Cochrane Library

**Cochrane** Database of Systematic Reviews

# Interventions for intra-operative pain relief during postpartum mini-laparotomy tubal ligation (Review)

Werawatakul Y, Sothornwit J, Laopaiboon M, Lumbiganon P, Kietpeerakool C

Werawatakul Y, Sothornwit J, Laopaiboon M, Lumbiganon P, Kietpeerakool C.
Interventions for intra-operative pain relief during postpartum mini-laparotomy tubal ligation.
*Cochrane Database of Systematic Reviews* 2019, Issue 2. Art. No.: CD011807.
DOI: 10.1002/14651858.CD011807.pub2.

**www.cochranelibrary.com**




WILEY

# TABLE OF CONTENTS

[Intervention Review]

# Interventions for intra-operative pain relief during postpartum mini-laparotomy tubal ligation

Yuthapong Werawatakul[1], Jen Sothornwit[1], Malinee Laopaiboon[2], Pisake Lumbiganon[3], Chumnan Kietpeerakool[3]

[1]Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand. [2]Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand. [3]Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

**Contact address:** Jen Sothornwit, Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand. jeneration_x021@hotmail.com.

**Editorial group:** Cochrane Fertility Regulation Group.
**Publication status and date:** New, published in Issue 2, 2019.

**Citation:** Werawatakul Y, Sothornwit J, Laopaiboon M, Lumbiganon P, Kietpeerakool C. Interventions for intra-operative pain relief during postpartum mini-laparotomy tubal ligation. *Cochrane Database of Systematic Reviews* 2019, Issue 2. Art. No.: CD011807. DOI: 10.1002/14651858.CD011807.pub2.



## ABSTRACT

### Background

Postpartum mini-laparotomy tubal ligation (PPTL) is a contraceptive method that works by interrupting the patency of the fallopian tubes. Several methods are used for intraoperative pain relief, such as systemic administration of opioids or intraperitoneal instillation of lidocaine.

### Objectives

To evaluate the effectiveness of and adverse effects associated with interventions for pain relief in women undergoing PPTL.

### Search methods

We searched for eligible studies published on or before 31 July 2017 in the CENTRAL Register of Studies Online, MEDLINE, Embase, PsycINFO, and CINAHL. We examined review articles and searched registers of ongoing clinical trials, citation lists of included studies, key textbooks, grey literature, and previous systematic reviews for potentially relevant studies.

### Selection criteria

We included randomised controlled trials (RCT) that compared perioperative pain relief measures during PPTL.

### Data collection and analysis

Two review authors independently assessed the titles, abstracts, and full-text articles of potentially relevant studies for inclusion. We extracted the data from the included studies, assessed risk of bias, and calculated and compared results. Discrepancies were resolved by discussion, or by consulting a third review author. We computed the inverse variance risk ratio (RR) with 95% confidence interval (CI) for binary outcomes, and the mean difference (MD) with 95% CI for continuous variables.

### Main results

We found only three RCTs, in which a total of 230 postpartum women participated. Most of our analyses were based on relatively small numbers of patients and studies. Overall, the certainty of evidence regarding the effectiveness of interventions was low, due to risk of bias and imprecision. We found very low-certainty evidence regarding the safety of interventions because of risk of bias and imprecision. Two studies had unclear risk of selection bias. One study had unclear risk of reporting bias and a high risk of other bias associated with the study protocol.

Women who received an intraperitoneal instillation of lidocaine experienced lower intensity intraperitoneal pain than those given a placebo (pooled MD -3.34, 95% CI -4.19 to -2.49, three studies, 190 participants, low-certainty evidence), or an intramuscular injection of morphine (MD -4.8, 95% CI -6.43 to -3.17, one study, 40 participants, low-certainty evidence). We found no clear difference in intraperitoneal pain between women who had an intramuscular injection of morphine added to an intraperitoneal instillation of lidocaine and those who had an intraperitoneal instillation of lidocaine alone (MD -0.40, 95% CI -1.52 to 0.72, one study, 40 participants, low-certainty evidence). An intramuscular injection of morphine alone was not effective for intraperitoneal pain relief compared to placebo (MD 0.50, 95% CI -1.33 to 2.33, one study, 40 women, low-certainty evidence). None of the studies reported any serious adverse events but the evidence was very low-certainty. Intraperitoneal instillation of lidocaine may reduce the number of women requiring additional pain control when compared to placebo (RR 0.27, 95% CI 0.17 to 0.44, three studies, 190 women, low-certainty evidence).

**Authors' conclusions**

An intraperitoneal instillation of lidocaine during postpartum mini-laparotomy tubal ligation before fallopian tubes were tied may offer better intraperitoneal pain control, although the evidence regarding adverse effects is uncertain. We found no clear difference in intraperitoneal pain between women who received a combination of an injection of morphine, and intraperitoneal instillation of lidocaine and those who received an intraperitoneal instillation of lidocaine alone. These results must be interpreted with caution, since the evidence overall was low to very low-certainty.

## PLAIN LANGUAGE SUMMARY

### Interventions for intra-operative pain relief during postpartum mini-laparotomy tubal ligation

**Review question**

The aim of this review was to compare interventions for intraoperative pain relief with other interventions or no intervention, during mini-laparotomy (small surgical incision through the abdominal wall) tubal ligation (uterine tubes tied) after delivery.

**Background**

Tubal ligation is a permanent form of birth control during which a woman's uterine tubes are surgically cut or blocked off, to prevent pregnancy. This surgery can be done through a mini-laparotomy. There are various methods used for pain relief during a mini-laparotomy tubal ligation. Some methods of pain relief include an injection of nonsteroidal anti-inflammatory drugs (a class of medication that can reduce pain and fever), opioids (a class of medications related in structure to opium), or pouring lidocaine (a medication used to numb tissue in a specific area) into the abdominal cavity.

**Study characteristics**

We included three randomised controlled trials involving a total of 230 women. These studies compared lidocaine poured into the abdominal cavity with a placebo, or other treatments, such as an injection of morphine (also known as an opioid) into the muscle, or combination of lidocaine and morphine. All studies took place in Thailand. The evidence described here are from studies published before 31 July, 2017.

**Key results**

Pouring lidocaine into the abdominal cavity during a mini-laparotomy tubal ligation before fallopian tubes were tied after delivery may offer better pain control than a placebo or morphine injection, although the evidence regarding adverse effects is uncertain. Women who received a combination of morphine injection and lidocaine poured into the abdominal cavity showed no clear difference in pain with those who received lidocaine alone. An injection of morphine into the muscle alone did not reduce pain more than a placebo.

**Certainty of the evidence**

The certainty of evidence regarding the effectiveness of these interventions was low due to risk of bias and imprecision of results. The certainty of evidence regarding the safety of the interventions was very low because of risk of bias and imprecision.

**Summary of findings for the main comparison. EMLA cream compared to placebo for pain during abdominal entry**

| EMLA cream compared to placebo cream for pain during abdominal entry | | | | | | |
|---|---|---|---|---|---|---|
| **Patient or population:** women undergoing PPTL under local anaesthesia<br>**Settings:** inpatient settings; tertiary hospitals<br>**Intervention:** EMLA cream<br>**Comparison:** placebo cream | | | | | | |
| **Outcomes** | **Illustrative comparative risks* (95% CI)** | | **Relative effect (95% CI)** | **No of women (studies)** | **Certainty of the evidence (GRADE)** | **Comments** |
| | **Risk with placebo** | **Risk with EMLA cream** | | | | |
| Pain during abdominal entry<br>(NRS; higher = more pain) | The mean pain score with placebo cream during abdominal entry was 4.6 | The mean pain score with EMLA cream was 3.18 lower (4.10 lower to 2.26 lower) | - | 90<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[1, 2] | MD -3.18, 95% CI -4.10 to -2.26 |
| Adverse events within 48 hours post operation | See comment | See comment | - | 90<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low[1, 3] | No reported adverse events occurred for this comparison |
| Number of women requiring rescue medication | 1000 per 1000 | 360 per 1000<br>(250 to 530) | RR 0.36 (0.25 to 0.53) | 90<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[1, 2] | |

*__The risk in the intervention group__ (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).

**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of the evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for imprecision of the data
[3]Downgraded two levels for serious imprecision of the data and/or sparseness of reported events

**Summary of findings 2. Lidocaine instillation compared to placebo for intra-operative intraperitoneal pain relief**

| **Lidocaine instillation compared to placebo for intra-operative intraperitoneal pain relief** | | | | | | |
|---|---|---|---|---|---|---|
| **Patient or population:** women undergoing PPTL under local anaesthesia<br>**Setting:** inpatient settings; tertiary hospitals<br>**Intervention:** lidocaine instillation<br>**Comparison:** placebo (normal saline instillation) | | | | | | |
| **Outcomes** | **Anticipated absolute effects* (95% CI)** | | **Relative effect (95% CI)** | **№ of women (studies)** | **Certainty of the evidence (GRADE)** | **Comments** |
| | **Risk with placebo instillation (normal saline)** | **Risk with lidocaine instillation** | | | | |
| Intraperitoneal pain<br><br>(NRS; higher = more pain) | The mean intraperitoneal pain score in the placebo group was 5.5 | The mean intraperitoneal pain score in the lidocaine was 3.34 lower (4.19 lower to 2.49 lower) | - | 190<br>(3 RCTs) | ⊕⊕⊖⊖<br>Low [1, 2] | MD -3.34, 95% CI -4.19 to -2.49 |
| Adverse events within 48 hours post operation | 100 per 1000 | 104 per 1000<br>(40 to 269) | RR 1.04<br>(0.40 to 2.69) | 150<br>(2 RCTs) | ⊕⊖⊖⊖<br>Very low [1,3] | |
| Number of women requiring rescue medication | 543 per 1000 | 147 per 1000<br>(92 to 239) | RR 0.27<br>(0.17 to 0.44) | 190<br>(3 RCTs) | ⊕⊕⊖⊖<br>Low [1, 2] | |

*__The risk in the intervention group__ (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).
**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for other potential risk of bias, as one study did have not a well-defined protocol for assessing adverse events, which might have impacted the reliability of reported results.
[3] Downgraded two levels for very serious imprecision (due to wide confidence intervals including benefit and harm, and sparseness of reported events)

### Summary of findings 3. Intramuscular morphine compared to placebo for intra-operative intraperitoneal pain relief

**Intramuscular (IM) morphine compared to IM placebo for intra-operative intraperitoneal pain relief**

**Patient or population:** women undergoing PPTL under local anaesthesia
**Setting:** inpatient setting; tertiary hospital
**Intervention:** IM morphine
**Comparison:** IM placebo (normal saline)

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of women (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Risk with IM placebo | Risk with IM morphine | | | | |
| Intraperitoneal pain<br><br>(NRS; higher = more pain) | The mean intraperitoneal pain score in the placebo group was 5.5 | The mean intraperitoneal pain score with IM morphine was 0.5 higher<br>(1.33 lower to 2.33 higher) | - | 40<br>(1 RCT) | ⊕⊕⊖⊖<br>Low [1, 2] | MD 0.50, 95% CI -1.33 to 2.33 |
| Adverse events within 48 hours post operation | See comment | See comment | - | 40<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low[1, 3] | There were 2 cases of vomiting in the IM morphine group, and no adverse events in the placebo group. |
| Number of women requiring rescue medication | 900 per 1000 | 900 per 1000<br>(729 to 1000) | RR 1.00<br>(0.81 to 1.23) | 40<br>(1 RCT) | ⊕⊕⊖⊖<br>Low [1, 2] | |

*__The risk in the intervention group__ (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).
**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for imprecision of the data
[3]Downgraded two levels for serious imprecision of the data and/or sparseness of reported events

### Summary of findings 4. Intraperitoneal lidocaine instillation compared to intramuscular morphine for intra-operative intraperitoneal pain relief

**Intraperitoneal lidocaine instillation compared to intramuscular (IM) morphine for intra-operative intraperitoneal pain relief**

**Patient or population:** women undergoing PPTL under local anaesthesia
**Setting:** inpatient setting; tertiary hospital
**Intervention:** lidocaine instillation
**Comparison:** IM morphine

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of women (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Risk with IM morphine | Risk with lidocaine instillation | | | | |
| Intraperitoneal pain<br><br>(NRS; higher = more pain) | The mean intraperitoneal pain score in the morphine group was 6.0 | The mean intraperitoneal pain score in the lidocaine group was 4.8 lower (6.43 lower to 3.17 lower) | - | 40<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[1, 2] | MD -4.80, 95% CI -6.43 to -3.17 |
| Adverse events within 48 hours post operation | See comment | See comment | - | 40<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low [1, 3] | There were 2 cases of vomiting in the IM morphine group, and no adverse events in the placebo group. |
| Number of women requiring rescue medication | 900 per 1000 | 198 per 1000<br>(81 to 486) | RR 0.22 (0.09 to 0.54) | 40<br>(1 RCT) | ⊕⊕⊖⊖<br>Low [1, 2] | |

*__The risk in the intervention group__ (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).
**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for imprecision of the data
[3]Downgraded two levels for serious imprecision of the data and/or sparseness of reported events

**Summary of findings 5. Combination of intraperitoneal lidocaine instillation and intramuscular morphine administration compared to placebo for intra-operative intraperitoneal pain relief**

**Intraperitoneal lidocaine instillation plus intramuscular (IM) morphine administration compared to placebo for intra-operative intraperitoneal pain relief**

**Patient or population:** women undergoing PPTL under local anaesthesia
**Setting:** inpatient setting; tertiary hospital
**Intervention:** intraperitoneal lidocaine instillation plus IM morphine
**Comparison:** placebo (intraperitoneal normal saline instillation plus IM normal saline)

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of women (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Risk with placebo | Risk with lidocaine instillation plus IM morphine | | | | |
| Intraperitoneal pain<br><br>(NRS; higher = more pain) | The mean intraperitoneal pain score in the placebo group was 5.5 | The mean intraperitoneal pain score in the lidocaine and morphine group was 4.7 lower<br>(6.09 lower to 3.31 lower) | - | 40<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[1, 2] | MD -4.70, 95% CI -6.09 to -3.31 |
| Adverse events within 48 hours post operation | See comment | See comment | - | 40<br>(1 RCT) | ⊕⊖⊖⊖<br>Very low [1, 3] | No adverse events occurred for this comparison |
| Number of women requiring rescue medication | 900 per 1000 | 99 per 1000<br>(27 to 378) | RR 0.11<br>(0.03 to 0.42) | 40<br>(1 RCT) | ⊕⊕⊖⊖<br>Low[1, 2] | |

