JOURNAL OF WORLD SCIENCE
https://jws.rivierapublishing.id/index.php/jws
Volume 4 No. 3. March 2025
P-ISSN: 2828-8726
E-ISSN: 2828-9307

THE EFFICACY OF LIPOSOMAL BUPIVACAINE IN MANAGING POSTOPERATIVE PAIN, A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROL TRIALS

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ABSTRACT
Postoperative pain, a significant surgical complication, presents a considerable challenge to the healthcare system, resulting in adverse outcomes, disability, prolonged hospitalization, and financial strain. This study seeks to evaluate the effectiveness of liposomal bupivacaine (LB) in postoperative pain management by a systematic review and meta-analysis of existing research. PubMed, CENTRAL, Embase, Web of Science, and Google Scholar were searched for randomized controlled trials (RCTs) published until January 2025, focusing on adults (18 years) undergoing surgical procedures where LB was administered via wound infiltration, nerve blocks, or periarticular injections. Primary outcomes included pain scores (VAS/NRS/BPI), opioid consumption, adverse events (e.g., nausea/vomiting), and patient satisfaction. A total of 763 papers were discovered in the literature, of which 21 (Barrington et al., 2017) were included. The pooled standardized mean difference (SMD) was -0.53, (95% CI, [-0.84, -0.23]; p = 0.0006) signifying a statistically significant decrease in pain levels favoring the intervention group. No significant disparity in opioid use was found between the two groups. The combined odds ratio (OR) was 0.78 (95% confidence interval (CI): [0.46 to 1.31]; [p = 0.35), indicating no significant difference in the incidence of nausea and vomiting. LB is effective in alleviating pain, diminishing opiate usage, and alleviating postoperative side effects.

Keyword: efficacy and safety; Liposomal Bupivacaine; Opioid reduction; postoperative analgesia; RCT

INTRODUCTION

Approximately 300 million surgeries are conducted annually worldwide for various reasons. Nonetheless, postoperative pain, a significant surgical complication, presents a considerable challenge to the healthcare system, resulting in adverse outcomes, disability, prolonged hospitalization, and financial strain. Insufficient management of acute postoperative pain may lead to additional complications, including respiratory infections, psychological issues, deep vein thrombosis, and chronic pain (Weiser et al., 2020). Optimal pain management during and after surgery enhances the patient's quality of life and satisfaction, improves clinical outcomes, accelerates patient discharge and recovery, reduces the incidence of postoperative chronic pain, and ultimately alleviates the economic burden (Gan, 2017).

In 2016 cross-sectional observational research including over 15,000 UK surgical patients revealed that 11 percent experienced severe pain, while 37 percent felt moderate discomfort during the first 24 hours post-surgery (Walker et al., 2016). Such information is not limited to the UK. A German prospective cohort study of 50,523 patients indicated that up to 47.2 percent suffered serious pain (NRS of at least 8) within the initial twenty-four hours post-surgery. Still, this prevalence varied according to the kind of operation

conducted. Moreover, moderate to severe pain persists during the prolonged surgical recovery period (Gerbershagen et al., 2013). Similarly, A cross-sectional study in China involving 26,193 adult patients revealed that 48.7% experienced moderate-to-severe pain on the first postoperative day. Furthermore, pain severity was linked to suboptimal recovery and decreased patient satisfaction (Liu et al., 2023). Opioids have historically been employed for the management of acute postsurgical and postprocedural pain; however, numerous studies indicate that adverse events associated with opioids negatively impact patient health outcomes (Phillips et al., 2017). A study published retrospective review of clinical and administrative records from over 135,000 patients treated using opioids following in-hospital Surgery or endoscopic interventions revealed that 10.6% experienced opioid-related adverse events (AEs). These AEs were linked to negative results, such as increased inpatient mortality, extended length of stay, and elevated 30-day rate of readmission (Ma et al., 2017).

Bupivacaine has been combined with liposomes to develop liposomal extended-release bupivacaine to deliver prolonged analgesia over 72 hours by single-dose administration. An instance of a bupivacaine liposome injectable solution is EXPAREL® (Pacira Pharmaceuticals, Inc., San Diego, CA, USA). EXPAREL® is an aqueous solution of multivesicular liposomes (DepoFoam® drug delivery system; Pacira Pharmaceuticals, Inc.) that contains bupivacaine at a concentration of 13.3 mg/ml. Following the administration of EXPAREL® into soft tissue, bupivacaine is gradually released from the multivesicular liposomes over time (Brown & Morrison, 2004).

