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Original Research Article

Evaluating the Efficacy of Intraperitoneal Bupivacaine Alone, or with Dexmedetomidine or with Tramadol for Pain Management Following Total Laparoscopic Hysterectomy

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Abstract

Introduction: Laparoscopic total hysterectomy (LTH) is a minimally invasive surgical procedure for gynecological conditions. Effective post-operative pain management is crucial for patient recovery and satisfaction. Intraperitoneal bupivacaine has shown promise as a method for providing analgesia in LTH. This study aims to compare the analgesic efficacy, opioid consumption, adverse effects, and patient satisfaction of intraperitoneal bupivacaine alone, dexmedetomidine, or tramadol in LTH.

Materials and Methods: A prospective, randomized, double-blind study was conducted at Padmakuvarba General Hospital Rajkot from June 2022 to Feb 2023. The study included 120 female patients undergoing elective laparoscopic hysterectomy. Patients were assigned to one of three groups: intraperitoneal bupivacaine alone, bupivacaine with tramadol, or bupivacaine with dexmedetomidine. Standardized surgical techniques and anesthesia were employed. Pain intensity was assessed using the Visual Analog Scale (VAS) at various time points post-surgery. Secondary outcomes included time to first analgesia request, total analgesic consumption, and occurrence of adverse effects.

Results: The study included 120 female patients undergoing laparoscopic hysterectomy, divided into three groups: Group A (intraperitoneal bupivacaine alone), Group B (bupivacaine with tramadol), and Group C (bupivacaine with dexmedetomidine). Patients in Groups B and C had significantly lower post-operative pain scores compared to Group A at all time points ($p < 0.001$). The time to first analgesia request was significantly longer in Groups B and C compared to Group A ($p < 0.001$). Total analgesic consumption over 24 hours was significantly lower in Groups B and C compared to Group A ($p < 0.001$). Adverse effects such as nausea, vomiting, pruritus, shoulder pain, and hypotension were more frequent in Group A compared to Groups B and C.

Conclusion: In conclusion, the addition of dexmedetomidine to intraperitoneal bupivacaine in patients undergoing laparoscopic hysterectomy resulted in better pain control, longer time to analgesic request, and lower analgesic consumption compared to bupivacaine alone or tramadol.

Keywords: Laparoscopic total hysterectomy, gynecological conditions, dexmedetomidine

Introduction

Laparoscopic total hysterectomy (LTH) has become a widely accepted surgical approach for the treatment of various gynecological conditions.[1] While this

minimally invasive technique offers advantages such as reduced post-operative pain and shorter hospital stays compared to open surgery, adequate post-operative pain management remains crucial for optimizing patient recovery and overall satisfaction.[2] Post-operative pain in Total Laparoscopic Hysterectomy (TLH) arises from factors such as intra-abdominal cavity stretching, peritoneal inflammation, and residual carbon dioxide irritation.[3] Various analgesic strategies have been explored to improve pain control following LTH, including the use of intraperitoneal local anesthetics and adjuvant medications.[1,2]

In recent years, intraperitoneal administration of bupivacaine has gained attention as a potential method to provide effective post-operative analgesia in LTH.[4] Bupivacaine, a long-acting local anesthetic, exerts its analgesic effect by inhibiting nerve conduction, thereby reducing pain perception in the operative site.[5] However, the addition of adjuvant medications, such as dexmedetomidine and tramadol, to intraperitoneal bupivacaine may offer additional benefits by enhancing analgesia through different mechanisms of action.[6]

Dexmedetomidine, an alpha-2 adrenergic agonist, possesses sedative, analgesic, and sympatholytic properties.[7] Studies have suggested that its use as an adjuvant to local anesthetics may prolong the duration of analgesia and reduce post-operative opioid consumption.[8] Tramadol, a centrally acting analgesic, exhibits dual mechanisms by inhibiting the reuptake of norepinephrine and serotonin, as well as acting as a weak mu-opioid receptor agonist.[9] Intraperitoneal tramadol has been investigated for its potential to provide effective post-operative pain relief with reduced opioid requirements.[10]

Despite the growing interest in the use of intraperitoneal bupivacaine alone or in combination with dexmedetomidine or tramadol for post-operative analgesia following LTH, there is a lack of comprehensive comparative evaluations to guide clinical decision-making. Therefore, this study aims to compare the analgesic efficacy, opioid consumption, adverse effects, and patient satisfaction associated with intraperitoneal bupivacaine alone, dexmedetomidine, or tramadol in patients undergoing LTH. Understanding the relative benefits and limitations of these analgesic regimens will aid in optimizing post-operative pain management in this patient population.

