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EDITED BY

Maria Caterina Pace,
University of Campania Luigi Vanvitelli,
Italy

REVIEWED BY

Vincenzo Pota,
University of Campania Luigi Vanvitelli,
Italy
Rajesh Kumar Kodali V.,
Sri Ramachandra University, India

*CORRESPONDENCE

Matheus Requena Escobar
✉ matheusrequena@hotmail.com

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Transversus abdominis plane block with liposomal bupivacaine versus standard bupivacaine for postoperative analgesia in elective cesarean section: a systematic review and meta- analysis

Matheus Requena Escobar^{1*} , Sara Amaral² , Leticia Oku¹ ,
Vitor Felippe³ , Carlos Darcy Bersot⁴ and
Thomas Rolf Erdmann⁵

¹Centro Universitário Lusiada, Santos, Brazil, ²Department of Anesthesiology, Duke University Medical Center, Durham, NC, United States, ³Departamento de Anestesiologia, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil, ⁴Universidade Federal de São Paulo (UNIFESP), Escola Paulista de Medicina, Programa de Pós-Graduação em Medicina Translacional, São Paulo, Brazil, ⁵Departamento de Cirurgia, Universidade Federal de Santa Catarina, Florianópolis, Brazil

Background: Transversus abdominis plane (TAP) block with bupivacaine is commonly used for analgesia after cesarean deliveries. Liposomal bupivacaine has been incorporated into TAP blocks to potentially prolong analgesic effects and reduce opioid use. However, its effectiveness for elective cesarean section remains uncertain.

Methods: This review was registered on PROSPERO (CRD420251046460). We systematically searched MEDLINE, EMBASE, and the Cochrane Library for studies comparing TAP block with liposomal bupivacaine plus conventional bupivacaine vs. conventional bupivacaine alone in women undergoing elective cesarean delivery. Meta-analyses were performed using random-effects models. Heterogeneity was assessed with I^2 statistics and Cochran's Q test.

Results: Three randomized controlled trials (meta-analysis) and one retrospective study (qualitative synthesis) were included, comprising 695 patients. Of these, 357 (51.4%) received TAP block with liposomal bupivacaine. Its use was associated with significantly decreased opioid consumption at 24 h (mean difference -0.76 mg IV morphine equivalents; 95% CI -1.46 to -0.07 ; $p = 0.03$; $I^2 = 20\%$). However, the absolute 24-hour reduction was small and well below the accepted minimal clinically important difference (MCID), suggesting no clinically meaningful opioid-sparing benefit. No significant differences were found in opioid consumption at 48 h, time to first rescue analgesia, or the incidence of nausea, dizziness, or serious adverse events.

Conclusion: In this meta-analysis, adding liposomal bupivacaine to TAP block resulted in a statistically significant but clinically trivial reduction in 24-hour opioid consumption (below accepted MCID thresholds), with no significant differences at 48 h. Time to first rescue analgesia and adverse events were similar between groups.

KEYWORDS

analgesia, bupivacaine, cesarean section, meta-analysis, nerve block, pain management

1 Introduction

Cesarean delivery is among the most common surgical procedures globally (1). Despite current multimodal approaches, many patients continue to experience moderate to severe pain in the early postoperative phase, often requiring increased opioid analgesia (2). The transversus abdominis plane (TAP) block is an increasingly used regional anesthesia technique that enhances analgesic results and reduces the requirement for systemic opioids (3). Liposomal bupivacaine, a long-acting formulation approved for surgical site infiltration, has recently been incorporated into TAP blocks to enhance analgesic duration and minimize opioid-related side effects (4).

The clinical efficacy of integrating liposomal bupivacaine into TAP blocks remains uncertain (4). Given the inconsistent findings regarding opioid use, pain scores, and side effects observed with conventional bupivacaine alone, liposomal formulations have been introduced as an attempt to improve analgesic duration and overall efficacy. Despite its increasing use, anesthesiologists and obstetric providers continue to debate its elevated cost and unclear additional benefits. There is ongoing discussion regarding the clinical significance of combining liposomal and conventional bupivacaine compared to traditional TAP block techniques (5).

Due to the lack of consistency, a systematic review and meta-analysis was conducted to compare the efficacy of TAP blocks using liposomal and conventional bupivacaine vs. bupivacaine alone in patients undergoing cesarean deliveries.

2 Materials and methods

This systematic review and meta-analysis was registered in PROSPERO database (CRD420251046460). It was performed and reported following the guidelines established by the Cochrane Collaboration Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (6, 7).