Notwithstanding these benefits, the clinical efficacy of liposomal bupivacaine is still contentious. Prior meta-analyses indicate that liposomal bupivacaine (LB) is effective in managing postoperative pain, diminishes opioid usage, and alleviates postoperative nausea and vomiting. However, numerous studies concentrate exclusively on wound infiltration techniques and are restricted to specific surgical interventions (Solis-Pazmino et al., 2024; Zhang et al., 2017). Conversely, other studies indicate that LB may be ineffective in specific contexts, demonstrating limited or inconsistent outcomes in postoperative pain management and opioid usage (Jiang et al., 2023).

The inconsistency in results highlights the necessity for a thorough assessment of the current evidence to ascertain the actual effectiveness of liposomal bupivacaine across various therapeutic contexts. This study seeks to evaluate the efficacy of liposomal bupivacaine in postoperative pain management by a systematic review and meta-analysis of existing research. The objective is to elucidate its effects on pain alleviation, opioid usage, unfavorable occurrences of postoperative nausea and vomiting, and overall patient contentment.

METHOD

This study employed a systematic review and meta-analysis approach following PRISMA 2020 guidelines to evaluate liposomal bupivacaine's (LB) effectiveness in

postoperative pain management. Randomized controlled trials (RCTs) published until January 2025 were included, focusing on adults (≥18 years) undergoing surgical procedures where LB was administered via wound infiltration, nerve blocks, or periarticular injections. Control groups received non-liposomal anesthetics or placebos. Primary outcomes included pain scores (VAS/NRS/BPI), opioid consumption, adverse events (e.g., nausea/vomiting), and patient satisfaction. Exclusion criteria removed non-human studies, non-RCTs, and small sample sizes (<10 participants). Searches were conducted in PubMed, CENTRAL, Embase, Web of Science, and Google Scholar using keywords like "Bupivacaine Liposomal" and "Postoperative Analgesia," with EndNote X9 used for deduplication. Two reviewers independently screened studies, extracted data (e.g., demographics, LB dosage, outcomes), and resolved discrepancies via a third reviewer. Missing data were excluded to maintain analysis integrity.

Study quality was assessed using Cochrane's Risk of Bias tool (v5.1.0), evaluating seven domains (e.g., randomization, blinding). Data synthesis was performed in RevMan 5.4 using random-effects models for continuous (SMDs) and dichotomous outcomes (ORs). Heterogeneity was measured via I^2 statistics (≥50% indicating significance), and publication bias was assessed through funnel plots and Egger's test. Subgroup analyses were omitted to focus on LB's aggregate effects. The methodology ensured rigorous, transparent evaluation of LB's efficacy in postoperative pain control.

RESULTS AND DISCUSSION

Results

Selection of Studies

A total of 763 papers were discovered in the literature search, of which 21 (Barrington et al., 2017; Cox et al., 2022; Egan et al., 2021; Elmer et al., 2022; Fidkowski et al., 2021; Hadzic et al., 2016; Hamilton et al., 2022; Hubler et al., 2021; Hungerford et al., 2021; James et al., 2023; Kim et al., 2022; Mazloomdoost et al., 2017; Meyer et al., 2021; Okoroha et al., 2016; Schroer et al., 2015; Schwartz et al., 2024; Sethi et al., 2019; Shih et al., 2022; Vandepitte et al., 2017; Yeap et al., 2022). were randomized controlled trials (RCTs) that satisfied the inclusion criteria. The cumulative sample size across all investigations was 2198 patients.

