Anaesthesia for evacuation of incomplete miscarriage. Cochrane Systematic Review.

Calvache JA, Delgado Noguera MF, Lesaffre E, Stolker RJ.

Cochrane Database of Systematic Reviews 2012, Issue 4. Art. No.: CD008681.

ABSTRACT

Background

An incomplete miscarriage occurs when all the products of conception are not expelled through the cervix. Curettage or vacuum aspiration have been used to remove retained tissues. The anaesthetic techniques used to facilitate this procedure have not been systematically evaluated in order to determine which provide better outcomes to the patients.

Objectives

To assess the effects of general anaesthesia, sedation or analgesia, regional or paracervical block anaesthetic techniques, or differing regimens of these, for surgical evacuation of incomplete miscarriage.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (23 January 2012), CENTRAL (*The Cochrane Library* 2012, Issue 1), PubMed (1966 to 23 January 2012), EMBASE (1974 to 23 January 2012), CINAHL (1982 to 23 January 2012), LILACS (1982 to 23 January 2012) and reference lists of retrieved studies.

Selection criteria

All published and unpublished randomised controlled trials (RCTs) or cluster-RCTs comparing the use of any anaesthetic technique (defined by authors as general anaesthesia, sedation/analgesia, regional or paracervical local block (PCB) procedures) to perform surgical evacuation of an incomplete miscarriage. We excluded quasi-randomised trials and studies that were only available as abstracts.

Data collection and analysis

Two review authors independently assessed studies for inclusion and assessed risk of bias. Data were independently extracted and checked for accuracy.

Main results

We included seven trials involving 800 women. The comparisons revealed a very high clinical heterogeneity. As a result of the heterogeneity in the randomisation unit, we did not combine trials but reported the individual trial results in the 'Data and analysis' section and in the text. Half of trials have unclear or high risk of bias in several domains.

We did not find any trial reporting data about maternal mortality. In terms of postoperative pain, PCB does not improve the control of postoperative pain when it is compared against sedation/analgesia or versus no anaesthesia/no analgesia. In the comparison of

PCB with lidocaine versus PCB with saline solution, significant differences favouring the group with lidocaine were found in one trial (moderate or severe postoperative pain) (risk ratio (RR) 0.32; 95% confidence interval (CI) 0.18 to 0.59).

When opioids were used, postoperative nausea and vomiting was more frequent in two trials comparing those versus PCB. In terms of requirement of blood transfusion, two trials showed conflicting results.

Authors' conclusions

Particular considerations that influence the choice of anaesthesia for this procedure such as availability, effectiveness, safety, side effects, practitioner's choice, costs and woman's preferences of each technique should continue to be used until more evidence supporting the use of one technique or another.

Keywords

Abortion, Incomplete [*surgery]; Anesthesia, General [*methods]; Anesthesia, Obstetrical [*methods]; Dilatation and Curettage [adverse effects, *methods]; Female; Humans; Hypnotics and Sedatives [therapeutic use]; Pain, Postoperative [*prevention & control]; Patient Satisfaction; Postoperative Nausea and Vomiting [etiology]; Pregnancy

BACKGROUND

Description of the condition

Miscarriage is when a pregnant woman loses her baby before the baby would be considered able to survive outside the womb, i.e. before 24 weeks' gestation. Miscarriage occurs in about 10% to 15% of pregnancies and the clinical signs are bleeding, usually with some abdominal pain and cramping (Shiers 2003).

An incomplete miscarriage occurs when all the products of conception are not expelled through the cervix (Bottomley 2009). After a clinical assessment suggesting complete miscarriage, 45% of women will have retained tissue on ultrasound (Alcazar 1995). Approximately 85% of incomplete miscarriages occur before the 12th week of pregnancy.

Traditionally, surgery (curettage or vacuum aspiration) has been the treatment used to remove any retained tissue and it is quick to perform. Nowadays, medical treatment is also available (Neilson 2010). This review is focused on anaesthesia used for surgical management.

Description of the intervention

Data from elective surgical abortions suggest that a major complication occurs in fewer than one in 100 women and mortality is around 0.7 in 100,000 (Bartlett 2004; Koonin 2000). Although the case-fatality-rate has decreased, anaesthesia-related events continue to be the leading cause of morbidity during the procedure (Lawson 1994).

To perform a surgical evacuation of incomplete miscarriage many anaesthetic techniques are used, including general anaesthesia, sedation/analgesia, regional and paracervical local block (PCB) anaesthesia. Key factors that influence the choice of anaesthesia include availability, effectiveness, safety, side effects, and costs. Other factors include woman preference, practitioner choice, facility resources and medical indications (Paul 1999).

How the intervention might work.

General anaesthesia and sedation/analgesia.

As defined by the American Society of Anesthesiologists, sedation/analgesia differ from anaesthesia because general anaesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to independently maintain ventilatory function is often impaired. Patients often require assistance in maintaining a permeable airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation. In this situation, drug-induced depression of neuromuscular function and cardiovascular alterations may be present (ASA 2004). General anaesthesia can be provided with inhalational halogen agents (e.g.

Sevofluorano), intravenous agents like thiopental or propofol or combinations of both and it can be supplemented or balanced with other intravenous agents such as opioids or benzodiazepines.

Sedation and analgesia comprise a continuum of states ranging from minimal sedation (anxiolysis) through general anaesthesia. It is difficult to establish an exact limit between them, but sedation/analgesia could be classified in accordance to ranges (minimal sedation, moderate sedation or conscious sedation and deep sedation/analgesia). Sedation/analgesia allows patients to tolerate unpleasant procedures by relieving anxiety, discomfort, or pain (ASA 2002). This is often used in combination with a local anaesthetic technique at the site of surgery. Oftentimes, sedation/analgesia can have fewer side effects than may occur with general anaesthesia.

General anaesthesia provides adequate operating conditions for cervical dilatation and uterine intervention. However, there are some situations when it is hazardous, for example, when the patient is in a poor medical condition. Observational studies have shown that general anaesthesia is associated with increased morbidity and mortality in the context of surgical evacuation compared with other techniques (Peterson 1981). Furthermore, it is associated with higher costs and use of personnel (Grimes 1979; Paul 1999; Raeder 1992). However, about 80% of procedures are performed under general anaesthesia currently (Grimes 1979; Osborn 1990; Peterson 1981; Soulat 2006).

Regional anaesthesia and PCB.

Several obstetric and gynaecologic procedures are currently performed under regional nerve block including cervical dilatation and uterine evacuation. PCB anaesthesia offers an alternative for cervical dilatation and uterine interventions. It is performed with injection of local anaesthetic around the cervix, at the 'three and nine o'clock' positions, anaesthetising the second to fourth sacral nerve roots as they pass through Frankenhauser's plexus at a depth of 2 to 4 mm (Piyamongkol 1998). The advantages of PCB compared to general anaesthesia are that it does not require general anaesthetic equipment nor personnel trained to administer general anaesthesia. The World Health Organization is seeking a reduction in the total number of surgical interventions performed under general anaesthesia, in favour of local anaesthesia (WHO 1978). However, PCB anaesthetic should be administered by trained staff and resuscitation facilities should be available.

This technique and regional anaesthesia can be provided with local anaesthetics drugs such as bupivacaine or lidocaine that differ by action onset, potency, duration and toxicity (Toledano 2009). Fatal complications (i.e. cardiac arrest) associated with local anaesthetic toxicity used for PCB are reported in the literature (Grimes 1976).

Other regional neuraxial techniques (spinal and epidural) are less used for short procedures. Some authors report the advantages of epidural anaesthesia, including

diminished psychological reaction and the possibility of performing surgical procedures without any additional anaesthesia (Grunstein 1976).

Paracervical local anaesthesia for cervical dilatation and uterine intervention was covered in another systematic Cochrane review (Tangsiriwatthana 2009). For this reason, we plan to include trials that use PCB anaesthesia in the context of incomplete miscarriage evacuation only.

Why it is important to do this review

Surgical evacuation of incomplete miscarriage is a frequent procedure. Renner reported that 46 million procedures are performed every year worldwide (Renner 2009).

Although the surgical evacuation of an incomplete miscarriage is a short anaesthetic procedure, it is not free of complications. The exposure to the anaesthetic procedure becomes a risk to the life of the patient. The mortality associated with general anaesthesia is 0.37/100,000 procedures, and the rate with local anaesthesia is estimated around 0.15/100,000. The use of general anaesthesia is associated with a two-fold to four-fold increased risk of death from abortion at less than or equal to 12 weeks' gestation (Peterson 1981).

Additionally, moderate to severe postoperative pain is reported and postoperative nausea and vomiting could be present. Many patients still find surgical evacuation extremely uncomfortable and it could affect maternal psychological status (Renner 2009).

Some observational studies show that some anaesthetic techniques could be better than others. Moreover, the different techniques currently used have not been evaluated through systematic methods and there is at present no consensus about the method or technique to provide better outcomes for women.

OBJECTIVES

To assess the effects of general anaesthesia, sedation or analgesia, regional or paracervical block anaesthetic techniques, or differing regimens of these, for surgical evacuation of incomplete miscarriage.

