



Original Article

A Comparative study evaluating efficacy of Intraperitoneal Bupivacaine-Fentanyl and Bupivacaine-Dexmedetomidine Combinations for Postoperative Analgesia Following Laparoscopic Cholecystectomy

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ABSTRACT

Effective control of postoperative pain is essential for faster recovery and better patient outcomes after laparoscopic cholecystectomy. Intraperitoneal instillation of local anesthetics, either alone or combined with adjuvant drugs, is a commonly used technique for postoperative analgesia. The purpose of this study was to evaluate and compare the pain-relieving effectiveness of intraperitoneal bupivacaine when used with fentanyl versus when used with dexmedetomidine in patients undergoing laparoscopic cholecystectomy.

Methods: This prospective, randomized, double-blind trial included sixty adult patients undergoing elective laparoscopic cholecystectomy, who were equally divided into two groups. At the end of the procedure, patients in Group BF received intraperitoneal instillation of 20 mL of 0.25% bupivacaine (50 mg) combined with fentanyl (1 µg/kg), with normal saline added to achieve a total volume of 30 mL. Patients in Group BD received 20 mL of 0.25% bupivacaine (50 mg) with dexmedetomidine (1 µg/kg), similarly diluted to a total volume of 30 mL. The final concentration of bupivacaine in both groups after dilution was approximately 0.167%. Postoperative pain was evaluated using the Visual Analogue Scale at 0.5, 1, 3, 5, 9, 14, 19, and 24 hours following surgery. The main outcome measured was the time to first request for rescue analgesia. Secondary outcomes included the total analgesic consumption within 24 hours and the occurrence of any side effects.

Results: Patients who received the combination of bupivacaine and dexmedetomidine experienced a markedly extended period of postoperative pain relief compared to those in the bupivacaine-fentanyl group. Visual Analogue Scale scores were consistently lower in Group BD, and these patients required fewer rescue analgesic doses within the first 24 hours after surgery. Hemodynamic parameters remained stable in both groups throughout the study. No major complications were observed in either group. The collected data were evaluated using suitable statistical methods, and a p-value below 0.05 was regarded as statistically significant.

Conclusion: Patients undergoing laparoscopic cholecystectomy, intraperitoneal delivery of bupivacaine with dexmedetomidine provided superior and longer-lasting postoperative analgesia compared to bupivacaine with fentanyl. The dexmedetomidine combination was associated with a lower need for rescue analgesia without compromising hemodynamic stability. These findings indicate that dexmedetomidine is a more effective adjuvant to bupivacaine for intraperitoneal analgesia in this surgical setting.

Keywords: Intraperitoneal analgesia, Bupivacaine, Fentanyl, Dexmedetomidine, Laparoscopic cholecystectomy, Postoperative pain.

INTRODUCTION

Laparoscopic cholecystectomy has become the preferred management option for symptomatic gallstone disease and has substantially overtaken the conventional open procedure [1,2]. The minimally invasive nature of this procedure results in less surgical trauma, shorter hospital stay, and faster return to daily activities [1]. Despite these advantages, a considerable number of patients continue to experience postoperative pain, which may adversely affect early mobilization and overall recovery [3,4].

Pain following laparoscopic cholecystectomy is multifactorial in origin [3,5]. It includes visceral pain due to manipulation of intra-abdominal organs, peritoneal irritation caused by carbon dioxide insufflation, incisional pain at trocar insertion sites, and referred shoulder pain resulting from diaphragmatic irritation [5]. Effective control of these pain components remains an important goal in perioperative management, as inadequate analgesia may delay discharge and reduce patient satisfaction.

Various analgesic techniques have been evaluated to improve postoperative pain control while minimizing opioid consumption [3]. Among these, intraperitoneal instillation of local anesthetic agents has gained attention because it directly targets peritoneal nociceptors and reduces visceral pain [4,6].

Bupivacaine is a long-acting amide-type local anesthetic that is widely utilized for intraperitoneal analgesia because of its extended duration of effect and well-documented safety profile [7]. However, the analgesic effect of bupivacaine alone may be insufficient to provide sustained postoperative pain relief. To enhance its efficacy, various adjuvant drugs have been combined with bupivacaine.

Fentanyl is a synthetic opioid and has been administered intraperitoneally as an adjuvant due to quick onset of analgesia [8]. Dexmedetomidine, a highly selective α -2 adrenergic receptor agonist, has recently gained attention as another adjuvant option because of its analgesic, sedative, and opioid-sparing properties [9,10]. Dexmedetomidine enhances analgesia by reducing sympathetic outflow and modulating nociceptive transmission, thereby prolonging the duration of local anesthetic action [10].