***The risk in the intervention group** (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).
**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for imprecision of the data
[3]Downgraded two levels for serious imprecision of the data and/or sparseness of reported events

## Summary of findings 6. Combination of lidocaine intraperitoneal instillation plus intramuscular morphine compared to lidocaine intraperitoneal instillation alone for intra-operative intraperitoneal pain relief

**Lidocaine intraperitoneal instillation plus intramuscular (IM) morphine compared to lidocaine intraperitoneal instillation alone for intra-operative intraperitoneal pain relief**

**Patient or population:** women undergoing PPTL under local anaesthesia
**Setting:** inpatient setting; tertiary hospital
**Intervention:** lidocaine intraperitoneal instillation plus IM morphine
**Comparison:** lidocaine intraperitoneal instillation alone

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of women (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Risk with lidocaine instillation alone | Risk with lidocaine instillation plus IM morphine | | | | |
| Intraperitoneal pain<br><br>(NRS; higher = more pain) | The mean intraperitoneal pain score in the lidocaine alone group was 1.2 | The mean intraperitoneal pain score in the lidocaine plus morphine group was 0.4 lower<br>(1.52 lower to 0.72 higher) | - | 40<br>(1 study) | ⊕⊕⊖⊖<br>Low[1, 2] | MD -0.40, 95% CI -1.52 to 0.72 |
| Adverse events within 48 hours post operation | See comment | See comment | - | 40<br>(1 study) | ⊕⊖⊖⊖<br>Very low [1, 3] | No adverse events occurred for this comparison |

| | | | | | |
|---|---|---|---|---|---|
| Number of women requiring rescue medication | 200 per 1000 | 100 per 1000 (20 to 486) | RR 0.50 (0.10 to 2.43) | 40 (1 study) | ⊕⊖⊖⊖ Low[1, 2] |

*__The risk in the intervention group__ (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).
**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for imprecision of the data
[3]Downgraded two levels for serious imprecision of the data and/or sparseness of reported events

### Summary of findings 7. Combination of lidocaine intraperitoneal instillation plus intramuscular morphine compared to intramuscular morphine alone for intra-operative intraperitoneal pain relief

**Lidocaine intraperitoneal instillation plus intramuscular (IM) morphine compared to IM morphine alone for intra-operative intraperitoneal pain relief**

**Patient or population:** women undergoing postpartum mini-laparotomy tubal ligation (PPTL) under local anaesthesia
**Setting:** inpatient setting; tertiary hospital
**Intervention:** lidocaine intraperitoneal instillation plus IM morphine
**Comparison:** IM morphine alone

| Outcomes | Anticipated absolute effects* (95% CI) | | Relative effect (95% CI) | № of women (studies) | Certainty of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Risk with IM morphine alone | Risk with lidocaine instillation plus IM morphine | | | | |
| Intraperitoneal pain<br><br>(NRS; higher = more pain) | The mean intraperitoneal pain score in the IM morphine alone group was 6.0 | The mean intraperitoneal pain score in the lidocaine plus morphine group was 5.2 lower (6.63 lower to 3.77 lower) | - | 40 (1 RCT) | ⊕⊕⊖⊖ Low[1, 2] | MD -5.20, 95% CI -6.63 to -3.77 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adverse events within 48 hours post operation | See comment | See comment | - | 40 (1 RCT) | ⊕⊖⊖⊖ Very low[1, 3] | There were only two cases of vomiting in the IM morphine group, and no adverse events in the lidocaine plus morphine group |
| Number of women requiring rescue medication | 900 per 1000 | 99 per 1000 (27 to 378) | RR 0.11 (0.03 to 0.42) | 40 (1 RCT) | ⊕⊕⊖⊖ Low[1, 2] | |

*__The risk in the intervention group__ (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).
**NRS**: numeric rating scale; **CI:** confidence interval; **RR:** risk ratio; **MD**: mean difference

**GRADEs (certainty) of evidence**

**High certainty:** we are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

**Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[1]Downgraded one level for unclear risk of selection bias
[2]Downgraded one level for imprecision of the data
[3]Downgraded two levels for serious imprecision of the data and/or sparseness of reported events

# BACKGROUND

## Description of the condition

Postpartum mini-laparotomy tubal ligation (PPTL) is the most common permanent contraception worldwide, with 18.9% of women choosing sterilization as their form of contraception (UN 2013). However, the fear of pain during this procedure is an important barrier for women undergoing this operation. One study found the mean intraoperative numerical rating scale (NRS) pain score for PPTL to be 5.5, and reported that some women (3.75%) required additional pain relief, or ended up undergoing general anaesthesia (Visalyaputra 1999). Pain usually occurs during the following three steps: skin incision, peritoneum stretching, and ligation of the fallopian tubes.

## Description of the intervention

Many techniques exist for intraoperative pain relief during PPTL, including general, regional, and local anaesthesia. General and regional anaesthesia are very effective for pain control during PPTL (Aaronson 2014). However, these interventions require facilities and anaesthesiologists, which might not be widely available, particularly in less economically developed countries. Other possible interventions include an injection of anaesthetic agents into the mesosalpinx (Benhamou 1994) or peritoneum (Ratanalappaiboon 2012), oral administration of non-steroidal anti-inflammatory drugs (NSAIDs; Putland 1999), analgesia, and parenteral administration of opioids (Visalyaputra 1999). These interventions can be more easily performed and do not require an anaesthesiologist. Thus, they might be more appropriate and practical for low-resource settings, if the safety can be ascertained.

## How the intervention might work

Local administration of lidocaine before the incision is only adequate for pain relief associated with the skin incision. It is not adequate for pain relief during the stretching of the peritoneum, or ligation of the uterine tubes (Visalyaputra 2002). An injection of anaesthetic agents (e.g. lidocaine or Marcaine) into the mesosalpinx, or peritoneum may inhibit pain by blocking the fast voltage-gated sodium channels in the neuronal cell membrane responsible for signal propagation, causing failure in transmitting action potential (Tetzlaff 2000). Intravenous injection or intramuscular injection of NSAIDs can inhibit cyclo-oxygenase-1 (COX-1) and COX-2 enzymes, which are involved in prostaglandin synthesis, resulting in their analgesic effects (Day 2013). Opioid administration can control the pain by acting as μ (mu) receptor agonists and agonist-antagonists (Trescot 2008). These interventions can prevent pain during peritoneal stretching and ligation of uterine tubes.

## Why it is important to do this review

The above-mentioned interventions have been widely used in low-resource settings due to their simplicity, and because they can be used on an outpatient basis (Chi 1992). Adequate pain management using local anaesthetic techniques could make PPTL available to more women who want sterilisation, particularly in low-resource settings. However, to our knowledge, there have been no systematic reviews determining the effectiveness of, and adverse events associated with interventions for intraoperative pain relief during PPTL.

See Appendix 1 for a list of abbreviations and Appendix 2 for a glossary of terms.

# OBJECTIVES

To evaluate the effectiveness of and adverse effects associated with interventions for pain relief in women undergoing postpartum mini-laparotomy tubal ligation (PPTL).

# METHODS

## Criteria for considering studies for this review

### Types of studies

We included all randomised controlled trials (RCTs) comparing one intervention to another intervention, placebo, or no treatment.

### Types of participants

Women undergoing PPTL under local anaesthesia.

### Types of interventions

We considered all interventions for intraoperative pain relief during PPTL. These included an injection of lidocaine into the mesosalpinx, intraperitoneal instillation of lidocaine, oral administration of non-steroidal anti-inflammatory drugs (NSAIDs), and an intramuscular injection (IM) injection of morphine.

### Types of outcome measures

#### *Primary outcomes*

1. Pain during PPTL, using validated rating measures, such as numerical rating scale (NRS), visual analogue scale (VAS), or the Faces Pain Scale-Revised (FPSR).

#### *Secondary outcomes*

1. Adverse effects, such as nausea, vomiting, urinary retention, or perioral numbness.
2. Requirement for additional medication, regional anaesthesia, or general anaesthesia, in order to complete the PPTL procedure.

We presented all outcomes for all comparisons of intraperitoneal pain relief measures in 'Summary of findings' tables.

## Search methods for identification of studies

### Electronic searches

We searched the following computerized databases:

- CENTRAL Register of Studies Online (CRSO) web platform (searched 31 July 2017 (Appendix 3));
- MEDLINE Ovid (1946 to 31 July 2017 (Appendix 4));
- Embase Ovid (1980 to 31 July 2017 (Appendix 5));
- PsycINFO Ovid (1806 to 31 July 2017 (Appendix 6));
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1961 to 31 July 2017 (Appendix 7)).

We also searched for ongoing clinical trials through ClinicalTrials.gov (www.clinicaltrials.gov) and the International Clinical Trials Registry Platform (ICTRP (www.who.int/ictrp/en/)). The former search strategy is detailed in Appendix 8.

An updated search was performed on 31 October 2018 which resulted in no new studies for inclusion.

### Searching other resources

#### *Unpublished and grey literature*

We searched electronic databases, including Greynet.org (www.greynet.org), WorldCat Dissertations and Theses (www.worldcat.org/title/worldcat-dissertations-and-theses/oclc), and Index to Theses (ProQuest Dissertations & Theses: UK & Ireland), to identify relevant conference abstracts and proceedings.

#### *Handsearch*

We searched previous systematic reviews and checked the citation lists of the included studies and key textbooks for potentially relevant references. We searched for papers in all languages and had them translated, if necessary.

## Data collection and analysis

### Selection of studies

Two review authors, Yuthapong Werawatakul (YW) and Jen Sothornwit (JS), independently assessed the titles and abstracts from our literature search. We excluded the studies that clearly did not meet inclusion criteria and evaluated the full-texts of all possibly relevant articles to determine eligibility. Discrepancies were resolved by discussion, or by consulting a third review author (CK or PL).

### Data extraction and management

Before examining the identified trials for possible inclusion, we developed and field tested a data collection form, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Two review authors, YW and JS, independently collected the data on the extraction forms and extracted the data under unblinded conditions. They resolved discrepancies by discussion, or by consulting a third review author, PL or Malinee Laopaiboon (ML). When necessary, we contacted the authors of the included studies to seek additional information. Correct entry of the data was verified by a third review author (PL or ML). As YW was the author of one of the included studies, JS and PL were responsible for assessing risk of bias and extracting data from this study (Ratanalappaiboon 2012).

We extracted the following data from the included studies:

- Author, year of publication and journal citation (including language)
- Country
- Setting
- Inclusion and exclusion criteria
- Study methodology
- Study population and disease characteristics, including total number of participant enrolled, participant characteristics, age, comorbidity, and other baseline characteristics
- Intervention details, including type, dosage, and pattern of administration
- Comparison(s): placebo or other treatment
- Risk of bias (see below)
- Duration of follow-up
- Outcomes: for each outcome, we extracted the outcome definition and unit of measurement; for adjusted estimates, we planned to record the variables adjusted for in the analyses
- Results: we extracted the number of women assigned to each comparison group, the total number analysed for each outcome, and the missing women
- Notes: funding and notable conflicts of interest of authors

### Assessment of risk of bias in included studies

Two review authors, YW and JS, independently assessed risk of bias for each included study, based on the guidance given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved any disagreements by discussion, or by consulting PL and ML. Specifically, we assessed the risk of bias in included studies for the following domains.

#### *1) Random sequence generation (checking for possible selection bias)*

For each included study, we described 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)*

For each included study, we described 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.

#### *3.1) Blinding of participants and personnel (checking for possible performance bias)*

For each included study, we described the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were 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 participants and personnel as:

- low, high, or unclear risk of bias for participants;
- low, high, or unclear risk of bias for personnel.

#### *3.2) Blinding of outcome assessment (checking for possible detection bias)*

For each included study, we described the methods used, if any, to blind outcome assessors from knowledge of which intervention a

participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high, or unclear risk of bias

#### *4) Incomplete outcome data (checking for attrition bias)*

For each included study, we described the completeness of data including attrition and exclusion from the studies. We assessed whether attrition and exclusion were reported and the numbers included in the analysis at each stage, reasons for attrition or exclusion where reported, and whether missing data were balanced across the groups.

We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups);
- unclear risk of bias.

#### *5) Selective reporting (checking for reporting bias)*

For each included study, we described 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 prespecified outcomes and all expected outcomes of interest to the review were reported);
- high risk of bias (where not all of the study's prespecified outcomes were reported, one or more reported primary outcomes were not prespecified, outcomes of interest were reported incompletely and so could be used, study failed 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)*

For each included study, we described 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 was risk of other bias.

#### *Overall risk of bias*

We made explicit judgements about whether trials were at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We considered an included trial to be at low risk of bias if the study was assessed to be at low risk of bias for all domains. Trials with uncertain risk of bias or with high risk of bias in one or more domains were considered to have a high risk of bias.

### Measures of treatment effect

For dichotomous data, such as nausea and vomiting, we presented results as summary risk ratios (RR) with 95% confidence intervals (Higgins 2011). For continuous data, we used the mean difference if outcomes were measured in the same way between trials. We had intended to use the standardized mean difference (SMD) to combine trials that measured the same outcome but use different methods (Higgins 2011). However, we did not calculate the SMD in the analyses, as all included studies used the same method for evaluating pain.

### Unit of analysis issues

The unit of analysis was the woman who was randomised. Cluster-randomised and cross-over trials were not appropriate study designs for the interventions that this review aimed to evaluate, and therefore, were ineligible for this review. We included multi-armed trials in the analyses along with individually-randomised trials. We included the relevant intervention groups in a pair-wise comparison of intervention groups that met the criteria for including studies in the review. We combined groups to create a single pair-wise comparison, using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

### Dealing with missing data

We planned to note the levels of attrition in the included studies, and to explore the impact of including studies with high levels of missing data (more than 20% of participants were lost to follow-up) on the overall assessment of treatment effect, using a sensitivity analysis. However, we did not perform this sensitivity analysis as none of the included studies had missing data. If feasible in future updates, we will perform a sensitivity analysis to assess the impact of a high level of missing data on the pooled results.

For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat basis. This means we attempted to include all randomised women in the analyses, and to analyse all women in the group to which they were allocated, regardless of whether they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any women whose outcomes were known to be missing.

