

ORIGINAL RESEARCH

The Efficacy and Safety of Local Anesthetic Techniques for Postoperative Analgesia After Cesarean Section: A Bayesian Network Meta-Analysis of Randomized Controlled Trials

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Objective: Cesarean section (CS) is one of the most frequently performed major surgical interventions. Local anesthetic techniques, a universal component of perioperative multimodal analgesia, are reportedly effective in reducing pain scores and opioid requirements. However, the optimal local anesthetic technique for postoperative CS pain remains unclear. **Methods:** Six databases were searched, and a Bayesian network meta-analysis was performed. The outcomes included cumulative morphine consumption and pain scores at four time points, time to first analgesic request, postoperative nausea and vomiting, pruritus, and sedation

Results: Sixty-eight studies with 5039 pregnant women were included. Six local anesthetic techniques were involved, including transversus abdominis plane block (TAPB), ilioinguinal and iliohypogastric nerve block, quadratus lumborum blocks, transversalis fascia plane block, erector spinae block, and wound infiltration. Compared to inactive controls, TAPB reduced cumulative morphine consumption at 6, 12, 24, and 48 h, pain scores at 6, 12, and 24 h (with the exception of 24 h at rest), the risk of postoperative nausea and vomiting, and sedation. Compared with inactive controls, ilioinguinal and iliohypogastric nerve block reduced cumulative morphine consumption at 6 and 24 h and pain scores at 6, 12, and 24 h during movement. Compared with inactive controls, quadratus lumborum blocks reduced cumulative morphine consumption at 24 and 48 h and pain scores at 6 and 12 h and lengthened the time to first analgesic request. Compared with inactive controls, wound infiltration reduced cumulative morphine consumption at 12 and 24 h, pain scores at 12 and 24 h during movement, and risk of sedation. Compared with inactive controls, erector spinae block reduced pain scores at 6 and 12 h. Transversalis fascia plane block was found to have similar outcomes to inactive controls.

Conclusion: TAPB is the most comprehensive local anesthetic technique for postoperative CS analgesia in the absence of intrathecal morphine.

Keywords: Cesarean section, postoperative pain, network meta-analysis, local anesthesia

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Introduction

Cesarean section (CS) is one of the most frequently performed major surgical interventions. In 2012, 23 million CS were performed worldwide.¹ Although CS has some benefits, such as lowering the risk of birth injuries (eg, asphyxia, shoulder dystocia, fractures²), it can cause moderate to severe postoperative pain.³ This pain

must be taken seriously and treated in a timely manner because it may delay recovery, affect daily activities, and impact maternal psychological well-being.⁴ Furthermore, insufficient treatment may cause pain to become persistent⁵ and chronic.⁶ Optimizing analgesic regimens is a crucial aspect of pain management and can be a cost-effective way to improve postoperative outcomes and patient satisfaction.

Although opioids are commonly used for relief of postoperative pain after CS, opioid-related adverse effects such as nausea, vomiting, sedation, itching, and risk of delayed maternal respiratory depression can lead to other problems for new mothers, such as delayed initiation of breastfeeding and impairment of mother-infant bonding,⁷ all of which reduce overall patient satisfaction.^{7,8} Many scholars have studied the safety and efficacy of interventions for postoperative CS pain management and have suggested that various local anesthetic techniques, such as transversus abdominis plane block (TAPB), ilioinguinal and iliohypogastric nerve block (IIIH), quadratus lumborum blocks (QLB), transversalis fascia plane block (TFBP), erector spinae block (ESB), and wound infiltration (WI), are effective in reducing pain scores and opioid requirements. Given that the potential side effects of these local analgesic techniques are limited, they are frequently recommended. However, to date, no randomized controlled trial (RCT) has directly compared the six methods. Hence, uncertainty exists among clinicians concerning the best method for postoperative CS pain management.

In the absence of an RCT directly comparing all interventions of interest, a network meta-analysis (NMA) provides the best evidence on the most effective intervention. NMA allows for indirect pairwise comparisons of interventions through the use of a common comparison group and subsequent ranking of the interventions. To date, this method has not been applied to the study of the six available interventions for postoperative CS pain management. Thus, our aim was to determine which of these six interventions is the ideal method of pain relief after CS.

