

# Extending epidural analgesia for emergency Caesarean section: a meta-analysis

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## Editor's key points

- Emergency Caesarean section requires a rapid onset of sustained analgesia.
- Topping-up an epidural that is already *in situ* is a good option, but the best local anaesthetic solution to use is not clear.
- This meta-analysis suggests that lidocaine 2% with epinephrine  $\pm$  fentanyl gives the fastest onset.
- Bupivacaine and levobupivacaine 0.5% were the least effective.

**Summary.** There is no high-level evidence supporting an optimal top-up solution to convert labour epidural analgesia to surgical anaesthesia for Caesarean section. The aim of this meta-analysis was to identify the best epidural solutions for emergency Caesarean section anaesthesia, with respect to rapid onset and low supplementation of intraoperative block. Eleven randomized controlled trials, involving 779 parturients, were identified for inclusion after a systematic literature search and risk of bias assessment. 'Top-up' boluses were classified into three groups: 0.5% bupivacaine or levobupivacaine (Bup/Levo); lidocaine and epinephrine, with or without fentanyl ( $LE \pm F$ ); and 0.75% ropivacaine (Ropi). Pooled analysis using the fixed-effects method was used to calculate the mean difference (MD) for continuous outcomes and risk ratio (RR) for dichotomous outcomes. Lidocaine and epinephrine, with or without fentanyl, resulted in a significantly faster onset of sensory block [MD  $-4.51$  min, 95% confidence interval (CI)  $-5.89$  to  $-3.13$  min,  $P < 0.00001$ ]. Bup/Levo was associated with a significantly increased risk of intraoperative supplementation compared with the other groups (RR 2.03; 95% CI 1.22–3.39;  $P = 0.007$ ), especially compared with Ropi (RR 3.24, 95% CI 1.26–8.33,  $P = 0.01$ ). Adding fentanyl to a local anaesthetic resulted in a significantly faster onset but did not affect the need for intraoperative supplementation. Bupivacaine or levobupivacaine 0.5% was the least effective solution. If the speed of onset is important, then a lidocaine and epinephrine solution, with or without fentanyl, appears optimal. If the quality of epidural block is paramount, then 0.75% ropivacaine is suggested.

**Keywords:** Caesarean section; epidural anaesthesia; epidural analgesia

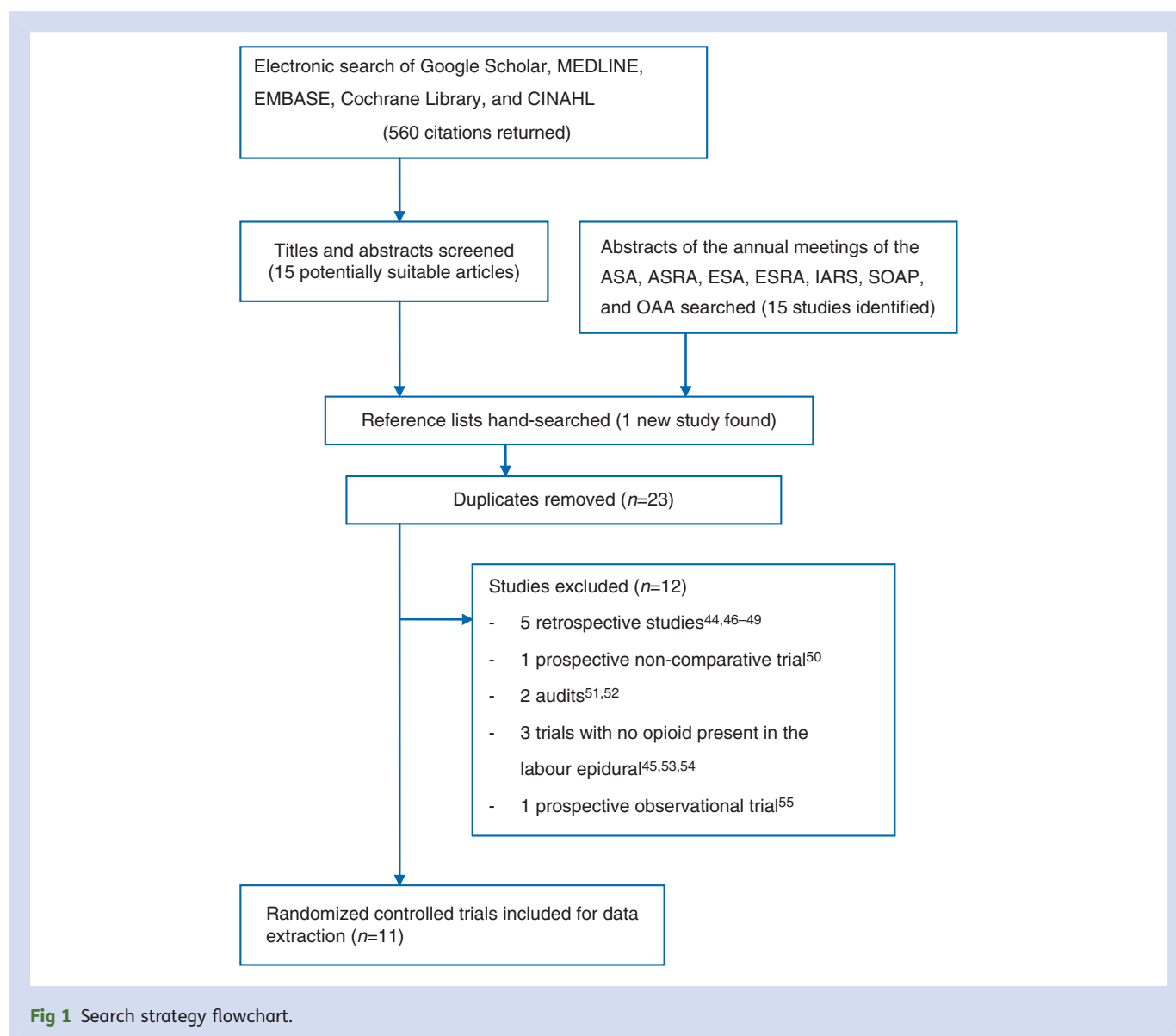
Converting labour epidural analgesia to surgical anaesthesia for Caesarean section is a common procedure. Over 93 000 emergency Caesarean sections (EmCS) were carried out in NHS hospitals in England from 2008 to 2009, and in 22% of these, an epidural anaesthetic was used.<sup>1</sup> This is consistent with the findings of a large-scale audit that noted that an epidural bolus ('top-up') was the mode of anaesthesia in 26% of EmCS.<sup>2</sup> Although many women are managed this way, the best way to convert epidural analgesia to anaesthesia for EmCS remains unclear. Opinion remains divided, with a survey indicating that a wide range of local anaesthetic (LA) solutions are used to achieve epidural anaesthesia.<sup>3</sup> There have been several randomized controlled trials examining the efficacy of different LAs and adjuncts, but none has clarified the optimal solution. The primary focus of these studies was to establish which epidural solution achieves anaesthesia in the fastest time. A lidocaine and epinephrine combination appears to result in a rapid onset of anaesthesia.<sup>4–7</sup> However, another important characteristic of the solution is that it should be fully effective for the