METHODS

Criteria for considering studies for this review

Types of studies. We considered all published and unpublished randomised controlled trials (RCTs) or cluster-RCTs without language restrictions that compared the use of anaesthetic techniques or drugs to perform surgical evacuation of an incomplete mis-

carriage for inclusion in the review. We excluded quasi-randomised trials. We did not include studies that were only available as abstracts.

Types of participants. Women with a diagnosis of incomplete miscarriage undergoing management by surgical evacuation performed with general, sedation/analgesia, regional or PCB anaesthesia.

Types of interventions. We considered trials if they compared any anaesthetic technique given preoperatively or intraoperatively (defined by authors as general anaesthesia, sedation/analgesia, regional or PCB procedures) to perform a surgical evacuation of incomplete miscarriage with another anaesthetic technique. We also included comparisons between different drugs, routes of administration, duration or timing of treatment if data were available. We did not include trials that compared systemic analgesia with non-steroidal analgesic drugs alone or cyclooxygenase (COX) inhibitors.

Types of outcome measures. Primary outcomes: (1) Women's satisfaction with procedure (as defined by the authors). (2) Pain during and/or after surgical evacuation of miscarriage, which was measured as categorical or continuous data (visual analogue scale, requirement for additional analgesia consumption (mg/kg). (3) Maternal mortality.

Secondary outcomes: (1) Adverse events (postoperative nausea and vomiting, blood loss, hypotension, postoperative sedation).

Search methods for identification of studies

Electronic searches. We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (23 January 2012).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from: quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL); weekly searches of MEDLINE; weekly searches of EMBASE; handsearches of 30 journals and the proceedings of major conferences; weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

In addition, we searched CENTRAL (*The Cochrane Library* 2012, Issue 1), PubMed (1966 to 23 January 2012), EMBASE (1974 to 23 January 2012), CINAHL (1982 to 23 January 2012), LILACS (1982 to 23 January 2012) using the search strategies detailed in Appendix 1, Appendix 2, Appendix 3, Appendix 4 and Appendix 5.

Searching other resources. We searched the reference lists of relevant studies. We did not apply any language restrictions.

Data collection and analysis

Selection of studies. Two review authors, Andrés Calvache (AC) and Mario Delgado (MD), independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted a referee.

Data extraction and management. We designed a form to extract data. For eligible studies, AC and MD extracted the data using the agreed form. We resolved discrepancies through discussion or, if required, we consulted a referee.

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies. Two review authors (AC, MD) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreement by discussion or by involving another review author.

(1) Random sequence generation (checking for possible selection bias). We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. We assessed the method as: low risk of bias (any truly random process, e.g. random number table; computer random number generator); high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias). We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We assessed the methods as: low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes); high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth); unclear risk of bias.

(3) Blinding of participants, personnel and outcome assessors (checking for possible performance bias). We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered studies to be at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as: low, high or unclear risk of bias for participants; low, high or unclear risk of bias for personnel; low, high or unclear risk of bias for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data). We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and 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 were balanced across groups or were related to outcomes. Where sufficient information was reported, or was supplied by the trial authors, we re-included missing data in the analyses which we undertook. We assessed methods as: low risk of bias (e.g. less than 20% missing data; missing outcome data balanced across groups); high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis carried out with substantial departure of intervention received from that assigned at randomisation); unclear risk of bias.

(5) Selective reporting (checking for reporting bias). We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found. We assessed the methods as: low risk of bias (where it was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported); high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported); unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above). We described for each included study any important concerns we had about other possible sources of bias. We assessed whether each study was free of other problems that could put it at risk of bias: low risk of other bias; high risk of other bias; unclear whether there is risk of other bias.

(7) Overall risk of bias. We made explicit judgements about whether studies were at high risk of bias according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses.

Measures of treatment effect. Dichotomous data. For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals. Continuous data. For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We used the standardized mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues. We included cluster-randomised trials in the analysis along with individually randomised trials. We adjusted their standard errors using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* using an estimate of the intracluster correlation co-efficient (ICC derived from the trial (if possible), or from another source. If ICCs from other sources were used, we reported this and conducted sensitivity analyses to investigate the effect of variation in the ICC. If we identified both cluster-randomised trials and individually-randomised trials, we planned to synthesise the relevant information. We considered it reasonable to combine the results from both if there was little heterogeneity between the study designs and the interaction between the effect of the intervention and the choice of randomisation unit was considered to be unlikely. We also acknowledged heterogeneity in the randomisation unit and performed a separate meta-analysis.

Dealing with missing data. For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis; i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity. We assessed statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if I^2 was greater than 30% and either T^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases. In future updates of this review, if there are 10 or more studies in a meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry. For continuous outcomes, we will use the test proposed by Egger 1997, and for dichotomous outcomes, the test proposed by Harbord 2006. If we detect asymmetry in any of these tests or if it is suggested by a visual assessment, we will performed exploratory analyses to investigate it.

Data synthesis. We carried out statistical analysis using the Review Manager software (RevMan 2008). We did not combine data in this review. In future updates, we will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will

be treated as the average range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials. If in future updates of this review we use random-effects analyses, the results will be presented as the average treatment effect with 95% confidence intervals, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity. In future updates, if we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, we will use random-effects analysis to produce it. We did not carry out our planned subgroup analyses, due to insufficient data. These will be carried out in future updates as more data become available. We will carry out the following subgroup analyses. (1) Gestational age (less than eight weeks and more than eight weeks), (2) Maternal age (less than 18 years, between 18 and 30 years and more than 30 years), (3) Type of surgical evacuation method used (any type of vacuum aspiration versus sharp metal curettage).

We will use the following outcomes in subgroup analysis: Women's satisfaction with procedure, Pain during or after surgical evacuation of miscarriage, or both and Maternal mortality.

For fixed-effect inverse variance meta-analyses, we will assess differences between subgroups by interaction tests. For random-effects and fixed-effect meta-analyses using methods other than inverse variance, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals being indicative of a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis. In future updates, we will carry out sensitivity analysis to assess variability of global effect estimation, in order to modify the incorporation of the clinical trials to analysis, according to its methodological quality (low bias risk versus moderate or high risk) and discussing why studies have a larger influence on the estimate.

RESULTS

Description of studies

Results of the search. The search of the databases yielded 292 references. Cochrane Pregnancy and Childbirth Group's Trials Register, CENTRAL, PubMed, EMBASE, CINAHL and LILACS retrieved 6, 13, 34, 35, 10 and 194 reports respectively. After applying the inclusion and exclusion criteria, we selected 22 studies from the search result and discarded 270 reports. From those, we excluded 14 duplicates. At the end, we selected eight trials for full paper review and inclusion. One trial was excluded after the full paper review. For details of the study selection process see the study flow diagram (Figure 1).

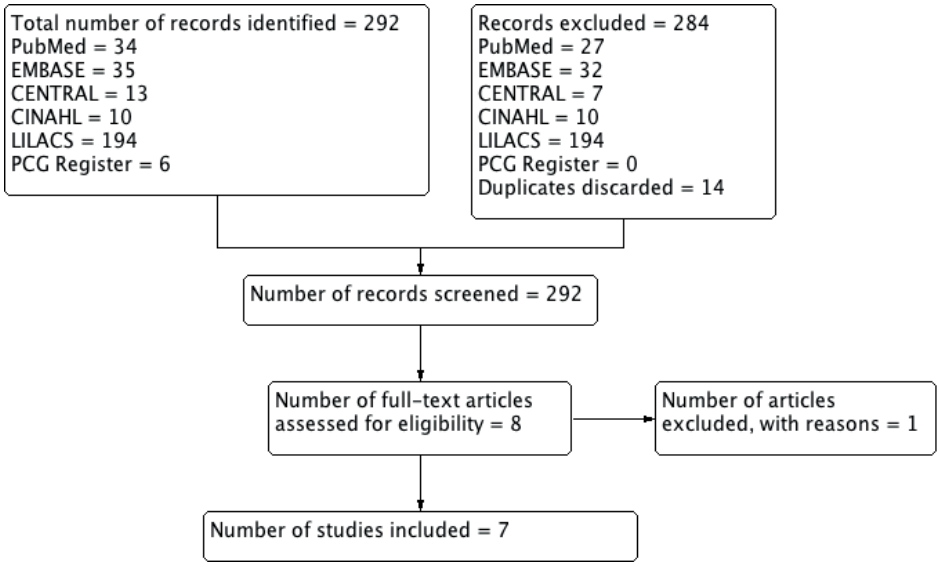

Figure 1. Study flow diagram.

Included studies. All the included trials used a randomised clinical trial design. Four of the trials were from developing countries; two were from the African continent (De Jonge 1994; Egziabher 2002), one from Panama (Lopez 2007) and one from Dominican Republic (Gomez 2004). From the remaining included studies, two were from United States (Kestin 1987; Rock 1977) and one was from Spain (Castillo 2004). Full details of all the included studies can be found in the Characteristics of included studies table.

One study did not have funding support (Egziabher 2002), one was supported by the David and Lucille Packard Foundation (Gomez 2004) and the others do not report any source of funding.

We included seven studies assessing different and diverse anaesthetic techniques on women with a prior diagnosis of incomplete miscarriage. All trials included participants with clinical or ultrasound diagnosis and up to 16 weeks of gestational age. One trial also included participants with missed abortions and anembryonic pregnancies (Lopez 2007). Most of the studies excluded women at high risk with cardiac, respiratory or other severe systemic disorders as well as women who were allergic to the anaesthetic drugs used. The majority of the studies selected women with open or dilated cervical canal and the most popular method used for the uterus evacuation was manual vacuum aspiration.