Methods

This NMA was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for NMA guidelines (<u>Supplemental Table S18</u>). A review protocol (number: CRD42021225699) was registered in the PROSPERO database (https://www.crd.york.ac.uk/PROSPERO). The Grading of Recommendations Assessment, Development and Evaluation (GRADE)

system was utilized to assess the certainty of the evidence using four levels (high, moderate, low, and very low). 10

Search Strategy

On December 12, 2020, two examiners independently searched for relevant studies in the following databases; PubMed, MEDLINE, Web of Science, EMBASE, ClinicalTrials.gov, and Cochrane Library. Search words included "cesarean section" ("transversus abdominis plane block," or "ilioinguinal and iliohypogastric nerve block," or "quadratus lumborum blocks," or "transversalis fascia plane block," or "erector spinae block," or "wound infiltration") and "postoperative pain." The details of the search strategy are shown in <u>Table S1</u>. At the same time, we searched the references of identified articles to find additional literature that met the inclusion criteria.

Data Extraction

Original studies were eligible if they met the following criteria: (I) was an RCT study; (II) full text available in English; and (III) assessed the efficacy and safety of local anesthetic techniques for postoperative analgesia after cesarean delivery in the absence of intrathecal morphine (ITM) or other long-acting neuraxial opioids. 11 Original studies were ineligible if they were (I) reviews, observational studies, case-control studies, abstracts, letters, or case reports; (II) studies involving combination blocks (ie, TAPB and rectus sheath); (III) studies with adjuncts; or (IV) laboratory animal literature. In the case of several publications from the same study, the study with the greatest number of cases and most relevant information was included.

For eligible studies, the first author, year of publication, anesthesia technique, groups and number of participants in each group, drug and dose, postoperative analgesia, and outcomes were extracted. Numeric data were gathered directly from tables or, when presented in graph form only, were inferred by digitizing the figure with GetData Graph Digitizer 2.26. 12

Outcomes

Cumulative morphine consumption and pain scores were the primary outcomes of this NMA. Four time points (6, 12, 24, and 48 h postoperatively) were chosen. Any opiate drugs other than intravenous morphine were converted to morphine equivalents. ¹³ Pain scores reported using visual analogue scales, verbal analogue scales, or numerical rating scores were converted to a standardized 0–100-point

score (where 0 = no pain and 100 = worst pain imaginable) for quantitative evaluations. Time to first analgesic request (min), postoperative nausea and vomiting (PONV), pruritus, and sedation were chosen as secondary outcomes.

Statistical Analysis

Prior to analysis, the risk of trial bias was assessed for the included studies using the Cochrane Collaboration's tool. Mean difference (MD) and 95% confidence interval (CI) were used to report cumulative morphine consumption, pain scores, and time to first analgesic request. Odds ratios (ORs) were used to report the risk of PONV, pruritus, and sedation. We evaluated the efficacy and safety of local anesthetic techniques for postoperative CS analgesia using an NMA. In this Bayesian NMA, random-effects and consistency models were used to analyze data and carry out the NMA (four chains, 50,000 iterations, 20,000 per chain). We assessed inconsistencies using the node-splitting method, and inconsistencies are reported by their Bayesian P values. An overall grading of the quality of evidence was conducted using the GRADE system. We

analyzed symmetry of comparison-adjusted funnel plots to evaluate possible small sample effects. All analyses were conducted using the "gemtc" package of R version 4.0.2 (R Foundation, Vienna, Austria) and Stata version 16.0 (StataCorp, College Station, TX, USA).

Results

Baseline Characteristics of Included **Studies**

A total of 602 potentially relevant publications were retrieved from six databases using our exhaustive search strategy (Supplemental Table S1). After screening, the full texts of 78 articles were reviewed. Finally, 68 RCTs were included in our final analysis (Figure 1). 14-81

The 68 RCTs were conducted between 1991 and 2021 and involved 5039 patients (Table 1). Six local anesthetic techniques were assessed in these studies, including ESB, IIIH, QLB, TAPB, TFPB, and WI (Figure 2). In total, 77.9% (53/68) involved spinal anesthesia; others involved general anesthesia or epidural anesthesia (3/68). Sixty-five were two-arm studies, and three were three-arm studies.