2.1 Eligibility criteria

This meta-analysis includes studies that fulfilled the specified inclusion criteria: (1) randomized controlled trials (RCTs); (2) adult women (≥ 18 years); (3) undergoing elective cesarean delivery and (4) reporting at least one prespecified outcome. Observational studies (prospective or retrospective) were eligible for inclusion in the systematic review for contextual completeness; however, due to confounding and higher risk of bias, quantitative synthesis (meta-analysis) was restricted to RCTs.

We excluded the following: (1) non-peer-reviewed studies, including preprints and conference abstracts without full-text access; (2) studies that did not specify the use of liposomal bupivacaine in the intervention group; and (3) studies with overlapping populations. No restrictions were imposed in terms of language or publication date. In case of missing relevant data, efforts were undertaken to reach out to the corresponding authors.

The research question was framed using a PICO approach: Population (adult women undergoing elective cesarean delivery);

Intervention (TAP block with liposomal bupivacaine plus conventional bupivacaine); Comparator (TAP block with conventional bupivacaine alone); Outcomes [opioid consumption (24 and 48 h, IV MME), pain scores at rest and with movement, time to first rescue analgesia and adverse events].

2.2 Search strategy and data extraction

MEDLINE, Embase, and the Cochrane Library were systematically searched from inception until April 10, 2025. The full electronic search strategies for MEDLINE (PubMed), Embase, and the Cochrane Library are provided in the [Supplementary Appendix](#). The search strategy included the terms “cesarean section,” “C-section,” “transversus abdominis plane block,” “TAP block,” “bupivacaine,” “liposomal,” and “Exparel.” Reference lists from all included studies and pertinent systematic reviews were manually examined for additional eligible studies. The search was conducted independently by two reviewers, who also extracted the data independently based on the predefined criteria. Discrepancies were addressed through consensus.

2.3 Endpoints

The main outcomes of interest were (1) postoperative opioid consumption at 24 and 48 h, measured in intravenous morphine milligram equivalents (IV MME); (2) postoperative pain scores at rest and during movement at 24 and 48 h postoperatively; (3) time to first rescue analgesia in hours; and (4) adverse events, which included nausea, vomiting, dizziness, and serious complications. A meta-analysis was conducted using pooled results when a minimum of three studies provided data for a specific endpoint.

2.4 Quality assessment

We evaluated the risk of bias using version 2 of the Cochrane Risk of Bias assessment tool (RoB 2) for all RCTs and the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) for observational studies (8, 9). All included studies were independently assessed by two authors, with any disagreements resolved through consensus. For RoB 2, risk of bias was classified into three categories: “low risk,” “some concerns,” and “high risk.” For ROBINS-I, risk of bias was categorized as “low,” “moderate,” “serious,” or “critical.”

2.5 Statistical analysis

For dichotomous outcomes, we calculated risk ratios (RR) with 95% confidence intervals (CI) using the Mantel-Haenszel method and for continuous outcomes, we calculated mean differences (MD) with 95% CI using the inverse-variance method. Random-effects models were used for all pooled analyses to account for clinical and methodological variability

across studies. *P*-values less than 0.05 were considered statistically significant.

Heterogeneity was assessed using the Cochran Q test and I^2 statistic, where I^2 values exceeding 40% were considered substantial heterogeneity. A *p*-value of less than 0.10 in the Q test was considered statistically significant for indicating heterogeneity, consistent with Cochrane guidelines (6). Random-effects models were used irrespective of the level of heterogeneity, consistent with Cochrane guidance when clinical and methodological diversity is anticipated (6). Sensitivity analyses were performed using a leave-one-out method, in which each included study was removed in turn to evaluate the stability and robustness of the overall effect estimates. This approach allows identification of potentially influential studies that may impact the direction or magnitude of the pooled outcomes. Funnel plots and formal tests for small-study effects were not performed because fewer than 10 studies were available for each meta-analysis. Therefore, publication bias could not be reliably assessed and cannot be excluded. Review Manager (RevMan) version 5.4.1 was used to perform all statistical analyses (10).

We assessed the certainty of evidence for each prespecified outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Evidence from randomized trials started as high certainty and was downgraded based on risk of bias, inconsistency, indirectness, imprecision, and publication bias. A Summary of Findings table is provided in the [Supplementary Appendix](#).

3 Results

3.1 Study selection and baseline characteristics

Our systematic search identified 545 records. After removing 167 duplicates, 378 records were screened by title and abstract; 12 articles were then reviewed in full text ([Figure 1](#)).

