ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

A comparative evaluation of intraperitoneal instillation and periportal infiltration of 0.375% ropivacaine with dexmedetomidine and nalbuphine as adjuvants for post-operative analgesia in laparoscopic cholecystectomy

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Submission: 16-03-2023 Revision: 04-06-2023 Publication: 01-07-2023

ABSTRACT

Background: Intraperitoneal instillation (IPI) of local anesthetic agents into peritoneal cavity has proved to be an effective method of post-operative analgesia in laparoscopic cholecystectomy (LC). The addition of adjuvants such as narcotics or α_2-agonists has been proposed to prolong the duration of post-operative analgesia. **Aims and Objectives:** This study aimed to compare post-operative analgesia of IPI and periportal infiltration of ropivacaine plus dexmedetomidine with ropivacaine plus nalbuphine in patients undergoing LC. **Materials and Methods:** This was a comparative, prospective, randomized controlled double-blind study conducted on total of 100 patients (American Society of Anesthesiologists class I and II) planned for LC who were randomly divided into two groups of 50 patients: Group Ropivacaine + Dexmedetomidine (RD) received IPI and periportal infiltration of 150 mg of ropivacaine (0.375%) and dexmedetomidine (1 μg/kg) diluted with normal saline to 40 mL and Group Ropivacaine + Nalbuphine (RN) received 150 mg of ropivacaine (0.375%) and 10 mg nalbuphine diluted with normal saline to 40 mL. Post-operative pain was assessed by Visual Analogue Score, time to first request of analgesia, and total amount of rescue analgesics given in 24 h and side effects were noted. Data were analyzed by Student's independent t-test and Chi-square test using SPSS version 20.0. **Results:** Overall Visual Analog Scale scores (1.38 ± 0.78 vs. 2.59 ± 1.15), time to first request of analgesia (7.3 ± 3.74 vs. 4.2 ± 2.71), and total analgesic consumption (82.4 ± 15.34 vs. 158.5 ± 16.19) were significantly lower in the RD group compared to the RN group. Among post-operative adverse events, the incidence of post-operative nausea and vomiting was significantly higher in the RN group. **Conclusion:** The addition of dexmedetomidine appears to be superior to nalbuphine in terms of prolonged post-operative analgesia, lesser requirement of rescue analgesia, and less complications.

Key words: Intraperitoneal; Laparoscopic cholecystectomy; Dexmedetomidine; Nalbuphine; Local anesthesia; Ropivacaine

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i7.53284

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Laparoscopic cholecystectomy (LC) as opposed to open cholecystectomy is currently the most accepted surgical technique for cholelithiasis. Laparoscopic procedure has many advantages over open procedure such as less hemorrhage, better cosmetic results, lesser post-operative pain, and shorter recovery time leading to shorter hospital

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stay and less health care expenditure.[1] Although it is a minimally invasive procedure, pain has been mentioned as a major complaint and a reason for delayed post-operative recovery. Post-operative pain is more common during the first few hours (h) after surgery and usually reduces over the next 48–72 h. Previous studies advocate the etiology of post-operative pain in patients who underwent LC as multifactorial consisting of visceral pain from the operation itself, parietal pain originating from the trauma to diaphragm as well as the peritoneum and the incision pain itself.[2-5] Intraperitoneal instillation (IPI) of the local anesthetic (LA) agent into gallbladder bed has been proven to be an effective method of post-operative analgesia in LC. It is an easy, non-invasive method associated with low pain scores, less opioid consumption, shoulder pain, and emetic symptoms.[6] However, the duration of analgesia may be limited for few hours. Hence, the addition of adjuvants such as narcotics or α2-agonists has been proposed to prolong post-operative analgesia.[7-10] There are very few if any studies comparing the effect of dexmedetomidine and nalbuphine as additives to ropivacaine in prolonging post-operative analgesia after LC, hence we have compared ropivacaine (0.375%) plus dexmedetomidine (1 mcg/kg) with ropivacaine (0.375%) plus nalbuphine (10 mg) to provide nearly total somatic and visceral pain block (post-operative analgesia) by IPI and infiltration at port site at the end of LC.

Aims and objectives

1. To determine the intensity and duration of pain.
2. Time to first analgesic request and total analgesic consumption in 24 hours.
3. Any side effects or complications.

MATERIALS AND METHODS

This comparative, prospective, randomized controlled double-blind hospital-based study was conducted in the department of anesthesiology, after taking approval from the institutional ethical committee (ref no IEC/GMCK/90) and informed consent from patient and their close relatives.

Inclusion criteria

A total of 100 patients in the age group of 18–60 years, of both sexes, belonging to American Society of Anesthesiologists (ASA) grade I or II, and scheduled to undergo LC under general anesthesia (GA) were included in the study.

Exclusion criteria

Patients with any chronic medical illness, allergy to study drug, previous abdominal surgery, or patients in whom surgery had to be converted to open cholecystectomy or with complications which could increase post-operative pain such as biliary spillage owing to puncture of the gallbladder or extensive dissection owing to adhesions were excluded from the study.