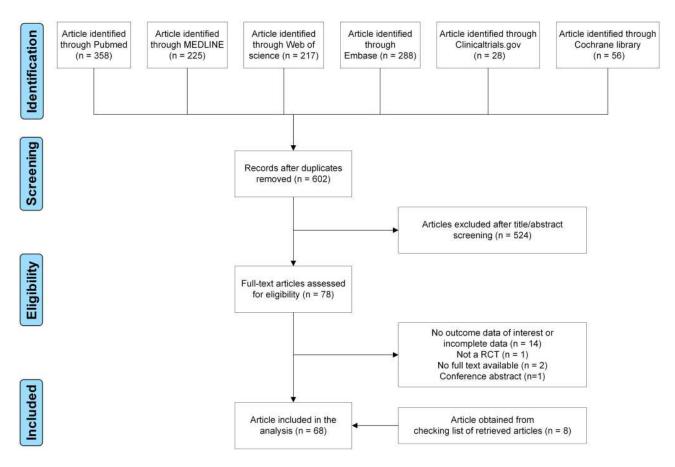


Figure I Flow-chart of study selection.

Table I Characteristics of Included Studies

| Author, year | Anesthesia technique | Groups (n) | Drug, dose | Postoperative analgesia | Outcomes |
|-------------------------------------|--|--------------|---|---|--|
| Trotter, 1991 ¹⁴ | GA | WI (14) | 20 ml of bupivacaine, maximum of 0.4 ml/kg | Morphine PCA | Cumulative morphine consumption, pain score |
| | | Control (14) | Saline | | |
| Ganta, 1994 ¹⁵ | GA | WI (20) | 20 ml of bupivacaine | Papaveretum, mefenamic acid | Pain score |
| | | Control (21) | No treatment | | |
| Mecklem, 1995 ¹⁶ | SA, 0.5% bupivacaine | WI (35) | 0.25% bupivacaine | Morphine PCA | PONV, pruritus |
| | | Control (35) | Saline | | |
| Fredman, 2000 ¹⁶ | SA, 8–10 mg of hyperbaric bupivacaine | WI (25) | 0.2% ropivacaine (100 mL) | Intravenous morphine, dipyrone | Cumulative morphine consumption, pain score |
| | | Control (25) | Sterile water | | |
| Bell, 2002 ¹⁸ | SA, 12 mg of 0.75% bupivacaine; EA | IIIH (31) | 12 mL of 0.5% bupivacaine on each side | Morphine PCA | Cumulative morphine consumption |
| | | Control (28) | Saline | | |
| Givens, 2002 ¹⁹ | EA | WI (20) | 0.25% bupivacaine | Morphine PCA | Cumulative morphine consumption, pain score |
| | | Control (16) | Saline | | |
| Zohar, 2006 ²⁰ | SA, 10 mg of hyperbaricbupivacaine | WI (30) | 0.25% bupivacaine | Intravenous morphine, diclofenac, ranitidine | Pain score |
| | | Control (30) | Sterile water | | |
| Lavand'homme, 2007 ²¹ | SA, 0.5% hyperbaric bupivacainewith sufentanil | WI (30) | 0.2% ropivacaine, 5 ml/h for 48 hours | Morphine PCA, diclofenac, acetaminophen | Cumulative morphine consumption, pain score |
| | | Control (30) | Saline | | |
| Al-Dehayat, 2008 ²² | GA | IIIH (30) | 10 ml of 0.5% bupivacaine on each side | Intramuscular morphine | Cumulative morphine consumption, pain score |
| | | Control (30) | Saline | 1 | |
| McDonnell, 2008 ²³ | SA, 12 mg of hyperbaricbupivacaine with fentanyl 25 µg | ТАРВ (25) | 0.75% bupivacaine 1.5 mg/kg on each side | Morphine PCA, acetaminophen, diclofenac | Cumulative morphine consumption, pain score, time to first analgesic request, sedation |
| | | Control (25) | Saline | | |

(Continued)

Table I (Continued).