Characteristics, and Patient Demographics

The trials were performed throughout several surgical disciplines, including 13 studies (Barrington et al., 2017; Elmer et al., 2022; Hadzic et al., 2016; Hamilton et al., 2022; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Okoroha et al., 2016; Schroer et al., 2015; Schwartz et al., 2024; Vandepitte et al., 2017) in Orthopedics, 1 study (Mazloomdoost et al., 2017) in Urology, 2 studies (Elmer et al., 2022; Meyer et al., 2021) in Gynecology, 1 study (Shih et al., 2022) in Cardiology, 1 study (Cox et al., 2022) in Ophthalmology, 1 study (Yeap et al., 2022) in Colorectal, 1 study (James et al., 2023) in oral

surgery and 1 study (Egan et al., 2021) in Reconstructive surgery. The publications were published between 2015 and 2024. The research showed variability in the application method of LB, where 7 studies (Cox et al., 2022; Egan et al., 2021; James et al., 2023; Mazloomdoost et al., 2017; Meyer et al., 2021; Okoroha et al., 2016; Sethi et al., 2019) reported in LI, 11 studies (Elmer et al., 2022; Fidkowski et al., 2021; Hadzic et al., 2016; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Schwartz et al., 2024; Shih et al., 2022; Vandepitte et al., 2017; Yeap et al., 2022) reported in NB, and 3 studies (Barrington et al., 2017; Hamilton et al., 2022; Schroer et al., 2015) reported in PAI. frequently in combination with general anesthesia.

The dosage of LB varied between 133 and 266 mg, where 8 studies (Barrington et al., 2017; Cox et al., 2022; James et al., 2023; Mazloomdoost et al., 2017; Okoroha et al., 2016; Sethi et al., 2019; Shih et al., 2022; Yeap et al., 2022) reported in volume, and 13 studies (Egan et al., 2021; Elmer et al., 2022; Fidkowski et al., 2021; Hadzic et al., 2016; Hamilton et al., 2022; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Meyer et al., 2021; Schroer et al., 2015; Schwartz et al., 2024; Vandepitte et al., 2017) reported in dose. Sample sizes in the studies varied from 12 to 267 people, for the type of pain scale, 11 studies (Barrington et al., 2017; Egan et al., 2021; Hamilton et al., 2022; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; Mazloomdoost et al., 2017; Okoroha et al., 2016; Schroer et al., 2015; Sethi et al., 2019; Yeap et al., 2022) were evaluated using VAS, 6 studies (Elmer et al., 2022; Fidkowski et al., 2021; Hadzic et al., 2016; Kim et al., 2022; Schwartz et al., 2024; Vandepitte et al., 2017) were evaluated using NRS, 1 study was evaluated using BPI (James et al., 2023) and 3 studies (Cox et al., 2022; Meyer et al., 2021; Shih et al., 2022) were not reported specific PS. For the intervention, 13 studies (Barrington et al., 2017; Cox et al., 2022; Egan et al., 2021; Fidkowski et al., 2021; Hadzic et al., 2016; Hubler et al., 2021; Hungerford et al., 2021; James et al., 2023; Mazloomdoost et al., 2017; Okoroha et al., 2016; Schwartz et al., 2024; Sethi et al., 2019; Shih et al., 2022) reported LB alone and 8 (Elmer et al., 2022; Hamilton et al., 2022; Hattrup et al., 2021; Kim et al., 2022; Meyer et al., 2021; Schroer et al., 2015; Vandepitte et al., 2017; Yeap et al., 2022) reported combined Liposomal Bupivacaine + Hydrochloride Bupivacaine study characteristics and patient demographics.

The average age of participants varied from 47.0 to 70.0 years, with three studies (Okoroha et al., 2016; Shih et al., 2022; Yeap et al., 2022) presenting age as median (IQR) and four studies (Fidkowski et al., 2021; Hubler et al., 2021; Mazloomdoost et al., 2017; Meyer et al., 2021) exclusively involving female participants, while three studies (Elmer et al., 2022; Sethi et al., 2019; Shih et al., 2022) included solely male participants. Overall, the data were quantified numerically across all studies, with female counts ranging from 5 to 151 and male counts from 2 to 130, although only two studies (Sethi et al., 2019; Shih et al., 2022) provided gender distribution in percentage form. The findings indicated variability, with pain ratings for both groups averaging between 0.9 and 565 (SD: 0.3 to 135) at 24, 48, and 72 hours, and opioid use averaging from 0.4 to 66.1 (SD: 0.3 to 61.5) for both groups

during the same intervals. The incidence of adverse events such as nausea and vomiting ranged from 2 to 61, whereas patient satisfaction levels varied from 9 to 51 across both groups. Variations in reporting resulted in some studies presenting data solely on pain ratings, while others concentrated primarily on opiate intake, adverse events (nausea and vomiting), or patient satisfaction.