duration of surgery, thereby minimizing intraoperative breakthrough pain, an important medico-legal issue in obstetric anaesthesia. This outcome has often been a secondary endpoint in studies of anaesthesia for EmCS, so trials often have insufficient power to adequately assess this endpoint. Inadequate study power may also occur because of the unpredictable nature of EmCS, such that recruitment and data collection are difficult. Several trials were halted before the planned number of patients had been recruited.<sup>6,8,9</sup>

The aim of this meta-analysis was to identify whether the current evidence supported significant differences between the various epidural 'top-up' solutions with respect to the time to the onset of surgical anaesthesia and the incidence of intraoperative supplementation.

## Methods

We identified studies that evaluated conversion of epidural analgesia during labour to surgical anaesthesia for EmCS (Fig. 1). This involved searching Google Scholar, MEDLINE



(1950 to 2010), EMBASE (1974 to 2010), CINAHL (1982 to 2010), and the Cochrane Library. For these database searches, we used the following exploded medical subject headings (MeSH), text words, and Boolean operators: 'epidural' OR 'extradural' AND 'c\*esarean section' OR 'c\*esarean delivery' AND 'urgent' OR 'emergency'. The search was not limited to publications in the English language and was last conducted on September 14, 2010. The authors then examined available abstracts from the 2000–2010 meetings of The American Society of Anesthesiologists, The American Society of Regional Anesthesia and Pain Medicine, The European Society of Anaesthesia, The European Society of Regional Anaesthesia and Pain Therapy, The International Anesthesia Research Society, and the Society for Obstetric Anesthesia and Perinatology. Abstracts from the 1991–2010 meetings of the Obstetric Anaesthetist's Association were also reviewed. The reference lists of all the relevant

articles generated by the above searches were then hand-searched for further studies.

Duplicates were removed and the remaining references analysed independently by two investigators to determine whether they met the inclusion criteria. Studies were considered eligible if they were randomized controlled trials comparing differing epidural top-up solutions, to extend labour analgesia achieved using a low-dose mixture of LA and opioid, for an EmCS.

Data from the trials included were extracted individually by two of the authors (S.G.H. and T.E.B.) on to a predetermined spreadsheet, with any discrepancies resolved by re-examining the original article or consulting a third author (T.B.C.). The authors of the selected trials were contacted to determine whether supplementary or unpublished data were available. The primary outcome measures were time to onset of a block adequate for surgery and the need

for supplementation of the block intraoperatively. Secondary outcomes included: nausea and vomiting, pruritis, shivering, sedation, cardiovascular changes, motor block, maternal satisfaction scores, Apgar scores, and cord gases. Details of labour analgesia, methods of the epidural top-up, block assessment, and the duration of surgery were also recorded. Information on sequence generation, allocation concealment, blinding, outcome details, and other potential sources of bias were noted, to allow implementation of The Cochrane Collaboration's tool for assessing the risk of bias.<sup>10</sup>

The individual trials evaluated a variety of epidural top-up solutions made up of differing LAs and adjuncts. For analysis, the epidural solutions were classified into three groups based on the LA that each contained: 0.5% bupivacaine or levobupivacaine (group Bup/Levo); 0.2% lidocaine with 1:200 000 epinephrine, with or without fentanyl (group LE $\pm$ F), and 0.75% ropivacaine (group Ropi).