Material and Methods

This prospective, randomized, double-blind study was conducted at Padmakuvarba General Hospital Rajkot between June 2022 and Feb 2023. Ethical approval was obtained from the Institutional Ethical Committee, and written informed consent was obtained from all patients. The study included a total of 120 female patients classified as American Society of Anesthesiologists (ASA) physical status I-II, aged between 18 and 60 years, who were scheduled for elective Total Laparoscopic Hysterectomy (TLH). Patients with contraindications to laparoscopic surgery, known allergies to local anesthetics or study medications, or a history of severe cardiac, pulmonary, or neurological diseases were excluded from the study.

Sample Size Calculation:

The sample size of 120 patients (40 patients in each group) was determined using the Power and Sample Size Calculator (PS version 3.0.0.34). The calculation was based on the assumption of a 30% improvement in pain scores, with an alpha error (α) of 0.05 and a power of 80%. Initially, a total of 129 patients were included in the study, but 9 patients were subsequently excluded based on predefined exclusion criteria.

Patient Randomization and Study Groups:

Patients were randomly allocated to one of the three study groups using a table of randomization. Group A (n = 40) received intraperitoneal bupivacaine 50 ml 0.25% + 5 ml normal saline (NS), Group B (n = 40) received intraperitoneal bupivacaine 50 ml 0.25% + tramadol 1 mg/kg (diluted in 5 ml NS), and Group C (n = 40) received intraperitoneal bupivacaine 50 ml 0.25% + dexmedetomidine 1 µg/kg (diluted in 5 ml NS). The study drugs were prepared by an anesthesiologist who was not involved in the study. The anesthesiologist observing the patient and the surgeon remained blinded to the study group assignments until the end of the study.

Surgical Technique and Anesthesia:

All patients underwent TLH under general anesthesia. Standard monitoring, including electrocardiography, non-invasive blood pressure measurement, pulse oximetry, and end-tidal carbon dioxide monitoring, was performed. Anesthesia induction was achieved using intravenous fentanyl 1.5 µg/kg, propofol 2.0-2.5 mg/kg, followed by succinylcholine 2 mg/kg to facilitate orotracheal intubation. Anesthesia was maintained with 60% N2O in oxygen with 0.5-1% isoflurane. TLH was performed using trocars and specialized instruments according to the standard procedure. Intra-abdominal pressure was maintained at 12-14 mm Hg during the surgery.

Administration of Study Solution:

After the TLH procedure and removal of the uterus, the carbon dioxide (CO2) in the peritoneal cavity was released by manual compression of the abdomen with an open trocar. Subsequently, the study solution, prepared by an anesthesiologist not involved in the study, was administered through intraperitoneal infusion into left, middle and right upper quadrants of abdomen at the end of TLH. The composition of the study solution varied based on the assigned group.

Postoperative Care and Outcome Measures:

Neuromuscular blockade was reversed using neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg, and tracheal extubation was performed. The nasogastric tube was removed, and patients were then transferred to the post-anesthesia care unit (PACU).

All patients remained in the PACU for 2 hours after the completion of surgery. The primary outcome variable was pain intensity, which was assessed using the Visual Analog Scale (VAS) score at various time points (0.5, 1, 2, 4, 6, 12, and 24 hours) post-surgery, as well as the overall VAS score (mean of all VAS scores). The secondary outcomes included the time to the first request for analgesia in the postoperative period, the total dose of analgesics used within a 24-hour period, and the occurrence of any adverse/side effects, such as postoperative nausea and vomiting.