| Author, year | Anesthesia technique | Groups (n) | Drug, dose | Postoperative analgesia | Outcomes | |
|-----------------------------------|---|--------------|--|--|--|--|
| Belavy, 2009 ²⁴ | SA, 11 mg of 0.5% bupivacaine with fentanyl 15 µg | TAPB (23) | 20 ml of 0.5% ropivacaine on each side | Morphine PCA, acetaminophen, diclofenac, ibuprofen | Cumulative morphine consumption, pain score, PONV, sedation, pruritus | |
| | | Control (24) | Saline | | | |
| Baaj, 2010 ²⁵ | SA, 10 mg of 0.5% bupivacaine with fentanyl 20 µg | TAPB (20) | 20 ml of 0.25% ropivacaine on each side | Morphine PCA | Cumulative morphine consumption, pain score, PONV | |
| | | Control (20) | Saline | | | |
| Sakalli, 2010 ²⁶ | GA | IIIH (30) | Neostigmine 0.04 mg/kg and atropine 0.02 mg/ kg | Tramadol PCA, meperidin | Pain score, PONV, sedation | |
| | | Control (30) | Saline | | | |
| McMorrow, 2011 ²⁷ | SA, 11–12.5 mg of hyperbaricbupivacaine with fentanyl 10 µg | TAPB (20) | 0.375 % bupivacaine 2 mg/ kg on each side | Morphine PCA, paracetamol, diclofenac | Pain score, pruritus | |
| | | Control (20) | Saline | | | |
| Sekhavat, 2011 ²⁸ | GA | WI (52) | 2% lidocaine | Morphine, mefenamic | Pain score | |
| | | Control (52) | 0.9% Sodium chloride | acid | | |
| Boztosun, 2012 ²⁹ | GA | IIIH (30) | 15 ml of 0.5% levobupivacaine on each side | Morphine PCA, diclofenac sodium, paracetamol | Cumulative morphine consumption, pain score, PONV, pruritus | |
| | | Control (30) | Saline | | | |
| Eslamian, 2012 ³⁰ | GA | TAPB (24) | I5 ml of 0.25% bupivacaine on each side | Intravenous tramadol, diclofenac | Cumulative morphine equivalents consumption, pain score, time to first analgesic request | |
| | | Control (24) | No treatment | | | |
| Hussein, 2012 ³¹ | SA, 2.5–3 ml of 0.5% heavy bupivacaine | TAPB (30) | 10 ml/h of 0.125% bupivacaine for 48 hours | Morphine PCA, paracetamol | Cumulative morphine consumption, PONV, sedation, pruritis | |
| | | WI (30) | 10 ml/h of 0.125% bupivacaine for 48 hours | | | |
| | | Control (30) | No treatment | | | |
| Jabalameli, 2012 ³² | SA, 2.5 ml hyperbaric bupivacaine 0.5% in dextrose 8.25% | WI (30) | 0.7 mg/kg of 0.25% bupivacaine | Morphine | Pain score, PONV | |
| | | Control (30) | Saline | | | |

(Continued)

Wang et al **Dove**press

Table I (Continued).

| Author, year | Anesthesia technique | Groups (n) | Drug, dose | Postoperative analgesia | Outcomes | |
|---------------------------------|--|--------------|---|--|---|--|
| Kessous, 2012 ³³ | GA or SA (7.5–10 mg of heavy bupivacaine) | WI (77) | 20 mL solution of 1% lidocaine | Propoxyphene hydrochloride, | Pain score | |
| | | Control (76) | Saline | paracetamol, diclofenac, meperidine | | |
| Sriramka, 2012 ³⁴ | SA, 7.5 mg of 0.5% hyperbaric bupivacaine and fentanyl 25 µg | TAPB (25) | 20 ml of 0.5% ropivacaine on each side | Intravenous morphine, acetaminophen | Cumulative morphine consumption | |
| | | Control (25) | Saline | | | |
| Tan, 2012 ³⁵ | GA | TAPB (20) | 20 ml of 2.5 mg/ ml levobupivacaine on each side | Morphine PCA | Cumulative morphine consumption, pain score, PONV, sedation | |
| | | Control (20) | No treatment | | | |

Abbreviations: EA, epidural anesthesia; ESB, erector spinae block; GA, general anesthesia; IIIH, ilioinguinal and iliohypogastric nerve block; PCA, patient-controlled analgesia; PONV, postoperative nausea and vomiting; QLB, quadratus lumborum block; SA, spinal anesthesia; TAPB, transversus abdominis plane block; TFPB, transversalis fascia plane block; WI, wound infiltration.