### Assessment of heterogeneity

We planned to assess statistical heterogeneity in each meta-analysis using the $Tau^2$, $I^2$, and $Chi^2$ statistics (Higgins 2011). We intended to regard heterogeneity as substantial if $I^2$ was greater than 30%, and either $Tau^2$ was greater than zero, or there was a low P value (less than 0.10) in $Chi^2$ test for heterogeneity (Higgins 2011).

### Assessment of reporting biases

As only three RCTs met the review inclusion criteria, we were unable to construct funnel plots to determine the possibility of publication bias (see Differences between protocol and review).

### Data synthesis

We carried out statistical analysis using Review Manager 5 software (Review Manager 2014). We used fixed-effect meta-analysis to combine data where it was reasonable to assume that studies were estimating the same underlying treatment effect (i.e. where trials were examining the same intervention,

and the trials' populations and methods were judged sufficiently similar). If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, as long as an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average range of possible treatment effects, and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we had intended to not combine trials. Had we used random-effects analyses, we would have presented the results as the pooled treatment effect with 95% confidence intervals, and the estimates of $Tau^2$ and $I^2$ (DerSimonian 1986).

#### *'Summary of findings' table and assessing the certainty of evidence*

We prepared 'Summary of findings' tables to display the results of the meta-analyses, based on the methods described in Chapter 11 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011).

We presented the results of the meta-analyses and overall certainty of the evidence obtained from all comparisons regarding intraperitoneal pain relief measures for all outcomes of interest (pain relief, adverse effects, additional medication required), according to the GRADE approach.

We created a 'Summary of findings' table using GRADEpro GDT (GRADEpro GDT 2015). We downgraded the evidence from high certainty by one level for each serious limitation, or by two levels for any very serious limitation, for study limitations, indirectness of the evidence, inconsistency of results, imprecision of results, and probability of publication bias. We interpreted the GRADE levels of evidence as:

- High certainty: the true effect lies close to that of the estimate of the effect.
- Moderate certainty: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low certainty: the true effect may be substantially different from the estimate of the effect.
- Very low certainty: the true effect is likely to be substantially different from the estimate of effect.

### Subgroup analysis and investigation of heterogeneity

We performed no subgroup analysis, as only three RCTs, assessing 230 women, met our inclusion criteria. However, we considered the type of intervention and volume of anaesthetic agent in the interpretation of findings. In future updates, we will perform subgroup analysis according to these factors, if feasible.

### Sensitivity analysis

We performed no sensitivity analysis, as only three trials met our inclusion criteria. In future updates, if we detect statistical heterogeneity, and there is a sufficient number of included studies, we will conduct a sensitivity analysis for primary outcomes to determine the possible contribution of other clinical or methodological differences across the included studies (i.e. high or unclear risk of bias for allocation concealment or publication status).

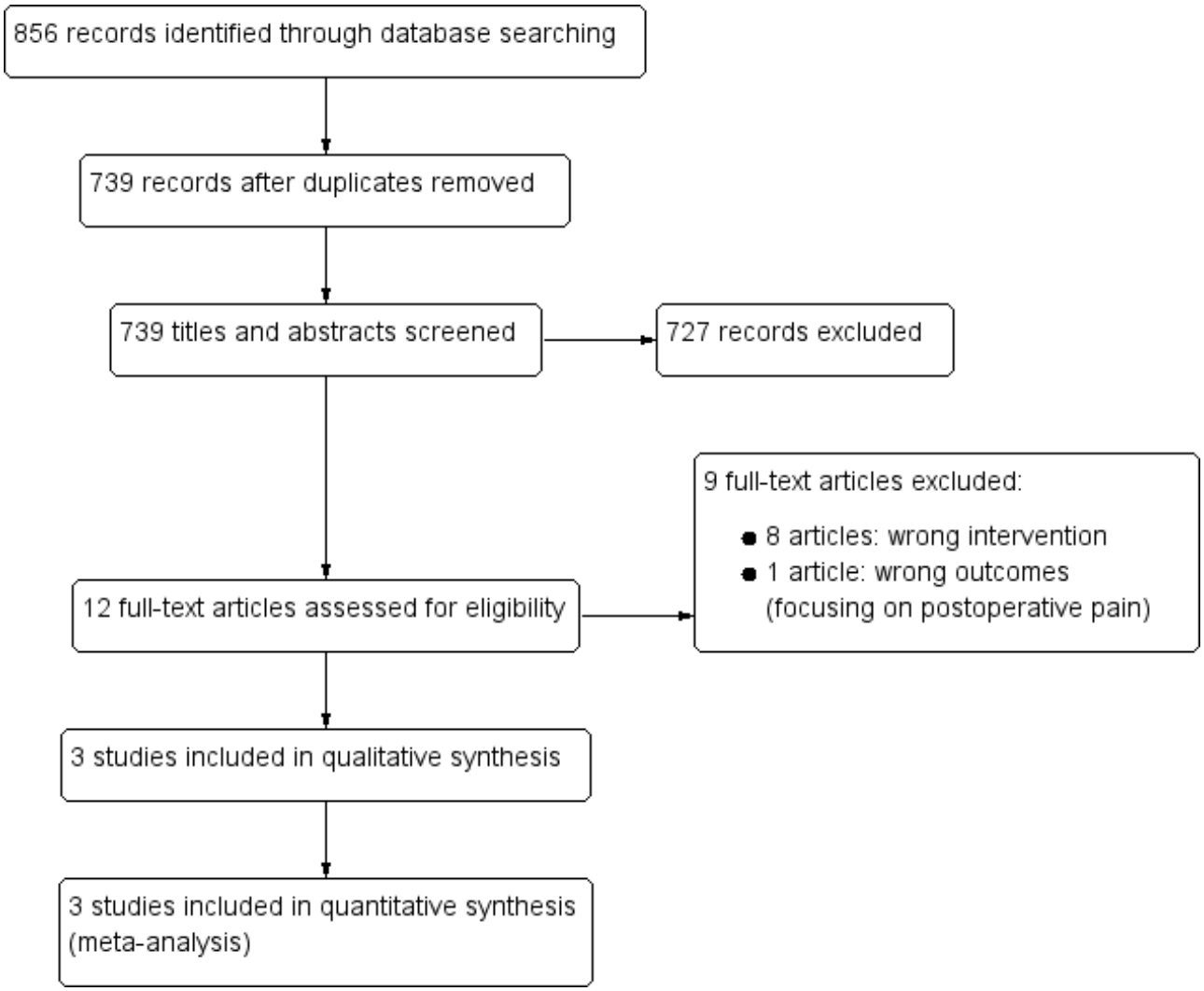
## RESULTS

## Description of studies

### Results of the search

We identified 856 records from the combined searches. After removing 117 duplicate records, we screened the titles and abstracts of 739 records, and discarded 727 records, as they did not meet the inclusion criteria. We obtained the full text of 12 articles for in-depth review, and excluded nine, leaving three randomised controlled trials (RCT) with 230 women to be included in this review. We checked the reference lists of included studies, key textbooks, and previous systematic reviews for potentially relevant references, but found no further relevant studies. We did not find any ongoing studies. See the PRISMA flow diagram in Figure 1.

**Figure 1. Study flow diagram**




## Included studies

Full details of included studies are provided in the 'Characteristics of included studies' section.

### *Study design and setting*

We included three RCTs; all were double-blinded placebo-controlled studies. Two RCTs were conducted in the same tertiary hospital in Bangkok, Thailand (Visalyaputra 1999; Visalyaputra 2002). The third RCT took place in a university hospital in northeast Thailand (Ratanalappaiboon 2012).

### *Participants*

All three RCTs recruited healthy women who agreed to undergo PPTL. Exclusion criteria were history of pelvic inflammatory disease, asthma, liver disease, allergy to lidocaine, or obesity (body mass index > 32 kg/m$^2$).

### *Sample sizes*

The sample sizes of the RCTs ranged from 60 to 90 women.

### *Outcomes and interventions*

#### Pain during PPTL

The included studies reported two time points of pain assessment during PPTL: pain during abdominal wall entry and intraperitoneal pain. Pain was assessed using the numeric rating scale (NRS), which ranged from 0 to 10 in all included studies, with higher scores indicating more pain.

#### Pain during abdominal entry

One study evaluated the efficacy of applying EMLA cream (eutectic mixture of lidocaine and prilocaine creams) compared to a placebo cream before the incision was made, for alleviating pain (Visalyaputra 2002). Two hours after applying the cream, forceps were used to assess pain, before making the skin incision, measured with the NRS. If the NRS score was ≥ 3, women received 10 ml of 1% lidocaine, infiltrated into the skin and subcutaneous tissue.

#### Intraperitoneal pain

Interventions were performed immediately after entry into the intraperitoneal cavity and before manipulation of the fallopian tubes.

Ratanalappaiboon 2012 assessed intraperitoneal pain in a total of 60 women. The study measured pain between three groups of women, one minute after the instillation into the peritoneal cavity (intraperitoneal), of 100 mg of lidocaine, 200 mg of lidocaine, or normal saline (as a placebo).

Visalyaputra 1999 assessed a total of 80 women. The study evaluated intraperitoneal pain between four study arms: (1) a placebo group, given an intramuscular injection and an intraperitoneal instillation of normal saline, (2) a morphine group, which received an intramuscular injection of 10 mg of morphine with an intraperitoneal instillation of normal saline, (3) a lidocaine group, given an intramuscular injection of normal saline and an intraperitoneal instillation of 80 mL of 0.5% lidocaine, and (4) a morphine and lidocaine group, which received either an intramuscular injection of 10 mg of morphine, or an intraperitoneal instillation of 80 mL of 0.5% lidocaine. Intraperitoneal pain was assessed three minutes after instillation.

Visalyaputra 2002 assessed a total of 90 women, comparing three groups of women who received either 1% or 2% lidocaine for intraperitoneal instillation, or normal saline as a placebo. Intraperitoneal pain was assessed one minute after instillation.

#### Adverse effects

All three studies reported adverse effects. Visalyaputra 1999 and Visalyaputra 2002 stated their protocol for monitoring the potential adverse effects throughout the operation. Ratanalappaiboon 2012 had no a well-defined protocol for assessing perioperative adverse effects.

#### Requirement for additional medication, regional or general anaesthesia for completing PPTL procedure

In all studies, women received regional or general anaesthesia if the pain was not adequately controlled after additional medication was administered. Table 1 shows the number of women who required regional or general anaesthesia for pain control during PPTL.

### Excluded studies

We excluded nine studies for the reasons described in the 'Characteristics of excluded studies' section. The common reasons were that the intervention used in the study was regional anaesthesia, or that postoperative pain was the outcome measure and not intra-operative pain.

## Risk of bias in included studies

See Figure 2 and Figure 3 for full details regarding risk of bias assessment in the included studies.

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

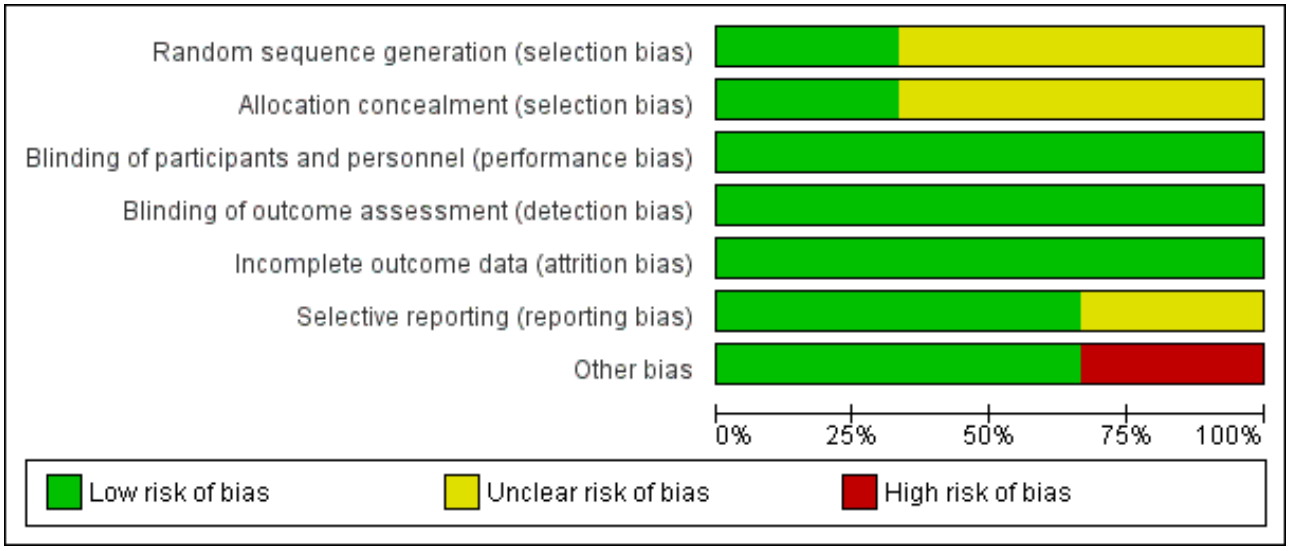
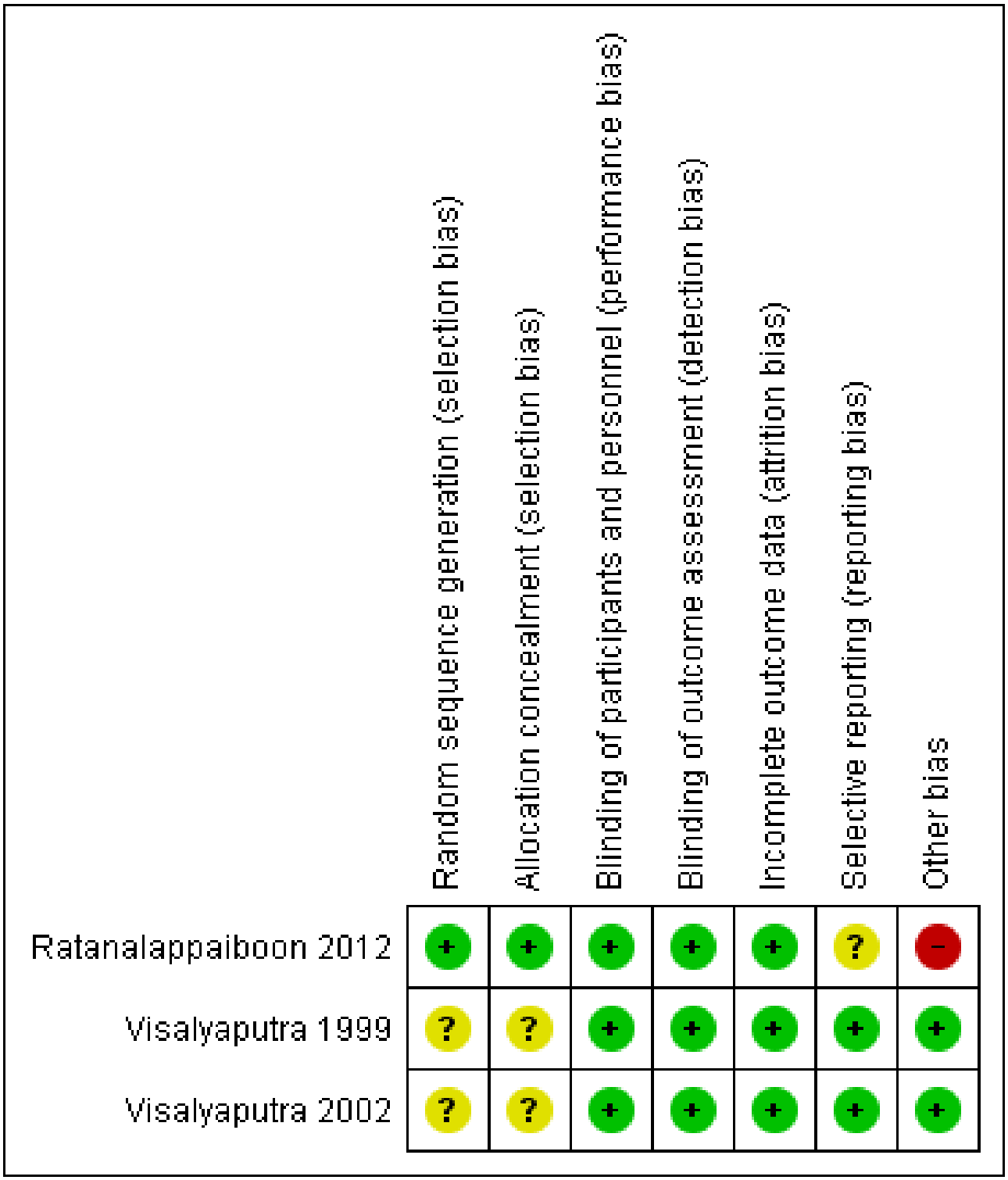


**Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study**




**Allocation**

Ratanalappaiboon 2012 reported that the researchers randomly assigned women to the groups using sealed opaque envelopes, which contained a computer-generated random number. We therefore judged this study to be at low risk of selection bias (Ratanalappaiboon 2017 [pers comm]). There was no statement regarding the method used to generate and conceal the allocation sequences in Visalyaputra 1999 and Visalyaputra 2002. Therefore, we rated Visalyaputra 1999 and Visalyaputra 2002 as having an unclear risk of selection bias.

### Blinding

Two studies blinded either women or outcome assessors, which led us to judge them as being at low risk of bias in this domain (Visalyaputra 1999; Visalyaputra 2002). There was no detailed description regarding the blinding of women and personnel in Ratanalappaiboon 2012.

Additional information provided by the first author of Ratanalappaiboon 2012 confirmed that this study minimized performance bias and detection bias by blinding the women and the outcome assessor (Ratanalappaiboon 2017 [pers comm]). Therefore, we also judged this study as having low risk of bias in this domain.

### Incomplete outcome data

We judged all three studies as having low risk of attrition bias because all outcomes were completely measured during operation.

### Selective reporting

There was little information regarding adverse effects in Ratanalappaiboon 2012, so we judged this study as having unclear risk of bias for this domain. We judged the remaining two included studies as having low risk of selective reporting bias because all expected outcomes described in the methods were reported in the results.

### Other potential sources of bias

Ratanalappaiboon 2012 contained no well-defined protocol for assessing perioperative adverse effects, so we judged this study as high risk of bias in this domain. We identified no other potential sources of bias in Visalyaputra 1999 or Visalyaputra 2002. Therefore, we determined that these two studies were at low risk of bias in this domain.

## Effects of interventions

See: **Summary of findings for the main comparison** EMLA cream compared to placebo for pain during abdominal entry; **Summary of findings 2** Lidocaine instillation compared to placebo for intra-operative intraperitoneal pain relief; **Summary of findings 3** Intramuscular morphine compared to placebo for intra-operative intraperitoneal pain relief; **Summary of findings 4** Intraperitoneal lidocaine instillation compared to intramuscular morphine for intra-operative intraperitoneal pain relief; **Summary of findings 5** Combination of intraperitoneal lidocaine instillation and intramuscular morphine administration compared to placebo for intra-operative intraperitoneal pain relief; **Summary of findings 6** Combination of lidocaine intraperitoneal instillation plus intramuscular morphine compared to lidocaine intraperitoneal instillation alone for intra-operative intraperitoneal pain relief; **Summary of findings 7** Combination of lidocaine intraperitoneal instillation plus intramuscular morphine compared to intramuscular morphine alone for intra-operative intraperitoneal pain relief

### 1. Any intervention versus no intervention or placebo

#### *1.1 EMLA cream versus placebo*

##### Primary outcome

##### Pain during abdominal entry

Pain during abdominal entry was reported in only one study. Visalyaputra 2002 evaluated the effectiveness of EMLA cream in alleviating pain during the skin incision. Women received either EMLA cream or a placebo. There was less pain reported during the forceps check when EMLA cream was used, then when they used a placebo (mean difference (MD) -3.18, 95% confidence interval (CI) -4.10 to -2.26; 1 RCT, 90 women; Analysis 1.1).

##### Secondary outcomes

##### Adverse effects

No adverse effects were reported for these two comparison groups.

##### Requirement for additional medication, regional anaesthesia, or general anaesthesia

Fewer women required additional lidocaine infiltration in the EMLA group then in the placebo group (risk ratio (RR) 0.36, 95% CI 0.25 to 0.53; 1 RCT, 90 women; Analysis 1.2).

#### *1.2 lidocaine instillation versus placebo (normal saline)*

A total of 190 women were randomised to receive various doses of lidocaine for intraperitoneal instillation versus normal saline (Ratanalappaiboon 2012; Visalyaputra 1999; Visalyaputra 2002).

##### Primary outcome

##### Intraperitoneal pain

Women who received lidocaine, regardless of the concentration, reported less intraperitoneal pain intensity then those who received normal saline (MD -3.34, 95% CI -4.19 to -2.49; 3 RCTs, 190 women; Analysis 2.1).

##### Secondary outcomes

##### Adverse effects

Two studies reported adverse effects, including dizziness and vomiting from the lidocaine instillation (Ratanalappaiboon 2012; Visalyaputra 2002). However, the pooled analysis showed no clear difference in the risk of adverse effects between the comparison groups (RR 1.04, 95% CI 0.40 to 2.69; 2 RCTs, 150 women; Analysis 2.2 ).

##### Requirement for additional medication, regional anaesthesia, or general anaesthesia

Pooled analysis indicated that there were fewer women who requiring additional pain relief measures when lidocaine was used for intraperitoneal instillation compared to placebo (RR 0.27, 95% CI 0.17 to 0.44; 3 RCTs, 190 women; Analysis 2.3).

#### *1.3 IM morphine versus placebo (normal saline)*

Visalyaputra 1999 evaluated the efficacy of an intramuscular (IM) injection of 10 mg of morphine compared to normal saline, given as a placebo, in 40 women.

**Primary outcome**

**Intraperitoneal pain**

There was no clear difference between the groups in their reports of intraperitoneal pain (MD 0.50, 95% CI -1.33 to 2.33; 1 RCT, 40 women; Analysis 3.1).

**Secondary outcomes**

**Adverse effects**

Two women who received IM morphine complained of vomiting; none of the women in the placebo group reported any adverse effects.

**Requirement for additional medication, regional anaesthesia, or general anaesthesia**

There was no clear difference between the groups in the rate of women who required additional medication, regional anaesthesia, or general anaesthesia (RR 1.00, 95% CI 0.81 to 1.23, 1 RCT, 40 women; Analysis 3.2).

### 2. Intervention versus intervention

Visalyaputra 1999, compared an intraperitoneal instillation of 0.5% lidocaine with 10 mg IM morphine in 40 women.

***Primary outcome***

**Intraperitoneal pain**

Women who received an intraperitoneal instillation of lidocaine experienced significantly less pain intensity than those who received IM morphine (MD -4.80, 95% CI -6.43 to -3.17; 1 RCTs, 40 women; Analysis 4.1).

***Secondary outcomes***

**Adverse effects**

Two women who received IM morphine complained of vomiting; none of the women who received an intraperitoneal instillation of lidocaine reported any adverse effects.

**Requirement for additional medication, regional anaesthesia, or general anaesthesia**

Significantly fewer women who received an intraperitoneal instillation of lidocaine required additional pain control measures compared to those who received IM morphine (RR 0.22, 95% CI 0.09 to 0.54; 1 RCT, 40 women; Analysis 4.2).

### 3. Combination of interventions versus no intervention or placebo

Visalyaputra 1999 compared a combination of an intraperitoneal instillation of 0.5% lidocaine instillation plus 10 mg IM morphine with a placebo of normal saline in 40 women.

***Primary outcome***

**Intraperitoneal pain**

Women who were given a combination of IM morphine and intraperitoneal lidocaine instillation reported significantly less pain than those who were given a placebo (MD -4.70, 95% CI -6.09 to -3.31; 1 RCT, 40 women; Analysis 5.1).

***Secondary outcomes***

**Adverse effects**

There were no adverse events observed in this comparison.

**Requirement for additional medication, regional anaesthesia, or general anaesthesia**

Significantly fewer women who were given a combination of IM morphine and intraperitoneal lidocaine instillation required additional medication, regional anaesthesia, or general anaesthesia than those in the placebo group (RR 0.11, 95% CI 0.03 to 0.42; 1 RCT, 40 women; Analysis 5.2).

### 4. Combination of interventions versus single intervention

***4.1 Combination of lidocaine instillation and IM morphine versus instillation of lidocaine alone***

A single study, involving 40 women, measured outcomes for this comparison (Visalyaputra 1999).

**Primary outcome**

**Intraperitoneal pain**

There was no clear difference in pain relief between the groups (MD -0.40, 95% CI -1.52 to 0.72; 1 RCT, 40 women; Analysis 6.1).

**Secondary outcomes**

**Adverse effects**

There were no adverse events observed in this comparison.

**Requirement for additional medication, regional anaesthesia, or general anaesthesia**

There was no clear difference in the number of women who required additional medication, regional anaesthesia, or general anaesthesia between the groups (RR 0.50, 95% CI 0.10 to 2.43, 1 RCT, 40 women; Analysis 6.2).

***4.2 Combination of lidocaine instillation and IM morphine versus IM morphine alone***

A single study, involving 40 women, measured outcomes for this comparison (Visalyaputra 1999).

**Primary outcome**

**Intraperitoneal pain**

Women who received a combination of lidocaine instillation and IM morphine reported less pain than those who received IM morphine alone (MD -5.20, 95% CI -6.63 to -3.77; 1 RCT, 40 women; Analysis 7.1).

**Secondary outcomes**

**Adverse effects**

Two women who received IM morphine alone complained of vomiting; no women who received a combination of lidocaine and IM morphine reported any adverse effects.

**Requirement for additional medication, regional anaesthesia, or general anaesthesia**

Significantly fewer women who received a combination of lidocaine plus IM morphine required additional medication, regional anaesthesia, or general anaesthesia than those who received IM

morphine alone (RR 0.11, 95% CI 0.03 to 0.42; 1 RCT, 40 women; Analysis 7.2).

## DISCUSSION

### Summary of main results

The findings of this review are based on three small RCTs, which analysed a total of 230 PPTL under local anaesthesia. One of the studies assessed pain intensity during abdominal entry, comparing the results of women who had EMLA cream applied prior to the incision, and those who had a placebo cream applied. The interventions for intraperitoneal pain relief evaluated in the three studies consisted of intraperitoneal instillation of various concentrations of lidocaine, an intramuscular injection of morphine, or a combination of intraperitoneal instillation of lidocaine and an intramuscular injection of morphine. However, most of the review findings are based on a small number of women from a single small study.

We observed the following main findings:

- EMLA, a topical anaesthetic agent, significantly reduced pain during abdominal entry more than placebo, as evidenced by lower pain intensity during a pain test conducted using forceps (Analysis 1.1), and significantly reduced the need for subcutaneous lidocaine during the procedure (Analysis 1.2).
- Women receiving intraperitoneal instillation of lidocaine (regardless of dose) experienced significantly less intraperitoneal pain intensity than those given placebo (Analysis 2.1), or IM morphine (Analysis 4.1). Adding IM morphine to an intraperitoneal instillation of lidocaine did not clearly reduce intraperitoneal pain compared to intraperitoneal instillation of lidocaine alone (Analysis 6.1). An intramuscular injection of morphine alone was not effective for intraperitoneal pain relief compared to placebo (Analysis 3.1).
- Adverse effects of local anaesthetic techniques assessed among the included studies were relatively infrequent, and no serious adverse effects were reported, only vomiting and dizziness.

### Overall completeness and applicability of evidence

The primary outcome of this review was pain intensity during PPTL. Only one included study measured pain during the incision for abdominal entry. All included studies reported intensity of intraperitoneal pain within a few minutes following the instillation of lidocaine. Visalyaputra 1999 evaluated intraperitoneal pain at three minutes after instillation. The remaining two studies evaluated intraperitoneal pain at one minute after instillation. The secondary outcomes of interest in this review included perioperative adverse effects and the number of women who required additional medication, regional anaesthesia, or general anaesthesia for pain relief during the procedure. None of the studies reported on the severity of adverse effects. Visalyaputra 1999 and Visalyaputra 2002 described their protocol for evaluating adverse effects during the procedure, but Ratanalappaiboon 2012 did not, which may raise the uncertainty of adverse effects reported in this included study. All included studies reported the number of women requiring additional medication, regional anaesthesia, or general anaesthesia for pain relief during the procedure. None of the studies reported on measures of satisfaction.

Although the interventions evaluated in this review varied across studies, the main intervention was the intraperitoneal instillation of lidocaine, either alone or combined with an injection of morphine. In addition, none of the included studies provided any pre-emptive analgesia (initiation of an anaesthetic agent before surgical incision), which has been reported as a promising strategy for better pain control throughout the perioperative period (Campiglia 2010). Therefore, the evidence presented is not applicable to patients undergoing different local anaesthetic techniques (i.e. injection of anaesthetic agents into the mesosalpinx, or those given pre-emptive analgesic agents).