Patients were educated about the use of the VAS score before anesthesia induction. A VAS score of 0 indicated no pain, while a VAS score of 10 represented the worst possible pain. Patients reporting a VAS score of 3 or higher were administered rescue analgesia in the form of intramuscular diclofenac 75 mg. Postoperative nausea and vomiting were managed by administering intravenous ondansetron 4 mg as necessary.

Statistical Analysis:

Data analysis was performed using SPSS version 21.0. Continuous variables were presented as mean ± standard deviation or median (interquartile range) based on their distribution. Categorical variables were reported as frequencies and percentages. For group comparisons, appropriate statistical tests, such as t-tests or analysis of variance (ANOVA) for continuous variables, and chi-square tests for categorical variables, were used. A significance level of $p < 0.05$ was considered statistically significant.

Results

The analysis of the demographic characteristics and operative data revealed that there were no significant differences observed among the three study groups (Group A, Group B, and Group C). (Table 1) The mean age of patients in each group showed no statistically significant variation (p = 0.721*). The distribution of male and female patients was similar across all groups (p = 0.654). The mean weight of patients in each group indicated no significant difference (p = 0.936*).

Table 1: Demographic characteristics of study groups

Variable	Group A (n=40)	Group B (n=40)	Group C (n=40)	p-value
Age (years)	42.16 ± 7.82	41.94 ± 8.12	43.02 ± 8.35	0.721*
Sex				
Males	10 (40%)	11 (40%)	12 (40%)	0.654
Females	30 (40%)	29 (40%)	28 (40%)	
Weight (kg)	68.40 ± 9.05	68.60 ± 9.28	67.90 ± 8.92	0.936*

The distribution of patients according to ASA classification (I or II) was comparable among the groups, with 28 patients (40%) in Group A, 29 patients (40%) in Group B, and 28 patients (40%) in Group C falling into ASA class I (p = 0.8792). For ASA class II, there were 12 patients (40%) in Group A, 11 patients (40%) in Group B, and 12 patients (40%) in Group C (p = 0.8792). The duration of surgery and anesthesia time did not significantly differ between the groups, with similar mean values observed (p = 0.964* and p = 0.821* respectively).

Figure 1 illustrates the mean post-operative VAS scores in the studied groups (Group B, Group BT, and Group BD) over different time intervals. At 0.5 hours post-operation, Group B had a mean VAS score of 4.20 ± 1.55, while Group BT and Group BD had mean scores of 3.80 ± 1.02 and 2.10 ± 0.78, respectively. The p-values associated with the pairwise comparisons between the groups were 0.035*, 0.000†, and 0.000‡, indicating statistically significant differences in scores.