Continuous outcomes were most often reported as median, inter-quartile range (IQR), and range. We calculated the mean and standard deviation via a validated technique before meta-analysis.<sup>11</sup> Descriptive statistics were then used to calculate the mean difference (MD), using the fixed-effects inverse variance approach. Results are expressed as MD with 95% confidence interval (CI) and results considered significant if the *P*-value was <0.05. For dichotomous outcomes, a meta-analysis was performed using risk ratio (RR) and the Mantel-Haenszel fixed-effects method.<sup>12 13</sup> Results are given as RR, with 95% CI. A *P*-value of <0.05 was considered significant.

The degree of heterogeneity was measured and expressed as the  $\chi^2$ -statistic. Inconsistency was assessed using the  $I^2$ -statistic,<sup>14 15</sup> with a value of >40% indicative of significant heterogeneity.

Sensitivity analysis based on the outcomes of onset of block and intraoperative supplementation was performed by excluding trials that did not have double blinding, adequate allocation concealment, or a loss to follow-up of >10%. A funnel plot of each primary outcome was used to assess publication bias. All statistical analysis was conducted using Review Manager version 5.0.25 for Windows.<sup>16</sup>

## Results

A total of 11 randomized controlled trials involving 779 parturients met the criteria for inclusion<sup>4-9 17-21</sup> (Table 1). The trials were predominantly conducted in the UK,<sup>4-9 19 21</sup> with three from Asia,<sup>17 18 20</sup> and all published in English. Two of the trials were presented only as conference abstracts,<sup>19 21</sup> and further trial details were obtained directly from the authors. Overall, the trials were of high quality (risk of bias summary, Fig. 2).

All trials recruited labouring women who had epidural catheters *in situ* and were receiving a low-dose mixture of LA and fentanyl, administered by various methods.

Inclusion and exclusion criteria were similar among the individual trials. All but one trial<sup>18</sup> were limited to singleton pregnancies, four were restricted to nulliparous women,<sup>7-9 17</sup> and the rest

recruited women of any parity.<sup>4-6 18-21</sup> One trial was limited to category 3 EmCS<sup>17</sup> and four to category 2 and 3 EmCS,<sup>5 6 18 20</sup> while the others included all categories of EmCS.<sup>4 7-9 19 21</sup>

## Onset of surgical block

In many studies, the onset of surgical block was assessed using more than one modality of block assessment or sought different dermatomal levels before surgery was allowed to proceed (Table 2). Most of the studies used loss of 'cold' to T4,<sup>4 7-9 17 19-21</sup> but two measured 'touch' to T5<sup>4 9</sup> and two 'touch' to T7.<sup>5 6</sup> Loss of 'sharp' sensation was also assessed in three trials, but at different levels, namely T4,<sup>17</sup> T6,<sup>18</sup> and T7<sup>6</sup> (Table 2).

Analysis indicated a significant reduction in the time to the onset of block when LE $\pm$ F solutions were compared with either Bup/Levo or Ropi (overall MD -1.66 min, 95% CI -2.40 to -0.91 min, *P*<0.0001; Fig. 3). There was, however, considerable heterogeneity among the trials (*P*<0.0001 and  $I^2$ =83%) which appeared to be accounted for mainly by one trial.<sup>20</sup> Removal of this trial from the meta-analysis, due to its markedly different protocol, reduced the time to the onset of block after LE $\pm$ F solutions further (MD -4.51 min, 95% CI -5.89 to -3.13 min, *P*≤0.00001), with a concurrent decrease in the degree of heterogeneity (*P*=0.74 and  $I^2$ =0%). Adding 50–75 µg of fentanyl to a top-up solution decreased the onset time to surgical anaesthesia (overall MD -2.02 min, 95% CI -3.31 to -0.73 min, *P*=0.002). The two trials in this meta-analysis showed low heterogeneity (*P*=0.29 and  $I^2$ =11%; Fig. 4).