From these trials, we explored nine comparisons. Of them, three were related with PCB (Egziabher 2002; Gomez 2004; Lopez 2007). Two trials studied comparisons of sedation (with intravenous opioids and/or benzodiazepines at different doses) versus general

anaesthesia performed with induction agents, opioids and supported with halogens agents or nitrous oxide (De Jonge 1994; Rock 1977). Two studies explored comparisons between modalities of general anaesthesia using different drugs or doses (Castillo 2004). The last comparison was made between intramuscular (IM) NSAIDs and IM opioids (Lopez 2007). We have provided full details of the comparisons in the Characteristics of included studies table. Aditionally, Figure 2 illustrates the comparisons performed in the trials.

The most common outcome assessed was intra or postoperative pain measured in different ways. Two trials reported pain score as a continuous variable (using verbal numerical scales in the postoperative period) (Gomez 2004; Lopez 2007). Egziabher 2002 and De Jonge 1994 reported postoperative pain using a categorical scale with five levels (verbal rating scales). Castillo 2004 used a four-level categorical scale and Kestin 1987 and Rock 1977 did not report intra or postoperative pain.

One trial reported the quality of anaesthesia as a dichotomous result, according to participant rating (success or failure). This was assessed during the postoperative period (Rock 1977). No other studies reported women's satisfaction-related outcomes.

Six trials presented data of postoperative nausea or vomiting as a dichotomous result (Castillo 2004; Egziabher 2002; Gomez 2004; Kestin 1987; Lopez 2007; Rock 1977). Two trials reported the requirement of blood transfusion in the postoperative period (De Jonge 1994; Rock 1977). We found no trials that reported outcomes about mortality or other secondary or adverse effects.

To describe our results we classified the comparisons into four groups. In the first group, PCB was compared against other techniques. The second group presented comparisons between sedation and general anaesthesia. The third one compared diverse modalities of general anaesthesia and the fourth group with other comparisons.

The comparisons revealed a very high clinical heterogeneity and this represented a major issue in order to provide a single effect estimate for the outcomes. In fact, we organised the comparisons and the outcomes to improve the description of the findings. However, each comparison by itself was done with different drugs (with different pharmacological profiles), doses and routes of administration. For this reason, we did not perform any meta-analysis technique in this review.

Excluded studies. We excluded one trial because its participants were out of the scope of this review. For further details, see the Characteristics of excluded studies table.

Risk of bias in included studies

Allocation (selection bias). Of the seven trials, four were classified as having an adequate randomisation sequence generation (Gomez 2004; Egziabher 2002; Lopez 2007; Rock 1977) and the other three studies were rated as having 'unclear' risk of bias.

Table 1. Characteristics of included studies

Castillo 2004

Methods	This study was designed to determine which single bolus dose of remifentanil in combination with propofol and nitrous oxide is best to control the haemodynamic, autonomous and somatic responses in women scheduled for dilatation and curettage of the uterine cervix. They evaluated the adequacy of different bolus doses of remifentanil, associated with propofol and nitrous oxide, for dilatation and curettage in a prospective double-blind study.
Participants	Inclusion criteria: healthy females scheduled for dilation and curettage after spontaneous abortion were enrolled. Exclusion criteria: ASA classification III or worse, history of cardiac, pulmonary, endocrine, hepatic or renal disease, morbid obesity, neuropsychiatric disorders, antihypertensive medication, emergency curettage for massive bleeding or haemodynamic instability, age less than 18 years. Source: Hospital General Universitario Gregorio Marañón, Spain. Date: not reported.
Interventions	3 groups. - Group A. Remifentanil 0.5 mcg/kg single bolus intravenously plus propofol 2 mg/kg. Mantained with nitrous oxide 60% plus oxygen. - Group B. Remifentanil 1 mcg/kg single bolus intravenously plus propofol 2 mg/kg. Mantained with nitrous oxide 60% plus oxygen. - Group C. Remifentanil 1.5 mcg/kg single bolus intravenously plus propofol 2 mg/kg. Mantained with nitrous oxide 60% plus oxygen. Total number of participants randomised = 34. Group A = 4, Group B = 15, Group C = 15.
Outcomes	- Haemodynamic stability, autonomic, somatic signs of light anaesthesia. - Adverse events (hypotension, bradycardia). - Total dose of remifentanil and number of additional doses. - Emergence time. - Time to response to a single verbal command. - Postoperative pain. Reported as categorical data (none, light, moderate, severe). - Nausea/vomiting postoperative. As dichotomous outcome.
Notes	ASA classification: American Society of Anesthesiologists (ASA) Physical Status.

Castillo 2004: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Women were assigned to 1 of the 3 groups according to the bolus dose of remifentanil to be administered".
Allocation concealment (selection bias)	Unclear risk	There is no information available.
Blinding (performance bias and detection bias)	Low risk	Blood pressure, heart rate and oxygen saturation were recorded by a blinded observer 1 minute before induction, at the end of propofol injection, during the first minute of curettage and just after completion of the procedure.
Incomplete outcome data (attrition bias)	Low risk	There is no description of incomplete data during follow-up period. As far as can tell, all patients appear to be evaluated.
Selective reporting (reporting bias)	Unclear risk	As far as can tell, outcomes reported were those pre-specified, however the trial protocol was not assessed.
Other bias	Low risk	No apparent biases from other sources.

De Jonge 1994

Methods	Randomised clinical trial to test the following hypotheses: (i) evacuation under systemic analgesia for uncomplicated incomplete abortion is safe, effective and acceptable; (ii) the delay between admission and the evacuation procedure is shorter for ward evacuations than for evacuations done in theatre; and (iii) blood loss for the ward group is less than for the theatre group.
Participants	Inclusion/exclusion criteria: uterine size equivalent to a pregnancy duration of 14 weeks or less, a dilated cervical canal, a haemoglobin concentration more than 8 g/dL after resuscitation and no signs of sepsis (temperature > 37.5°C, foul-smelling vaginal discharge). No women refused to participate. Source: Kalafong Hospital, a tertiary medical centre serving a black urban population. University of Pretoria. Date: between February and May 1992.
Interventions	2 groups. - Group 1. Sedation: It was provided by an opioid analgesic, fentanyl, and a benzodiazepine, midazolam. For the ward evacuation, the analgesic technique was as follows: pre-oxygenation for at least 3 minutes with 6-7 litres oxygen delivered through a close-fitting mask; fentanyl 1.5 mcg/kg given slowly intravenously up to a maximum of 100 mcg/kg, followed by midazolam administered slowly intravenously and titrated against the consciousness level of the participant to a maximum of 15 mg. Oxygenation was monitored by pulse-oximetry for the entire procedure. - Group 2. General anaesthesia. The anaesthetic technique for the evacuation in theatre was: pre-oxygenation; thiopental. 3.0-5.0 mg/kg intravenously, succinyldicholine 1.0 mg/kg intravenously; routine intubation because none of the women were starved; inhalation of oxygen and nitrous oxide (50/50) 70 ml/kg and halothane 0.5% to 1.0% with spontaneous respiration. • All the evacuations, both in the ward and in theatre, were performed with a sharp curette by a trained house officer or registrar. Total number of participants randomised = 142. Group 1 = 73, Group 2 = 68.
Outcomes	- Time delay between admission and evacuation. - Complications (anaesthetic- and procedure-related). - Acceptability, measured retrospectively by the level of fear and/or pain experienced by the woman grading: 1 - none; 2 - mild; 3 - moderate; 4 - severe; 5 - very severe. - Requirement for blood transfusion. - Need for re-evacuation.

De Jonge 1994: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	There is no information available.
Allocation concealment (selection bias)	Low risk	"Randomisation was done using numbered sealed opaque envelopes drawn by the clinician on a consecutive basis".
Blinding (performance bias and detection bias)	Unclear risk	There is no information available.
Incomplete outcome data (attrition bias)	Unclear risk	There is no information available.
Selective reporting (reporting bias)	Unclear risk	Appears to be free of selective reporting bias but we did not assess the trial protocol.
Other bias	High risk	The number of women was less than the number calculated in the protocol. Quote: "The sample size of 182 could not be achieved because of hospital strikes and unrest".