This review included only those studies that evaluated the effectiveness and safety of local anaesthetic techniques for pain relief during postpartum mini-laparotomy tubal ligation, therefore, we cannot generalize the review findings to non-postpartum women undergoing interval tubal ligation procedures.

A previous systematic review observed a considerably high rate of anaesthetic-related mortality among patients in low-resource settings, which is partly explained by the inability to support investment in technology, techniques, and training necessary to improve patient safety (Bainbridge 2012). The strength of this review is that it addressed a clinically relevant and pragmatic question for low- and middle-income countries (LMIC). This review, which included three studies conducted in Thailand, indicated that intraperitoneal instillation of a local anaesthetic agent could be an acceptable anaesthetic method that could offer good pain control for women who undergo PPTL.

The review findings can apply to other LMIC, as intraperitoneal instillation of local anaesthetic agent is an easy, cheap, and a less invasive method that does not require an anaesthesiologist or advanced anaesthetic equipment. Therefore, this would make PPTL more available to more women in LMIC settings who wish to be sterilized.

### Quality of the evidence

The main limitation of this review is that we only identified three small RCTs, involving a total of 230 women. Most of the analyses were based on a small number of studies and women. Using GRADE criteria, we judged the overall certainty of evidence in this review as low to very low. We downgraded the certainty of the evidence to low for all comparisons of intraperitoneal instillation of lidocaine versus placebo or other interventions, due to unclear risk of selection bias in two of the three studies, and imprecision of reported estimations (Visalyaputra 1999; Visalyaputra 2002). We downgraded the evidence to very low certainty for adverse effects for all comparisons, because of unclear risk of selection bias in two of the three included studies and imprecision of the data. Another potential source of bias was that one study had no well-defined protocol for assessing adverse effects, which may have impacted the credibility of reported data (Ratanalappaiboon 2012).

### Potential biases in the review process

We conducted a comprehensive search of the grey literature, conference proceedings, key textbooks, citation lists of included studies, and registered databases of ongoing trials, with assistance from the Gynaecology and Fertility Group information specialist. We followed MECIR standards, which are the methodological

requirements for preparing Cochrane Protocols and Reviews (Higgins 2016).

However, we were unable to determine the possibility of reporting bias, or assess heterogeneity, because of the limited numbers of studies for each outcome. One included study was co-authored by YW (Ratanalappaiboon 2012). We minimized the potential bias by inviting PL to assess risk of bias and extract data from this included study. None of the review authors have any links to drug companies or a financial interest in the prescription of the medication under evaluation.

### Agreements and disagreements with other studies or reviews

To our knowledge, this is the first systematic review conducted to assess the effectiveness and adverse effects of local anaesthetic techniques for pain control during PPTL. The evidence we found in our review showed that intraperitoneal instillation of a local anaesthetic agent provided good analgesia without any reported serious adverse effects.

Using a combination of analgesic agents with different mechanisms (multimodal analgesia), can improve pain control through the synergistic effects among the agents used (Elvir-Lazo 2010; Gritsenko 2014). Perioperative pain management with multiple analgesic agents has been shown to offer significantly better analgesia than single agent use (Lee 2013; Rafiq 2014). We did not find that adding an injection of morphine to the intraperitoneal instillation of lidocaine clearly reduced intraperitoneal pain when compared to intraperitoneal instillation of lidocaine alone, but the findings should be interpreted with caution, as the certainty of this evidence is low.

## AUTHORS' CONCLUSIONS

### Implications for practice

Intraperitoneal instillation of lidocaine during PPTL seems to offer better intraperitoneal pain control than a placebo or an injection of morphine, without any reported serious adverse events. The combination of an injection of morphine with intraperitoneal instillation of lidocaine however did not clearly reduce intraperitoneal pain when compared to intraperitoneal instillation of lidocaine alone. These results should be interpreted with caution, since they are based on low to very low certainty evidence.

### Implications for research

Due to insufficient current data, there is a need for adequately sized, high-quality, randomised trials to determine the effects of a combination of intraperitoneal instillation of anaesthetic agents with other local anaesthesia as a multimodal pain management strategy for postpartum women undergoing mini-laparotomy tubal ligation. Further studies should also establish a well-defined protocol for assessing the rate and severity of perioperative adverse events, such as vomiting and hypotension, and the satisfaction of women and their healthcare providers, in order to better understand the potential harms and benefits of these local anaesthetic techniques.

## ACKNOWLEDGEMENTS

We would like to thank Anja Helmerhorst, Helen Nagels, and Makalapua Motu'apuaka for their contributions to the editorial process and clinical advice; Carol Manion and Marian Showell for designing the search strategies and running the search; Dylan Southard for assisting with the English language presentation; and the referees for their useful suggestions and comments during the prepublication editorial process.

# REFERENCES

## References to studies included in this review

**Ratanalappaiboon 2012** *{published data only}*

Rattanalappaiboon D, Werawatakul Y, Tharnprisan P, Prasit M. Intraperitoneal lidocaine for decreasing intra-operative pain during postpartum tubal resection in Srinagarind Hospital. *Journal of the Medical Association of Thailand* 2012;**95**(4):477-81.

**Visalyaputra 1999** *{published data only}*

Visalyaputra S, Lertakyamanee J, Pethpaisit N, Somprakit P, Parakkamodom S, Suwanapeum P. Intraperitoneal lidocaine decreases intraoperative pain during postpartum tubal ligation. *Anesthesia and Analgesia* 1999;**88**(5):1077-80.

**Visalyaputra 2002** *{published data only}*

Visalyaputra S, Pethpaisit N, Ariyanon P, Parakkamodom S, Permpolprasert L, Apidechakul P, et al. EMLA cream and intraperitoneal lidocaine decrease intraoperative pain during postpartum tubal sterilization. *Journal of the Medical Association of Thailand* 2002 Sep;**85**(Suppl 3):S942-7.

## References to studies excluded from this review

**Campbell 2001** *{published data only}*

Campbell DC, Riben CM, Rooney ME, Crone LA, Yip RW. Intrathecal morphine for postpartum tubal ligation postoperative analgesia. *Anesthesia and Analgesia* 2001 Oct;**93**(4):1006-11.

**Grace 2001** *{published data only}*

Grace RF, Lesteour T, Sala T, Stewart J. A randomized comparison of low-dose ketamine and lignocaine infiltration with ketamine-diazepam anaesthesia for post partum tubal ligation in Vanuatu. *Anaesthesia and Intensive Care* 2001;**29**(1):30-3.

**Habib 2005** *{published data only}*

Habib AS, Muir HA, White WD, Spahn TE, Olufolabi AJ, Breen TW. Intrathecal morphine for analgesia after postpartum bilateral tubal ligation. *Anesthesia and Analgesia* 2005 Jan;**100**(1):239-43.

**Huffnagle 2002** *{published data only}*

Huffnagle SL, Norris MC, Huffnagle HJ, Leighton BL, Arkoosh VA. Intrathecal hyperbaric bupivacaine dose response in postpartum tubal ligation patients. *Regional Anesthesia and Pain Medicine* 2002 May-Jun;**27**(3):284-8.

**Marcus 2005** *{published data only}*

Marcus RJ, Wong CA, Lehor A, McCarthy RJ, Yaghmour E, Yilmaz M. Postoperative epidural morphine for postpartum tubal ligation analgesia. *Anesthesia and Analgesia* 2005 Sep;**101**(3):876-81.

**Norris 1996** *{published data only}*

Norris MC, Honet JE, Leighton BL, Arkoosh VA. A comparison of meperidine and lidocaine for spinal anesthesia for postpartum tubal ligation. *Regional Anesthesia and Pain Medicine* 1996 Mar-Apr;**21**(2):84-8.

**Panni 2010** *{published data only}*

Panni MK, George RB, Allen TK, Olufolabi AJ, Schultz JR, Okumura M, et al. Minimum effective dose of spinal ropivacaine with and without fentanyl for postpartum tubal ligation. *International Journal of Obstetric Anesthesia* 2010 Oct;**19**(4):390-4.

**Rorarius 1999** *{published data only}*

Rorarius M, Suominen P, Baer G, Pajunen P, Tuimala R, Laippala P. Peripherally administered sufentanil inhibits pain perception after postpartum tubal ligation. *Pain* 1999 Jan;**79**(1):83-8.

**Toledo 2009** *{published data only}*

Toledo P, McCarthy RJ, Ebarvia MJ, Huser CJ, Wong CA. The interaction between epidural 2-chloroprocaine and morphine: a randomized controlled trial of the effect of drug administration timing on the efficacy of morphine analgesia. *Anesthesia and Analgesia* 2009 Jul;**109**(1):168-73.

## Additional references

**Aaronson 2014**

Aaronson J, Goodman S. Obstetric anesthesia: not just for cesareans and labor. *Seminars in Perinatology* 2014;**38**(6):378-85.

**Bainbridge 2012**

Bainbridge D, Martin J, Arango M, Cheng D, Evidence-based Peri-operative Clinical Outcomes Research (EPiCOR) Group. Perioperative and anaesthetic-related mortality in developed and developing countries: a systematic review and meta-analysis. *Lancet* 2012;**380**(9847):1075-81.

**Benhamou 1994**

Benhamou D, Narchi P, Mazoit JX, Fernandez H. Postoperative pain after local anesthetics for laparoscopic sterilization. *Obstetrics Gynecology* 1994;**84**(5):877-80.

**Campiglia 2010**

Campiglia L, Consales G, De Gaudio AR. Pre-emptive analgesia for postoperative pain control: a review. *Clinical Drug Investigation* 2010;**30 Suppl 2**:15-26.

**Chi 1992**

Chi IC, Gates D, Thapa S. Performing tubal sterilizations during women's postpartum hospitalization: a review of the United States and international experiences. *Obstetrical and Gynecological Survey* 1992 Feb;**47**(2):71-9.

**Day 2013**

Day RO, Graham GG. Non-steroidal anti-inflammatory drugs (NSAIDs). *BMJ* 2013;**346**:f3195.

**DerSimonian 1986**

DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clinical Trials* 1986;**7**(3):177–88.

**Elvir-Lazo 2010**

Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. *Current Opinion in Anesthesiology* 2010 Dec;**23**(6):697-703.

**GRADEpro GDT 2015 [Computer program]**

McMaster University (developed by Evidence Prime). GRADEpro GDT. Version accessed 30 November 2017. Hamilton (ON): McMaster University (developed by Evidence Prime), 2015.

**Gritsenko 2014**

Gritsenko K, Khelemsky Y, Kaye AD, Vadivelu N, Urman RD. Multimodal therapy in perioperative analgesia. *Best Practice and Research Clinical Anaesthesiology* 2014 Mar;**28**(1):59-79.

**Higgins 2011**

Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

**Higgins 2016**

Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. Methodological Expectations of Cochrane Intervention Reviews. Cochrane: London, Version 1.02 2016.

**Lee 2013**

Lee SK, Lee JW, Choy WS. Is multimodal analgesia as effective as postoperative patient-controlled analgesia following upper extremity surgery?. *Orthopaedics and Traumatology: Surgery and Research* 2013 Dec;**99**(8):895-901.

**Putland 1999**

Putland AJ, McCluskey A. The analgesic efficacy of tramadol versus ketorolac in day-case laparoscopic sterilisation. *Anaesthesia* 1999;**54**(4):382-5.

**Rafiq 2014**

Rafiq S, Steinbrüchel DA, Wanscher MJ, Andersen LW, Navne A, Lilleoer NB, et al. Multimodal analgesia versus traditional opiate based analgesia after cardiac surgery, a randomized controlled trial. *Journal of Cardiothoracic Surgery* 2014;**9**:52.

**Ratanalappaiboon 2017 [pers comm]**

Ratanalappaiboon D (Khon Kaen University, Khon Kaen, Thailand). [personal communication]. Conversation with: Sothornwit J (Khon Kaen University, Khon Kaen, Thailand) 2 December 2017.

**Review Manager 2014 [Computer program]**

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5. Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

**Schünemann 2011**

Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

**Sterne 2011**

Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;**343**:d4002.

**Tetzlaff 2000**

Tetzlaff JE. The pharmacology of local anesthetics. *Anesthesiology Clinics of North America* 2000;**18**(2):217-33.

**Trescot 2008**

Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. *Pain Physician* 2008;**11**:133-53.

**UN 2013**

United Nations (UN), Department of Economic and Social Affairs, Population Division. World Contraceptive Patterns 2013. www.un.org/en/development/desa/population/publications/pdf/family/worldContraceptivePatternsWallChart2013.pdf (accessed January 2018).