Finally, 3 RCTs (4, 5, 11) and 1 retrospective observational study (12) were included, comprising 695 patients, of whom 357 (51.4%) received TAP block with liposomal bupivacaine combined with bupivacaine ([Figure 1](#)). All studies evaluated patients undergoing elective cesarean delivery under spinal anesthesia, with morphine administered intrathecally in three of the four studies (4, 11, 12). TAP blocks were administered either at the conclusion of the procedure (4, 5, 12) or intraoperatively during surgical closure (11). Further baseline characteristics are summarized in [Table 1](#). Quantitative synthesis was restricted to randomized controlled trials; the retrospective observational study was included for contextual completeness and summarized qualitatively due to serious risk of bias.

3.2 Pooled analysis

Postoperative opioid consumption at 24 h was reported in 3 studies including 294 patients. The TAP block with liposomal bupivacaine resulted in significantly lower opioid use compared to bupivacaine alone (MD -0.76 mg IV MME; 95% CI -1.46 to

-0.07 ; $p=0.03$; $I^2=20\%$; [Figure 2A](#)). At 48 h, opioid use was comparable between groups (MD -1.62 mg IV MME; 95% CI -4.85 to 1.60 ; $p=0.32$; $I^2=62\%$; [Figure 2B](#)). Additionally, there was no statistically significant difference regarding time to first rescue analgesia (MD 3.08 h; 95% CI -1.96 to 8.12 ; $p=0.23$; $I^2=10\%$; [Figure 2C](#)).

The incidence of nausea and vomiting was similar between groups (RR 1.52; 95% CI 0.79 to 2.92; $p=0.21$; $I^2=19\%$; [Figure 3A](#)). Likewise, no statistically significant difference was observed for dizziness (RR 1.04; 95% CI 0.43 to 2.54; $p=0.93$; $I^2=0\%$; [Figure 3B](#)). Serious adverse events were rare and comparably distributed between groups (RR 0.92; 95% CI 0.24 to 3.60; $p=0.91$; $I^2=0\%$; [Figure 3C](#)). All randomized trials explicitly reported no occurrences of block-related complications or local anesthetic systemic toxicity (LAST).

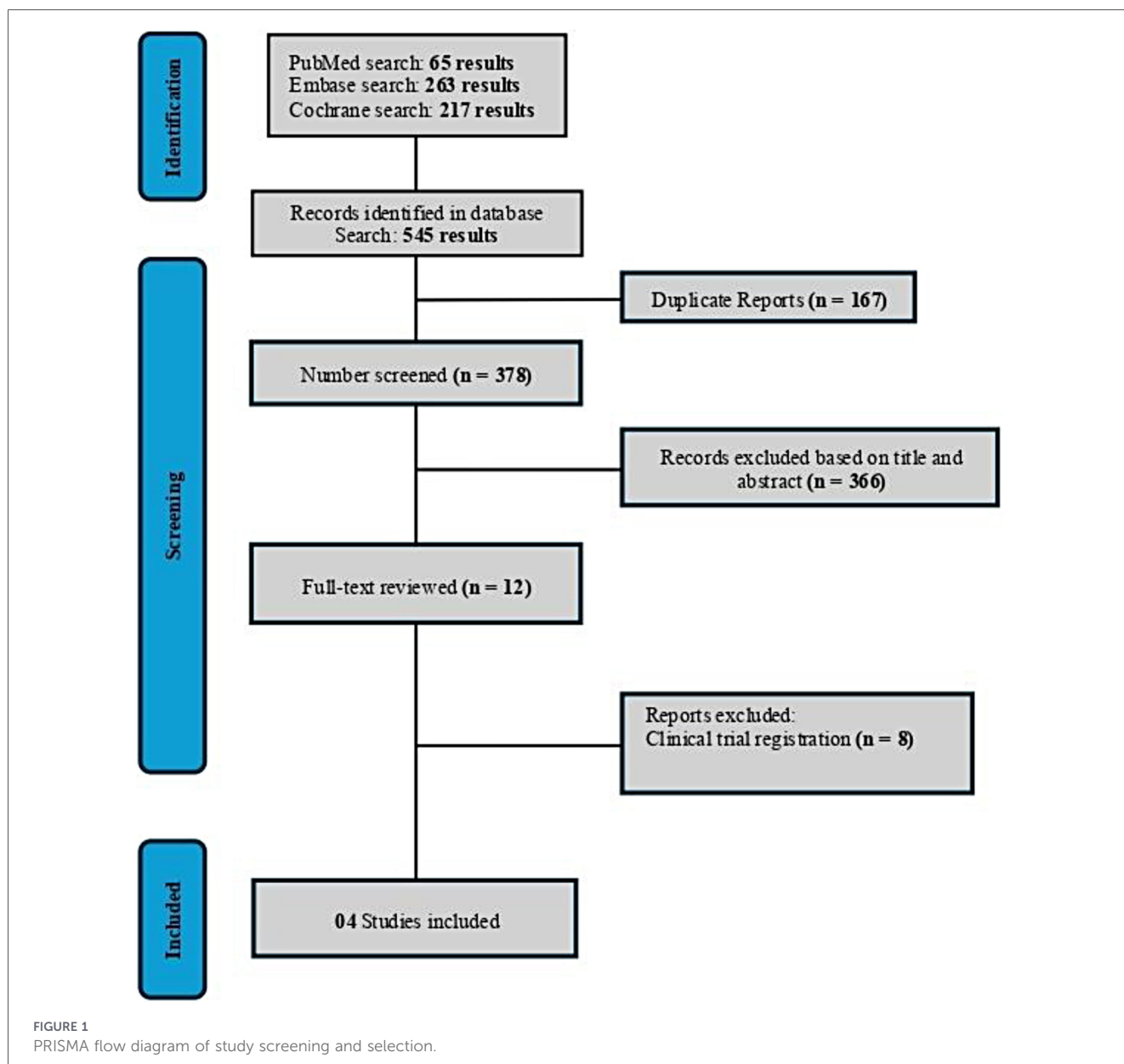
Pain outcomes were reported heterogeneously across trials. Liu et al. reported pain at rest and with movement (VAS 0-10) at multiple points, whereas Nedeljkovic et al. summarized pain as AUC through 72 h and Antony et al. reported interval-based nurse-recorded pain ratings. Given differences in scales, time points, and summary metrics, pain outcomes were not pooled and are summarized descriptively.