A total of 21 studies compared WI with a control; 17 studies compared TAPB with a control; ten studies compared IIIH with a control; seven studies compared QLB

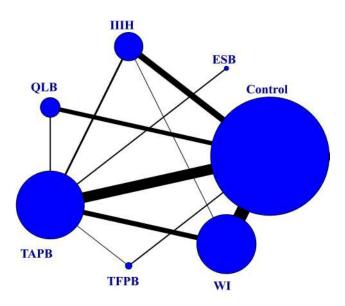


Figure 2 A network plot of eligible comparisons among different local anesthetic techniques.

All included studies

Notes: Circles represent the intervention as a node in the network, lines represent direct comparisons using randomized controlled trials and the thickness of lines corresponds to the number of randomized controlled trials included in each comparison. Abbreviations: ESB, erector spinae block; IIIH, ilioinguinal and iliohypogastric nerve block; QLB, quadratus lumborum blocks; TAPB, transversus abdominis plane block; TFBP, transversalis fascia plane block; WI, wound infiltration.

with a control; and two studies compared TFPB with a control. No study compared ESB with a control. TAPB was compared with all other local anesthetic techniques. Drugs and dose, postoperative analgesia, and outcomes are shown in Table 1. Evaluation of bias risk for all RCTs is presented in Supplemental Figures S1 and S2

Primary Outcomes

Eleven studies reported cumulative morphine consumption at 6 h. Cumulative morphine consumption at 6 h was significantly lower for TAPB and IIIH than for controls (MD = -9.37, 95% CI: -14.52 to -4.11; MD = -15.29, 95% CI: -26.95 to -3.63, respectively). Fourteen studies reported cumulative morphine consumption at 12 h. Cumulative morphine consumption at 12 h was significantly lower for TAPB and WI than for controls (MD = -13.62, 95% CI: -21.59 to -5.54; MD = -13.36, 95% CI: -24.74 to -2.05, respectively). Thirty-five studies reported cumulative morphine consumption at 24h. Cumulative morphine consumption at 24h was significantly lower for TAPB, QLB, IIIH, and WI than for controls (Figure 3). Twelve studies reported cumulative morphine consumption at 48 h. Cumulative morphine consumption at 48 h was significantly lower for TAPB and QLB than for controls (MD = -24.81, 95% CI: -48.92 to -2.36; MD = -25.28, 95% CI: -48.82 to -1.78, respectively).

Pain scores at 6 and 12 h both at rest and during movement and at 24 h during movement were lower for

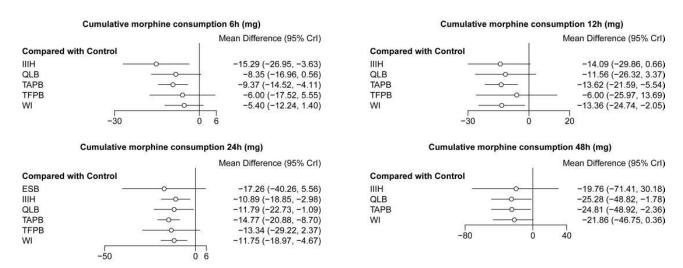


Figure 3 Forest plots of network meta-analysis of all trials for cumulative morphine consumption at each time point. Abbreviations: ESB, erector spinae block; IIIH, ilioinguinal and iliohypogastric nerve block; QLB, quadratus lumborum blocks; TAPB, transversus abdominis plane block; TFBP, transversalis fascia plane block; WI, wound infiltration.

TAPB both than for controls (Figure 4). Pain scores were lower for ESB and QLB at 6 and 12 h both at rest and during movement than for controls (Figure 4). Pain scores were lower for IIIH at 6, 12, and 24 h during movement than for controls (Figure 4). Pain scores were lower for WI at 12 and 24 h during movement than for controls (Figure 4). Pain scores were similar between TFPB and controls (Figure 4). Pairwise comparisons are shown in Supplemental Tables S2-S13.

Secondary Outcomes

QLB lengthened the time to first analgesic request compared with controls (MD = 966.76, 95% CI: 262.82-1662.52). TAPB reduced the risk of PONV compared with controls (OR = 0.37, 95% CI: 0.15-0.86). TAPB and WI reduced the risk of sedation compared with controls (OR = 0.19, 95% CI: 0.05-0.58; OR = 0.17, 95% CI: 0.03-0.69, respectively, Figure 5). Pairwise comparisons are shown Supplemental Tables S14-S17.

