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Systematic review

Prolonging the duration of single-shot intrathecal labour analgesia with morphine: A systematic review

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HIGHLIGHTS

- Meta-analysis of RCTs of duration of analgesia after spinal morphine during labour.
- Adding morphine (≤250 mcg) to spinal bupivacaine + fentanyl or sufentanil may prolong pain relief.
- Spinal bupivacaine + morphine may be a cost effective alternative to epidural analgesia for labour-pain.

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ABSTRACT

Background and aims: Single-shot spinal with bupivacaine plus fentanyl or sufentanil is commonly used as analgesia during labour, but the short duration limits the clinical feasibility. Different drugs have been added to prolong the analgesic duration. The additional effect of intra-thecal morphine has been studied during labour pain as well as after surgery. We assessed whether adding morphine to intra-thecal bupivacaine + fentanyl or sufentanil prolongs pain relief during labour.

Methods: Meta-analysis of placebo-controlled randomized clinical trials of analgesia prolongation after single-shot intrathecal morphine ≤250 μg during labour when given in combination with bupivacaine + fentanyl or sufentanil. After identifying 461 references, 24 eligible studies were evaluated after excluding duplicate publications, case reports, studies of analgesia after caesarean delivery, and epidural labour analgesia. Mean duration in minutes was the primary outcome measure and was included in the calculation of the standardized mean difference. Duration was defined as the time between a single shot spinal until patient request of rescue analgesia. All reported side effects were registered. Results of individual trials were combined using a random effect model. Cochrane tool was used to assess risk of bias.

Results: Five randomized placebo-controlled clinical trials (286 patients) were included in the meta-analysis. A dose of 50–250 μg intrathecal morphine prolonged labour analgesia by a mean of 60.6 min (range 3–155 min). Adding morphine demonstrated a medium beneficial effect as we found a pooled effect of standardized mean difference = 0.57 (95% CI: −0.10 to 1.24) with high heterogeneity (I^2 = 88.1%). However, the beneficial effect was statistically non-significant (z = 1.66, p = 0.096). The lower-bias trials showed a small statistically non-significant beneficial effect with lower heterogeneity. In influential analysis, that excluded one study at a time from the meta-analysis, the effect size appears unstable and the results indicate no robustness of effect. Omitting the study with highest effects size reduces the pooled effect markedly and that study suffers from inadequate concealment of treatment allocation and blinding. Trial quality was generally low, and there were too few trials to explore sources of heterogeneity in meta-regression and stratified analyses. In general, performing meta-analyses on a small number of trials are possible and may be helpful if one is aware of the limitations. As few as one more placebo-controlled trial would increase the reliability greatly.

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Conclusions: Evidence from this systematic review suggests a possible beneficial prolonging effect of adding morphine to spinal analgesia with bupivacaine + fentanyl or +sufentanil during labour. The study quality was low and heterogeneity high. No severe side effects were reported. More adequately-powered randomized trials with low bias are needed to determine the benefits and harms of adding morphine to spinal local anaesthetic analgesia during labour.

Implications: Epidural analgesia is documented as the most effective method for providing pain relief during labour, but from a global perspective most women in labour have no access to epidural analgesia. Adding morphine to single shot spinal injection of low dose bupivacaine, fentanyl or sufentanil may be efficacious but needs to be investigated.

Contents

Epidural analgesia (EDA) is the most effective method of providing pain relief during labour [1]. From a global perspective, most women in labour have no access to EDA, either because hospitals lack anaesthesiologist or the facilities for EDA in the hospital is limited for economic reasons. Single-dose spinal analgesia, if proven safe and efficient, may be a feasible option under such circumstances. Compared with EDA, this technique is easier to administer and monitor and the costs may be significantly reduced [2]. After introducing thin (25-27G) non-traumatic spinal needles, the risk of post dura puncture headache is minimal. The use of single-shot spinal analgesia during labour has been limited due to its short duration of action.

The local anaesthetic bupivacaine combined with a lipophilic, rapidly absorbed and removed, and therefore short-acting opioid, usually fentanyl or sufentanil, are common drugs used for spinal analgesia during labour. These combinations produce analgesia for up to 3 h [3].

The duration of spinal analgesia can be prolonged by adding the hydrophilic morphine that stays in the CSF longer, increasing the duration of analgesia [4]. Published studies of morphine added to spinal anaesthesia for surgery have documented this effect [5]. Studies on morphine added to spinal analgesia for labour-pain are mostly small-number studies and the results are conflicting.

The aim of this study was to perform a systematic review of randomised controlled trials assessing the prolongation of analgesia after adding morphine to local anaesthetic spinal analgesia during labour.

1. Methods

Because the review was based on previously published studies, research ethical board approval of the protocol was not necessary. The protocol for this systematic review was registered on the International Prospective Registry of Systematic Reviews (PROSPERO, CRD42013005402).

1.1. Literature search

A qualified medical librarian was consulted at the medical library of Oslo University Hospital. Electronic searches in Ovid Medline, EMBASE, Cochrane Library, PubMed, and Google were performed with reference to the following definitions of participants, interventions, comparators, and outcomes (PICO): labouring women, single-shot spinal analgesia with intrathecal morphine compared to placebo, and with prolongation of analgesia duration as an outcome. We also performed hand searches of the reference lists of the obtained articles. Search terms were as follows: “intrathecal opioid in labour analgesia”, “intrathecal analgesia in labour”, “spinal analgesia in labour”, “labour pain”, “obstetric analgesia”, “labour management” or “vaginal delivery”, and “morphine in labour analgesia”. Authors were contacted for detailed information when needed.

1.2. Trial selection

All studies that used intrathecal morphine during labour for analgesia published after 1946 up to 15th March 2016 were assessed. Only placebo-controlled randomised clinical trials evaluating the prolongation of analgesia after adding morphine to spinal analgesia (bupivacaine, fentanyl and/or sufentanil) during labour, and not during caesarean section, were considered eligible for inclusion in the systematic review. Studies of single shot spinal and combined spinal epidural technique were included. After identifying 461 references, 61 were removed due to duplicate publications. Three hundred forty-six references were excluded for the following reasons: case reports, intrathecal analgesia during caesarean delivery, and epidural labour analgesia. Of the 54 studies screened, 30 were excluded because drugs other than intrathecal morphine were studied (Fig. 1), leaving 24 eligible studies.