3.3 Sensitivity and exploratory analyses

Postoperative opioid consumption within the first 24 h was reported by all RCTs (4, 5, 11). The pooled analysis showed a statistically significant reduction in opioid use, favoring the TAP block with liposomal bupivacaine (MD -0.76 mg IV MME; 95% CI -1.46 to -0.07 ; $p=0.03$; $I^2=20\%$; [Figure 2A](#)). The leave-one-out sensitivity analysis ([Supplementary Figures A and B](#)) found notable variability across studies: exclusion of Liu et al. (5) reduced the effect size and made the result non-significant (MD -0.40 mg IV MME; 95% CI -1.56 to 0.76 ; $p=0.27$; $I^2=16\%$), while exclusion of Antony et al. (11) increased the magnitude and statistical significance (MD -1.03 mg IV MME; 95% CI -1.65 to -0.41 ; $p=0.001$; $I^2=0\%$).

For opioid consumption at 48 h, the pooled result did not reach statistical significance in the overall analysis (MD -1.62 mg IV MME; 95% CI -4.85 to 1.60 ; $p=0.32$; $I^2=62\%$; [Figure 2B](#)). Sensitivity analysis revealed fluctuation: exclusion of Liu et al. (5) yielded a statistically significant benefit (MD -3.78 mg IV MME; 95% CI -7.24 to -0.33 ; $p=0.03$; $I^2=0\%$; [Supplementary Figure D](#)), while exclusion of Antony et al. (11) or Nedeljkovic et al. (4) resulted in non-significant findings ($p=0.53$ and $p=0.81$, respectively), as seen in [Supplementary Figures E and C](#).

Time to first rescue analgesia was assessed in all RCTs (4, 5, 11). Leave-one-out analysis indicated that Liu et al. (5) exerted a strong influence on the effect size: when excluded, the pooled result inverted direction and became non-significant (MD -1.00 h; 95% CI -9.96 to 7.97 ; $p=0.83$; $I^2=0\%$; [Supplementary Figure G](#)). Exclusion of Antony et al. (11) increased the mean difference and nearly achieved statistical significance (MD 4.70 h; 95% CI -0.16 to 9.57 ; $p=0.06$; $I^2=0\%$; [Supplementary Figure F](#)), while exclusion of Nedeljkovic et al. (4) had a minimal impact on the overall effect estimate, with a modest



rise in heterogeneity (MD 2.78 h; 95% CI -2.94 to 8.50; $p = 0.24$; $I^2 = 28\%$; [Supplementary Figure H](#)).

[Tables 2, 3](#). The certainty of evidence was moderate for opioid consumption at 24 h and low to very low for the remaining outcomes (GRADE; [Supplementary Appendix](#)).