## CHARACTERISTICS OF STUDIES

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

**Ratanalappaiboon 2012**

| | |
|---|---|
| Methods | A randomised double-blinded controlled trial conducted in Khon Kaen, Thailand.<br><br>Both women and outcome assessor were blinded in this study. Duration of enrolment was not mentioned. |
| Participants | Included 60 women with ASA physical status I who had no contraindication for surgery and agreed to undergo postpartum tubal sterilisation.<br><br>Excluded women who had a history of pelvic inflammatory disease, asthma, liver disease, allergy to lidocaine, or body mass index > 32 kg/m$^2$. |

**Ratanalappaiboon 2012** *(Continued)*

| | |
|---|---|
| Interventions | Women were assigned to three groups: 20 mL of isotonic normal saline (NSS) versus 20 mL NSS containing 100 mg lidocaine versus 20 mL NSS containing 200 mg lidocaine |
| Outcomes | Pain scores using verbal numerical rating scale |
| Notes | Power and type I error for sample size calculation were not provided in this study. Tubal ligation could be performed in all women, with three women requiring additional meperidine administration for severe pain. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Randomisation was performed by drawing lots. |
| Allocation concealment (selection bias) | Low risk | Sealed envelopes were used for allocation concealment. |
| Blinding of participants and personnel (performance bias)<br>All outcomes | Low risk | Double-blinded (this information provided by the study author (Ratanalappaiboon 2017 [pers comm]) |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Double-blinded (this information provided by the study author (Ratanalappaiboon 2017 [pers comm]) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All outcomes were assessed during the operation. |
| Selective reporting (reporting bias) | Unclear risk | Little information regarding perioperative adverse effects reported. |
| Other bias | High risk | The study had no well-defined protocol for assessing perioperative adverse effects. |

**Visalyaputra 1999**

| | |
|---|---|
| Methods | A randomised controlled trial conducted in a large hospital in Bangkok, Thailand.<br>Method of randomisation was not reported. Duration of enrolment was not mentioned. |
| Participants | Included 80 women with ASA physical status I or II who agreed to undergo postpartum tubal ligation under local anaesthesia.<br><br>Excluded women who had a history of pelvic inflammatory disease, asthma, liver disease, allergy to local anaesthetics, or body mass index > 32 kg/m$^2$. |
| Interventions | Group M: intramuscular (IM) injection of morphine 10 mg 1 hour before surgery and intraperitoneal instillation of 80 mL isotonic sodium chloride solution during surgery<br><br>Group L: isotonic sodium chloride solution IM and intraperitoneal instillation of 80 mL 0.5% lidocaine<br><br>Group ML: IM injection of morphine 10 mg IM 1 hour before surgery and intraoperative intraperitoneal instillation of 80 mL 0.5% lidocaine |

**Visalyaputra 1999** *(Continued)*

| | |
|---|---|
| | Group P (placebo): isotonic sodium chloride solution IM and intraperitoneal instillation of 80 mL isotonic sodium chloride solution during surgery |
| Outcomes | Pain scores using verbal numerical rating scale |
| Notes | Surgery was not conducted in three women. Two women in Group P and one in Group L required general anaesthesia with endotracheal intubation. |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Mentioned randomisation but no description was reported |
| Allocation concealment (selection bias) | Unclear risk | Method of allocation concealment not mentioned |
| Blinding of participants and personnel (performance bias)<br>All outcomes | Low risk | Both women and physician were blinded to intervention allocated |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Outcome assessors were blinded to intervention given |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All outcomes were assessed during the operation. |
| Selective reporting (reporting bias) | Low risk | All potentially relevant outcomes were reported |
| Other bias | Low risk | All subjects were analysed in the group to which they were randomised. In addition, the study had a well-defined protocol for assessing perioperative adverse effects |

**Visalyaputra 2002**

| | |
|---|---|
| Methods | A randomised controlled trial conducted in a large hospital in Bangkok, Thailand.<br>Method of randomisation was not reported. Duration of enrolment was not mentioned. |
| Participants | Included 90 women with ASA physical status I or II who agreed to undergo postpartum tubal ligation under local anaesthesia<br><br>Excluded women who had history of pelvic inflammatory disease, liver disease, allergy to local anaesthetics, or body mass index > 32 kg/$m^2$ |
| Interventions | Women were randomly assigned to have EMLA cream or placebo cream applied to the skin two hours before they entered the operating room. After the peritoneal cavity was approached, women were assigned to three groups receiving 20 mL intraperitoneal instillation of 1% lidocaine, 2% lidocaine, and normal saline (NS). |
| Outcomes | Pain scores using verbal numerical rating scale were assessed during forceps check. If the NRS score was ≥ 3, the women received 10 mL of 1% lidocaine infiltrated into the skin and subcutaneous tissue. |

**Visalyaputra 2002** *(Continued)*

| | |
|---|---|
| | When the peritoneal cavity was approached, and the lidocaine or NS was instilled into the intra-abdominal cavity, NRS pain scores were assessed again |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | There were no details regarding random sequence generation applied in this study. |
| Allocation concealment (selection bias) | Unclear risk | The authors did not mention the method applied for allocation concealment |
| Blinding of participants and personnel (performance bias)<br>All outcomes | Low risk | Both women and physician were blinded |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | The authors blinded outcome assessors to intervention assigned. |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | All outcomes were assessed during the operation. |
| Selective reporting (reporting bias) | Low risk | All potentially relevant outcomes were reported. |
| Other bias | Low risk | All women were analysed in the group to which they were randomised. In addition, the study had a well-defined protocol for assessing perioperative adverse effects. |

The American Society of Anesthesiologists (ASA) physical status classification system is a system for assessing the fitness of patients before surgery which is based upon the patient's physical health status. Normal healthy patients and those who have mild systematic disease are classified as ASA physical status I and II, respectively.

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Campbell 2001 | Wrong intervention |
| Grace 2001 | Wrong intervention |
| Habib 2005 | Wrong intervention |
| Huffnagle 2002 | Wrong intervention |
| Marcus 2005 | Wrong intervention |
| Norris 1996 | Wrong intervention |
| Panni 2010 | Wrong intervention |

| Study | Reason for exclusion |
|---|---|
| Rorarius 1999 | The study focused on postoperative pain |
| Toledo 2009 | Wrong intervention |

## DATA AND ANALYSES

### Comparison 1. EMLA cream versus placebo cream for pain associated with abdominal entry

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Pain during forceps check | 1 | 90 | Mean Difference (IV, Fixed, 95% CI) | -3.18 [-4.10, -2.26] |
| 2 Number of women requiring lidocaine instillation for rescue medication | 1 | 90 | Risk Ratio (IV, Fixed, 95% CI) | 0.36 [0.25, 0.53] |

### Analysis 1.1. Comparison 1 EMLA cream versus placebo cream for pain associated with abdominal entry, Outcome 1 Pain during forceps check.

| Study or subgroup | EMLA cream N | EMLA cream Mean(SD) | Placebo cream N | Placebo cream Mean(SD) | Mean Difference Fixed, 95% CI | Weight | Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Visalyaputra 2002 | 45 | 1.5 (1.9) | 45 | 4.6 (2.5) | | 100% | -3.18[-4.1,-2.26] |
| **Total ***** | **45** | | **45** | | | **100%** | **-3.18[-4.1,-2.26]** |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z=6.79(P<0.0001) | | | | | | | |




### Analysis 1.2. Comparison 1 EMLA cream versus placebo cream for pain associated with abdominal entry, Outcome 2 Number of women requiring lidocaine instillation for rescue medication.

| Study or subgroup | EMLA cream n/N | Placebo cream n/N | Risk Ratio IV, Fixed, 95% CI | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|
| Visalyaputra 2002 | 16/45 | 45/45 | | 100% | 0.36[0.25,0.53] |
| **Total (95% CI)** | **45** | **45** | | **100%** | **0.36[0.25,0.53]** |
| Total events: 16 (EMLA cream), 45 (Placebo cream) | | | | | |
| Heterogeneity: Not applicable | | | | | |
| Test for overall effect: Z=5.13(P<0.0001) | | | | | |

## Comparison 2. Lidocaine instillation versus placebo for intraperitoneal pain

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Intraperitoneal pain | 3 | 190 | Mean Difference (IV, Fixed, 95% CI) | -3.34 [-4.19, -2.49] |
| 2 Adverse events | 2 | 150 | Risk Ratio (IV, Fixed, 95% CI) | 1.04 [0.40, 2.69] |
| 3 Number of women requiring rescue medication | 3 | 190 | Risk Ratio (IV, Fixed, 95% CI) | 0.27 [0.17, 0.44] |

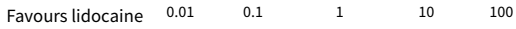
### Analysis 2.1. Comparison 2 Lidocaine instillation versus placebo for intraperitoneal pain, Outcome 1 Intraperitoneal pain.

| Study or subgroup | Lidocaine N | Lidocaine Mean(SD) | Placebo N | Placebo Mean(SD) | Mean Difference Fixed, 95% CI | Weight | Mean Difference Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Ratanalappaiboon 2012 | 40 | 3.5 (3.6) | 20 | 6.6 (3.3) | | 21.92% | -3.1[-4.91,-1.29] |
| Visalyaputra 1999 | 20 | 1.2 (2.2) | 20 | 5.5 (2.9) | | 28.28% | -4.3[-5.9,-2.7] |
| Visalyaputra 2002 | 60 | 2.3 (2.1) | 30 | 5.2 (3) | | 49.79% | -2.9[-4.1,-1.7] |
| **Total ***** | **120** | | **70** | | | **100%** | **-3.34[-4.19,-2.49]** |
| Heterogeneity: Tau²=0; Chi²=1.97, df=2(P=0.37); I²=0% | | | | | | | |
| Test for overall effect: Z=7.72(P<0.0001) | | | | | | | |



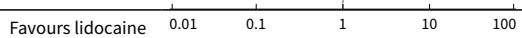

### Analysis 2.2. Comparison 2 Lidocaine instillation versus placebo for intraperitoneal pain, Outcome 2 Adverse events.

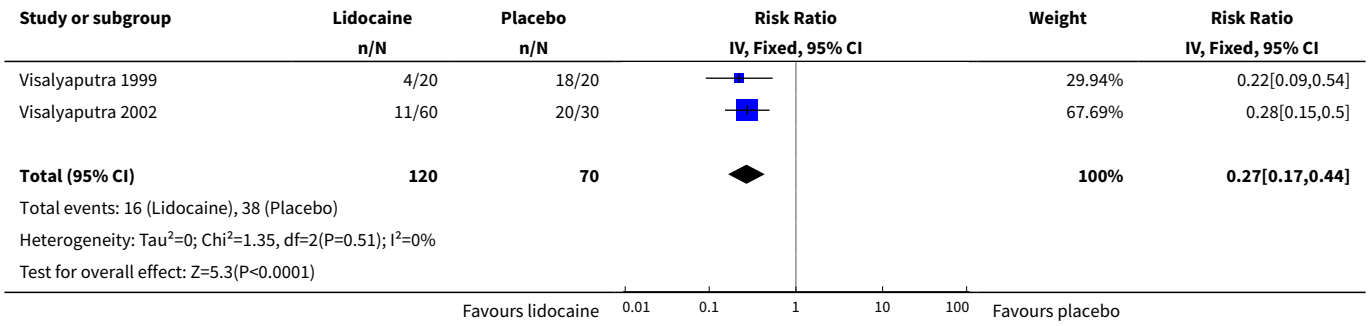
| Study or subgroup | Lidocaine n/N | Placebo n/N | Risk Ratio IV, Fixed, 95% CI | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|
| Ratanalappaiboon 2012 | 3/40 | 0/20 | | 10.55% | 3.59[0.19,66.22] |
| Visalyaputra 2002 | 9/60 | 5/30 | | 89.45% | 0.9[0.33,2.45] |
| **Total (95% CI)** | **100** | **50** | | **100%** | **1.04[0.4,2.69]** |
| Total events: 12 (Lidocaine), 5 (Placebo) | | | | | |
| Heterogeneity: Tau²=0; Chi²=0.77, df=1(P=0.38); I²=0% | | | | | |
| Test for overall effect: Z=0.08(P=0.93) | | | | | |




### Analysis 2.3. Comparison 2 Lidocaine instillation versus placebo for intraperitoneal pain, Outcome 3 Number of women requiring rescue medication.

| Study or subgroup | Lidocaine n/N | Placebo n/N | Risk Ratio IV, Fixed, 95% CI | Weight | Risk Ratio IV, Fixed, 95% CI |
|---|---|---|---|---|---|
| Ratanalappaiboon 2012 | 1/40 | 0/20 | | 2.37% | 1.54[0.07,36.11] |

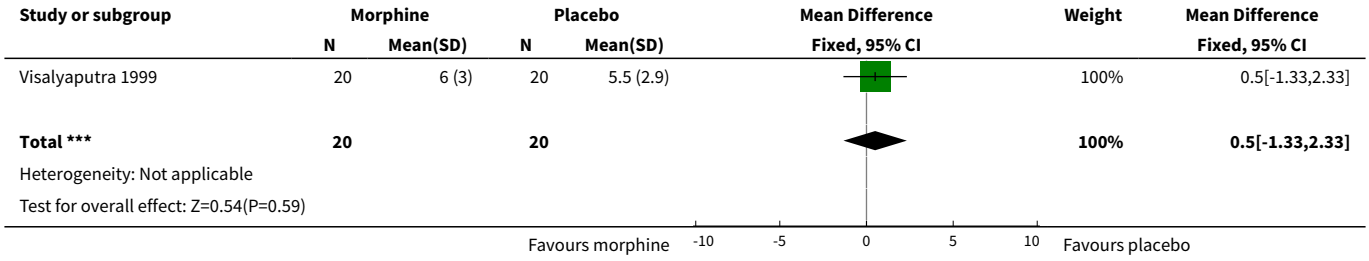




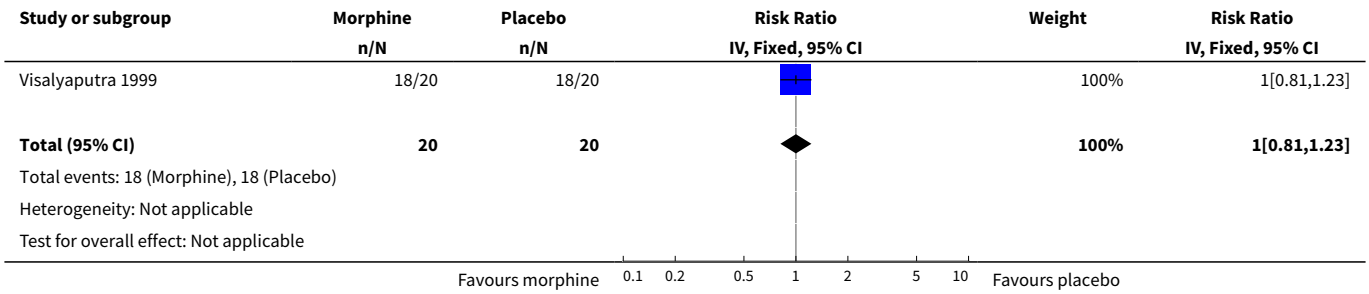

## Comparison 3. IM morphine versus placebo for intraperitoneal pain

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Intraperitoneal pain | 1 | 40 | Mean Difference (IV, Fixed, 95% CI) | 0.5 [-1.33, 2.33] |
| 2 Number of women requiring rescue medication | 1 | 40 | Risk Ratio (IV, Fixed, 95% CI) | 1.0 [0.81, 1.23] |

### Analysis 3.1. Comparison 3 IM morphine versus placebo for intraperitoneal pain, Outcome 1 Intraperitoneal pain.



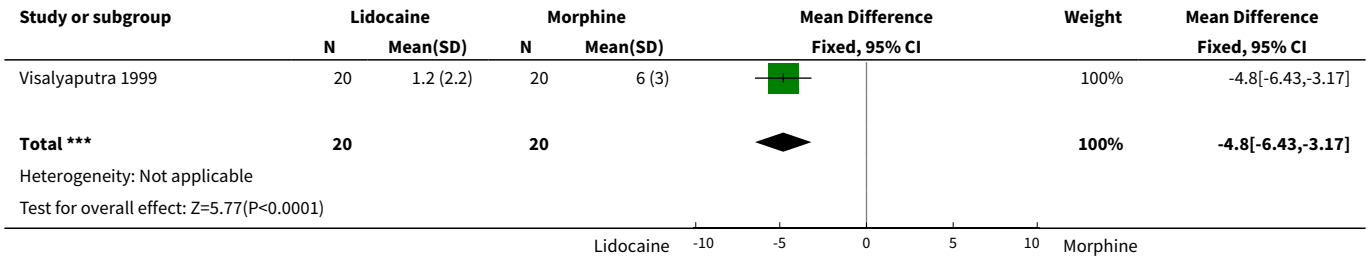

### Analysis 3.2. Comparison 3 IM morphine versus placebo for intraperitoneal pain, Outcome 2 Number of women requiring rescue medication.