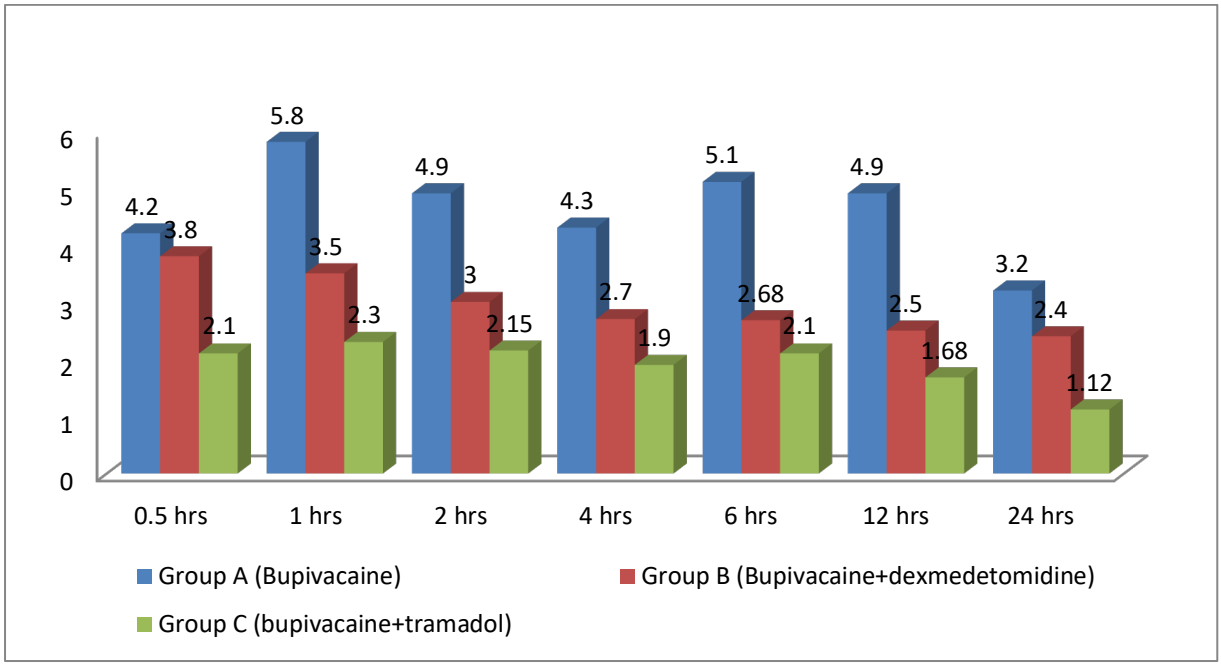

Fig 1: Mean post-operative VAS scores

Over the course of the study, the mean VAS scores in Group B remained consistently higher compared to Group BT and Group BD at all time points (1, 2, 4, 6, 12, and 24 hours). The differences in scores were statistically significant for all time intervals, as denoted by the p-values of 0.000* (Group B vs. Group BT), 0.000† (Group B vs. Group BD), and 0.000ǂ (Group BT vs. Group BD).

Table 2 presents the findings of the study, comparing the variables in three groups: Group A (n=40), Group B (n=40), and Group C (n=40). The overall VAS scores over 24 hours post-operatively were significantly higher in Group A (3.9 ± 0.67) compared to Group B (1.43 ± 0.58) and Group C (2.60 ± 0.46) (p = 0.000*). The time to first request of analgesia in the postoperative period was significantly shorter in Group A (49 ± 23 min) compared to Group B (129 ± 32 min) and Group C (105 ± 23 min) (p = 0.0000*). Furthermore, the total dose of diclofenac in 24 hours was significantly higher in Group A (143 ± 48 mg) compared to Group B (41 ± 29 mg) and Group C (68 ± 19 mg) (p = 0.000*). These results highlight the superior pain control and delayed analgesic requirement in the groups receiving bupivacaine plus dexmedetomidine (Group B) and bupivacaine plus tramadol (Group C) compared to Group A (bupivacaine only).

Table 2: Post-operative overall VAS# score and analgesic requirements (mean±SD) in studied groups

Variable	Group A (n=40)	Group B (n=40)	Group C (n=40)	P value
Overall VAS over 24 h post-operatively	3.9 ± 0.67	1.43 ± 0.58	2.60 ± 0.46	0.000* 0.00000† 0.0000ǂ
Time to first request of analgesia in post-op period (min)	49 ± 23	129 ± 32	105 ± 23	0.0000* 0.025† 0.0000ǂ
Total dose of diclofenac (mg) in 24 h	143 ± 48	41 ± 29	68 ± 19	0.000* 0.00000† 0.0000ǂ

*Level of significance between Group A and Group B; †Level of significance between Group B and Group C; ǂLevel of significance between Group C and A; #VAS: Visual analogue scale, SD: Standard deviation

In our study involving 120 participants across three groups, adverse effects were evaluated post-operatively. (Fig 2) Group A had higher frequencies of nausea (20%), vomiting (12.5%), pruritus (12.5%), shoulder pain (5%), and hypotension (12.5%) compared to Group B and Group C. Urine retention was reported in Group A (2.5%) and Group C (2.5%), while Group B had no cases. These findings suggest a potential association between the interventions in Group A and a higher risk of adverse effects.