3.4 Quality assessment

The risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool for RCTs (8). One study (Nedeljkovic et al., 2020) was judged to have a low risk of bias across all domains. Two studies (Liu et al., 2024, and Antony et al., 2024) were rated as having “some concerns” overall due to issues related to the selection of the reported result, despite showing low risk of bias in all other domains. The retrospective study by Feerman et al., 2021 (12), was evaluated using the ROBINS-I tool (9) and was judged to have an overall serious risk of bias due to the lack of adjustment for key confounders. A detailed summary of the risk of bias assessment is presented in

4 Discussion

This systematic review and meta-analysis evaluated the effect of incorporating liposomal bupivacaine into TAP blocks in patients undergoing cesarean delivery. The findings show a statistically significant association between this combination and a reduction in opioid consumption during the first 24 postoperative hours (4, 5, 11). However, pain outcomes were reported heterogeneously across trials and did not demonstrate a consistent clinically meaningful improvement; likewise, no significant differences were observed regarding time to first rescue analgesia, or the incidence of adverse events such as

TABLE 1 Baseline characteristics of included studies.

Characteristics	Nedeljkovic, 2020 (4) TAP LB (n = 97) TAP BUPI (n = 89)	Liu, 2024 (5) TAP BUPI + LB (n = 49) TAP BUPI (n = 49)	Feierman, 2021 (12) TAP LB (n = 116) TAP BUPI 2020 (n = 82) TAP BUPI (2012) (n = 30)	Antony, 2024 (12) TAP LB (n = 31) TAP BUPI (n = 29)
Study design	Randomized controlled trial	Randomized controlled trial	Retrospective cohort	Randomized controlled trial
Country	United States	China	United States	United States
Study duration	2017–2018	2024	2020	2021–2022
Age, years	34/33	32 (4.8)/31 (4.9)	33 ± 10/30 ± 5/30 ± 5	33.0 ± 3.8/33.7 ± 5.3
ASA score II (%)	93.8/91.0	100/100	–	–
ASA score III (%)	6.2/9.0	–	–	–
Weight, kg (mean ± SD)	86.7 ± 17.8/87.5 ± 17.5	79 ± 11.6/80 ± 13.2	84 ± 22/79 ± 17/76 ± 18	27.9/36.0
BMI (mean ± SD)	–	30 (27,32)/30 (27,34)	32 ± 9/30 ± 6/28 ± 9	36 ± 7.4/32.6 ± 4.9
Height, cm (mean ± SD)	163.3 ± 6.6/163.5 ± 7.8	161 (158,167)/160 (158,165)	160.02 ± 7.62/162.56 ± 15.24/ 162.54 ± 12.7	–
Race (%) - Caucasian	69.1/71.9	–	–	–
Race (%) - Black	13.4/16.9	–	–	–
Race (%) - Asian	5.2/5.6	–	–	–
Race (%) - Other	12.4/5.6	–	–	–
Prior C-section (%)	35.1/39.3	59.2/67.3	–	64.5/72.4

Age, mean; BMI, Body Mass Index in kg/m², median; ASA, American Society of Anesthesiologists physical status classification; C-section, cesarean section; TAP, transversus abdominis plane; LB, liposomal bupivacaine; BUPI, conventional bupivacaine.

nausea, vomiting, and dizziness. Notably, none of the included studies reported complications related to the block, such as local anesthetic systemic toxicity (LAST) (4, 5, 11, 12).