Egziabher 2002

Methods	Randomised clinical trial comparing PCB with lidocaine versus placebo in the control of pain during manual vacuum aspiration.
Participants	Inclusion criteria: women with diagnosis of incomplete miscarriage before 16 weeks of gestation. Participants without evidence of infections, blood pressure less than 140/90 mmHg, non-diabetic or cardiac disease, free from severe anaemia, cervical dilation at least 1.5-2 cm and free from acute pelvic inflammatory disease. Exclusion criteria: abortion occurring 16 weeks and over of gestation, blood pressure greater or equal to 140/90 mmHg, infections of cervix, uterus and pelvis, diabetic and cardiac disease, allergy to lidocaine and respiratory distress. Source: Marie Stopes Health Centres, Nairobi, Kenia. Date: period from September 1997 to October 1997.
Interventions	2 groups. - Group 1. PCB (2 mL of lidocaine injection at the cervical-vaginal juncture at 3 and 9 o'clock positions). - Group 2. PCB (2 mL of normal saline solution injection at the cervical-vaginal juncture at 3 and 9 o'clock positions). Total number of participants randomised = 142. Group 1 = 71, Group 2 = 71.
Outcomes	- Postoperative pain. Using Mc Gill scale (none pain, mild, moderate, severe, very severe). The assessment was performed before, during, after and 30 minutes after the end of surgical procedure. The results are reported as categorical data. - Postoperative nausea-vomiting. Reported as dichotomous outcome.
Notes	PCB: Paracervical block

Egziabher 2002: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"142 randomly selected participants, using random tables".
Allocation concealment (selection bias)	Unclear risk	There is no information available.
Blinding (performance bias and detection bias)	Low risk	The investigator, participant and the nurse filling out the questionnaire were blinded to allocation. 1 nurse who gave out the medication was not blinded.
Incomplete outcome data (attrition bias)	Unclear risk	No loss of participants nor exclusions reported.
Selective reporting (reporting bias)	Unclear risk	Seems to be free of bias here. However, we did not assess the trial protocol.
Other bias	High risk	The reported results of McGill scale per each category does not add 100% per each arm of treatment.

Gomez 2004

Methods	To estimate the effectiveness of PCB in controlling pain among women treated with manual vacuum aspiration for an incomplete abortion. An open parallel, randomised clinical trial was designed comparing 2 groups.
Participants	Women attending Maternidad Nuestra Señora de la Altagracia who were diagnosed as having an incomplete abortion and who fulfilled all the selection criteria. Inclusion criteria: women with incomplete abortion, open cervix, and pregnancies of 12 weeks or less gestational age, women aged 18 to 45 years, women able to and capable of giving written informed consent. Exclusion criteria: women with septic abortion, psychiatric or neurological disease, hypovolaemic or septic shock, abdominal rebound pain or signs of peritonitis, allergies to lidocaine, any observable pelvic mass, previous enrolment in the study, a severe medical condition (neoplasia), live fetus in utero, suspicions or presence of a sexually transmitted infection. Source: women attending Maternidad Nuestra Señora de la Altagracia located in Santo Domingo, Dominican Republic. Date: period from April 2, 2002 to October 23, 2002.
Interventions	2 groups. - Group 1. Without anaesthesia. - Group 2. PCB with 1% lidocaine during manual vacuum aspiration. The PCB was performed with a 23-gauge needle used to inject 5 mL of lidocaine slowly to a depth of 0.5 cm in the cervix–vaginal joint at 4- or 5- and 7- or 8-o'clock positions. All participants received counselling and psychological support before, during and after the procedure. Used a total of 10 mL of lidocaine (5 mL in each site). 5 minutes after applying the lidocaine, the gynaecologist, using the manual vacuum aspiration technique, evacuated the uterus. Total number of participants randomised = 215. Group 1 = 108, Group 2 = 107.
Outcomes	- Intraoperative pain as evaluated by the woman and external observer. The pain expressed by the woman at various points of treatment also was measured both as a discrete variable and as a categorical variable: no pain (0 points) or slight pain (1–3 points), moderate pain (4–6 points), and severe pain (7–10 points). - Changes in the level of pain on the basis of a comparison of pain before the procedure and pain reported during the procedure. - The need to suspend the procedure or administer anaesthetics medicaments or parenteral sedatives; the need for other parenteral analgesics. - Existence of intraoperative and postoperative complications (infection, haemorrhage uterine perforation, and incomplete evacuation), the need for further surgery, the presence of adverse events, and the presence of serious adverse events.
Notes	PCB: Paracervical block

Gomez 2004: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Women were assigned to 1 of the 2 groups by means of a random number table, generated by a computational algorithm based on a block size of 2 (20%), 4 (40%), and 6 (40%) to generate a list of treatment allocation.

Allocation concealment (selection bias)	Low risk	The randomisation distribution was kept in sealed, sequential opaque envelopes kept at the Reproductive Health Department's office at Maternidad Nuestra Señora de la Altagracia and only opened when a study participant had consented to the study and was in the operating theatre for treatment.
Blinding (performance bias and detection bias)	Low risk	Consenting participants were treated in the operating theatre, where the randomisation group assignment was opened to determine the pain control to be received. An external trained observer evaluated pain levels. The biostatistician responsible for processing and analysing data was blinded regarding the 2 groups being studied.
Incomplete outcome data (attrition bias)	Low risk	No losses and no exclusions were reported. All patients after randomisation were evaluated.
Selective reporting (reporting bias)	Unclear risk	Pre-specified outcomes reported on, but the trial protocol not assessed.
Other bias	Low risk	There was no other information which would suggest other biases.

Kestin 1987

Methods	This study was undertaken to compare the newer IV agents, alfentanil and etomidate with fentanyl and thiopental. Quality of recovery and the frequency of side effects were assessed.
Participants	Inclusion/exclusion criteria: Women presenting for evacuation of retained products of conception after spontaneous inevitable abortion (within 16 weeks of gestation) were studied. No participants had received any sedative or analgesic medication before the study. Source: Princess Anne Hospital, Southampton. Date: not reported.
Interventions	2 groups. - Group 1. General anaesthesia with fentanyl-thiopental. Fentanyl intravenous 1 mcg/kg followed after 2 minutes by an induction dose of thiopental (until loss of the eyelash reflex). Mantained with nitrous oxide 70% plus oxygen. - Group 2. General anaesthesia with alfentanil-etomidate group received alfentanil 10 mcg/kg followed immediately by an induction dose from a syringe containing etomidate 20 mg intravenous. Mantained with nitrous oxide 70% plus oxygen. Total number of participants randomised = 44. Group 1 = 22, Group 2=22.
Outcomes	- Recovery from anaesthesia. It was assessed using a modification of the coin counting test. 10 coins, 2 of each denomination less than 50 pence, were used. 3 coins were removed at random and the remaining 7 coins presented in a column to the participant, who was instructed to pick them from the top of the column 1 by 1, keeping a verbal. Reported as dichotomous outcome. - Time to opening eyes after procedure. Reported in minutes. - Time to showing thumb on command. Reported in minutes.

Kestin 1987: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	They were then randomly allocated to receive either alfentanil and etomidate or fentanyl and thiopental.
Allocation concealment (selection bias)	Unclear risk	There is no information available.

Blinding (performance bias and detection bias)	Unclear risk	There is no information available.
Incomplete outcome data (attrition bias)	Unclear risk	There is no information available.
Selective reporting (reporting bias)	Unclear risk	Pre-specified outcomes reported on, but the trial protocol not assessed.
Other bias	Low risk	"There were no significant difference between the two groups in baseline characteristics".

Lopez 2007

Methods	The objective of this study was to compare the effectiveness and the adverse effects of analgesics most commonly used in daily practice for the treatment of incomplete abortion with MVA.
Participants	Inclusion criteria: women with ultrasound diagnosis of incomplete miscarriage before 12 weeks of gestation (53%). They also included women with missed abortions (35%) and anembryonic pregnancies (12%). The women were included once the uterine cervix was pharmacologically dilated. Exclusion criteria: women who had history of allergy to any of the analgesics used and participants who did not want to participate in the study. Source: women who attended the gynaecology department of the Complejo Hospitalario "Arnulfo Arias Madrid", Caja de Seguro Social, Panama. Date: period from March 1 to June 13, 2004.
Interventions	3 groups. - Group 1. IM diclofenac (1 mg/kg) plus PCB (1 mg/kg of lidocaine at the cervical-vaginal juncture at 3, 5, 7, and 9 o'clock positions). - Group 2. IM diclofenac (1 mg/kg) plus meperidine IM (1 mg/kg). - Group 3. IM meperidine (1 mg/kg) alone A latency period of at least 30 minutes was given before starting the procedure. All participants received psychological support before, during, and after the procedure. Total number of participants randomised = 113. Group 1 = 37, Group 2 = 39, Group 3 = 37.
Outcomes	1. Postoperative pain. Using Wong scale (visual analogue scale) ranked from 0 to 10. The assessment was performed 3 minutes after the end of surgical procedure. The results are reported as continuous and categorical data. 2. Postoperative nausea. Reported as dichotomous outcome.
Notes	IM: intramuscular. MVA: Manual vacuum aspiration. PCB: Paracervical block.

Lopez 2007: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Women were assigned to the 3 groups by means of a random table generated by a computational algorithm based on a block size of 9, to generate a list of treatment allocation.
Allocation concealment (selection bias)	Low risk	The randomisation distribution was kept in sealed, sequential opaque envelopes, which were opened after admission and the analgesic was administered before the participant entered the operating room.
Blinding (performance bias and detection bias)	Unclear risk	The analgesic was administered before the participant entered the operating room. It is unclear for the outcome evaluation. It does not apply for the woman because it is a non-pharmacological intervention.

Incomplete outcome data (attrition bias)	Low risk	Of the 117 participants, 4 were excluded because of missing data including 1 woman who decided not to participate after randomisation. Of the 113 recruited, 37 participants were enrolled to group 1, 39 participants to group 2 and 37 participants to group 3.
Selective reporting (reporting bias)	Unclear risk	Seem to have reported all pre-specified outcomes, but we did not access the trial protocol.
Other bias	Low risk	There was nothing to suggest any other risk of bias.

