Efficacy of low-dose bupivacaine in spinal anaesthesia for caesarean delivery: systematic review and meta-analysis

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CRD summary
The review concluded that low dose bupivacaine for Caesarean delivery spinal anaesthesia compromised anaesthetic efficacy despite the benefit of lower maternal hypotension and nausea/vomiting. The review was well conducted and the results seem reliable; however, an arbitrary cut-off value for low dose bupivacaine means that a degree of caution is warranted when interpreting the authors’ conclusions.

Authors’ objectives
To compare the efficacy and adverse effects of low dose spinal bupivacaine compared with conventional dose spinal bupivacaine for elective Caesarean delivery.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and LILACS were searched to October 2008 for articles in any language published in peer-reviewed journals. Search terms were reported. Reference lists of retrieved articles and relevant journals were handsearched. The MEDLINE search was updated in December 2010.

Study selection
Randomised controlled trials (RCTs) of low dose spinal bupivacaine (≤8mg) versus conventional dose spinal bupivacaine (>8mg) in elective or semi-urgent caesarean delivery under neuraxial spinal anaesthesia were eligible for inclusion. Trials were limited to American Society of Anaesthesiologist I-II term parturients. Primary outcomes were frequency of intraoperative analgesic supplementation by any route and conversion to general anaesthesia. Secondary outcomes were maternal adverse effects, neonatal outcomes, patient satisfaction during the intraoperative period and surgical conditions as assessed by the surgeon.

The included trials studied low dose spinal bupivacaine (4mg to 8mg) versus conventional dose spinal bupivacaine (8.7mg to 12.5mg) in patients with a mean age of 24 to 37 years. Various neuraxial techniques were used. Various concomitant drugs were administered. The trials were published between 2000 and 2010 and conducted in North America, South America, Europe, Asia and Africa. The mean weight of patients ranged from 58kg to 85kg.

Two reviewers independently performed study selection. Disagreements were resolved by consensus.

Assessment of study quality
Trial quality was assessed using the Jadad scale of randomisation, blinding and withdrawals to give a score out of five. The Cochrane Handbook was used to assess trial quality on the basis of randomisation, allocation concealment, blinding, incomplete outcome data, selective reporting and other biases. Evidence for each outcome was graded according to the GRADE criteria.

The two authors performed quality assessment independently.

Data extraction
Data were extracted on primary and secondary outcomes and used to calculate relative risks (RRs), together with 95% confidence intervals (CIs).

The two authors extracted data independently. Disagreements were resolved by discussion.

Methods of synthesis
Random-effects meta-analysis was undertaken to calculate pooled relative risks and 95% CIs. Fixed-effect meta-analysis was used for one outcome. Statistical heterogeneity was assessed using the I² statistic. The weighted rounded
dose for low dose was 7mg and for conventional dose bupivacaine 11 mg. The number needed to harm was calculated.

Sensitivity analysis excluded one study at a time. Subgroup analyses and meta-regression were performed on prespecified confounding factors: bupivacaine baricity, position during injection, uterine exteriorisation, original groups versus re-grouping, short-acting intrathecal opioid use and study population.

Publication bias was assessed using Egger's test and Begg’s funnel plots.

**Results of the review**

Fifteen RCTs were included in the review (1,004 patients, range 32 to 239) and 12 of these were included in the meta-analysis (693 patients). Three trials scored the maximum of 5 on the Jadad scale, five scored 4, five scored 3 and two scored 2.

**Primary outcomes:** Compared with conventional dose bupivacaine, low dose bupivacaine was associated with a significantly higher risk of analgesic supplementation during caesarean delivery (RR 3.76, 95% CI 2.38 to 5.92; I²=0%; 10 RCTs). The evidence was graded as high quality. The number needed to harm was four patients. There was no evidence of publication bias.

Sensitivity analysis using odds ratios and a fixed-effect model did not alter results. Subgroup analyses and meta-regression that assessed possible confounding variables did not reveal interaction or effect modification. Conversion to general anaesthesia occurred in only one trial that reported two events from 21 patients in the low dose group and none in the conventional dose group.

**Secondary outcomes:** Compared with conventional dose bupivacaine, low dose bupivacaine was associated with a statistically significantly lower risk of hypotension (RR 0.78, 95% CI 0.65 to 0.93; I²=29%; nine RCTs), lower risk of nausea and vomiting (RR 0.71, 95% CI 0.55 to 0.93; I²=6%; 11 RCTs). The evidence was graded as moderate quality. Other secondary outcomes could not be calculated.

**Authors’ conclusions**

Low dose bupivacaine in spinal anaesthesia compromised anaesthetic efficacy despite the benefit of lower maternal hypotension and nausea/vomiting.

**CRD commentary**

Inclusion criteria for the review were clearly defined. Several relevant data sources were searched. There were no language restrictions. There was a restriction on publication status. Publication bias was assessed and was not detected, although the authors stated correctly that it could not be ruled out totally. Attempts were made to reduce reviewer error and bias throughout the review. Quality assessment indicated that the quality of the evidence was generally good. Evidence for the primary outcomes was deemed high quality. The authors noted that there were differences across the trials in terms of definitions and cut-off values for low dose bupivacaine. Trials were combined using standard statistical techniques. Statistical heterogeneity was assessed appropriately.

This review was well conducted and the results seem reliable; however, an arbitrary cut-off value for low dose bupivacaine means that a degree of caution is warranted when interpreting the authors’ conclusions.

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

**Practice:** The authors stated that lower bupivacaine doses could not be recommended unless an epidural catheter was in place to rescue the block if anaesthesia was inadequate or became inadequate during surgery. They summarised that the problem of ensuring better anaesthesia while avoiding the higher incidence and severity of hypotension was not resolved.

**Research:** The authors did not state any implications for research.

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