Although both fentanyl and dexmedetomidine have been shown to improve postoperative analgesia when combined with intraperitoneal bupivacaine, direct comparisons between these two adjuvants are limited [6,8–10]. Accordingly, this study was undertaken to evaluate and compare the effectiveness of intraperitoneal bupivacaine combined with fentanyl versus bupivacaine combined with dexmedetomidine in managing postoperative pain among patients undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS

The study was designed as a prospective, randomized, double-blind comparative trial and was carried out after approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before their inclusion in the study. A total of sixty adult patients who were scheduled to undergo elective laparoscopic cholecystectomy under general anesthesia were enrolled.

Study Population

Patients aged 18–60 years with American Society of Anesthesiologists (ASA) physical status I or II who were scheduled for elective laparoscopic cholecystectomy were included in the study. Patients who did not meet these criteria were excluded, if they had known hypersensitivity to study drugs, history of chronic pain or long-term analgesic use, significant hepatic, renal, cardiac, or psychiatric illness, pregnancy or lactation, or if intraoperative conversion to open cholecystectomy was required.

Randomization and Blinding

Participants who met the eligibility criteria were randomly assigned into two groups of 30 patients each using a computer-generated randomization method. Preparation of the study medication was carried out by an anesthesiologist who was not involved in patient care or data collection. Both the patients and the investigator responsible for evaluating postoperative pain were unaware of the group assignments.

Study Groups

Group BF (Bupivacaine–Fentanyl group):

Patients in this group received intraperitoneal instillation of 20 mL of 0.25% bupivacaine (50 mg) combined with fentanyl at a dose of 1 μ g/kg. The mixture was diluted with normal saline to obtain a total volume of 30 mL.

Group BD (Bupivacaine–Dexmedetomidine group):

Patients in this group received intraperitoneal instillation of 20 mL of 0.25% bupivacaine (50 mg) with dexmedetomidine at a dose of 1 μ g/kg. The solution was similarly diluted with normal saline to make the total volume 30 mL.

The final concentration of bupivacaine in both groups after dilution was approximately 0.167%.

Anesthetic Technique

All participants were premedicated with intravenous midazolam (0.03 mg/kg) and glycopyrrolate (0.004 mg/kg). Induction of general anesthesia was achieved using propofol (2 mg/kg) and fentanyl (2 µg/kg), followed by vecuronium (0.1 mg/kg) to enable endotracheal intubation. Anesthesia was maintained with a mixture of oxygen, nitrous oxide, and isoflurane.

Continuous intraoperative monitoring was performed using electrocardiography, non-invasive blood pressure measurement, pulse oximetry, and end-tidal carbon dioxide monitoring throughout the procedure.

Intraperitoneal Drug Administration

At the completion of surgery and before removal of the trocars, the prepared study solution (30 mL) was instilled into the peritoneal cavity under direct laparoscopic visualization. The solution was distributed around the gallbladder bed and beneath both hemidiaphragms.

Postoperative Pain Assessment and Analgesia

Postoperative pain intensity was assessed using the Visual Analogue Scale (VAS), where a score of 0 represented no pain and a score of 10 corresponded to the most severe pain imaginable. Pain assessments were performed at 0.5, 1, 3, 5, 9, 14, 19, and 24 hours following surgery.

As part of standard postoperative analgesic management, all patients were administered intravenous paracetamol 1 g every 8 hours. Additional (rescue) analgesia was provided with intravenous diclofenac 75 mg whenever the VAS score reached or exceeded 4. Intravenous diclofenac (75 mg) was used as the sole rescue analgesic and was administered only when the VAS score was ≥ 4 .

Following administration of diclofenac, pain was reassessed clinically using VAS score. If pain recurred (VAS ≥ 4), an additional dose of diclofenac (75 mg IV) was administered, maintaining a minimum interval of 8 hours between doses.

The main outcome evaluated in the study was the time to first request for rescue analgesia. Secondary outcomes included the total amount of analgesic used during the first 24 hours (calculated as the cumulative dose of diclofenac given within 24 hours) and the occurrence of side effects such as nausea, vomiting, bradycardia, hypotension, respiratory depression, and sedation.

RESULTS

Sixty patients were included in the study, with thirty participants assigned to each group (Group BF and Group BD). All enrolled patients completed the study, and their data were analyzed.

Baseline demographic variables such as age, body weight, gender distribution, and American Society of Anesthesiologists Physical Status Classification System status were similar in both groups. There were no statistically significant differences between Group BF and Group BD for any of these characteristics (Table 1).

