/ or Drug comparison/ or Comparative study/ or (comparative adj5 trial\$).ti,ab,hw. or (control\$ or prospectiv\$ or volunteer \$).ti,ab,hw. or exp "Evaluation and Follow Up"/ or Prospective study/) not (animal/ not (human/ and animal/))
17. 16 and 15

Appendix 3. Search strategy for CENTRAL

- #1 MeSH descriptor Air explode all trees
- #2 MeSH descriptor Sodium Chloride explode all trees
- #3 (injection* near air) or air or (Sodium Chloride) or (Saline Solution*)
- #4 (#1 OR #2 OR #3)
- #5 MeSH descriptor Epidural Space explode all trees

#6 MeSH descriptor Injections, Epidural explode all trees
 #7 MeSH descriptor Analgesia, Epidural explode all trees
 #8 MeSH descriptor Anesthesia, Epidural explode all trees
 #9 (resistance techniq*) or ((an?esthesia or analgesia) near (Epidural or Peridural or Extradural)) or (Epidural Space*)
 #10 (#5 OR #6 OR #7 OR #8 OR #9)
 #11 (#4 AND #10)

Appendix 4. Search strategy for CINAHL (EBSCO host)

#1 (MM "Air+")
 #2 (MH "Sodium Chloride+")
 #3 "air" or "Sodium Chloride" or "Saline Solution*"
 #4 S1 or S2 or S3
 #5 (MM "Epidural Space")
 #6 (MH "Injections, Epidural+")
 #7 (MM "Analgesia, Epidural") or (MM "Anesthesia, Epidural")
 #8 TX Epidural Space*
 #9 S5 or #6 or #7 or #8
 #10 #4 and #9

Appendix 5. Search strategy for ISI Web of Science

#1 TS=Sodium Chloride or TS=air or TS=Saline Solution*
 #2 TS=Epidural Space* or TS=((an?esthesia or analgesia) SAME (Epidural or Peridural or Extradural)) or TS=resistance techniq*
 #3 #2 AND #1
 #4 TS=random* or TS=(clinical SAME trial*) or TS=controlled stud* or TS=((doubl* or singl* or tripl* or trebl*) SAME (blind* or mask*)) or TS=placebo* or TS=latin square* or TS=cross-over or TS=Multicenter or TS=crossover or TS=Comparative study
 #5 #4 AND #3

Appendix 6. Search strategy for LILACS (BIREME)

("air" or "Saline Solution\$" or "Sodium Chloride") and ("EPIDURAL SPACE/" or "EPIDURAL ANALGESIA/" or "EPIDURAL ANESTHESIA/" or "Epidural Space\$")

Appendix 7. Study selection, quality assessment and data extraction form

First author; journal/conference proceedings etc; year

Study eligibility

RCT/Quasi/CCT (delete as appropriate); relevant participants; relevant interventions; relevant outcomes

Yes/No/Unclear Yes/No/Unclear Yes/No/Unclear Yes/No*/Unclear

** Issue relates to selective reporting? When authors may have taken measurements for particular outcomes, but not reported these within the paper(s). Reviewers should contact trial lists for information on possible non-reported outcomes and reasons for exclusion from publication. Study should be listed in 'Studies awaiting assessment' until clarified. If no clarification is received after three attempts, study should then be excluded.*

Do not proceed if any of the above answers is 'No.' If study is to be included in the 'Excluded studies' section of the review, record below the information to be inserted into 'Table of excluded studies.'

References to trial

Check other references identified in searches. If further references to this trial are found, link the papers now and list below. All references to a trial should be linked under one study ID in RevMan.

Code each paper Author(s); Journal/Conference Proceedings etc; Year

Participants and trial characteristics

Participant characteristics

Further details

Age (mean, median, range, etc)

Sex of participants (numbers/%, etc)

Disease status/type, etc (if applicable)

Other

Trial characteristics

Methodological quality

Allocation of intervention

State here method used to generate allocation and reasons for grading Grade (circle)

Low risk (random)

High risk (e.g. alternate)

Unclear

Concealment of allocation

Process used to prevent foreknowledge of group assignment in an RCT, which should be seen as distinct from blinding

State here method used to conceal allocation and reasons for grading Grade (circle)

Low risk

High risk

Unclear

Blinding

Person responsible for participant care Yes/No

Participant Yes/No

Outcome assessor Yes/No

Other (please specify) Yes/No

Intention-to-treat

An intention-to-treat analysis is one in which all participants in a trial are analysed according to the intervention to which they were allocated, whether or not they received it.

All participants entering trial

15% or less excluded

Not analysed as 'intention-to-treat'

Unclear

Were withdrawals described? **Yes** **No** **Not clear?**

Discuss if appropriate

Data extraction

Outcomes relevant to your review

Copy and paste from 'Types of outcome measures'

Reported in paper (circle)

Inability to insert an epidural catheter; consequently occurrence of anaesthesia failure Yes/No

Accidental intravascular catheter placement

Yes/No

Unblocked segment

Yes/No

Inadvertent dural puncture

Yes/No

Complications (paraesthesia, air venous embolism, neurological complications, accidental puncture of the dura mater, total subarachnoid block, epidural haematoma due to blood vessel lesions, epilepsy, pneumoencephalo) Yes/No

Adverse events (head and neck pain, subcutaneous emphysema, migraine post puncture of the dura mater, difficulty to progress the catheter, inefficient block, hypotension) Yes/No

Quality of analgesia

Yes/No

Length of stay in hospital

Yes/No

Or continuous data

Code of paper/n/Outcomes (rename)/Unit of measurement/Mean (SD)/Intervention group/n/Control group/Mean (SD)/Details if outcome described only in text

Outcome A

Outcome B

Outcome C

Outcome D

Outcome E

Outcome F

Or dichotomous data

Code of paper/Outcomes (rename)/Intervention group (n) n = number of participants, not number of events/Control group (n)

n = number of participants, not number of events

Other information that you feel is relevant to the results

Indicate if any data were obtained from the primary author or if results were estimated from graphs etc, or were calculated by you using a formula (this should be stated and the formula given). In general, if results are not reported in paper(s) obtained, this should be made clear here to be cited in the review.

