Efficacy and safety of paravertebral blocks in breast surgery: a meta-analysis of randomized controlled trials
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CRD summary
This review concluded that paravertebral blocks (alone or in combination with general anaesthetic) provided better postoperative pain control with few adverse effects compared with other analgesic treatment strategies in women undergoing breast surgery, although the results were limited by the diversity of surgical procedures and anaesthetics. Limitations in the data presented mean that these conclusions should be interpreted with caution.

Authors' objectives
To assess the efficacy and safety of paravertebral blocks compared with other analgesic and anaesthetic regimes on pain management in women undergoing breast surgery

Searching
Cochrane Central Register of Controlled Clinical Trials (CENTRAL), MEDLINE and EMBASE were searched from inception to 'present' (latest trials published in 2009) following Cochrane Collaboration recommendations. Search terms were provided. No language or publication type restrictions were used. Reference lists of retrieved articles were checked for additional publications. Relevant research groups were contacted to retrieve information about ongoing trials.

Study selection
Randomised controlled trials that compared paravertebral blocks with sham procedures or with any other analgesic modality in women undergoing breast surgery were eligible for inclusion. Data from all age groups and types of breast surgery were eligible.

The primary outcomes were: acute postoperative pain (defined as worst acute postoperative pain score, acute postoperative pain scores at rest or at movement) at up to two hours, two to 24 hours and 24 to 48 hours; chronic postoperative pain at six and 12 months; and the need for rescue analgesic. Secondary outcomes included the time to the need for rescue analgesics, the number of patients with postoperative nausea and vomiting, the number of patients with a technique failure of paravertebral blocks, and the number of patients with adverse events.

Included trials compared paravertebral blocks with or without general anaesthetic versus general anaesthetic alone or general anaesthetic in combination with a continuous wound catheter. Where paravertebral blocks was administered alone, patients were sedated with propofol and/or midazolam. Paravertebral blocks were a single injection, multiple injections, or continuous catheter. Local anaesthetics used included bupivacaine, ropivacaine, and lidocaine. Analgesic opioids were used in all trials. Postoperative nausea and vomiting prophylaxis included dexamethasone and/or ondansetron. Patients underwent minor and major elective breast tumour resection or mastectomy, with or without axillary dissection.

Two authors independently applied the inclusion criteria to the full-text articles.

Assessment of study quality
The Jadad scale was used to assess trial quality; items included random allocation, concealment of allocation, blinding technique and description of drop-outs. Trials were rated as high (3 or more points) or low (under 3 points).

Quality assessment was performed independently by two authors.

Data extraction
Standardised forms were used for data extraction. Relative risks (RR), with 95% confidence intervals (CIs), were calculated for dichotomous outcomes. Mean differences (MD), with 95% confidence intervals, were calculated for continuous outcomes. Pain scores were converted to a scale ranging from zero (no pain) to 10 (worst pain). Where
necessary, the worst pain score given was extracted for the relevant time period. Where separate data on postoperative nausea and vomiting were given, only the number of patients vomiting was extracted. If continuous data were reported only as median and range, the mean was considered equivalent to the median. Standard deviation (SD) was estimated assuming that the width of the interquartile range was 1.35 standard deviation for a normal distribution of outcome.

Data extraction was performed independently by two authors; any discrepancies were resolved by consulting a third author or by discussion between authors.

Methods of synthesis
A fixed-effect model was used to pool data unless significant heterogeneity was identified, then a random-effects model was used. Heterogeneity was assessed using $I^2$; it was assumed to be present if $I^2$ was over 30%.

Subgroup analyses were planned according to type of paravertebral block modality (single injection, multiple injections and catheter), use of a fixed additional analgesic, and use of a postoperative nausea and vomiting prophylaxis regime. Sensitivity analyses were planned according to trial quality (low versus high) and to assess the influence of different reported outcomes (median versus mean).

Publication bias was assessed using funnel plots.

Results of the review
Fifteen RCTs were included in the review (925 patients in Table 1; data from 877 patients with breast cancer analysed). Trial quality was classed as high in 10 trials and low in five trials.