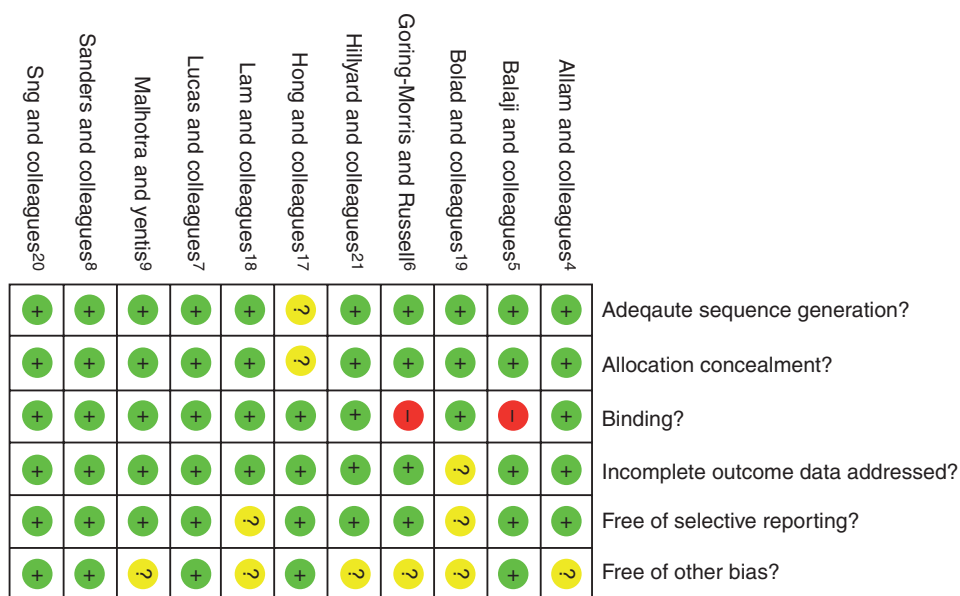
## Intraoperative block supplementation

Meta-analysis showed a significant increase in the incidence of supplementation for intraoperative pain when Bup/Levo was compared with either LE $\pm$ F or Ropi (pooled RR 2.03, 95% CI 1.22–3.39, *P*=0.007; Fig. 5). There was no heterogeneity among these trials (*P*=0.73 and  $I^2$ =0%). This increased risk of intraoperative supplementation was highest in the pooled subgroup analysis of Bup/Levo compared with Ropi (RR 3.24, 95% CI 1.26–8.33, *P*=0.01). Again there was no heterogeneity (*P*=0.57 and  $I^2$ =0%). When Bup/Levo was compared with LE $\pm$ F, the results were not significant (RR 1.60, 95% CI 0.86–2.98, *P*=0.13), with no evidence of heterogeneity (*P*=0.80 and  $I^2$ =0%). Removal of the only unpublished study included in the meta-analysis of intraoperative supplementation<sup>21</sup> resulted in a marginal reduction in the relative risk of intraoperative supplementation associated with Bup/Levo (RR 1.95, 95% CI 1.15–3.30, *P*=0.01), with no implications for heterogeneity (*P*=0.66 and  $I^2$ =0%).

The addition of fentanyl to an epidural top-up did not decrease the need for intraoperative supplementation (pooled values RR 0.66, 95% CI 0.33–1.33, *P*=0.25), although there was heterogeneity among these trials (*P*=0.01 and  $I^2$ =85%; Fig. 6).