Quality of assessment

The quality of assessment indicates that all included studies were evaluated as having a low risk of bias across all seven domains.

1) Primary outcomes:
    a) Effectiveness of Liposomal Bupivacaine (Pain Assessment): A pooled study of postoperative pain ratings at 24, 48, and 72 hours was performed utilizing a random-effects model. Pain ratings were presented as the mean and standard deviation (SD) in all trials examined.

        24 hours: Sixteen studies (Barrington et al., 2017; Cox et al., 2022; Egan et al., 2021; Elmer et al., 2022; Hadzic et al., 2016; Hamilton et al., 2022; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Mazloomdoost et al., 2017; Okoroha et al., 2016; Schroer et al., 2015; Schwartz et al., 2024; Sethi et al., 2019; Vandepitte et al., 2017) documented pain levels at 24 hours following surgery. The standardized mean difference (SMD) of -0.53, (95% CI, [-0.84, -0.23]; $p = 0.0006$) signifying a statistically significant decrease in pain levels favoring the intervention group. Significant heterogeneity was noted among studies ($X^2 = 138.81$; $df = 15$; $p < 0.00001$; $I^2 = 89\%$), indicating considerable variety in effect sizes among the included trials.

        Fifteen research (Barrington et al., 2017; Cox et al., 2022; Egan et al., 2021; Elmer et al., 2022; Hamilton et al., 2022; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; James et al., 2023; Kim et al., 2022; Mazloomdoost et al., 2017; Okoroha et al., 2016; Schroer et al., 2015; Schwartz et al., 2024; Sethi et al., 2019) yielded data on pain ratings at 48 hours. The study indicated a standardized mean difference (SMD) of -0.41 (95% CI, [-0.64, -0.18]; $p = 0.0005$), signifying a moderate decrease in pain levels. Consistent with the 24-hour result, heterogeneity persisted at a high level ($X^2 = 66.09$; $df = 14$; $p < 0.00001$; $I^2 = 79\%$), indicating variability in the effects among trials.

        At 72 hours, pain ratings were documented in fifteen investigations (Barrington et al., 2017; Cox et al., 2022; Egan et al., 2021; Elmer et al., 2022; Hadzic et al., 2016; Hamilton et al., 2022; Hattrup et al., 2021; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Mazloomdoost et al., 2017; Okoroha et al., 2016; Schroer et al., 2015; Schwartz et al., 2024; Sethi et al., 2019), yielding a standardized mean difference (SMD) of -0.35 (95% CI, [-0.53, -0.17]; $p < 0.0001$). This outcome also indicates a substantial decrease in

discomfort. The heterogeneity was considerable (X^2 = 42.09; df = 14; p = 0.0001; I^2 = 67%), showing reduced variability relative to the 24- and 48-hour periods, although still implying some discrepancies across the research findings.

2) Secondary Outcomes:
   a) Opioid Utilization: Opioid usage was evaluated at 24-, 48-, and 72-hours post-surgery, utilizing the mean and standard deviation for both the intervention and control cohorts.

      Twelve studies (Egan et al., 2021; Elmer et al., 2022; Hamilton et al., 2022; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Mazloomdoost et al., 2017; Meyer et al., 2021; Okoroha et al., 2016; Sethi et al., 2019; Shih et al., 2022; Vandepitte et al., 2017) documented opioid use at 24 hours following surgery. The pooled standardized mean difference (SMD) was -0.15 (95% CI, [-0.40, 0.09]; p = 0.22), indicating no statistically significant decrease in opioid intake relative to controls. Significant heterogeneity was observed among the studies (X^2 = 44.24; df = 11; p < 0.00001; I^2 = 75%), signifying a considerable degree of variability in the outcomes.

      48 hours: Thirteen research (Egan et al., 2021; Elmer et al., 2022; Hamilton et al., 2022; Hubler et al., 2021; Hungerford et al., 2021; James et al., 2023; Kim et al., 2022; Mazloomdoost et al., 2017; Meyer et al., 2021; Okoroha et al., 2016; Sethi et al., 2019; Shih et al., 2022; Vandepitte et al., 2017) supplied data on opioid use at the 48-hour mark. The aggregated standardized mean difference (SMD) was -0.08 (95% CI, [-0.39, 0.23]; p = 0.61), indicating no significant disparity in opioid use. The heterogeneity was substantial (X^2 = 72.23; df = 12; p < 0.00001; I^2 = 83%), indicating significant variability among the studies.