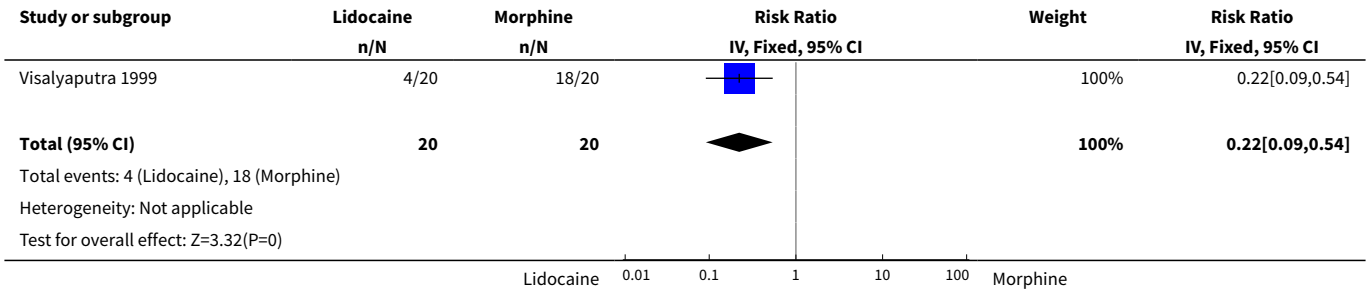
**Comparison 4. Lidocaine instillation versus IM morphine for intraperitoneal pain**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Intraperitoneal pain | 1 | 40 | Mean Difference (IV, Fixed, 95% CI) | -4.8 [-6.43, -3.17] |
| 2 Number of women requiring rescue medication | 1 | 40 | Risk Ratio (IV, Fixed, 95% CI) | 0.22 [0.09, 0.54] |

**Analysis 4.1. Comparison 4 Lidocaine instillation versus IM morphine for intraperitoneal pain, Outcome 1 Intraperitoneal pain.**



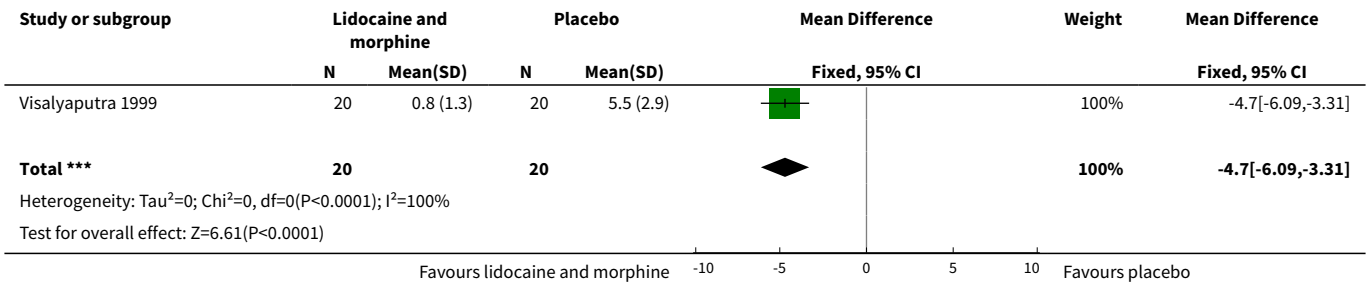

**Analysis 4.2. Comparison 4 Lidocaine instillation versus IM morphine for intraperitoneal pain, Outcome 2 Number of women requiring rescue medication.**



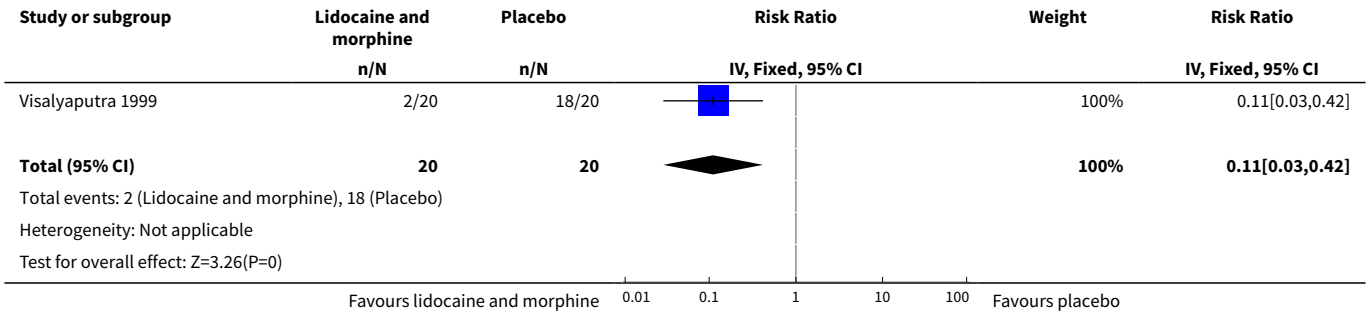

**Comparison 5. Lidocaine instillation plus IM morphine versus placebo for intraperitoneal pain**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Intraperitoneal pain | 1 | 40 | Mean Difference (IV, Fixed, 95% CI) | -4.70 [-6.09, -3.31] |
| 2 Number of women requiring rescue medication | 1 | 40 | Risk Ratio (IV, Fixed, 95% CI) | 0.11 [0.03, 0.42] |

### Analysis 5.1. Comparison 5 Lidocaine instillation plus IM morphine versus placebo for intraperitoneal pain, Outcome 1 Intraperitoneal pain.



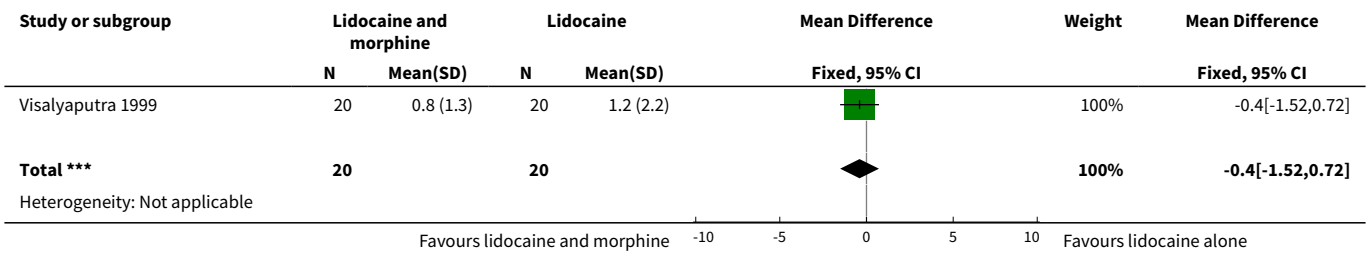

### Analysis 5.2. Comparison 5 Lidocaine instillation plus IM morphine versus placebo for intraperitoneal pain, Outcome 2 Number of women requiring rescue medication.

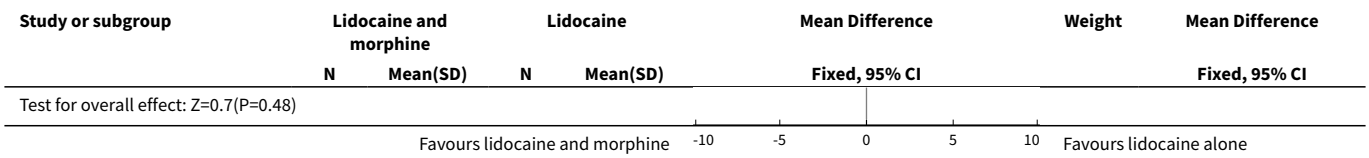



## Comparison 6. Lidocaine instillation plus IM morphine versus lidocaine instillation alone for intraperitoneal pain

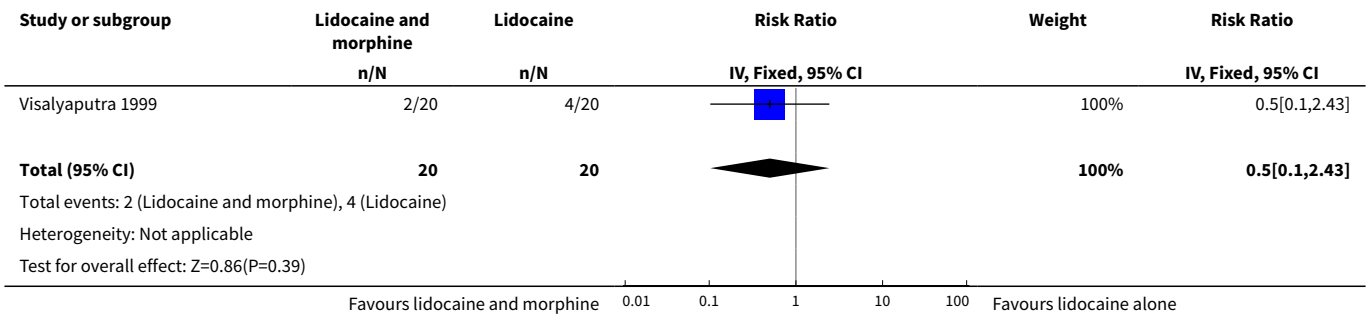
| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Intraperitoneal pain | 1 | 40 | Mean Difference (IV, Fixed, 95% CI) | -0.40 [-1.52, 0.72] |
| 2 Number of women requiring rescue medication | 1 | 40 | Risk Ratio (IV, Fixed, 95% CI) | 0.5 [0.10, 2.43] |

### Analysis 6.1. Comparison 6 Lidocaine instillation plus IM morphine versus lidocaine instillation alone for intraperitoneal pain, Outcome 1 Intraperitoneal pain.





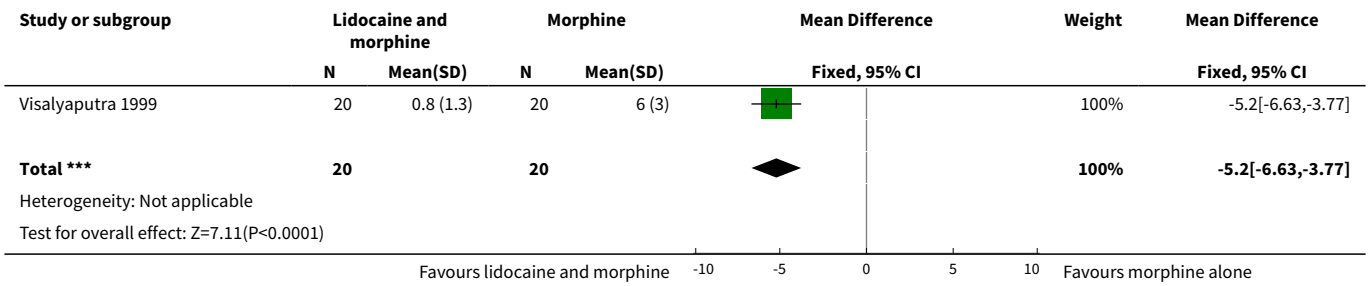

**Analysis 6.2. Comparison 6 Lidocaine instillation plus IM morphine versus lidocaine instillation alone for intraperitoneal pain, Outcome 2 Number of women requiring rescue medication.**



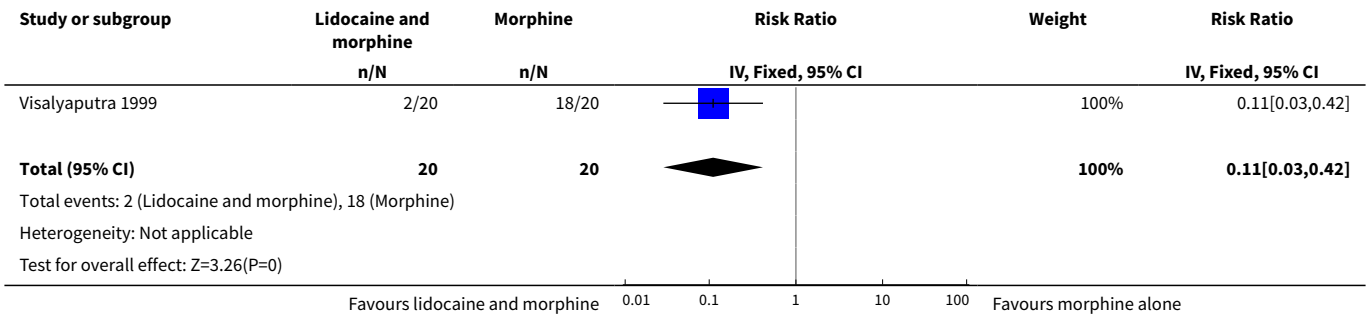

## Comparison 7. Lidocaine instillation plus IM morphine versus IM morphine alone for intraperitoneal pain

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Intraperitoneal pain | 1 | 40 | Mean Difference (IV, Fixed, 95% CI) | -5.2 [-6.63, -3.77] |
| 2 Number of women requiring rescue medication | 1 | 40 | Risk Ratio (IV, Fixed, 95% CI) | 0.11 [0.03, 0.42] |

**Analysis 7.1. Comparison 7 Lidocaine instillation plus IM morphine versus IM morphine alone for intraperitoneal pain, Outcome 1 Intraperitoneal pain.**



**Analysis 7.2. Comparison 7 Lidocaine instillation plus IM morphine versus IM morphine alone for intraperitoneal pain, Outcome 2 Number of women requiring rescue medication.**