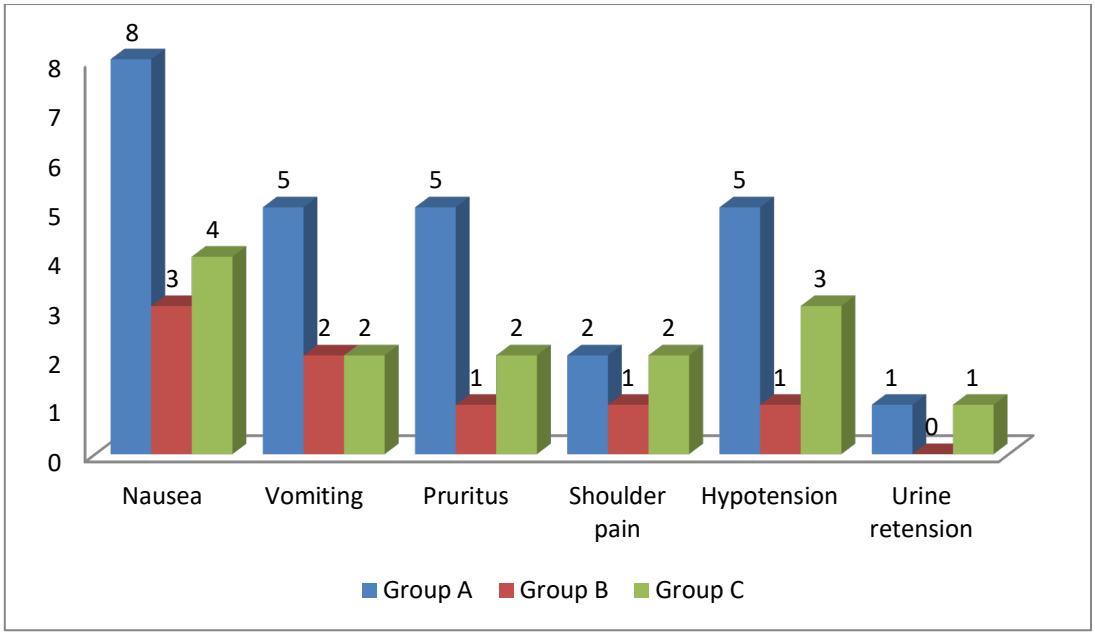

Fig 2: Post-operative adverse/side effects

Discussion

In recent years, there has been a growing interest in exploring less invasive surgical techniques for various gynecological procedures, including total laparoscopic hysterectomy (TLH). TLH offers numerous potential benefits, such as reduced post-operative pain, shorter hospital stays, and faster recovery compared to traditional open surgery. This has led to an increased adoption of TLH in clinical practice. However, despite its widespread use, there is still a need for further research to evaluate the efficacy and safety of TLH in various patient populations.

In our study on TLH, we assessed the mean post-operative VAS scores in three groups: Group B, Group BT, and Group BD. At 0.5 hours post-operation, Group B had a mean VAS score of 4.20 ± 1.55, Group BT had a mean score of 3.80 ± 1.02, and Group BD had the lowest mean score of 2.10 ± 0.78. These findings indicate that Group BD had the least post-operative pain compared to the other groups.

In comparison to other studies, the addition of dexmedetomidine to bupivacaine (Group BD) yielded significantly lower VAS scores than bupivacaine alone (Group B), as shown by Punyani et al.[11] Similarly, Shukla et al.[12] demonstrated that Group BD had lower VAS scores than bupivacaine with tramadol (Group BT) and bupivacaine alone (Group B). Furthermore, Narasimhan et al.[13] found that combining bupivacaine with dexmedetomidine (Group C) resulted in significantly lower VAS scores compared to bupivacaine alone (Group A) and bupivacaine with tramadol (Group B) in laparoscopic cholecystectomies. These consistent findings highlight the superior analgesic effect achieved by combining bupivacaine with dexmedetomidine.

Taken together, the consistent results across these studies indicate that the addition of dexmedetomidine or tramadol to bupivacaine can result in significantly lower VAS scores, indicating improved post-operative pain control. These findings suggest that these combination therapies may have potential benefits for managing pain in laparoscopic procedures, including TLH. However, further research is warranted to assess additional outcome measures and potential adverse effects to

fully evaluate the effectiveness and safety of these interventions in TLH and other surgical procedures.