      72 Hours: Thirteen trials (Egan et al., 2021; Elmer et al., 2022; Hamilton et al., 2022; Hubler et al., 2021; Hungerford et al., 2021; Kim et al., 2022; Mazloomdoost et al., 2017; Meyer et al., 2021; Okoroha et al., 2016; Schroer et al., 2015; Sethi et al., 2019; Shih et al., 2022; Vandepitte et al., 2017) documented opioid usage at 72 hours, yielding a pooled standardized mean difference (SMD) of -0.24 (95% CI, [-0.43, -0.04]; p = 0.02), indicating a modest although statistically significant decrease in opioid consumption favoring the intervention. The heterogeneity was modest (X^2 = 28.14; df = 12; p = 0.005; I^2 = 57%), suggesting reduced outcome variability compared to prior time points.
   b) Post-operative nausea and vomiting: Five articles (Barrington et al., 2017; Hadzic et al., 2016; Hubler et al., 2021; Schroer et al., 2015; Schwartz et al., 2024) documented that Seventy-five patients in the liposomal bupivacaine (LB) group felt nausea, compared to ninety-four in the control group. The combined odds ratio (OR) was 0.78 (95% CI: [0.46 to 1.31]; p = 0.35), indicating no

statistically significant difference in the incidence of nausea between the two groups. The heterogeneity was minimal, evidenced by an X^2 value of 0.95 (df = 4, p = 0.92) and I^2 = 0%, signifying no significant variability across the studies included for nausea.

Two studies (Hadzic et al., 2016; Schwartz et al., 2024) documented that Vomiting occurred in 30 patients in the LB group and 45 in the control group. The aggregated odds ratio (OR) was 0.68 (95% CI, [0.24 to 1.93]; p = 0.46), indicating no statistically significant difference between the groups. The heterogeneity for vomiting was minimal, evidenced by an X^2 value of 0.28 (df = 1, p = 0.59) and I^2 = 0%, signifying low variability across the trials. Refer to Figure.5. Liposomal bupivacaine (LB) did not markedly decrease the occurrence of nausea or vomiting relative to the control group. The minimal variation among trials indicates uniform results for these outcomes. Consequently, LB does not seem to exert a substantial influence on the mitigation of postoperative nausea or vomiting.

c) Patient Satisfaction: Patient satisfaction was documented by 184 individuals in the liposomal bupivacaine (LB) cohort, in contrast to 192 individuals in the control cohort. The odds ratio (OR) was 0.82 (95% CI, [0.50, 1.35]; p = 0.44), suggesting no statistically significant disparity in satisfaction between the two groups. The heterogeneity was limited (X^2 = 4.86; df = 5; p = 0.43; I^2 = 0%), indicating uniform results across the trials with negligible variability.

3) Publication Bias: Publication bias was assessed with a funnel plot diagram. The funnel plot depicting pain scores, opioid intake, adverse events (nausea and vomiting), and patient satisfaction was symmetrical, suggesting a little risk of publication bias, and Egger's regression test was not performed.

Discussion

This meta-analysis assesses the effectiveness of liposomal bupivacaine (LB) in alleviating postoperative pain, minimizing opiate usage, lowering side effects such as nausea and vomiting, and enhancing patient satisfaction across different surgical procedures.

The meta-analysis showed that VAS scores went down significantly 24, 48, and 72 hours after surgery. This suggests that liposomal bupivacaine (LB), either by itself or in combination with bupivacaine hydrochloride (BH), effectively reduced pain after several surgeries. In line with what Nguyen et al. (2023) found, that pain scores went down significantly at all time points tested (24, 48, and 72 hours) when they compared the pain-relieving effects of LB versus long-acting LA for peripheral nerve block following a variety of surgical procedures. Similarly, Zhang et al. (2017) reported that bupivacaine diminished pain scores at 12-, 24-, and 48-hours post-total hip arthroplasty. However, our study further evaluated the 72-hour outcome across various surgical types, offering a more comprehensive perspective on pain management. Zhang et al. (2017) showed that liposomal

bupivacaine provided better pain relief than regular bupivacaine 24 and 48 hours after total knee arthroplasty. However, our results are different from those of Kolade et al. (2019) who found that liposomal bupivacaine (LB) was the same as non-liposomal agents (NLAs) after shoulder surgery, with no significant improvement in VAS ratings at 24 and 48 hours. Ma et al. (2017) also revealed non-significant variations in VAS at 48- and 72-hours post-total hip arthroplasty, akin to Cao & Pan (2017) who found that VAS did not diminish at 24, 48, and 72 hours following total shoulder arthroplasty. Disparities in research demographics, surgical procedures, and postoperative care regimens may further highlight the diversity in results.