Freehand space for writing actions such as contact with study authors and changes

References to other trials

Did this report include any references to published reports of potentially eligible trials not already identified for this review? First author

Journal/Conference

Year of publication

Did this report include any references to unpublished data from potentially eligible trials not already identified for this review? If yes, list contact names and details

Appendix 1

Trial characteristics

Further details

Single-centre/Multi-centre

Country/Countries

How was participant eligibility defined?

How many people were randomly assigned?

Number of participants in each intervention group

Number of participants who received intended treatment

Number of participants who were analysed

Drug treatment(s) used

Dose/Frequency of administration

Duration of treatment (state weeks/months, etc; if cross-over trial, give length of time in each arm)

Median (range) length of follow-up reported in this paper (state weeks, months or years, or if not stated)

Time points when measurements were taken during the study

Time points reported in the study

Time points you are using in RevMan

Trial design (e.g. parallel/cross-over*)

Other

WHAT'S NEW

Date	Event	Description
28 May 2015	Amended	Typo in affiliations corrected

HISTORY

Protocol first published: Issue 1, 2011

Review first published: Issue 7, 2014

Date	Event	Description
31 May 2012	Amended	Contact details updated.
22 February 2012	Amended	Contact details updated.
18 January 2012	Amended	Contact details updated.

Date	Event	Description
2 May 2011	Amended	Co-authors contact details amended and protocol updated to RevMan 5.1
4 February 2011	Amended	Contact details updated.

CONTRIBUTIONS OF AUTHORS

Pedro L Antibas (PA), Paulo do Nascimento Junior (PNJ), Leandro G Braz (LGB), João Vitor Pereira Doles (JVD), Norma SP Módolo (NSPM) and Regina El Dib (RED)

Conceiving of the review: PA and RED.

Co-ordinating the review: RED.

Undertaking manual searches: JVD.

Screening search results: PA and RED.

Organizing retrieval of papers: PNJ and LGB.

Screening retrieved papers against inclusion criteria: PNJ and LGB.

Appraising quality of papers: PA and RED.

Abstracting data from papers: RED and NSPM.

Writing to authors of papers to ask for additional information: JVD and LGB.

Providing additional data about papers: PNJ and JVD.

Obtaining and screening data on unpublished studies: PA and JVD.

Managing data for the review: PA, RED and NSPM.

Entering data into Review Manager ([RevMan 5.1](#)): PA.

Entering RevMan statistical data: RED.

Performing other statistical analyses not using RevMan: RED.

Performing double entry of data (data entered by person one: PA; data entered by person two: RED).

Interpreting data: PA, PNJ, LGB, NSPM and RED.

Making statistical inferences: PA and RED.

Writing the review: PA, PNJ, LGB, NSPM and RED.

Securing funding for the review: RED.

Serving as guarantor for the review (one review author): RED.

Taking responsibility for reading and checking the review before submission: PA and RED.

DECLARATIONS OF INTEREST

Pedro L Antibas: none known.

Paulo do Nascimento Junior: none known.

Leandro G Braz: none known.

Joao VP Doles: none known.

Air versus saline in the loss of resistance technique for identification of the epidural space (Review)

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Norma SP Módulo: none known.

Regina El Dib: none known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Karen Hovhannisyanyan, Denmark.

Help with designing search strategies

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Primary and secondary outcomes were slightly changed from the published protocol ([Antibas 2011](#)). For item one of the primary outcomes, we decided to interpret this as a negative outcome. We included a definition for it, as "inability to locate the epidural space and/or unintentional dural puncture by epidural needle." We included both accidental subarachnoid catheter placement and combined spinal epidural anaesthesia failure as primary outcomes because of their clinical relevance. Furthermore, we considered paraesthesia, dysaesthesia and catheter replacement as adverse events. We added pain to the list of secondary outcomes, however defined by the included studies.

We amended the items of the "Subgroup analysis and investigation of heterogeneity" section; however, the content remains the same, with the exception of a new item that we have added with the aim of investigating the difference between residents and professional anaesthesiologists regarding inability to locate the epidural space, defined as inability to identify the epidural space and/or unintentional dural puncture by epidural needle.

We have added to the sensitivity analyses rates of withdrawal for each outcome (< 20% vs greater than and/or equal to 20%).

We changed the wording of the approved published protocol regarding the intervention of interest and the control group to fit better with the title. The published protocol stated the intervention of interest as saline (fluid) and the control intervention as air. Now, the review reads "intervention of interest: air and control intervention: saline (fluid)."

Authorship changed from the published protocol to the review, and new members joined the review author team.

INDEX TERMS

Medical Subject Headings (MeSH)

*Air; *Sodium Chloride [administration & dosage]; Anesthesia, Epidural [instrumentation] [*methods]; Catheterization [adverse effects] [instrumentation]; Elasticity [physiology]; Epidural Space [*anatomy & histology]; Ligamentum Flavum [physiology]; Medical Errors [statistics & numerical data]; Paresthesia [etiology]; Post-Dural Puncture Headache [etiology]; Pressure; Randomized Controlled Trials as Topic

MeSH check words

Adult; Humans