In our study, we assessed the post-operative pain levels using the Visual Analog Scale (VAS) in three groups: Group A, Group B, and Group C. The VAS scores over 24 hours post-operatively were significantly higher in Group A (3.9 ± 0.67) compared to Group B (1.43 ± 0.58) and Group C (2.60 ± 0.46) (p = 0.000*). This aligns with the study by Punyani et al.[11], where they found significantly lower VAS scores in the bupivacaine combined with dexmedetomidine group (Group BD) compared to the bupivacaine-only group (Group B). Our findings are consistent with previous studies regarding the analgesic effects of α-2 agonists intraperitoneally. Ahmed et al.[14] demonstrated that intraperitoneal instillation of mepiridine or dexmedetomidine in combination with bupivacaine 0.25% significantly reduced post-operative analgesic requirements and the incidence of shoulder pain in laparoscopic gynecological surgeries.

In terms of the time to the first request of analgesia in the post-operative period, our study showed a significant delay in Group BD compared to Group B, supporting the findings of Govil et al.[15] who found no difference between tramadol and clonidine groups. However, in our study, the time was significantly shorter in the tramadol group compared to the dexmedetomidine group. Similarly, Shukla et al.[12] reported delayed analgesic requirement in the bupivacaine plus dexmedetomidine group (Group BD) compared to the bupivacaine with tramadol group (Group BT) and bupivacaine-only group (Group B).

In our study, we observed higher doses of diclofenac in Group B compared to Group BD and Group BT, consistent with the findings of Memis et al.[16], Acharya et al.[4] and Ahmed et al.[14] However, our study did not find higher doses in the clonidine group compared to the tramadol group, contrary to Deshmukh et al.[17] Furthermore, the total dose of diclofenac in 24 hours was significantly higher in Group A (143 ± 48 mg) compared to Group B (41 ± 29 mg) and Group C (68 ± 19 mg) (p = 0.000*). This corresponds to the study by Narasimhn et al.[13], where bupivacaine combined with dexmedetomidine (Group C) resulted in significantly lower VAS scores compared to bupivacaine alone (Group A) and bupivacaine with tramadol (Group B).

These collective findings emphasize the superior pain control and delayed analgesic requirement in the groups receiving bupivacaine plus dexmedetomidine (Group B) and bupivacaine plus tramadol (Group C) compared to bupivacaine alone (Group A). The consistent results across our study and the mentioned studies highlight the potential benefits of combining bupivacaine with dexmedetomidine or tramadol for effective pain management in laparoscopic procedures, including TLH.

In our study, there was no statistically significant difference in adverse effects among the three study groups (p = 0.4010). However, the incidence of shoulder pain was lower in Group BD (12.5%) compared to Group BT (40%) and the bupivacaine alone group (70%), which is consistent with findings from Govil et al.[15]'s study. Additionally, Punyani et al.[11] and Shukla et al.[12] reported a lower incidence of nausea and vomiting in the bupivacaine-dexmedetomidine group compared to other groups. Furthermore, Narasimhn et al.[13] found a lower incidence of sedation and respiratory depression in the bupivacaine-dexmedetomidine group. These findings suggest that adding dexmedetomidine to the analgesic regimen may reduce shoulder pain, as well as protect against nausea, vomiting, sedation, and respiratory depression.

Several limitations should be acknowledged in this study. Firstly, the study was conducted at a single center, which may limit the generalizability of the findings. Secondly, the blinding of patients, surgeons, and anesthesiologists to the study group assignments may have been challenging due to the nature of the intervention. Lastly, the follow-up period was limited to 24 hours, which may not capture long-term outcomes and potential complications.

Conclusion

Our study focused on evaluating the efficacy and safety of different analgesic regimens in TLH. We found that combining bupivacaine with dexmedetomidine resulted in significantly lower post-operative pain scores compared to bupivacaine alone or combination with tramadol. These findings support the notion that multimodal analgesic approaches can effectively manage pain in TLH. Additionally, our study observed no significant differences in adverse effects among the three study groups, indicating a favorable safety profile for the examined regimens. However, further research is needed to assess long-term outcomes, patient satisfaction, and cost-effectiveness to fully understand the implications of these analgesic strategies in TLH and optimize perioperative pain management protocols.