Rock 1977

Methods	Prospective, randomised clinical trial seeks to compare the choice of analgesia and anaesthesia in women with early spontaneous incomplete or inevitable abortion, undergoing suction curettage with regards to pain relief, post procedure rehabilitation, and hospitalisation time.
Participants	Inclusion/exclusion criteria: women with diagnosis of uncomplicated spontaneous incomplete or inevitable abortion were included. Women without signs or symptoms of sepsis or history or findings suggestive of instrumentation was included. Women with at least 6 hours of fasting. Women with a uterus greater than 12 weeks of gestational size were excluded. Source: Duke University Medical Center, Durham, North Carolina. Date: period from January 1, 1973 to December 31, 1974.
Interventions	2 groups. - Group 1. Intravenous analgesia. Diazepam 10 mg intravenous given 5-10 minutes before the procedure and meperidine 0.5 to 0.8 mg per pound with promethazine 25 mg. - Group 2. General anaesthesia. Thyamilal 75-250 mg or thiopental sodium 200-250 mg intravenous with 70% nitrous oxide and 30% oxygen by mask. Cervical dilation was performed when advisable. Curettage was performed with a translucent suction curette of the aspirator. Total number of participants randomised = 115. Group 1 = 59, Group 2 = 56.
Outcomes	- Quality of anaesthesia and analgesia. As dichotomous result of success/failure. Failues were based on the lack of participant cooperativeness during the procedure and complaints of discomfort during and following surgery. - Participant evaluation of success/failure. As dichotomous result. - Time from procedure to discharge. - Time from admission to discharge.

Rock 1977: Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	On the basis of a card drawn from an index file in which the order of the cards had been previously mathematically randomised.
Allocation concealment (selection bias)	Unclear risk	There is no information available.
Blinding (performance bias and detection bias)	Unclear risk	There is no information available.
Incomplete outcome data (attrition bias)	Unclear risk	No losses and no exclusions were reported, but nothing is described.
Selective reporting (reporting bias)	Unclear risk	Appears to be free of selective reporting bias but we did not assess the trial protocol.
Other bias	Unclear risk	No imbalances in baseline data identified.

Randomised clinical trial	Comparisons performed	
Group 1. Comparisons incluiding PCB		
Egziabher 2002	PCB with lidocaine	PCB with saline solution
Lopez 2007	PCB plus IM diclofenac	IM diclofenac plus IM meperidine
Lopez 2007	PCB plus IM diclofenac	IM meperidine
Gomez 2004	PCB with lidocaine	No anaesthesia
Group 2. Comparisons of sedation versus general anaesthesia		
De Jonge 1994	Sedation: fentanyl plus IV midazolam	General anaesthesia: thiopental plus halothane
Rock 1977	Sedation: IV meperidine plus IV diazepam	General anaesthesia: thiopental plus nitrous oxide
Group 3. Comparisons of modalities of general anaesthesia		
Kestin 1987	General anaesthesia: etomidate, alfentanil and nitrous oxide	General anaesthesia: thiopental, fentanyl and nitrous oxide
Castillo 2004	General anaesthesia: propofol, remifentanil 1 mcg/kg	General anaesthesia: propofol, remifentanil 1.5 mcg/kg
Group 4. Other comparisons		
Lopez 2007	IM diclofenac plus IM meperidine	IM meperidine

Figure 2. Comparisons performed among trials.

Table 2. Characteristics of excluded studies

Grunstein 1976

Reason for exclusion	The participants of this study are out of the scope of this review. In this study, epidural analgesia was performed in 78 women with abortion in the midtrimester or preterm delivery of up to 27 weeks of pregnancy. Women were divided into 3 groups. The first group included 30 women with signs of inevitable abortion. The second group comprised of 9 cases of induced abortion and the third one of 39 cases of preterm delivery.

Allocation concealment was adequate in three studies (Gomez 2004; De Jonge 1994; Lopez 2007). For the remainder it was unclear.

Blinding (performance bias and detection bias). Three studies were categorised as 'low' risk of bias for blinding (Castillo 2004; Egziabher 2002; Gomez 2004). The remaining trials were rated as having an 'unclear' risk of bias for this domain.

Incomplete outcome data (attrition bias). Three studies were categorised as 'low' risk of bias for this domain (Gomez 2004; Lopez 2007; Castillo 2004). The remaining studies were classified as having 'unclear' risk of bias.

Selective reporting (reporting bias). It was unclear to us whether any of the studies were free of selective reporting bias as we were unable to assess the protocols for the studies.

Other potential sources of bias. Two trials (De Jonge 1994; Egziabher 2002) were classified as 'high' risk of bias. De Jonge 1994 was stopped early and failed to recruit the participants planned.

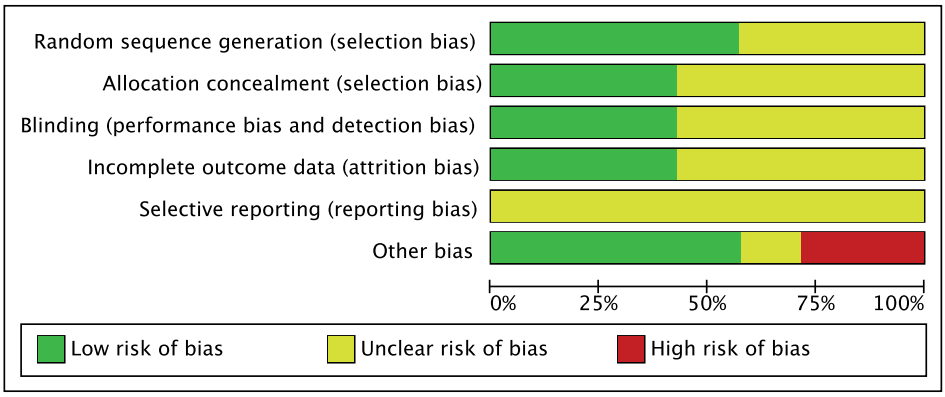

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

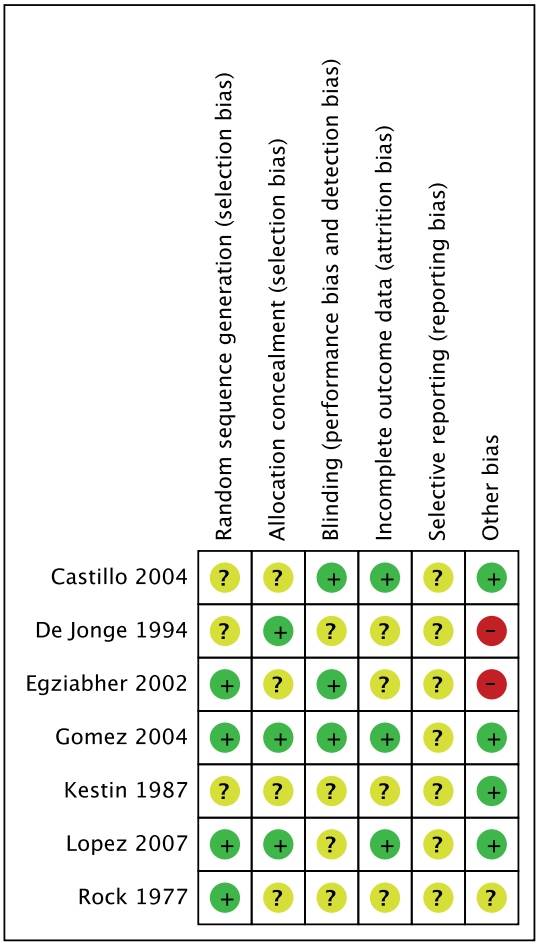

Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

In conclusion, the trials included in this review have several risks of bias. The domain most achieved was adequate sequence generation. The remaining domains of evaluation were reached in less than 50% of the studies. We have included a summary of the 'Risk of bias' assessment in the Characteristics of included studies table, in the 'Risk of bias' graph (Figure 3) and in the 'Risk of bias' summary graph (Figure 4).

Effects of interventions

We present our results organised hierarchically by outcome. As mentioned above, we have four comparison groups. For more details please refer to (Figure 2). We show each category only where studies assessing the outcome were available.

Primary outcomes: Postoperative pain

Group 1 - comparisons including PCB

Egziabher 2002 compared the use of PCB with lidocaine versus block with saline solution. Significant differences favouring the group with lidocaine were found (moderate or severe postoperative pain) (risk ratio (RR) 0.32; 95% confidence interval (CI) 0.18 to 0.59 (Analysis 1.1)).

Lopez 2007 made two comparisons. In the first one, PCB plus IM diclofenac versus IM diclofenac plus IM meperidine, using the dichotomous outcome (moderate or severe postoperative pain) no significant differences were found (RR 0.98; 95% CI 0.73 to 1.30 (Analysis 2.1)). Furthermore, they reported a mean pain of 5.4 (standard deviation (SD) 2.8) (n = 37) and 5.0 (SD 2.6) (n = 39) respectively. No significant differences were found between these interventions (mean difference (MD) 0.40; 95% CI -0.82 to 1.62 (Analysis 2.2)).

In the other comparison, PCB plus IM diclofenac versus IM meperidine, using the dichotomous outcome (moderate or severe postoperative pain) no significant differences were found (RR 1.00; 95% CI 0.74 to 1.35 (Analysis 3.1)). They also reported a mean pain of 5.4 (SD 2.8) (n = 37) and 5.7 (SD 3.2) (n = 37) respectively. No significant differences were found between these interventions (MD -0.30; 95% CI -1.67 to 1.07 (Analysis 3.2)).