Postoperative pain severity was evaluated using the Visual Analogue Scale for Pain at fixed time intervals during the initial 24-hour postoperative period. During the early postoperative period (0.5, 1, 3 and 5 hours), Mean VAS scores were similar in both groups, and no statistically significant differences were noted. From the ninth postoperative hour onward, A higher percentage of patients in Group BF demonstrated a progressive increase in pain scores VAS ≥ 4 . In contrast, A higher percentage of patients in Group BD maintained VAS scores < 4 throughout the observation period. A statistically significant difference in pain scores was observed between the two groups from the ninth hour and persisted until 24 hours (Table 2). Analysis of analgesic requirements revealed a statistically significant difference between the two groups. The average time to first request for rescue analgesia was considerably longer in Group BD (9.6 ± 2.1 hours) compared with Group BF (5.2 ± 1.3 hours), with a p-value < 0.001 . Total analgesic consumption (diclofenac, mg) during the first 24 hours was also lower in Group BD (90 ± 15 mg) compared with Group BF (125 ± 20 mg), and this difference was statistically significant ($p < 0.001$). Diclofenac was administered in fixed 75 mg doses, and cumulative consumption values represent mean total dose per patient during the first 24 postoperative hours (Table 3). A higher proportion of patients in Group BF required rescue analgesia intravenous diclofenac compared with those in Group BD. Rescue analgesia was required by 26 patients (86.7%) in Group BF, whereas only 14 patients (46.7%) in Group BD required additional analgesia, and The observed difference was statistically significant ($p 0.002$). No complications such as nausea, vomiting, bradycardia, hypotension, respiratory depression, or excessive sedation were noted in either group during the study period.

STATISTICAL ANALYSIS

Data were analyzed using the IBM SPSS Statistics. Continuous variables were presented as mean $\pm$ standard deviation, whereas categorical variables were summarized as frequencies and percentages.

For comparison of continuous variables between the two groups, the Student's t-test was applied. Categorical variables were evaluated using the Chi square test or the Fisher's exact test based on the distribution of data and expected cell counts. A p-value of less than 0.05 was considered statistically significant.

TABLE 1 Demographic Characteristics of Patients

Parameter	Group BF	Group BD	P-value	Interpretation
Average Age	36.1 ± 3.2 years	34.5 ± 3.6 years	0.07	No significant difference (t-test)
Average Weight	63.4 ± 6.2 kg	60.8 ± 6.7 kg	0.08	No significant difference (t-test)
Sex Distribution	14 males / 16 females	11 males / 19 females	0.18	No significant difference (Chi-square)
ASA I (out of 30)	15	19	0.30	No significant difference (Chi-square)
ASA II (out of 30)	15	11		No significant difference

TABLE 2 Proportion of Patients with VAS ≥ 4 in the Postoperative Period (n = 30 per group)

Time (hours)	Group BF (VAS ≥ 4)	Mean VAS±SD	Group BD (VAS ≥ 4)	Mean VAS±SD	P-value	Interpretation
0.5	0 / 30 (0%)	1.3 ± 0.5	0 / 30 (0%)	1.2 ± 0.4	0.396	No difference
1	0 / 30 (0%)	1.7 ± 0.6	0 / 30 (0%)	1.5 ± 0.5	0.166	No difference
3	2 / 30 (6.7%)	1.8 ± 0.8	0 / 30 (0%)	1.7 ± 0.6	0.586	Not significant
5	5 / 30 (16.7%)	2.4 ± 0.9	2 / 30 (6.7%)	2.1 ± 0.7	0.155	Not significant
9	12 / 30 (40%)	4.0 ± 1.0	4 / 30 (13.3%)	3.1 ± 0.8	<0.001	significant
14	18 / 30 (60%)	4.3 ± 1.2	8 / 30 (26.7%)	3.6 ± 0.9	0.013	significant
19	23 / 30 (76.7%)	4.8 ± 1.5	12 / 30 (40.0%)	4.0 ± 1.2	0.026	significant
24	26 / 30 (86.7%)	5.6 ± 1.1	14 / 30 (46.7%)	4.2 ± 1.1	<0.001	significant

TABLE 3 Time to First Analgesia and Total Analgesia Consumption in Groups BF and BD

Parameter	Group BF	Group BD	P-value	Interpretation
Time to First Analgesia (hours)	5.2 ± 1.3	9.6 ± 2.1	< 0.001	Significantly delayed in BD group
Mean Analgesia Consumption (mg)	125 ± 20	90 ± 15	< 0.001	Significantly lower in BD group
Patients Requiring Rescue Analgesia (Diclofenac)	26 / 30 (86.7%)	14 / 30 (46.7%)	0.002	Significantly fewer patients in BD group

DISCUSSION

Postoperative pain following laparoscopic cholecystectomy continues to be a relevant clinical issue despite the minimally invasive nature of the procedure. Pain after laparoscopy is multifactorial and results from visceral irritation due to surgical handling, peritoneal inflammation caused by carbon dioxide insufflation, incisional pain at trocar insertion sites, and diaphragmatic irritation that may lead to referred shoulder pain [5,11]. Effective postoperative analgesia must therefore address both visceral and somatic components of pain to facilitate early mobilization and recovery.