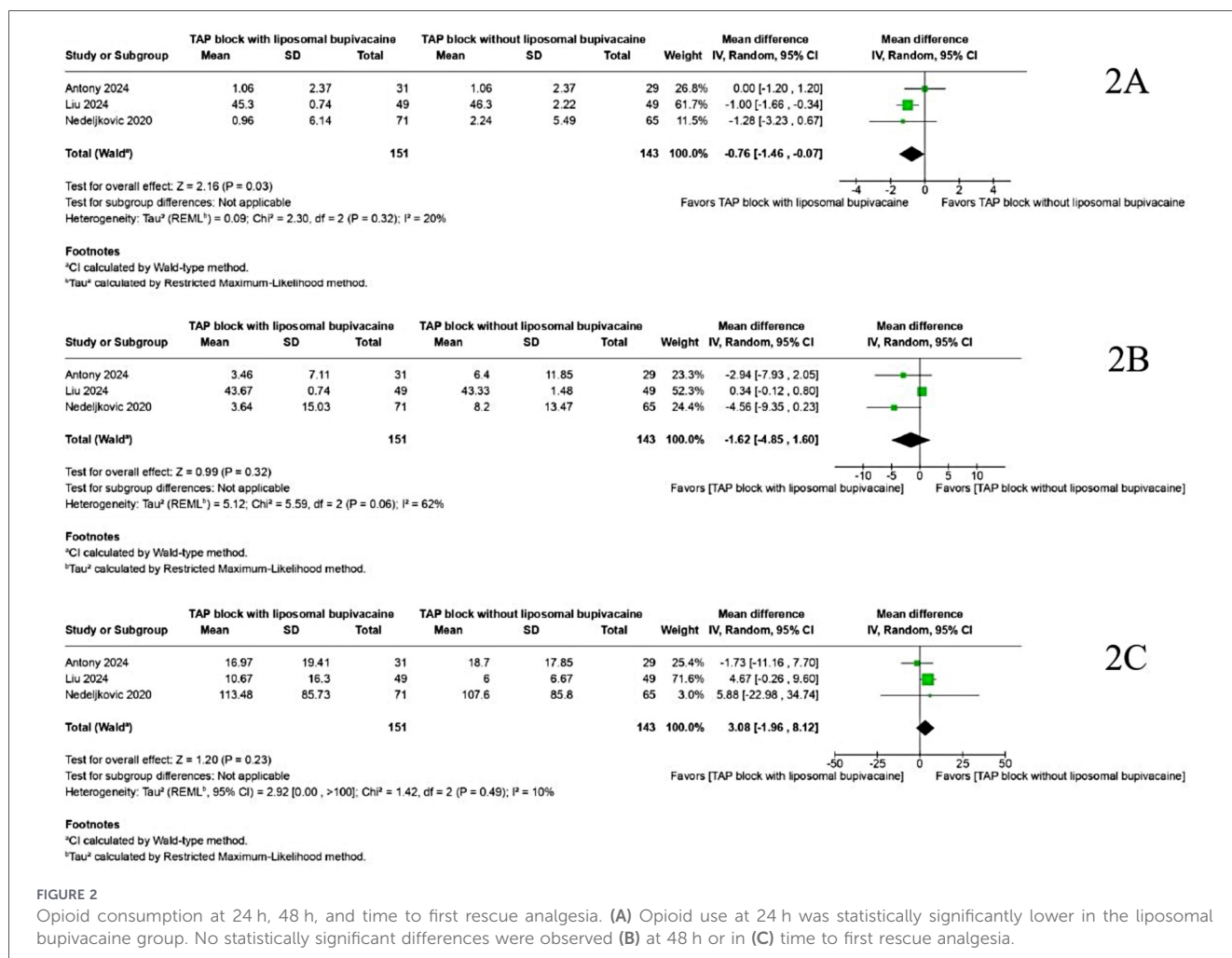
Although the first 24 h postoperatively showed a statistically significant decrease in opioid consumption, this difference did not meet the minimal clinically important difference (MCID), usually estimated at 10 mg of MME in the context of postoperative analgesia (13). The MCID serves as a clinical threshold that helps distinguish between statistical significance and a perceptible therapeutic benefit. Interventions that do not exceed this threshold are unlikely to meaningfully impact patient-centered outcomes or justify changes in clinical practice, particularly in settings where opioid-sparing strategies, such as intrathecal morphine, are already in place (14).

Liu et al. (5) reported similar opioid consumption between treatment groups, while Antony et al. (11) observed a reduction in opioid requirements only at hospital discharge, with no significant difference during the immediate postoperative period. These individual findings align with the overall pattern observed in our meta-analysis, which revealed a statistically significant reduction in opioid consumption at 24 h that did not exceed the clinical threshold of the MCID of 10 mg MME (13). Previous reviews, such as that by Hussain et al., have similarly reported modest and inconsistent reductions associated with the use of the liposomal formulation, particularly in interfascial blocks (15). Taken together, the available evidence suggests that the routine use of liposomal bupivacaine in TAP blocks does not

confer a clinically meaningful reduction in opioid consumption following cesarean delivery.

Our findings did not show any advantage of liposomal bupivacaine in prolonging the time to first rescue analgesia. Despite the theoretical advantage of sustained drug release, no significant prolongation of the time to supplemental analgesia was found in the pooled analysis. Pain outcomes were inconsistently reported across trials (rest vs. movement, varying time points, and different summary metrics), limiting direct comparisons. Where differences in pain intensity were observed, they were small and did not consistently reach commonly accepted MCID thresholds for acute pain on 0-10 scales (13). These findings are consistent with those of Hamilton et al., who reported limited benefits of liposomal bupivacaine in interfascial plane blocks, in contrast to more favorable results observed with direct surgical site infiltration (16). The absence of effect in these outcomes may be attributable to the concomitant use of intrathecal morphine, the short duration of postoperative assessment, and the inherent limitations of unidimensional pain scales.