Gomez 2004 comparing PCB with lidocaine versus No anaesthesia/No sedation, reported no significant differences in moderate or severe postoperative pain (RR 1.00; 95% CI 0.86 to 1.16 (Analysis 4.1)). Similar results were reported using a continuous scale (MD -0.43; 95% CI -1.29 to 0.43 (Analysis 4.2)).

Group 2 - comparisons of sedation versus general anaesthesia

De Jonge 1994 compared a sedation strategy (intravenous (IV) fentanyl, IV midazolam) versus general anaesthesia (thiopental and halothane). No significant differences were found between these interventions (moderate or severe postoperative pain) (RR 0.07; 95% CI 0.00 to 1.23 (Analysis 5.1)).

Group 3. Comparisons of modalities of general anaesthesia

Castillo 2004 compared two bolus doses of remifentanil (1 mcg/kg versus 1.5 mcg/kg) with a fixed dose of propofol. No significant differences in moderate or severe post-operative pain were found between these interventions (RR 3.00; 95% CI 0.13 to 68.26 (Analysis 8.1)).

Group 4 - other comparisons

Lopez 2007 compared the effect of IM diclofenac plus IM meperidine versus IM meperidine alone. No significant differences were found between these interventions in moderate or severe postoperative pain (RR 1.02; 95% CI 0.77 to 1.36 (Analysis 9.1). The result was presented as a continuous scale with similar findings (MD -0.70; 95% CI -2.01 to 0.61 (Analysis 9.2)).

Primary outcomes: Women's satisfaction

Group 2 - comparisons of sedation versus general anaesthesia

Rock 1977 presented a comparison of general anaesthesia (thiopental, nitrous oxide) versus sedation (IV meperidine and IV diazepam). In terms of participant satisfaction, this study reported the outcome quality of anaesthesia (assessed by the woman). Significant differences were found between groups (RR 1.25; 95% CI 1.10 to 1.43 (Analysis 6.1)).

Secondary outcomes: Postoperative nausea and vomiting

Group 1 - comparisons including PCB

Egziabher 2002 showed a significant difference favouring the PCB with Lidocaine versus PCB with saline solution (RR 0.56; 95% CI 0.40 to 0.79 (Analysis 1.2)).

In the comparison of PCB plus IM diclofenac versus IM diclofenac plus IM meperidine, Lopez 2007 presented a significant difference favouring the PCB plus IM diclofenac group (RR 0.19; 95% CI 0.05 to 0.81 (Analysis 2.3)).

In the PCB plus IM diclofenac versus IM meperidine alone group, significant differences favouring the PCB plus IM diclofenac were found (RR 0.18; 95% CI 0.04 to 0.76 (Analysis 3.3)).

In the last comparison of this category (PCB with lidocaine versus No anaesthesia/No sedation) no events of nausea or vomiting were reported (Gomez 2004) (Analysis 4.3).

Group 2 - comparisons of sedation versus general anaesthesia

No significant differences were found between these interventions in the Rock 1977 trial (RR 0.26; 95% CI 0.03 to 2.29 (Analysis 6.2)).

Group 3 - comparisons of modalities of general anaesthesia

Kestin 1987 compared two modalities of general anaesthesia: etomidate plus alfentanil versus thiopental plus fentanyl. Significant differences were found favouring the thiopental-fentanyl combination (RR 0.22; 95% CI 0.05 to 0.91 (Analysis 7.1)).

Castillo 2004 compared two bolus doses of remifentanil with a fixed dose of propofol. They did not find significant differences (RR 3.00; 95% CI 0.13 to 68.26 (Analysis 8.2)).

Group 4 - other comparisons

Lopez 2007 found no significant differences between IM diclofenac plus IM meperidine versus IM meperidine alone (RR 0.95; 95% CI 0.47 to 1.92 (Analysis 9.3)).

Table 3. Data and analyses

1. PCB with lidocaine versus PCB with saline solution

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Postoperative pain (moderate or severe)	1	142	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.18, 0.59]
1.2 Nausea/vomiting	1	142	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.40, 0.79]

2. PCB with lidocaine plus IM diclofenac versus IM diclofenac plus IM meperidine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Postoperative pain (moderate or severe)	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.73, 1.30]
2.2 Postoperative pain	1	76	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.82, 1.62]
2.3 Nausea/vomiting	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.05, 0.81]

3. PCB with lidocaine plus IM diclofenac versus IM meperidine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 Postoperative pain (none/mild)	1	74	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.74, 1.35]
3.2 Postoperative pain	1	74	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.67, 1.07]
3.3 Nausea/vomiting	1	74	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.04, 0.76]

4. PCB with lidocaine versus no anaesthesia/no sedation

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 Postoperative pain (moderate or severe)	1	215	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.86, 1.16]
4.2 Postoperative pain	1	215	Mean Difference (IV, Fixed, 95% CI)	-0.43 [-1.29, 0.43]

4.3 Nausea/vomiting	1	215	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

5. General anaesthesia (thiopental, halothane) versus sedation (fentanyl, midazolam)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 Postoperative pain (moderate or severe)	1	141	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.00, 1.23]
5.2 Requirement of blood transfusion	1	141	Risk Ratio (M-H, Fixed, 95% CI)	1.98 [1.10, 3.57]

6.General anaesthesia (thiopental, nitrous oxide) versus sedation (meperidine, diazepam)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 Quality of anaesthesia (satisfaction)	1	115	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [1.10, 1.43]
6.2 Nausea/vomiting	1	115	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.03, 2.29]
6.3 Requirement of blood transfusion	1	115	Risk Ratio (M-H, Fixed, 95% CI)	3.16 [0.13, 75.94]

7. General anaesthesia (thiopental, fentanyl, nitrous oxide) versus general anaesthesia (etomidate, alfentanil, nitrous oxide)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
7.1 Nausea/vomiting	1	44	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.05, 0.91]

8. General anaesthesia (remifentanil 1 mcg/kg bolus, propofol) versus general anaesthesia (remifentanil 1.5 mcg/kg bolus, propofol)

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
8.1 Postoperative pain (moderate or severe)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	3.00 [0.13, 68.26]
8.2 Nausea/vomiting	1	30	Risk Ratio (M-H, Fixed, 95% CI)	3.00 [0.13, 68.26]

9. IM diclofenac plus IM meperidine versus IM meperidine

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
9.1 Postoperative pain (moderate or severe)	1	76	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.77, 1.36]
9.2 Postoperative pain	1	76	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.01, 0.61]
9.3 Nausea/vomiting	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.47, 1.92]

Secondary outcomes: Requirement of blood transfusion

Group 2 - comparisons of sedation versus general anaesthesia

De Jonge 1994 compared a sedation strategy (IV fentanyl, IV midazolam) versus general anaesthesia (thiopental and halothane). They found significant differences favouring the general anaesthesia arm (RR 1.98; 95% CI 1.10 to 3.57 (Analysis 5.2)).

Rock 1977 reported no significant differences between groups (RR 3.16; 95% CI 0.13 to 75.94 (Analysis 6.3)).

DISCUSSION

The surgical management of an incomplete miscarriage is a common procedure in the practice of clinical anaesthesia. However, the different techniques currently used have not been evaluated through systematic methods and there is at present no consensus about the method or technique to provide better outcomes for women under this procedure.

This review examined randomised controlled trials comparing any anaesthetic technique (general anaesthesia, sedation/analgesia, regional or PCB) in this special type of population. We included seven trials in this review, but the information available in this area remains scarce.

Summary of main results

None of the included studies reported data about maternal mortality. One study reported maternal satisfaction (Rock 1977). In this trial, significant differences were found favouring the use of general anaesthesia in comparison with sedation/analgesia. However, this trial was classified with unclear risk of bias in five of six domains.

The included studies used different approaches to assess the outcome of postoperative pain. Five studies reported data related to postoperative pain. Three studies (Castillo 2004; De Jonge 1994; Egziabher 2002) used ordinal categorical scales with four or five categories. The remaining two trials (Gomez 2004; Lopez 2007) used continuous and categorical scales.

PCB does not improve the control of postoperative pain when it is compared against sedation/analgesia or versus no anaesthesia/no analgesia (Gomez 2004; Lopez 2007). When it is compared with PCB with saline solution, the women under block with lidocaine present less moderate or severe postoperative pain (Egziabher 2002). Nowadays, the postoperative pain level of women under surgical evacuation of incomplete miscarriage remain without complete relief.

For secondary outcomes, six trials reported the outcome nausea and vomiting (Castillo 2004; Egziabher 2002; Gomez 2004; Kestin 1987; Lopez 2007; Rock 1977) and two stud-

ies reported the need for postoperative blood transfusion (De Jonge 1994; Rock 1977). The results show a consistent finding. When opioid drugs were compared versus other strategies, these participants had more events of nausea and vomiting (Lopez 2007). In addition, when both arms has opioids the differences disappear (Castillo 2004). Kestin 1987 show a reduction in the risk of nausea and vomiting using a combination of general anaesthesia using thiopental, fentanyl versus etomidate, alfentanil (one trial, 44 participants). In the PCB scenario, the risk of postoperative nausea and vomiting was reduced using local anaesthetics versus saline solution (Egziabher 2002).