Inconsistencies, Certainty of Evidence, and Publication Bias

Evaluations of inconsistencies for all outcomes are presented in Supplemental Figures S3-S5. We noted a significance level of P > 0.05 for most cases, which indicates that inconsistencies were not sufficient to influence the conclusions of this NMA. We used the GRADE system to evaluate the certainty of evidence (Table 2). No significant asymmetry was found in the funnel plots of major primary and secondary outcomes.

Discussion

This NMA is the largest review assessing the efficacy and safety of local anesthetic techniques after CS. A total of 68 RCTs involving 5039 patients were included. Our analysis provided the opportunity to both explore the network of evidence and combine all data available for treatment comparisons. In this first comprehensive NMA, we found that TAPB had many advantages, including reduced cumulative morphine consumption at 6, 12, 24, and 48 h, reduced pain scores at 6, 12, and 24 h, reduced risk of PONV, and reduced risk of sedation compared with inactive controls. IIIH, QLB, ESB, and WI each had their own limited advantages. However, TFPB was found to have similar outcomes to inactive controls. Using this fairly new method for comparing these six interventions for postoperative CS pain management, TAPB appeared to be the most comprehensive option.

Opioid use has risen dramatically in the past three decades. ITM and intrathecal diamorphine are currently considered the gold standard for analgesia following elective CS in the USA and United Kingdom, respectively.82 However, opioid overdose has become a leading cause of unintentional deaths, surpassing motor vehicle accidents in the USA.83 In the last decades, doctors have begun to reduce opioid use during and after CS. Because operations such as CS are a vulnerable time when most patients are first exposed to opioids, utilizing a different local anesthetic technique could play a large role in decreasing opioid exposure.

Various local anesthetic techniques, which are a universal component of any perioperative multimodal analgesia, have

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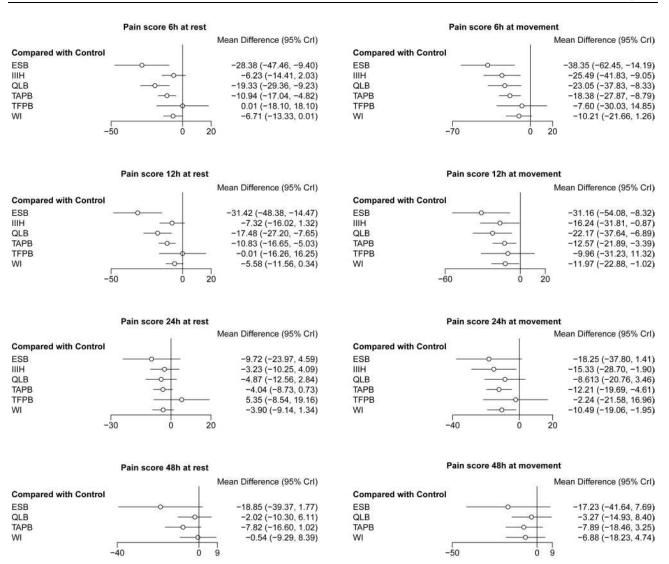


Figure 4 Forest plots of network meta-analysis of all trials for pain scores at each time point.

Abbreviations: ESB, erector spinae block; IIIH, ilioinguinal and iliohypogastric nerve block; QLB, quadratus lumborum blocks; TAPB, transversus abdominis plane block; TFBP, transversalis fascia plane block; WI, wound infiltration.

been explored in the last two decades. ⁸² TAPB, WI, IIIH, and QLB are the most widely used local anesthesia techniques, and recently an increasing number of doctors have employed ESB and TFPB for postoperative analgesia after CS. These six local anesthetic techniques can also be used together with non-opioid medications. Thus, patients may be able to remain opioid-free in the first few hours after CS.