**Table 1** Description of included studies

Study	n	Top-up solution A (volume in ml)	Top-up solution B (volume in ml)	Top-up solution C (volume in ml)	Details of labour analgesia	Administration details of epidural top-up	Primary outcome/s	Median pre-top-up level of blockade A/B/C
Sanders and colleagues <sup>8</sup>	47	0.5% bupivacaine (20)		0.75% ropivacaine (20)	Midwife top-up: 10 ml of 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	Total volume over 3 min	Time from end of top-up until onset of block to cold at T4	T10/T10 (cold)
Hillyard and colleagues <sup>21</sup>	61	0.5% levobupivacaine (15)		0.75% ropivacaine (15)	PCEA: 9.9 ml (20 min lockout) 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	Total volume over 3 min	Time from end of top-up until onset of block to cold at T4	T9/T9 (cold)
Sng and colleagues <sup>20</sup>	90	0.5% levobupivacaine (15)	2% lidocaine, epinephrine 1:200 000 and 50 µg fentanyl (15)	0.75% ropivacaine (15)	CSE : 2 mg ropivacaine+15 µg fentanyl IT, then infusion: 0.1% ropivacaine and 2 µg ml <sup>-1</sup> fentanyl	Total volume over 3 min	Time from end of top-up until onset of block to cold at T4	T9/T8/T9 (cold)
Balaji and colleagues <sup>5</sup>	100	0.5% levobupivacaine (20)	2% lidocaine, epinephrine 1:200 000 and 100 µg fentanyl (22.1)		Intermittent top-up: 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	3 ml test dose over 90–120 s, the rest over 1–2 min	Time from end of top-up until onset of block to touch at T7	T11/T11 (sharp) L3/L2 (touch)
Goring-Morris and Russell <sup>6</sup>	68	0.5% bupivacaine (20)	2% lidocaine, epinephrine 1:200 000 and 100 µg fentanyl (22.1)		Intermittent top-up: 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	3 ml test dose over 2 min, the rest over 1 min	Time from beginning of top-up until block to touch at T7	T11/T11 (sharp) L2/L2 (touch)
Lucas and colleagues <sup>7</sup>	90	0.5% bupivacaine (20)	2% lidocaine and epinephrine 1:200 000 (20)	50:50, 0.5% bupivacaine and 2% lidocaine and epinephrine 1:200 000 (20)	Midwife top-up: 10 ml of 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl (max every 30 min)	Total volume over 3 min	Time from end of top-up until onset of block to cold at T4	T10/T10/T10 (cold)
Allam and colleagues <sup>4</sup>	46	0.5% levobupivacaine (20)	1.8% lidocaine, epinephrine 1:200 000 and HCO <sub>3</sub> (20.1)		PCEA: 5 ml (15 min lockout)+3 ml background. 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	Total volume over 3 min	Time from end of top-up until onset of block to light touch at T5	T10/T8 (cold) T12/T11 (touch)
Lam and colleagues <sup>18</sup>	40	2% lidocaine, epinephrine 1:200 000 75 µg fentanyl and HCO <sub>3</sub> (16.2)	2% lidocaine, epinephrine 1:200 000 and 75 µg fentanyl (16.2)		Infusion: 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	3 ml test dose over 3 min, the rest over 1 min	Time from end of top-up until loss of sharp discrimination at T6	T11/T11 (sharp)
Hong and colleagues <sup>17</sup>	62	2% lidocaine, epinephrine 1:200 000 and 100 µg fentanyl (22)	2% lidocaine and epinephrine 1:200 000 (22)		Infusion: 0.1% ropivacaine and 2 µg ml <sup>-1</sup> fentanyl	Total volume over 5 min	Time from end of top-up until onset of block to cold at T4	T12/L1 (cold) L1/L2 (sharp)
Bolad and colleagues <sup>19</sup>	63	0.5% bupivacaine (15)	0.5% levobupivacaine (15)	0.75% levobupivacaine (15)	PCEA: 9.9 ml (20 min lockout) 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl	Total volume over 3 min	Time from end of top-up until onset of block to cold at T4	Not available
Malhotra and Yentis <sup>9</sup>	112	0.5% levobupivacaine and 75 µg fentanyl (21.5)	0.5% levobupivacaine (21.5)		Midwife top-up: 10–15 ml of 0.1% bupivacaine and 2 µg ml <sup>-1</sup> fentanyl (max every 30 min)	Total volume over 3 min	Time from end of top-up until onset of block to cold at T4, to touch at T5 and intraoperative supplementation	T9/T8 (cold) T8/T10 (touch)

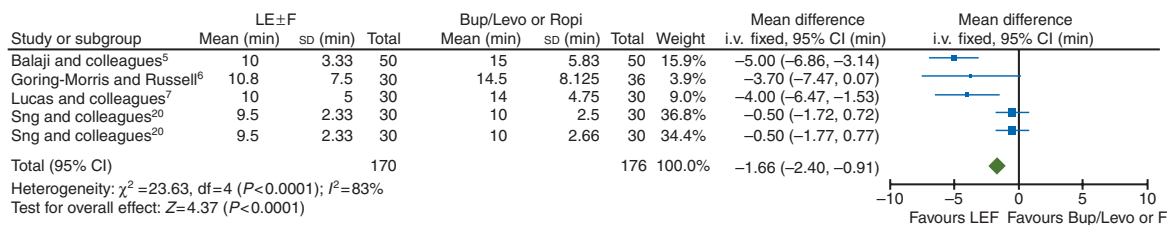


Bupivacaine and levobupivacaine solutions were compared with other LAs as the control group in the meta-analysis of intraoperative supplementation because they are the most widely used top-up solutions in the UK<sup>3</sup> and thereby represent a 'standard' solution. In contrast, LE + F solutions were compared with the control group of

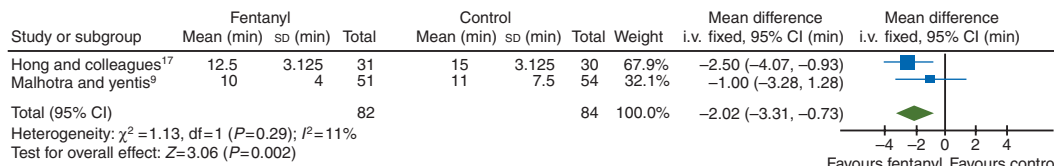


**Table 2** Time to onset of block for each of the epidural top-up solutions, modality through which this was assessed and from which point after administration of the top-up this time commenced. Values are median [IQR (range)]