De Jonge 1994 reported a significant increment on the risk of blood transfusion with general anaesthesia versus sedation/analgesia. Nevertheless, Rock 1977 does not report any difference between general anaesthesia and sedation/analgesia. However, both studies used different drugs. In addition, the result presented by De Jonge 1994 could be influenced by the comparison under study. Patients allocated to sedation in the ward probably were evacuated more quickly than patients in the operating room under general anaesthesia.

Overall completeness and applicability of evidence

We included seven trials involving 800 women. Although we had planned to combine the estimates, explore the sources of heterogeneity and to carry out a subgroup/sensitivity analysis, the available studies and their comparisons allowed only a descriptive systematic review without meta-analysis. However, it shows an interesting overview of the great amount of heterogeneity in the clinical practice of anaesthesia.

From these seven trials, we evaluated nine comparisons. Four included PCB versus other modalities of anaesthesia and the remaining five included general anaesthesia versus sedation/analgesia or other type of general anaesthesia. No trials were found that compared PCB versus general anaesthesia.

The most frequent primary outcome reported was postoperative pain. It was reported in different ways using categorical or continuous scales. Only one study reported maternal satisfaction with the anaesthesia. No trials were found that reported maternal mortality with the procedure. From all trials, six reported postoperative nausea and vomiting and two reported postoperative requirement of blood transfusion.

Most women included in this review were diagnosed with incomplete miscarriage and the evacuation was done using manual vacuum aspiration or curettage. Only one trial included patients with missed abortions and anembryonic pregnancies.

Quality of the evidence

The quality of the evidence was intermediate. Only one of the seven included studies (Gomez 2004) was rated as being low risk of bias in six of seven domains of the risk of bias tool. Of the remaining six trials, four have an adequate sequence generation and

three had adequate allocation concealment. Also, of these six trials, three reported some form of blinding. In addition, it is hard to assess if there was selective reporting bias.

The risk of bias of the trial that reported an increase in the requirement of blood transfusion was unclear or high in several domains.

Potential biases in the review process

We attempted to minimise serious bias by the following; two review authors assessed eligibility for inclusion and two authors carried out data extraction and assessed risk of bias. Data entry into RevMan (RevMan 2008) was undertaken by one author. However, many of these steps involve subjective assessments and thus may carry some risk of bias.

Agreements and disagreements with other studies or reviews

We are unaware of other systematic reviews on this specific clinical question.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence found presents conflicting results with the use of PCB. Most trials do not show differences with use of PCB. Unfortunately, in this anatomical area, it is difficult to assess the effectiveness and quality of the block. However, the pain perception remains significant among these patients. In addition, significant results shown by Egziabher 2002 in terms of pain could be explained by placebo effect taking into account that the Gomez 2004 trial comparison with no treatment failed to show an effect.

One trial suggested that women's satisfaction could be improved using general anaesthesia. The use of perioperative opioids was associated with an increase of postoperative nausea and vomiting in this scenario.

Key factors that influence the choice of anaesthesia for this procedure include availability, effectiveness, safety, side effects, practitioner choice and costs. These considerations should continue to be used to select the individual approach to each patient until more evidence is available. Furthermore, it is also important to consider the woman's preferences after anaesthesiologist advice about each technique.

Implications for research

Researchers in all medical specialties are increasingly studying non-traditional, patient-centred outcomes such as patient satisfaction and quality of life to assess quality of health care. Only one study examined this type of outcome and they did so in a very simple way (Rock 1977). Currently, we know that the assessment of patient satisfaction is a complex procedure because satisfaction is a multi-dimensional concept with determi-

nants that are not yet clearly defined (Pascoe 1983). Many studies use only simple overall questions and the reliability of single-item global satisfaction is poor and inadequate to address the complexity of satisfaction (Chanthong 2009; Fung 1998; Ware 1983).

Valid and reliable assessment of pain is essential for both clinical trials and pain management in clinical practice. One-dimensional tools such as numeric rating scales or visual analogue scales are available. Both are more powerful in detecting changes in pain intensity than a verbal categorical rating scale. In addition, it can be very useful to use baseline assessments to detect meaningful treatment effects (Breivik 2008).

To conclude, we consider that further studies in this context should be conducted. It should address important patient-oriented outcomes (i.e. patient satisfaction). In terms of pain management, appropriate methods to assess acute and long-term pain should be used. These trials should be large enough and well conducted. We identified several comparisons in our review process. With our current pharmacological agents and the development of anaesthetic methods, probably several forms could be available to perform this procedure nowadays.

ACKNOWLEDGEMENTS

To Alberto Giraldo and Nayibe Salamanca from Colombia for their input into the protocol for this review.

Departments of Anesthesiology and Pediatrics, Health Sciences Faculty, University of Cauca, Popayan, Colombia.

To the Netherlands Institute for Health Sciences NIHES from Erasmus University Rotterdam, The Netherlands.

To Mr Louis Volkers, Drs/MSc Information Specialist from the Medical Library Helpdesk, Erasmus MC Hospital, Rotterdam for his help in the search process for this review and Jorge Cardenas MD for his advice and comments during the writing process.

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

SOURCES OF SUPPORT

- Universidad del Cauca, Colombia
- Iberoamerican Cochrane Centre, Spain
- Department of Anesthesiology, Erasmus MC Hospital, Rotterdam, The Netherlands
- Department of Biostatistics, Erasmus MC Hospital, Rotterdam, The Netherlands

APPENDIX

Table. Search strategies

CENTRAL search strategy. The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2012, Issue 1).
#1 (incomplete near miscarr*)
#2 (incomplete near abort*)
#3 MeSH descriptor Abortion, Spontaneous explode all trees
#4 products near conception
#5 (rpoc)
#6 MeSH descriptor Anesthesia explode all trees
#7 anesthe* or anaesthe*
#8 MeSH descriptor Anesthetics explode all trees
#9 (#1 OR #2 OR #3 OR #4 OR #5)
#10 (#6 OR #7 OR #8)
#11 (#9 AND #10)
PubMed search strategy (1966 to 23 January 2012)
#1 "Abortion, Spontaneous"[Mesh]
#2 "Anesthetics"[Mesh]
#3 "Anesthesia"[Mesh]
#4 #2 OR #3
#5 #1 AND #4
#6 randomized controlled trial [pt]
#7 controlled clinical trial [pt]
#8 randomized [tiab]
#9 placebo [tiab]
#10 drug therapy [sh]
#11 randomly [tiab]
#12 trial [tiab]
#13 groups [tiab]
#14 #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
#15 animals [mh] NOT (humans [mh] and animals [mh])
#16 #14 AND #5
#17 #16 NOT #15
EMBASE search strategy (1974 to 23 January 2012, via OVID)
1 exp Abortion/
2 incomplete miscarr*.ti,ab.
3 exp Anesthesia/
4 exp Anesthetic agent/
5 1 or 2
6 3 or 4

7 5 and 6
8 Clinical trial/
9 Randomized controlled trials/
10 Random Allocation/
11 Single-Blind Procedure/
12 Double-Blind Procedure/
13 Cross-Over Procedure/
14 Placebos/
15 Randomi?ed controlled trial$.tw.
16 RCT.tw.
17 Random allocation.tw.
18 Randomly allocated.tw.
19 Allocated randomly.tw.
20 (allocated adj2 random).tw.
21 Single blind$.tw.
22 Double blind$.tw.
23 ((treble or triple) adj blind$).tw.
24 Placebo$.tw.
25 Prospective Studies/
26 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27 Case study/
28 Case report.tw.
29 Abstract report/ or letter/
30 27 or 28 or 29
31 26 not 30
32 animal/ not human/
33 7 and 31
34 33 not 32
CINAHL search strategy. (1982 to 23 January 2012)
1 exp Abortion, spontaneous/
2 incomplete adj2 miscarr*
3 exp Anesthesia/
4 exp Anesthetics/
5 1 or 2
6 3 or 4
7 5 and 6
LILACS search strategy (searched 23 January 2012)
First block

((Pt ENSAIO CONTROLADO ALEATORIO OR Pt ENSAIO CLINICO CONTROLADO OR Mh ENSAIOS CONTROLADOS ALEATORIOS OR Mh DISTRIBUICAO ALEATORIA OR Mh MÉTODO DUPLO-CEGO OR Mh MÉTODO SIMPLES-CEGO) AND NOT (Ct ANIMALS AND NOT (Ct HUMANO AND Ct ANIMALS)) OR (Pt ENSAIO CLÍNICO OR Ex E05.318.760.535$) OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple$ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh PLACEBOS OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR (Mh PROJETOS DE PESQUISA) AND NOT (Ct ANIMALS AND NOT (Ct HUMANO AND Ct ANIMALS)) OR (Ct ESTUDO COMPARATIVO OR Ex E05.337$ OR Mh SEGUIMENTOS OR Mh ESTUDOS PROSPECTIVOS OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct ANIMALS AND NOT (Ct HUMANO AND Ct ANIMALS))) AND NOT Mh ANIMALS
Second block
Mh Abortion OR Mh Curettage OR Mh Miscarriage OR Mh miscarry$ OR abort$ OR surgical abortion OR abortion OR manual suction aspiration OR electric suction aspiration OR first trimester
Third block
Mh Thiopental OR Mh Propofol OR Mh Ketamine OR Mh Lidocaine OR Mh Bupivacaine OR thiop$ OR sodip$ OR pento$ OR tiop$ OR propof$ OR dipriv$ OR keta$ OR remifen$ OR remyfen$ OR Mh fentanyl OR narcot$ OR Mh morphine OR trama$ OR midazolam OR diazepam OR sedat$ OR anxiolyt$ OR Mh Nitrous oxide OR Sevo$ OR Isof$ OR Halot$ OR Enflu$ OR general ane$ OR general anae$ OR conduct$ OR region$ OR spin$ OR lidoc$ OR lydo$ OR xilo$ OR xylo$ OR bupiv$ OR bupyv$ OR bupi$
The three blocks were combined with 'AND'