The overall quantity of opioid use was a significant metric for assessing the analgesic efficacy of liposomal bupivacaine. Our research found significant opioid use only at 72 hours, with non-significant findings at 24 and 48 hours. This contrasts with the findings of DInges et al. (2021) and Wang et al. (2017) who saw considerable opioid decreases at postoperative day one, but no significant reductions at 48 and 72 hours, suggesting an early opioid-sparing impact Wang et al. (2017) underscored the efficacy of periarticular injection in total knee arthroplasty. Chen et al. (2023) documented a substantial reduction in opioid usage after 48 hours, although the reductions at 24 and 72 hours were not statistically significant following total knee arthroplasty. Kuang et al. (2017) talked about how well periarticular injections work for total knee arthroplasty and found that opioid use didn't go down significantly within 72 hours. On the other hand, Zhao et al. (2019) showed a significant reduction in total morphine consumption 24- and 48-hours post-infiltration for total joint arthroplasty. The opioid-sparing effect of LB can change depending on the time after surgery, the injection technique, the type of surgery, and the person's recovery pattern. Understanding these changes is important for making the best postoperative pain management plans for each surgical procedure.

Our research revealed no substantial changes in nausea and vomiting, aligning with several prior studies concerning orthopedic operations. In particular, Zhao et al. (2019) conducted a study on total joint arthroplasty, focusing exclusively on nausea. Our study, which evaluated both nausea and vomiting, found no significant differences, while Chen et al. (2023) presented data related to total knee arthroplasty. In contrast, Wang et al. (2017) and Zhang et al. (2017) found a significantly reduced incidence of nausea and vomiting in the Liposomal bupivacaine groups linked with periarticular and infiltration administration of LB, respectively, in total knee arthroplasty and total hip arthroplasty. Differences in patient demographics, surgical procedures, or anesthesia methods may account for the disparities in nausea and vomiting outcomes, potentially influencing the prevalence of postoperative nausea and vomiting. This implies that LB may provide benefits in specific surgical scenarios, underscoring the necessity for additional research into how surgical techniques and individual patient characteristics impact LB's effectiveness in addressing postoperative complications.

Although several studies, such as those by Vyas, et al [38] indicate that LB enhances patient satisfaction with ratings above 80%, our research did not reveal a notable increase. This suggests that while LB may effectively manage pain and reduce opioid usage, it may not consistently enhance the overall patient experience, as measured by satisfaction.

The findings underscore the intricacy of satisfaction as an outcome, potentially affected by other aspects outside pain management, such as expectations, recovery experiences, and side effects. Our data suggest that LB has the potential to alleviate pain and decrease opioid usage, especially after 72 hours; however, the impact on nausea, vomiting, and patient satisfaction varies among trials. Divergences in the administration of LB, patient attributes, surgical methodologies, and varying anesthetic approaches likely account for the observed disparity in results.

CONCLUSION

Liposomal bupivacaine effectively reduces pain ratings at 24, 48, and 72 hours postoperatively, with a notable decrease in opioid usage only observed at 72 hours. Both intervention and control groups reported similar levels of nausea, vomiting, and patient satisfaction. The study, which included only randomized controlled trials (RCTs), aimed to minimize bias and enhance reliability across various surgical procedures, although it highlighted significant heterogeneity in outcomes. Limitations included a small sample size in several RCTs and variability in administration methods, which may have contributed to inconsistent results. The findings suggest a need for larger studies with standardized reporting to accurately assess side effects and patient satisfaction. Future research should focus on the long-term effects of liposomal bupivacaine, exploring different dosing strategies and multimodal analgesic techniques, as well as patient-reported outcomes related to recovery quality and long-term satisfaction.

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