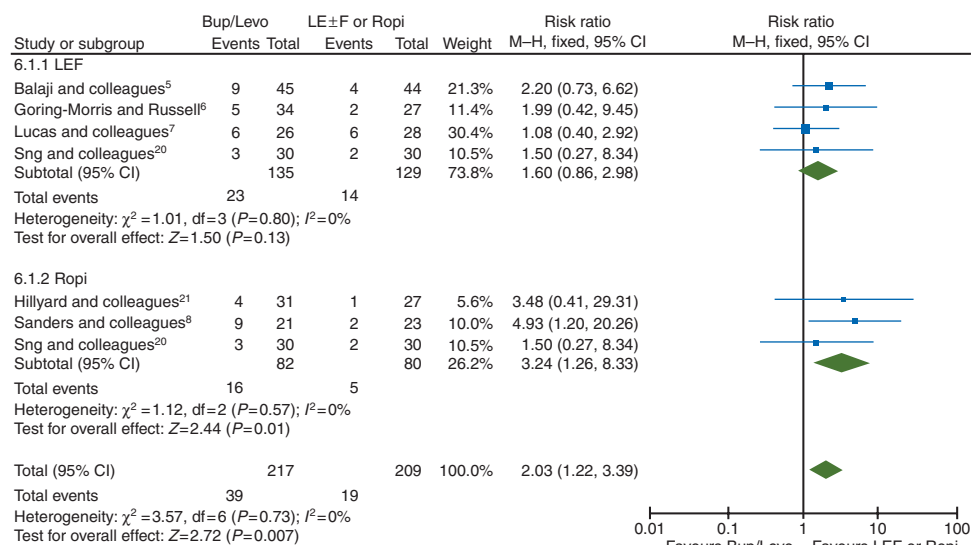
Study	Top-up solution A	Top-up solution B	Top-up solution C	Assessment method 1	Time for A	Time for B	Time for C	Assessment method 2	Time for A	Time for B	Time for C
Sanders and colleagues <sup>8</sup>	0.5% Bup		0.75% Ropi	Cold T4 (end of top-up)	11 [7.3–19.5 (5.0–45.0)]		11 [8.5–15.5 (4.0–20.0)]				
Hillyard and colleagues <sup>21</sup>	0.5% Levo		0.75% Ropi	Cold T4 (end of top-up)	7.5 [5.0–15.0 (5.0–35.0)]		10 [7.5–15.0 (5.0–35.0)]				
Sng and colleagues <sup>20</sup>	0.5% Levo	2% Lido/Epi and 50 µg Fent	0.75% Ropi	Cold T4 (end of top-up)	10.0 [7.0–15.0 (5.0–20.0)]	9.5 [7.0–13.3 (5.0–19.0)]	10.0 [7.0–15.0 (4.0–20.0)]				
Balaji and colleagues <sup>5</sup>	0.5% Levo	2% Lido/Epi and 100 µg Fent		Touch T7 (end of top-up)	15 [10.0–20.0 (5.0–40.0)]	10 [8.0–13.0 (5.0–25.0)]					
Goring-Morris and Russell <sup>6</sup>	0.5% Bup	2% Lido/Epi and 100 µg Fent		Touch T7 (start of top-up)	17.5 [12.5–25.0 (7.5–40.0)]	13.8 [10.0–26.9 (2.5–32.5)]		Sharp T7 (start of top-up)	10.0 [5.0–10.0 (2.5–30.0)]	10.0 [6.3–11.3 (2.5–25.0)]	
Lucas and colleagues <sup>7</sup>	0.5% Bup	2% Lido/Epi	0.5% Bup and 2% Lido/Epi	Cold T4 (end of top-up)	14 [11.0–19.3 (6.0–25.0)]	10 [9.0–18.5 (6.0–36.0)]	10 [8.8–17.0 (6.0–36.0)]				
Allam and colleagues <sup>4</sup>	0.5% Levo	1.8% Lido/Epi and HCO <sub>3</sub>		Cold T4 (end of top-up)	11 [9.0–14.0 (6.0–30.0)]	7 [5.0–8.0 (4.0–17.0)]		Touch T5 (end of top-up)	14 [10.0–17.0 (9.0–31.0)]	7 [6.0–9.0 (5.0–17.0)]	
Lam and colleagues <sup>18</sup>		2% Lido/Epi 100 µg Fent and HCO <sub>3</sub>	2% Lido/Epi and 100 µg Fent	Sharp T6 (end of top-up)		6 [4.0–6.0 (2.0–8.0)]	10 [8.0–10.0 (4.0–12.0)]				
Hong and colleagues <sup>17</sup>		2% Lido/Epi	2% Lido/Epi and 100 µg Fent	Cold T4 (end of top-up)		15.0 [12.5–17.5 (7.5–20.0)]	12.5 [10.0–17.5 (5.0–17.5)]	Sharp T4 (end of top-up)		17.5 [15.0–20.0 (12.5–25.0)]	15.0 [15.0–17.5 (7.5–17.5)]
Bolad and colleagues <sup>19</sup>	0.5% Levo	0.75% Levo	0.5% Bup	Cold T4 (end of top-up)	15 [5.0–30+]	15 [5.0–40.0]	20 [5.0–40.0]				
Malhotra and Yentis <sup>9</sup>	0.5% Levo		0.5% Levo and 75 µg Fent	Cold T4 (end of top-up)	11 [7.0–16.0 (3.0–48.0)]		10 [5.0–14.0 (5.0–29.0)]	Touch T5 (end of top-up)	12 [9.0–19.0 (3.0–85.0)]		11 [7.0–16.0 (5.0–29.0)]



**Fig 3** The onset time of a block suitable to allow surgery, comparing LE ± F (2% lidocaine, epinephrine, and fentanyl) top-up solutions with either Bup/Levo (0.5% bupivacaine, 0.5% levobupivacaine), or Ropi (0.75% ropivacaine) solutions.