Bibliography

1. Yang CY, Shen TC, Lin CL, Chang YY, Huang CC, Lin WC. Surgical outcomes of hysterectomy by transvaginal natural orifice transluminal endoscopic surgery (vNOTES) compared with laparoscopic total hysterectomy (LTH) in women with non-prolapsed and benign uterine diseases. Taiwan J Obstet Gynecol. 2020;59(4):565–9.
2. Potnis AR, Boralkar AK, Varudkar AS. Post-Operative Outcomes within Enhanced Recovery after Surgery: A Comparative Study of Multisystem Outcomes. 2020;
3. Sallam HF, Shady NW, Aly HF, Elfadl GMA, Abbas AM. Low pressure pneumoperitoneum and intraperitoneal infusion of normal saline for reducing shoulder tip pain after gynecologic laparoscopy: randomized controlled trial. Int Surg J. 2018;5(3):959–64.
4. Acharya R, Karan D, Khetan M. Postoperative analgesia with intraperitoneal ropivacaine with and without dexmedetomidine after total laparoscopic hysterectomy: a randomized, double-blind, controlled trial. Asian J Pharm Clin Res. 2016;9(3):76–9.
5. Catterall WA, Mackie K. Local anesthetics. Goodman Gilman's Pharmacol Basis Ther 11th Ed N Y McGraw-Hill. 2006;369–85.
6. Modir H, Yazdi B, Piri M, Almasi-Hashiani A. An investigation of the effects of dexmedetomidine and fentanyl as an adjuvant to ropivacaine on pain scores and hemodynamic changes following laparoscopic cholecystectomy. Med Gas Res. 2021;11(3):88.
7. Talke P, Richardson CA, Scheinin M, Fisher DM. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg. 1997;85(5):1136–42.
8. Kang R, Jeong JS, Yoo JC, Lee JH, Choi SJ, Gwak MS, et al. Effective dose of intravenous dexmedetomidine to prolong the analgesic duration of interscalene brachial plexus block: a single-center, prospective, double-blind, randomized controlled trial. Reg Anesth Pain Med. 2018;43(5):488–95.
9. Reeves RR, Burke RS. Tramadol: basic pharmacology and emerging concepts. Drugs Today Barc Spain 1998. 2008;44(11):827–36.
10. Yadava A, Rajput SK, Katiyar S, Jain RK. A comparison of intraperitoneal bupivacaine-tramadol with bupivacaine-magnesium sulphate for

pain relief after laparoscopic cholecystectomy: A prospective, randomised study. Indian J Anaesth. 2016;60(10):757.
11. Punyani M, Bhandari G, Singh K. Comparative Study of Post Operative Analgesic Effect of Intraperitoneal and Port Site Instillation of Dexmedetomidine with Bupivacaine and Bupivacaine Alone After Laparoscopic Cholecystectomy. EAS J Anaesthesiol Crit Care. 2019;1(2):19–24.
12. Shukla U, Prabhakar T, Malhotra K, Srivastava D, Malhotra K. Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy: A comparative evaluation. Indian J Anaesth. 2015;59(4):234.
13. Narasimham ML, Rao BD. Comparison of intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy. Indian J Clin Anaesth. 2017;4(1):143–6.
14. Ahmed B, Elmawgoud A, Doaa R. Antinociceptive effect of (a2-adrenoceptor agonist) dexmedetomedine vs meperidine, topically, after laparoscopic gynaecologic surgery. J Med Sci. 2008;8(4):400–4.
15. Govil N, Kumar P. Intraperitoneal levobupivacaine with or without clonidine for pain relief after laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled trial. Anesth Essays Res. 2017;11(1):125.
16. Memis D, Turan A, Karamanlioglu B, Tükenmez B, Pamukçu Z. The effect of tramadol or clonidine added to intraperitoneal bupivacaine on postoperative pain in total abdominal hysterectomy. J Opioid Manag. 2005;1(2):77–82.
17. Deshmukh P, Takalkar S, Chaudhari A, Chakole V. A prospective comparative study to assess-post operative analgesic effect of intraperitoneal instillation of bupivacaine with dexmedetomidine to bupivacaine with tramadol in patients undergoing laparoscopic cholecystectomy. Indian J Forensic Med Toxicol. 2020;14(4):6546–51.