One of the most widely discussed hypotheses for the inconsistent results of liposomal bupivacaine in fascial plane blocks centers on its limited physical dispersion. As a multivesicular formulation composed of large and dense liposomes, its diffusion across interfascial planes may be limited (17). In blocks such as the TAP block, which relies on a broad spread of the anesthetic solution between the internal oblique



and transversus abdominis muscles, this property may result in incomplete coverage of the abdominal somatic nerves. Studies as Ilfeld et al. (17) explore this possibility, suggesting that while liposomal bupivacaine may be effective in localized surgical site infiltration, its mechanical structure may limit its efficacy in interfascial plane blocks due to impaired spread along tissue planes.

The heterogeneous findings regarding the efficacy of liposomal bupivacaine observed in cesarean deliveries are not unique to this surgical context. Studies across various surgical specialties, including abdominal, orthopedic, and urologic procedures, have also reported variable results, with significant differences attributed to the mode of administration, type of regional block, and use of adjunctive analgesic strategies (18, 19). While some studies suggest clinical benefit when liposomal bupivacaine is used for localized surgical infiltration, such as in total knee arthroplasty or mastectomy (20, 21), others have found no advantage over conventional bupivacaine, particularly in fascial plane blocks. Systematic reviews by Hamilton et al. (16) and Hussain et al. (15) highlight this inconsistency, pointing to the absence of a clear clinical benefit in settings where broad anatomical dispersion of the anesthetic is required. These findings suggest that the performance of liposomal bupivacaine may be influenced more by the pattern of application and underlying anatomical considerations than by the type of surgical procedure itself.

Several previous meta-analyses have evaluated the use of liposomal bupivacaine in interfascial plane blocks; however, they differ substantially from the present review in terms of clinical focus and inclusion criteria. For instance, the meta-analysis by Hussain et al. (15) examined various abdominal blocks across multiple surgical procedures, including non-obstetric interventions, with considerable heterogeneity in comparators and anesthetic techniques. In contrast, our meta-analysis was strictly limited to patients undergoing elective cesarean delivery, comparing the combination of liposomal and conventional bupivacaine vs. conventional bupivacaine alone, exclusively within the context of TAP blocks. This more homogeneous approach allows for clinically specific and practice-relevant interpretations relevant to obstetric anesthesia. Furthermore, by including only studies with complete datasets and standardized outcome reporting, we reduced the risk of methodological bias often associated with broader systematic reviews (6).

From a value-based care perspective, liposomal bupivacaine has a substantially higher acquisition cost than plain bupivacaine. In the absence of clinically meaningful improvements in opioid consumption and pain outcomes, routine use of liposomal bupivacaine for TAP block after elective cesarean delivery may represent low-value care. Formal cost-effectiveness evaluations in obstetric populations remain