**Fig 4** The effect of the addition of fentanyl to a top-up solution on the onset time of a block suitable to allow surgery.



**Fig 5** The need for intraoperative supplementation, comparing Bup/Levo (0.5% bupivacaine or 0.5% levobupivacaine) top-up solutions to LE ± F (2% lidocaine, epinephrine, and fentanyl), or Ropi (0.75% ropivacaine) solutions.

other LAs in the meta-analysis of onset time, because they have been found consistently to have faster onset.<sup>4–7 25 26</sup>

Drawing conclusions from this meta-analysis is complicated by the diversity of protocols and endpoints, this being most apparent in the investigation of onset. In total, six different combinations of sensory block testing modality and level of block were recorded, adding complexity to interpretation of results. The implications for research

generated by the lack of consensus relating to suitable block levels and methods of measurement have been highlighted before.<sup>27</sup> The starting point for recording onset time also varied, with the majority of trials using the end of administration of the epidural top-up, but one the beginning<sup>6</sup> and another including a 3 min test dose before using the end of the main epidural top-up.<sup>17</sup> Such diversity may affect the validity of the meta-analytical techniques applied to this

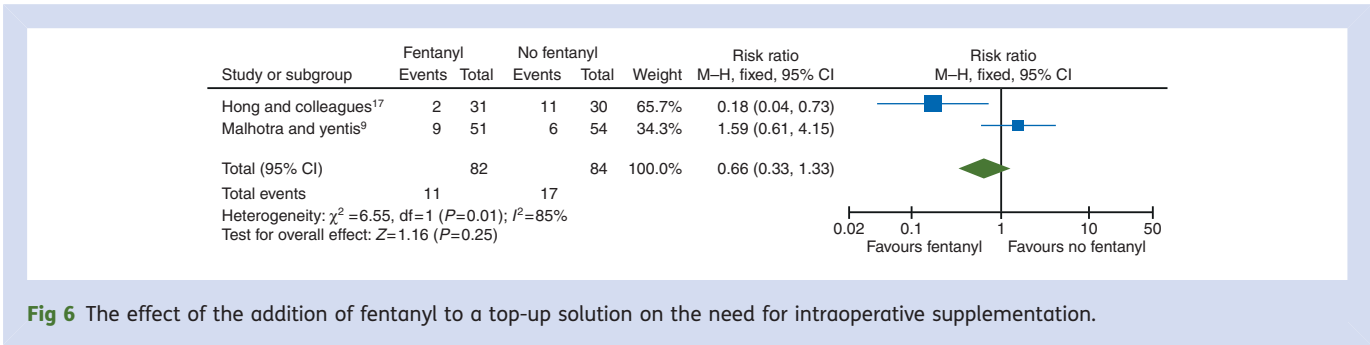


Fig 6 The effect of the addition of fentanyl to a top-up solution on the need for intraoperative supplementation.

endpoint. However, in each study, these different endpoints were all considered similarly to indicate surgical readiness, arguably assessing the same clinical endpoint and therefore making meta-analysis appropriate.

If the upper limit of the range of onset times is considered to be the longest expected time for an epidural top-up to achieve anaesthesia for surgical readiness, then all of the solutions studied could be considered appropriate for a category 3 EmCS,<sup>28</sup> for which a suggested decision to delivery interval is <75 min.<sup>29</sup> When there is maternal or fetal compromise, delivery should be accomplished as quickly as possible, taking into account that rapid delivery has the potential to do harm.<sup>28</sup> A category 1 EmCS has an accepted audit standard of <30 min for the decision-to-delivery interval,<sup>28</sup> so most of the top-up solutions would be suitable for most of these circumstances, as indicated by their IQR and range for onset time. Inevitably, there are possible exceptions, such that the reduction in onset time by 4.5 min after administration of lidocaine 2% and epinephrine, with or without fentanyl, appears attractive.

The recent ‘Saving Mothers Lives’ report emphasizes the importance of fast speed of block onset after an epidural top-up in certain situations.<sup>30</sup> One of the deaths directly due to anaesthesia resulted from inability to ventilate the lungs during general anaesthesia for a Category 1 Caesarean section. This woman had a functioning epidural catheter which the anaesthetist elected not to top-up because of the perceived delay before achieving surgical readiness. In all the trials included in this meta-analysis, solutions containing lidocaine and epinephrine, with or without fentanyl, showed median onset times <15 min. Using this solution to top-up an epidural catheter in the delivery room, that location being recommended in the report providing an anaesthetist and suitable equipment is available, creates the opportunity for surgical readiness comparable with administering general anaesthesia, which has a higher risk of serious complications.