Paravertebral blocks versus general anaesthetic (six RCTs, n=344 patients)

Worst postoperative pain scores were significantly lower for paravertebral blocks at up to two hours post operation (MD -2.47, 95% CI -3.06 to -1.88; five RCTs; $I^2$=71%), two to 24 hours post operation (MD -1.77, 95% CI -2.42 to -1.12; five RCTs; $I^2$=84%) and at 24 to 48 hours post operation (MD -1.75, 95 CI -3.19 to -0.31; three RCTs; $I^2$=83%). Significant heterogeneity was observed for each comparison. Funnel plots demonstrated asymmetry (plots not shown). Subgroup analyses showed better results in multiple injection paravertebral block trials for all time periods, but heterogeneity remained (results not presented in paper).

The number of patients who required postoperative rescue opioids was significantly lower for those who received paravertebral blocks (five RCTs) up to 24 hours (RR 0.16, 95% CI 0.04 to 0.57; four RCTs) and at 24 to 48 hours (RR 0.18, 95% CI 0.06 to 0.54; one RCT) after surgery.

Paravertebral blocks plus general anaesthetic versus general anaesthetic alone (five RCTs, n=215)

Worst postoperative pain scores were significantly lower in the combined paravertebral block plus general anaesthetic group at up to two hours post operation (MD -1.87, 95% CI -2.53 to -1.21; $I^2$=2%) and at two to 24 hours (MD -2.21, 95% CI -3.07 to -1.35; $I^2$=0). No significant heterogeneity was observed for either comparison. Funnel plots demonstrated no asymmetry. Subgroup analyses (results not reported in paper) showed better results in catheter paravertebral block trials at up to two hours and in single injection paravertebral block trials at two to 24 hours post operation. No other statistically significant results were observed.

Results were also presented for adverse events and other outcomes, and for the one trial that compared paravertebral blocks with continuous wound infusion.

Authors' conclusions
Paravertebral blocks (alone or in combination with general anaesthetic) provided better postoperative pain control with few adverse effects compared with other analgesic treatment strategies in women undergoing breast surgery, although the results were limited by the diversity of surgical procedures and anaesthetics.

CRD commentary
The aim and inclusion criteria for this review were clear and appropriate. Three major medical databases were searched with no language restrictions. An attempt was made to identify grey literature, which reduced the risk of publication.
bias. Some evidence of publication bias was detected using funnel plots, but given the small number of included trials, the reliability of these findings was unclear. All of the main stages of the review were carried out in duplicate, which reduced the risk of reviewer bias.

A well-recognised tool for the quality assessment of RCTs was used to evaluate trials; most trials were found to be of high quality. Limited trial details were provided, which made it hard to judge the generalisability of trials and the appropriateness of statistical synthesis. The authors did not clearly state whether the mean differences were standardised or weighted. It was unclear what effect this, and the assumption that mean and median results were equivalent, had on the results. Confidence intervals were wide for some outcomes.

The review was carried out to a reasonable standard, but given the limited number of trials, wide confidence intervals and difficulty in judging the appropriateness of the statistical synthesis, the authors’ conclusions should be interpreted with caution.

**Implications of the review for practice and research**

**Implications for practice:** The authors stated that the optimal dose and type of local anaesthetic/additives used and the optimal technique to establish a sufficient and reliable paravertebral blocks for breast surgery had not yet been clarified. They suggested that a catheter paravertebral block combined with general anaesthetic may provide the most effective perioperative analgesia for breast surgery, but that further studies were needed.

**Implications for research:** The authors stated that further studies to assess the optimal risk-benefit ratio for the different paravertebral block techniques were needed. Larger studies were needed to investigate a possible preventative role of paravertebral blocks on the incidence of chronic postoperative pain after breast surgery. Studies were also needed to compare the rate of failure and incidence of adverse events of an ultrasound guided paravertebral blocks with other approaches including nerve stimulation and loss of resistance technique. Further studies should investigate whether the combination of general anaesthetic with a continuous local anaesthetic wound infusion provide comparable effects in the postoperative period compared with a catheter paravertebral block.

**Funding**

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**Bibliographic details**


**PubMedID**

20947592

**DOI**

10.1093/bja/aeq265

**Original Paper URL**

http://bja.oxfordjournals.org/content/105/6/842.abstract

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Analgesics, Opioid /administration & dosage; Anesthesia, General; Drug Administration Schedule; Female; Humans; Mastectomy /adverse effects; Nerve Block /adverse effects /methods; Pain Measurement /methods; Pain, Postoperative /etiologie /prevention & control; Randomized Controlled Trials as Topic; Treatment Outcome

**AccessionNumber**

12011000085
Date bibliographic record published
11/05/2011

Date abstract record published
05/03/2012

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.