Safety-related outcomes of local anesthetic techniques may include opioid-related side effects (ie, PONV, pruritus, sedation, respiratory depression, hypotension, and urinary retention), block-related complications (ie, hematoma, organ injury, local anesthetic systemic toxicity, and block failure), and effects on breastfeeding or mother-infant interaction. Respiratory depression, 14,37,51,78 hypotension, 32,37,38,53 urinary retention, 31,37,68,72 effects

on breastfeeding or mother-infant interaction, 43,65,77 and block-related complications 37,39,41,43,50,73,80 were rarely reported in the involved study. Therefore, we selected PONV, pruritus, and sedation as the safety outcomes of this NMA. Although their incidence is low, block-related complications, especially local anesthetic systemic toxicity, deserve attention, as pregnant women have increased cardiac output and reduced $\alpha 1$ -acid glycoprotein levels, which can increase perfusion speed at injection sites, enhance local anesthetic absorption, and increase peak free local anesthetic concentrations. 87

The efficacy outcomes of local anesthetic techniques usually include cumulative morphine consumption, pain scores, and time to first analgesic request. In this NMA, cumulative morphine consumption and pain scores were

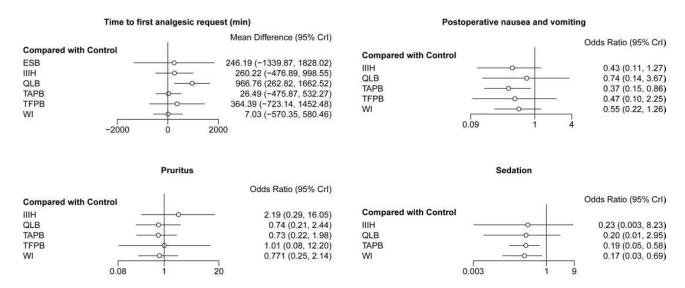


Figure 5 Forest plots of network meta-analysis of all trials for secondary outcomes. Abbreviations: ESB, erector spinae block; IIIH, ilioinguinal and iliohypogastric nerve block; QLB, quadratus lumborum blocks; TAPB, transversus abdominis plane block; TFBP, transversalis fascia plane block; WI, wound infiltration.

the primary outcomes. Time to first analgesic request, also called the duration of the local anesthetic technique, was also assessed. The results revealed that QLB lengthened the time to first analgesic request compared with TAPB, WI, and controls. QLB also effectively reduced pain scores 12 h after CS, which was consistent with the results of previous studies. 86,88,89 A recently published study revealed that QLB not only reduced acute pain scores (with similar efficacy to TAPB during the acute phase) but also reduced the severity of persistent postoperative pain months after CS (with better efficacy than TAPB during the chronic phase). 90 More RCTs are needed to confirm these findings. The durations of other local anesthetic techniques were similar.

TAPB was first described by Rafi et al in 200191 and has rapidly gained popularity in the study of local anesthesia for CS. TAPB is useful as a primary mode of analgesia in women undergoing CS who are not receiving neuraxial morphine for any reason.⁹² TAPB is also guite useful for opioid-tolerant patients, who often have poorly controlled postoperative pain. The major disadvantage of TAPB is that it does not provide visceral analgesia. This omission likely explains why multiple studies have failed to show that TAPB is superior to standard multimodal analgesia with ITM and why TAPB has not been shown to offer any additional analysesic benefits in the presence of ITM. In the present NMA, all included studies were conducted in the absence of ITM.

We found that TAPB decreased cumulative morphine consumption at each time point studied and reduced pain scores within 24 h. In addition, opioid-related side effects, such as PONV and risk of sedation, were also reduced, which may be related to the reduction in opioid consumption after TAPB. Although TAPB did not show an overwhelming advantage over the other five local anesthetic techniques in pairwise comparisons, the benefits of TAPB were clear, and we conclude that this is the most comprehensive local anesthetic technique. This is in agreement with previous meta-analysis studies. 11,93

We found that IIIH reduced pain scores at 6, 12, and 24 h during movement, and WI reduced pain scores at 12 and 24 h during movement. However, neither IIIH nor WI showed greater benefits in relieving resting pain. Due to the absence of a study directly comparing ESB and controls, the results of indirect comparisons showing that ESB reduced pain scores at 6 and 12 h need to be further confirmed. 74,76 Finally, we found that TFPB was not superior to controls for all outcomes we analyzed.