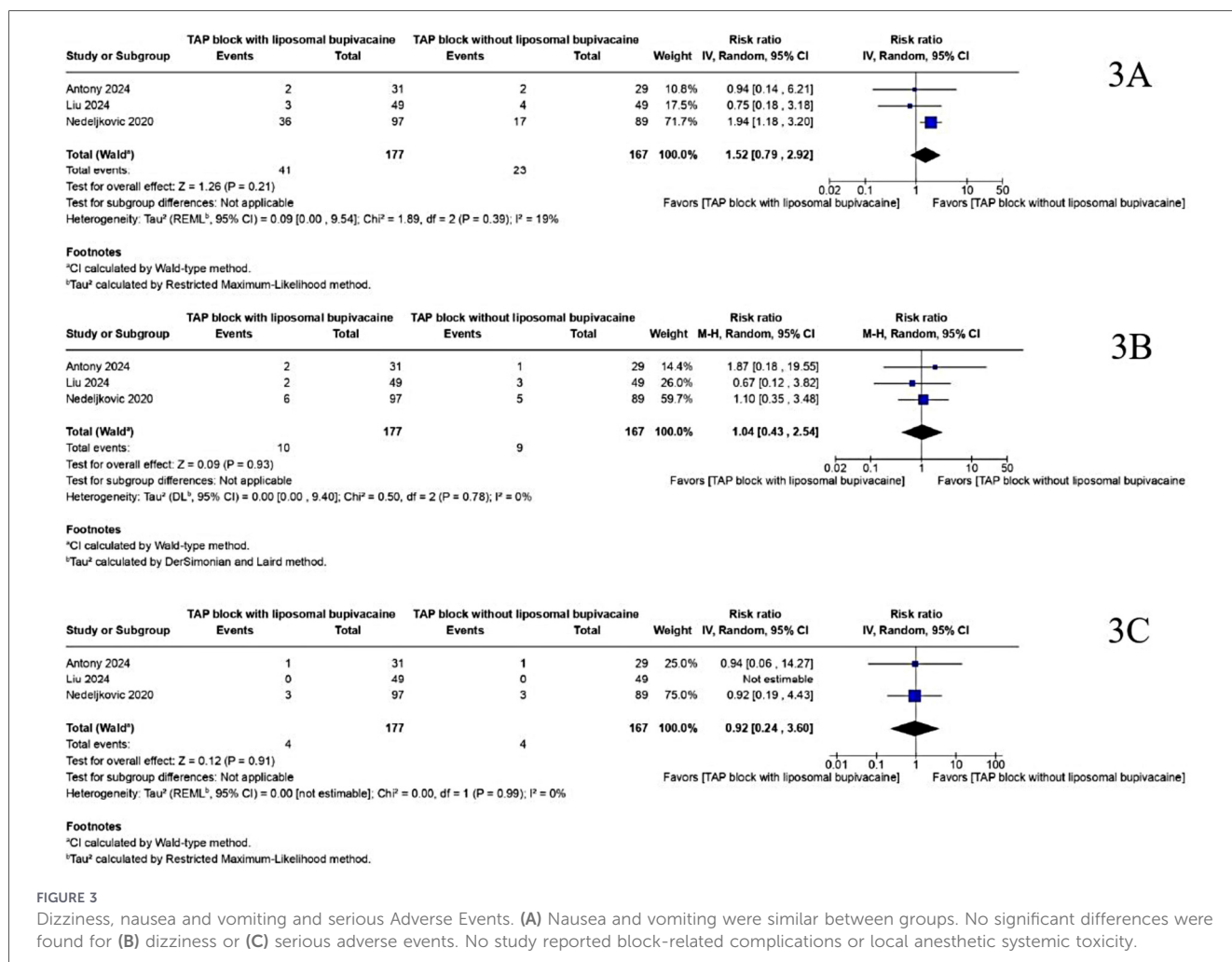


FIGURE 3

Dizziness, nausea and vomiting and serious Adverse Events. (A) Nausea and vomiting were similar between groups. No significant differences were found for (B) dizziness or (C) serious adverse events. No study reported block-related complications or local anesthetic systemic toxicity.

TABLE 2 Risk of bias assessment (RoB-2).

Study	Bias from randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in measurement of the outcomes	Bias in selection of the reported result	Overall risk of bias
LIU 2024	Low	Low	Low	Low	Some concerns	Some concerns
ANTONY 2024	Low	Low	Low	Low	Some concerns	Some concerns
NEDLJKOVIC 2020	Low	Low	Low	Low	Low	Low

limited and should be incorporated into future adequately powered pragmatic trials.

This review has limitations. The small number of included studies limited the statistical power of the meta-analysis, precluding analyses of additional outcomes and the formal assessment of publication bias (6). Although a statistically significant reduction in opioid consumption was noted at 24 h, the absolute effect size did not meet the threshold for clinical relevance (MCID) (13), potentially due to insufficient sample size. A major limitation is that intrathecal morphine was used in most included studies. Because intrathecal morphine is a key determinant of post-cesarean analgesia, it may create a ceiling

effect that masks any incremental opioid-sparing or analgesic benefit attributable to liposomal bupivacaine. Therefore, the applicability of these findings may be limited to settings in which neuraxial opioids are routinely used, and the results may not generalize to protocols that omit or minimize intrathecal opioids. Additional heterogeneity, such as variations in anesthetic concentration, volume administered, timing of TAP block placement, and multimodal regimens, may also have influenced the results. To reduce these limitations, we applied consistent outcome definitions and random-effects models. Furthermore, none of the included studies were adequately powered to detect rare adverse events, such as local anesthetic

TABLE 3 Risk of bias assessment (ROBINS-I).

Study	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias judgement
Feierman 2021	Serious	Low	Low	Low	Low	Moderate	Moderate	Serious

systemic toxicity (LAST), delayed mobilization, or sedation-related complications. These methodological limitations provide directions for future research. Subsequent studies should evaluate whether the presence or absence of intrathecal morphine modifies the effect of liposomal bupivacaine and should include patient-centered outcomes, such as quality of recovery, maternal satisfaction, and breastfeeding success, beyond traditional analgesic endpoints.

5 Conclusion

This meta-analysis showed no clinically meaningful reduction in opioid consumption with the addition of liposomal bupivacaine to TAP blocks during cesarean delivery. The statistically significant 24-hour reduction was small and below MCID thresholds. Additionally, there was no significant difference between groups regarding time to first rescue analgesia and incidence of adverse events.

Author contributions

MR: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. SA: Methodology, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. LO: Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. VF: Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. CB: Resources, Visualization, Writing – original draft, Writing – review & editing. TE: Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was not used in the creation of this manuscript.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fanes.2026.1731998/full#supplementary-material>

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