## ADDITIONAL TABLES

**Table 1. Number (%) of women undergoing postpartum mini-laparotomy tubal ligation who required regional or general anaesthesia, stratified by comparisons**

| | | |
|---|---|---|
| **Comparision I**<br>Lidocaine instillation versus placebo | Lidocaine group (N = 120) | Placebo group (N = 70) |
| Required regional or general anaesthesia | 1 (0.83) | 22 (31.43) |
| **Comparison II**<br>An intramuscular injection of morphine versus placebo | Morphine group (N = 20) | Placebo group (N = 20) |
| Required regional or general anaesthesia | 0 (0) | 2 (10.0) |
| **Comparison III**<br>Intraperitoneal instillation of lidocaine with IM morphine | Lidocaine group (N = 20) | Morphine group (N = 20) |
| Required regional or general anaesthesia | 0 (0) | 4 (20.0) |
| **Comparison IV**<br>Intraperitoneal instillation of lidocaine combined with an injection of morphine versus placebo | Lidocaine plus morphine group (N = 20) | Placebo group (N = 20) |
| Required regional or general anaesthesia | 0 (0) | 2 (10.0) |
| **Comparison V**<br>Intraperitoneal instillation of lidocaine combined with an injection of morphine versus intraperitoneal instillation of lidocaine alone | Lidocaine plus morphine group (N = 20) | Lidocaine alone group (N = 20) |
| Required regional or general anaesthesia | 0 (0) | 1 (5.0) |
| **Comparison VI**<br>Intraperitoneal instillation of lidocaine combined with an injection of morphine versus an injection of morphine alone | Lidocaine plus morphine group (N = 20) | Morphine alone group (N = 20) |

**Table 1. Number (%) of women undergoing postpartum mini-laparotomy tubal ligation who required regional or general anaesthesia, stratified by comparisons** *(Continued)*

| | | |
|---|---|---|
| Required regional or general anaesthesia | 0 (0) | 0 (0) |

Data are present as number of women (percentage)

## APPENDICES

### Appendix 1. Abbreviations

EMLA: trade name for lidocaine and prilocaine cream

FPSR: Faces Pain Scale-Revised

IM: intramuscular

IV: intravenous

NRS: numerical rating scale

NSAIDS: non-steroidal anti-inflammatory drugs

PPTL: postpartum mini-laparotomy tubal ligation

VAS: visual analogue scale

### Appendix 2. Glossary

| **Glossary** | |
|---|---|
| Anaesthesia | Relief of pain by loss of sensation |
| **Fallopian tubes** | Tubes through which an egg travels from the ovary to the uterus |
| **General** anaesthesia | The use of drugs that produce a sleep-like state to prevent pain during surgery |
| **Intraperitoneal instillation** | The process of administering a medicinal solution into the abdominal cavity |
| **Local** anaesthesia | The use of drugs that prevent pain in a part of the body |
| **Mini-laparotomy** | A small abdominal incision used for a sterilization procedure, in which the fallopian tubes are closed off |
| **Regional** anaesthesia | The use of drugs to block sensation in certain areas of the body |

### Appendix 3. CENTRAL register of Stuides Online (CRSO) search strategy

Searched 31 July 2017

Web platform

#1 MESH DESCRIPTOR Sterilization, Tubal EXPLODE ALL TREES 206

#2 (tub* adj2 sterili*):TI,AB,KY 95

#3 (tub* adj2 ligation*):TI,AB,KY 188

#4 (tub* adj2 resect*):TI,AB,KY 19

#5 (laparotom* adj5 sterili*):TI,AB,KY 8

#6 #1 OR #2 OR #3 OR #4 OR #5 376

#7 MESH DESCRIPTOR Postpartum Period EXPLODE ALL TREES 1232

#8 postpartum:TI,AB,KY 4571

#9 puerperi*:TI,AB,KY 773

#10 pain*:TI,AB,KY 98928

#11 analgesi*:TI,AB,KY 37878

#12 an?esthe*:TI,AB,KY 50901

#13 #7 OR #8 OR #9 OR #10 OR #11 OR #12 140875

#14 #6 AND #13 241

## Appendix 4. MEDLINE Ovid search strategy

Searched from 1946 to 31 July 2017

1 exp Sterilization, Tubal/ (4319)
2 (tub* adj2 sterili*).tw. (1985)
3 (tub* adj2 ligation*).tw. (2085)
4 (tub* adj2 excis*).tw. (197)
5 (tub* adj2 resect*).tw. (823)
6 (laparotom* adj5 sterili*).tw. (96)
7 or/1-6 (7223)
8 Postpartum Period/ or postpartum.tw. (56208)
9 puerperi*.tw. (5916)
10 pain*.tw. (590080)
11 analgesi*.tw. (108282)
12 an?esthe*.tw. (344555)
13 or/8-12 (996662)
14 7 and 13 (1591)
15 randomized controlled trial.pt. (470446)
16 controlled clinical trial.pt. (94472)
17 randomized.ab. (412793)
18 randomised.ab. (80959)
19 placebo.tw. (196985)
20 clinical trials as topic.sh. (187621)
21 randomly.ab. (286033)
22 trial.ti. (185390)
23 (crossover or cross-over or cross over).tw. (76340)
24 or/15-23 (1210406)
25 exp animals/ not humans.sh. (4445445)
26 24 not 25 (1116409)
27 14 and 26 (238)

## Appendix 5. Embase Ovid search strategy

Searched from 1980 to 31 July 2017

1 exp uterine tube sterilization/ (8025)
2 (tub* adj2 sterili?*).tw. (1926)
3 (tub* adj2 ligation).tw. (2110)
4 (tub* adj2 resect*).tw. (521)
5 (laparotomy adj5 sterili*).tw. (64)
6 or/1-5 (9833)
7 exp puerperium/ or postpartum.tw. (86204)

8 puerperi*.tw. (5486)
9 pain*.tw. (795262)
10 analgesi*.tw. (141390)
11 an?esthe*.tw. (406092)
12 or/7-11 (1281395)
13 6 and 12 (2118)
14 Clinical Trial/ (934406)
15 Randomized Controlled Trial/ (461605)
16 exp randomization/ (74957)
17 Single Blind Procedure/ (28656)
18 Double Blind Procedure/ (138538)
19 Crossover Procedure/ (52576)
20 Placebo/ (297062)
21 Randomi?ed controlled trial$.tw. (164014)
22 Rct.tw. (25050)
23 random allocation.tw. (1666)
24 randomly.tw. (354965)
25 randomly allocated.tw. (27912)
26 allocated randomly.tw. (2254)
27 (allocated adj2 random).tw. (781)
28 Single blind$.tw. (19520)
29 Double blind$.tw. (173719)
30 ((treble or triple) adj blind$).tw. (700)
31 placebo$.tw. (252974)
32 prospective study/ (392963)
33 or/14-32 (1976552)
34 case study/ (48774)
35 case report.tw. (334348)
36 abstract report/ or letter/ (1004831)
37 or/34-36 (1379919)
38 33 not 37 (1930713)
39 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.) (5811574)
40 38 not 39 (1797896)
41 13 and 40 (311)

## Appendix 6. PsycINFO Ovid search strategy

Searched from 1806 to 31 July 2017

1 exp Tubal Ligation/ (69)
2 (tub* adj2 sterili*).tw. (35)
3 (tub* adj2 ligation).tw. (78)
4 (tub* adj2 resect*).tw. (5)
5 (laparotom* adj5 sterili*).tw. (1)
6 or/1-5 (130)
7 postpartum.tw. (10093)
8 puerperi*.tw. (334)
9 pain*.tw. (98748)
10 analgesi*.tw. (13546)
11 an?esthe*.tw. (14761)
12 or/7-11 (125509)
13 6 and 12 (20)

## Appendix 7. CINAHL EBSCO search strategy

Searched from 1961 to 31 July 2017

| # | Query | Results |
|---|---|---|
| S27 | S14 AND S26 | 141 |

*(Continued)*

| | | |
|---|---|---|
| S26 | S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 | 1,150,085 |
| S25 | TX allocat* random* | 7,046 |
| S24 | (MH "Quantitative Studies") | 16,124 |
| S23 | (MH "Placebos") | 10,252 |
| S22 | TX placebo* | 46,769 |
| S21 | TX random* allocat* | 7,046 |
| S20 | (MH "Random Assignment") | 43,570 |
| S19 | TX randomi* control* trial* | 128,784 |
| S18 | TX ( (singl* n1 blind*) or (singl* n1 mask*) ) or TX ( (doubl* n1 blind*) or (doubl* n1 mask*) ) or TX ( (tripl* n1 blind*) or (tripl* n1 mask*) ) or TX ( (trebl* n1 blind*) or (trebl* n1 mask*) ) | 899,162 |
| S17 | TX clinic* n1 trial* | 209,068 |
| S16 | PT Clinical trial | 80,032 |
| S15 | (MH "Clinical Trials+") | 218,190 |
| S14 | S6 AND S13 | 601 |
| S13 | S7 OR S8 OR S9 OR S10 OR S11 OR S12 | 2,526,796 |
| S12 | TX an?esthe* | 2,434,221 |
| S11 | TX analgesi* | 42,154 |
| S10 | TX pain* | 258,139 |
| S9 | TX puerperi* | 1,054 |
| S8 | TX postpartum | 16,911 |
| S7 | (MM "Puerperium") OR (MM "Surgery, Obstetrical") | 621 |
| S6 | S1 OR S2 OR S3 OR S4 OR S5 | 943 |
| S5 | TX laparotom* N5 sterili* | 4 |
| S4 | TX tub* N2 resect* | 42 |
| S3 | TX tub* N2 ligation* | 306 |
| S2 | TX tub* N2 sterili* | 745 |
| S1 | (MM "Sterilization, Tubal") | 441 |

## Appendix 8. Search strategy prior to 2015

**PubMed**

((sterilization OR tubal ligation OR tubal resection) AND minilaparotomy AND pain), (sterilization OR tubal ligation OR tubal resection) AND postpartum AND pain

**CENTRAL**

Title, Abstract, Keywords: (sterilization OR tubal ligation OR tubal resection) AND minilaparotomy AND pain
AND Title, Abstract, Keywords: (sterilization OR tubal ligation OR tubal resection) AND postpartum AND pain

**POPLINE**

All fields: "female sterilization" OR "tubal ligation" OR "tubal resection"
Keyword: minilaparotomy
AND Keyword: pain

**EMBASE** (Elsevier)

(sterilization OR tubal ligation OR tubal resection) AND minilaparotomy AND postpartum AND pain

**Scopus**

(sterilization OR tubal ligation OR tubal resection) AND postpartum AND pain

**CINAHL Plus with Full Text**

(sterilization OR tubal ligation OR tubal resection) AND postpartum AND pain

**ClinicalTrials.gov**
Intervention: NOT (hysteroscop* OR laparoscop*)
Title acronym/Title: (sterilization OR tubal ligation OR tubal resection) AND pain

**ICTRP**

Title: pain
Intervention: (sterilization OR tubal ligation OR tubal resection)

## CONTRIBUTIONS OF AUTHORS

YW initiated the review topic, reviewed and approved the final version of the review

JS drafted the review, reviewed and approved the final version of the review

ML drafted the review, reviewed and approved the final version of the review

PL initiated the review topic, drafted the review, reviewed and approved the final version of the review

CK drafted the review, reviewed and approved the final version of the review

## DECLARATIONS OF INTEREST

YW: none known

JS: none known

ML: none known

PL: none known

CK: none known

## SOURCES OF SUPPORT

### Internal sources

- Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Thailand.

- Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Thailand.
- Cochrane Thailand, Thailand.

### External sources

- Thailand Research Fund (Distinguished Professor Award), Thailand.
- Long-term Institutional Development HUBs (LID-HUBs), the Human Reproduction Programme (HRP) Alliance for Research Capacity Strenghtening, Department of Reproductive Health and Research, World Health Organization, Switzerland.

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

### Authors

Chumnan Kietpeerakool joined the review team.

### Objectives

We added adverse effects as one of the objectives that this review aimed to evaluate.

### Searching other resources

In the review, we added Greynet.org (www.greynet.org), WorldCat Dissertations and Theses (www.worldcat.org/title/worldcat-dissertations-and-theses/oclc), and Index to Theses (ProQuest Dissertations & Theses: UK & Ireland) as sources for identifying potentially relevant conference abstracts and proceedings.

### Data extraction and management

We added the details of data extracted from each included study under this section.

### Measures of treatment effect

In the protocol, we stated that we intended to use the standardized mean difference to combine trials that measure the same outcome but use different methods (Higgins 2011). However, we did not follow this methodology, as all included studies applied the same method for evaluating pain.

### Dealing with missing data

In the protocol, we had planned to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect using a sensitivity analysis. However, we did not follow this methodology as none of the included studies had missing data. In future updates, we will use a sensitivity analysis to assess the impact of high level of missing data on the pooled results, if feasible.

### Assessment of reporting biases

As there were only three trials that met our inclusion criteria, we were unable to construct funnel plots to determine the possibility of publication bias, as previously stated in the review protocol. In a future update of this review, we will examine the funnel plots corresponding to meta-analysis of the primary outcome to assess the potential for small study effects, such as publication bias, if we are able to identify more than 10 studies. We plan to assess funnel plot asymmetry visually (Sterne 2011).

### Main outcomes for 'Summary of findings' table for assessing the certainty of the evidence

We added the details of preparing 'Summary of findings' table and assessing the certainty of the evidence

### Subgroup analysis and investigation of heterogeneity

We performed no subgroup analysis, as only three RCTs, which assessed a total of only 230 patients, met the inclusion criteria. However, we considered types of intervention and volume of anaesthetic agent in the interpretation of findings. In future updates, we will perform subgroup analysis according to these factors, if feasible.

### Sensitivity analysis

We performed no sensitivity analysis, as few trials met our inclusion criteria. In future updates, if statistical heterogeneity is detected and there is a sufficient number of included studies, we will conduct a sensitivity analysis for the primary outcome to determine the possible contribution of other clinical or methodological differences across the included studies (i.e. high or unclear risk of bias for allocation concealment or publication status).

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Laparotomy; Analgesics, Opioid [administration & dosage] [*therapeutic use]; Anesthetics, Local [administration & dosage] [*therapeutic use]; Infusions, Parenteral; Injections, Intramuscular; Intraoperative Care [methods]; Lidocaine [administration & dosage] [*therapeutic use]; Lidocaine, Prilocaine Drug Combination [administration & dosage] [therapeutic use]; Morphine [administration & dosage] [*therapeutic use]; Pain, Procedural [*therapy]; Placebos [administration & dosage] [therapeutic use]; Randomized Controlled Trials as Topic; Salvage Therapy [statistics & numerical data]; Sterilization, Tubal [*adverse effects] [methods]

### MeSH check words

Female; Humans