NMA can be used to estimate relative effects, even in the absence of pairwise clinical trials, through the use of a common comparator. Therefore, NMA is a particularly useful tool for decision-makers. Using NMA, we were able to compare six local anesthetic techniques. Altogether, the best available evidence suggests that TAPB is the most effective and safest local anesthetic technique for postoperative CS analgesia when ITM is

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Table 2 Summary of the Results of NMA and GRADE Quality Score Assessment for the Outcomes

| Outcome | Study Number | Participants Number | Conclusion | GRADE Quality Score |
|--|-----------------|------------------------|--|-----------------------|
| Cumulative morphine consumption 6h (mg) | П | 622 | TAPB and IIIH superior to the controls | Moderate [#] |
| Cumulative morphine consumption 12h (mg) | 14 | 813 | TAPB and WI superior to the controls | Moderate [#] |
| Cumulative morphine consumption 24h (mg) | 35 | 2308 | TAPB, QLB, WI, IIIH superior to the controls | Moderate [#] |
| Cumulative morphine consumption 48h (mg) | 12 | 702 | TAPB and QLB superior to the controls | Moderate [#] |
| Pain score 6h at rest | 50 | 3690 | TAPB, ESB, and QLB superior to the controls | Moderate [#] |
| Pain score 6h at movement | 30 | 2034 | TAPB, ESB, IIIH, and QLB superior to the controls | Moderate [#] |
| Pain score 12h at rest | 45 | 3182 | TAPB, ESB, and QLB superior to the controls | Moderate [#] |
| Pain score 12h at movement | 28 | 1937 | TAPB, ESB, QLB, IIIH and WI superior to the controls | Moderate [#] |
| Pain score 24h at rest | 49 | 3248 | No local anesthetic technique superior to the controls | Moderate [#] |
| Pain score 24h at movement | 33 | 2201 | TAPB, IIIH, and WI superior to the controls | Moderate [#] |
| Pain score 48h at rest | 16 | 951 | No local anesthetic technique superior to the controls | Low ^{#‡} |
| Pain score 48h at movement | 13 | 702 | No local anesthetic technique superior to the controls | Moderate [#] |
| Time to first analgesic request (min) | 23 | 1707 | QLB superior to the controls | Low ^{#‡} |
| PONV | 25 | 1864 | TAPB superior to the controls | Moderate [#] |
| Pruritus | 16 | 1199 | No local anesthetic technique superior to the controls | Moderate [#] |
| Sedation | 14 | 907 | TAPB and WI superior to the controls | Low ^{#‡} |

Notes: $^{\#}$ Rated down for serious imprecision; ‡ Rated down for serious inconsistency.

Abbreviations: ESB, erector spinae block; IIIH, ilioinguinal and iliohypogastric nerve block; PONV, postoperative nausea and vomiting; QLB, quadratus lumborum block; TAPB, transversus abdominis plane block; TFPB, transversalis fascia plane block; WI, wound infiltration.

not possible or desired, such as when general anesthesia is required for cesarean delivery.⁸⁵

Limitations

First, in some cases, the same intervention was performed in several different ways, but we pooled the different techniques into a single group for analysis. For example, two approaches to TAPB, lateral and posterior, were employed,

and QLB could be divided into QLB 1, QLB 2, and QLB 3.82 However, unlike previous studies, we could not perform subgroup analysis.11,94 Second, the drugs and doses used were not consistent across different studies of the same intervention, which limited the results of this NMA. Third, some included studies were single-center trials with limited sample sizes, which may have reduced the reliability of the results and conclusions of those studies.

Conclusion

The present NMA suggests that TAPB is the most comprehensive local anesthetic technique for postoperative CS analgesia in the absence of ITM.

Abbreviations

CI, confidence interval; CS, cesarean section; ESB, erector spinae block; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IIIH, ilioinguinal and iliohypogastric nerve block; ITM, intrathecal morphine; MD, mean difference; NMA, network metanalysis; OR, odds ratio; PONV, postoperative nausea and vomiting; QLB, quadratus lumborum blocks; RCT, randomized controlled trial; TAPB, transversus abdominis plane block; TFBP, transversalis fascia plane block; WI, wound infiltration.

Ethical Publication Statement

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Author Contributions

All authors contributed to data analysis and drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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Journal of Pain Research 2021:14 https://doi.org/10.2147/JPR.S313972 1569

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