Although there were insufficient trials to assess the effect of bicarbonate in this meta-analysis, the reduction in onset time appears more pronounced when bicarbonate is added.<sup>4 18</sup> Some of the time-saving might, however, be offset by drug preparation time,<sup>31</sup> and there are safety implications when mixing drugs in an emergency situation.<sup>32</sup> Despite an absence of case reports of clinical toxicity in

this setting in which plasma and tissue LA concentrations have already been established by epidural analgesia, lidocaine is a less cardiotoxic LA than bupivacaine, levobupivacaine, or ropivacaine.

The need for intraoperative supplementation of the epidural block was recorded more consistently across studies. If either levobupivacaine 0.5% or bupivacaine 0.5% is used then supplementation is more likely to be needed, especially compared with ropivacaine 0.75%. The potency ratio of levobupivacaine and bupivacaine to ropivacaine ranges from approximately 1:2 to 1:1.<sup>33 34</sup> At elective CS<sup>35 36</sup> or for labour analgesia,<sup>37 38</sup> potencies appear similar. It may be that preceding epidural analgesia causes a degree of tachyphylaxis to LA,<sup>39</sup> such that a larger dose is required in the emergency setting. If ropivacaine, bupivacaine, and levobupivacaine have similar potencies, then the more concentrated solution of ropivacaine (0.75% vs 0.5%) may explain why it appears a more effective solution.

The potency ratio of lidocaine to bupivacaine is commonly reported to be 1:4<sup>40</sup> and the doses administered in the trials reflect this. The risk of intraoperative supplementation was not significantly different between Bup/Levo and LE ± F solutions. This may be due to the use of similarly effective doses or the presence of epinephrine, which reduces vascular uptake of lidocaine<sup>41</sup> and prolongs its action.

Fentanyl is often added to an epidural top-up in this setting, but the meta-analysis did not support a benefit in reducing the need for supplementation of the block intraoperatively. A major limitation of the finding is that it was generated by pooling only two trials,<sup>9 16</sup> which reported contradicting results. In contrast, the addition of fentanyl significantly improves the quality of epidural anaesthesia for elective surgery.<sup>42</sup> It has been suggested that this difference observed in the emergency situation is because fentanyl in the labour epidural solution has already produced a near-maximal effect.<sup>9</sup> The onset time was reduced by the inclusion of fentanyl and it did not increase the incidence of vomiting, so further investigation of its effect on the quality of block appears warranted.

A potentially confounding factor in this meta-analysis was the inclusion of the study by Sng and colleagues<sup>20</sup> that had different methodology to the other trials. In that trial, labour epidural analgesia was initiated with a combined spinal-epidural technique and any epidural top-up that did



not produce a rapid effect was quickly topped up further before operation. This approach might account for the absence of a difference in onset time or intraoperative supplementation rate between the study solutions. When this study was excluded, lidocaine with epinephrine, with or without fentanyl, showed a greater, and clinically relevant, reduction in onset time compared with other solutions.

The merit of including unpublished studies in a meta-analysis can be questioned. Two unpublished trials met the inclusion criteria, one of which was used in the meta-analysis of intraoperative supplementation.<sup>21</sup> The majority of investigators involved in meta-analyses feel that unpublished studies should be included, with the caveat that it has been possible to assess their methodology adequately.<sup>4,3</sup> We were able to answer adequately the same risk of bias questions asked of the published trials and therefore were willing to include them. To investigate the effects of including unpublished material, we removed the one unpublished trial from the meta-analysis of intraoperative supplementation. This led to small reduction in the increased risk of supplementation associated with Bup/Levo, but the MD from other groups remained significant.

Another possible criticism of this meta-analysis is the absence of trials evaluating 3% 2-chloroprocaine, which is widely used as an epidural top-up solution for EmCS in North America. This LA has a rapid onset, but a short duration of action, and is not available in the UK. The two trials assessing its efficacy in these circumstances<sup>44, 45</sup> did not meet the inclusion criteria for this analysis.

In conclusion, the current literature does not strongly support one particular epidural top-up solution when converting labour epidural analgesia to epidural anaesthesia for surgery. Meta-analysis of the few trials investigating this topic was limited by both small numbers of trials and methodological variance, but indicates that bupivacaine or levobupivacaine 0.5% is the least efficacious with respect to both the speed of onset and quality of block. Ropivacaine 0.75% is most effective for reducing the need for supplementation of intraoperative block, while lidocaine 2% with epinephrine, with or without fentanyl, produces the fastest onset of surgical block.

This meta-analysis highlights the need for a multicentre, double-blinded, randomized controlled trial to address the question of the optimal solution for EmCS. Such a trial would need to be powered adequately for the incidence of intraoperative supplementation and onset time of block and should use a method of block assessment that is widely supported and clinically applicable. Until further information is available, if a rapid onset block is required, such as for a category 1 EmCS, using lidocaine 2% with epinephrine, and probably fentanyl, is recommended. Clinical trials also suggest that adding bicarbonate is beneficial in these circumstances, but there were insufficient such trials to perform meta-analysis and drug preparation time must be considered. When there is less time pressure, ropivacaine 0.75% appears optimal because it is associated with a reduced need for intraoperative supplementation.

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