REFERENCES

Included studies

Castillo 2004. Castillo T, Avellanal M, Garcia de Lucas E. Bolus application of remifentanil with propofol for dilatation and curettage. European Journal of Anaesthesiology 2004;21(5):408-11. [CRSREF: 3259485; PubMed: 15141801]

De Jonge 1994. De Jonge ET, Pattinson RC, Makin JD, Venter CP. Is ward evacuation for uncomplicated incomplete abortion under systemic analgesia safe and effective? A randomised clinical trial. South African Medical Journal 1994;84(8 Pt 1):481-3. [CRSREF: 3259487; PubMed: 7825081]

Egziabher 2002. Egziabher TG, Ruminjo JK, Sekadde-Kigondu C. Pain relief using paracervical block in patients undergoing manual vacuum aspiration of uterus. East African Medical Journal 2002;79(10):530-4. [CRSREF: 3259489; PubMed: 12635758]

Gomez 2004. Gomez PI, Gaitan H, Nova C, Paradas A. Paracervical block in incomplete abortion using manual vacuum aspiration: randomized clinical trial. Obstetrics & Gynecology 2004;103(5 Pt 1):943-51. [CRSREF: 3259491; PubMed: 15121569]

Kestin 1987. Kestin IG, Dorje P. Anaesthesia for evacuation of retained products of conception. Comparison between alfentanil plus etomidate and fentanyl plus thiopentone. British Journal of Anaesthesia 1987;59(3):364-8. [CRSREF: 3259493; PubMed: 3103663]

Lopez 2007. Lopez JC, Vigil-De Gracia P, Vega-Malek JC, Ruiz E, Vergara V. A randomized comparison of different methods of analgesia in abortion using manual vacuum aspiration. International Journal of Gynecology & Obstetrics 2007;99(2):91-4. [CRSREF: 3259495; PubMed: 17628562]

Rock 1977. Rock JA, Brame RG, Parker RT. Choice of analgesia or anesthesia for pain relief in suction curettage. Obstetrics & Gynecology 1977;49(6):721-3. [CRSREF: 3259497; PubMed: 865738]

Excluded studies

Grunstein 1976. Grunstein S, Jaschevatzky OE, Shalit A, Levy Y. Epidural analgesia in midtrimester abortion. International Journal of Gynecology & Obstetrics 1976;14(3):257-60. [CRSREF: 3259499; PubMed: 13014]

ADDITIONAL REFERENCES

Alcazar 1995. Alcazar JL, Baldonado C, Laparte C. The reliability of transvaginal ultrasonography to detect retained tissue after spontaneous first trimester abortion clinically thought to be complete. Ultrasound in Obstetrics and Gynecology 1995;6:126-9.

ASA 2002. American Society of Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96:1004–17.

ASA 2004. American Society of Anesthesiologists. Continuum of depth of sedation. Definition of general anesthesia and levels of sedation/analgesia. Approved by ASA House of Delegates; on October 13, 1999, amended October 27, 2004 (http://www.asahq.org/publicationsAndServices/standards/20.html) (accessed 2009) 2004.

Bartlett 2004. Bartlett LA, Berg CJ, Shulman HB, Zane SB, Green CA, Whitehead S, et al. Risk factors for legal induced abortion-related mortality in the United States. Obstetrics & Gynecology 2004;103(4):729-37. [PubMed: 15051566]

Bottomley 2009. Bottomley C, Bourne T. Diagnosing miscarriage. Best Practice & Research. Clinical Obstetrics & Gynaecology 2009;23(4):463-77.

Breivik 2008. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Breivik Hals EK, et al. Assessment of pain. British Journal of Anaesthesia 2008;101(1):17–24.

Chanthong 2009. Chanthong P, Abrishami A, Wong J, Herrera F, Chung F. Systematic review of questionnaires measuring patient satisfaction in ambulatory anesthesia. Anesthesiology 2009;110(5):1061-7.

Egger 1997. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315(7109):629-34.

Fung 1998. Fung D, Cohen MM. Measuring patient satisfaction with anesthesia care: a review of current methodology. Anesthesia and Analgesia 1998;87:1089-98.

Grimes 1976. Grimes DA, Cates W. Deaths from paracervical anesthesia used for first-trimester abortion, 1972-1975. New England Journal of Medicine 1976;295(25):1397-9.

Grimes 1979. Grimes DA, Schulz KF, Cates W Jr, Tyler CW Jr. Local versus general anesthesia: which is safer for performing suction curettage abortions? American Journal of Obstetrics and Gynecology 1979;135(8):1030-5. [PubMed: 517587]

Harbord 2006. Harbord RM, Egger M, Sterne JA. A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. Statistics in Medicine 2006;25(20):3443-57.

Higgins 2011. Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Koonin 2000. Koonin LM, Strauss LT, Chrisman CE, Parker WY. Abortion surveillance--United States, 1997. MMWR CDC Surveillance Summaries 2000;49(11):1-43. [PubMed: 11130580]

Lawson 1994. Lawson HW, Frye A, Atrash HK, Smith JC, Shulman HB, Ramick M. Abortion mortality, United States, 1972 through 1987. American Journal of Obstetrics and Gynecology 1994;171(5):1365-72. [PubMed: 7977548]

Neilson 2010. Neilson JP, Gyte GML, Hickey M, Vazquez JC, Dou L. Medical treatments for incomplete miscarriage (less than 24weeks). Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD007223. DOI: 10.1002/14651858.CD007223.pub2.

Osborn 1990. Osborn JF, Arisi E, Spinelli A, Stazi MA. General anaesthesia, a risk factor for complication following induced abortion? European Journal of Epidemiology 1990;6(4):416-22. [PubMed: 2091944]

Pascoe 1983. Pascoe GC. Patient satisfaction in primary health care: a literature review and analysis. Evaluation and Program Planning 1983;6:182-210.

Paul 1999. Paul M, Lichtenberg ES, Borgatta L, Grimes DA, Stubblefield PG, Maltzer DS. Pain management. In: A clinician's guide to medical and surgical abortion. 1st edition. Philadelphia. PA: Churchill Livingstone, 1999.

Peterson 1981. Peterson HB, Grimes DA, Cates W Jr, Rubin GL. Comparative risk of death from induced abortion at less than or equal to 12 weeks' gestation performed with local versus general anesthesia. American Journal of Obstetrics and Gynecology 1981;141(7):763-8. [PubMed: 7315903]

Piyamongkol 1998. Piyamongkol W. Obstetrics. In: Tongsong T, Wanapirak C, editor(s). Obstetric anaesthesiology. 4th Edition edition. Bangkok: P.B. Foreign Book Center, 1998.

Raeder 1992. Raeder JC. Propofol anaesthesia versus paracervical blockade with alfentanil and midazolam sedation for outpatient abortion. Acta Anaesthesiologica Scandinavica 1992;36(1):31-7. [PubMed: 1539476]

Renner 2009. Renner RM, Jensen JT, Nichols MD, Edelman A. Pain control in first trimester surgical abortion. Cochrane Database of Systematic Reviews 2009, Issue 2. Art. No.: CD006712. DOI: 10.1002/14651858.CD006712.pub2.

RevMan 2008. Review Manager (RevMan) [Computer program]. Version 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

Shiers 2003. Shiers C. Abnormalities of early pregnancy. In: Fraser DM, Cooper MA, editor(s). Myles textbook for midwives. 14th Edition edition. Edinburgh: Churchill Livingstone, 2003.

Soulat 2006. Soulat C, Gelly M. Immediate complications of surgical abortion [Complications immediates de l'IVG chirurgicale]. Journal de Gynecologie, Obstetrique et Biologie de la Reproduction 2006;35(2):157-62. [PubMed: 16575361]

Tangsiriwatthana 2009. Tangsiriwatthana T, Sangkomkamhang US, Lumbiganon P, Laopaiboon M. Paracervical local anaesthesia for cervical dilatation and uterine intervention. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD005056. DOI: 10.1002/14651858.CD005056.pub2.

Toledano 2009. Toledano RD, Kodali BS, Camann WR. Anesthesia drugs in the obstetric and gynecologic practice. Reviews in Obstetrics and Gynecology 2009;2(2):93-100.

Ware 1983. Ware JE Jr, Snyder MK, Wright WR, Davies AR. Defining and measuring patient satisfaction with medical care. Evaluation and Program Planning 1983;6:247-63.

WHO 1978. World Health Organization. Induced abortion. Technical report No. 623. Vol. 22. Geneva: World Health Organization, 1978.