In this randomized, double-blind study, intraperitoneal administration of bupivacaine with dexmedetomidine resulted in better postoperative analgesia compared with the combination of bupivacaine and fentanyl. The dexmedetomidine group showed a significantly longer duration of analgesia, lower pain scores during the later postoperative period, and a decreased need for rescue analgesics during the first 24 hours after surgery. These findings indicate that dexmedetomidine enhances the analgesic efficacy of intraperitoneal bupivacaine more effectively than fentanyl in patients undergoing laparoscopic cholecystectomy.

The improved analgesic profile observed with dexmedetomidine may be explained by its pharmacodynamic properties. Dexmedetomidine is a highly selective α_2 -adrenergic receptor agonist that produces analgesic effects primarily by reducing sympathetic nervous system activity and inhibiting the release of norepinephrine. Activation of α_2 receptors at peripheral and central sites results in neuronal hyperpolarization and attenuation of nociceptive signal transmission [15,16]. When administered as an additive to local anesthetics, dexmedetomidine has been reported to extend the duration of sensory blockade and improve the overall quality of analgesia without evidence of neurotoxicity [14,17].

The findings of the present study are consistent with previous experimental and clinical research. Brummett et al. demonstrated that the addition of dexmedetomidine to bupivacaine significantly prolonged sensory and motor blockade in animal models [14]. Clinical studies involving neuraxial and peripheral nerve block techniques have similarly reported prolonged analgesia and reduced postoperative analgesic requirements when dexmedetomidine was used as an adjuvant [13,18]. The current study extends these observations to the intraperitoneal route, supporting its role in multimodal analgesia for laparoscopic surgery.

Fentanyl provides analgesia primarily through activation of μ -opioid receptors at spinal and supraspinal levels, thereby inhibiting pain transmission [19,20]. Although intraperitoneal fentanyl has been shown to improve early postoperative pain control, its analgesic effect may be limited by rapid systemic absorption from the peritoneal cavity [12]. This pharmacokinetic characteristic may account for the earlier requirement for rescue analgesia and higher cumulative analgesic consumption observed in the fentanyl group in this study.

Hemodynamic variables were stable in both groups, and no clinically important adverse events were noted. Dexmedetomidine is recognized to produce dose-dependent bradycardia and hypotension as a result of its sympatholytic action [21,22]; however, at the dose administered intraperitoneally in this study, these effects were mild and did not require intervention. The absence of respiratory depression further supports the safety of dexmedetomidine as an opioid-sparing adjuvant.

From a clinical perspective, intraperitoneal administration of bupivacaine combined with dexmedetomidine offers a simple, safe, and effective strategy for postoperative pain management following laparoscopic cholecystectomy. By providing prolonged analgesia and reducing opioid consumption, this technique aligns well with improved postoperative recovery protocols that focus on multimodal pain management and promoting faster recovery after surgery.

Study Limitations

This study has certain limitations that should be recognized. As part of the standardized anesthesia protocol, intravenous fentanyl was given to patients in both groups during the induction of anesthesia. In addition, patients in the bupivacaine–fentanyl group also received fentanyl via the intraperitoneal route. Although the intravenous dose was identical in both groups, its systemic analgesic effect during the early postoperative period may have influenced pain assessment and partially reduced the observable difference between the study groups. Furthermore, the comparatively small sample size may restrict how widely these findings can be applied, and larger multicenter studies are needed to further validate the results.

CONCLUSION

The results of the current study suggest, intraperitoneal administration of Bupivacaine in combination with Dexmedetomidine offers more effective and prolonged postoperative pain analgesia than bupivacaine combined with fentanyl in patients undergoing laparoscopic cholecystectomy. The dexmedetomidine combination was associated with lower postoperative pain scores, delayed requirement of rescue analgesia and decreased the overall consumption of analgesic medications in the first 24 hours, without causing notable adverse effects. Because of its opioid-sparing effect and good safety profile, Dexmedetomidine appears to be a reliable and effective adjuvant to bupivacaine for intraperitoneal analgesia in laparoscopic cholecystectomy.

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