The patients were randomly allocated into two groups having 50 patients each, according to computer-generated numbers.

In Group Ropivacaine+Dexmedetomidine (RD), patients received IPI and periportal infiltration of 150 mg of ropivacaine (0.375%) and dexmedetomidine (1 μg/kg) diluted with normal saline to a total volume of 40 mL.

In Group Ropivacaine+Nalbuphine (RN), patients received IPI and periportal infiltration of 150 mg of ropivacaine (0.375%) and 10 mg nalbuphine, diluted with normal saline to a total volume of 40 mL.

For double blinding, the study solutions were drawn into pre-coded sterile syringes by an anesthetist not involved in the study and given to the surgeon for IPI and periportal infiltration. A detailed pre-operative assessment was done for the patients which included taking medical history and performing general physical and systemic examination. The relevant laboratory investigations were done. The Visual Analog Scale (VAS) was explained in great detail to every patient. VAS consists of a straight vertical 10 cm line where the bottom point (0 cm) represents no pain and the top (10 cm) represents the worst imaginable pain. Patients were kept fasting for 6 h for solids and 2 h for clear liquids before surgery. All the operations were performed by surgeons having at least 3 years of experience in laparoscopic surgery.

Anesthesia technique was same in all the patients. Tablet alprazolam 0.5 mg was administered the night before the surgery. The patients were shifted to operation theater and routine physiological monitoring was commenced including baseline heart rate (HR), pulse oximetry (SpO_2), noninvasive blood pressure (NIBP), and five-lead electrocardiogram. Then, peripheral intravascular (iv) access was obtained. Patients were pre-medicated with iv administration of glycopyrrolate 0.2 mg and midazolam 1 mg. Patients were pre-oxygenated with 100% O_2 for 3–5 min, and induction of anesthesia was done with iv fentanyl 1–2 μg/kg and propofol 1–2 mg/kg till loss of verbal response. Endotracheal intubation with an appropriate-size cuffed tube was facilitated using atracurium 0.5 mg/kg. The maintenance of anesthesia was done with isoflurane (1%–1.5%) along with O_2 and N_2O and atracurium. Ventilation was adjusted to keep end-tidal CO_2 at 35–40 mmHg. Nasogastric tube was inserted after intubation and removed at the end of surgery. Intraoperative analgesia was supplemented with iv infusion of acetaminophen (15 mg/kg). Patients were

placed in reverse Trendelenburg position of around 15° to 20°. Pneumoperitoneum was created by insufflating CO_2 at a rate of 5 L/min, and intra-abdominal pressure was kept between 12 and 15 mmHg throughout the surgery. After dissecting the gallbladder from liver bed, hemostasis, washing of the peritoneal cavity, and suctioning of the irrigating fluid were done. At the end of surgery, CO_2 was carefully evacuated by manual compression of abdomen with open trocar. Study drug (30 mL) according to the group was instilled IP by the surgeon under direct vision into the right hepatodiaphragmatic space, on the gallbladder bed, above and near hepatoduodenal ligament and sprayed on upper surface of liver. Patients were kept in Trendelenburg position of 15–20° for 10 min. After the removal of trocar, 10 mL of the study drug was infiltrated at port sites (4 mL at umbilical incision, 3 mL at epigastric incision, and 3 mL at working port). At the end of surgery, the reversal of residual neuromuscular blockade was done with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Then, patients were extubated and shifted to the recovery room, where HR, NIBP, and SpO_2 were monitored. The severity of pain was assessed using VAS ranging from 0 to 10. VAS score was recorded immediately after recovery (regarded as 0 h) and at 1, 2, 4, 8, 12, 18, and 24 h postoperatively. For patients with VAS score ≥4, rescue analgesia was given, using intramuscular injection diclofenac (75 mg). The time to first analgesic request and the total analgesic consumption in 24 h postoperatively were recorded. Adverse effects such as hypotension (>20% decrease of MAP from baseline), bradycardia (HR <60 bpm), post-operative nausea and vomiting (PONV), pruritus, respiratory depression (SpO_2<90% on room air or respiratory rate <10 breaths/min), shoulder tip pain, or sedation (Modified Ramsay Sedation Scale) were recorded.

Statistical analysis

The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar diagrams. Student's independent t-test or Mann–Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. P<0.05 was considered statistically significant.

RESULTS

There was no significant difference (P>0.05) with respect to age, gender, weight, body mass index (BMI), and ASA physical status and duration of surgery among the study groups (Table 1).

Regarding the intensity of post-operative pain, the VAS values were lower in the RD group as compared with the RN group throughout the whole study period up to 24 h, and the difference was found to be statistically significant (P<0.05) except at 0, 1, and 8 h (Figure 1).

Overall VAS scores were significantly lower in the RD group (P<0.05). The time to the first analgesic request was significantly longer (P<0.05) in the RD group (7.3±3.7 h) than that in the RN group (4.2±2.7 h), indicating better and longer duration of post-operative analgesia in the RD group (Table 2). The total dose of diclofenac used for rescue analgesia was significantly lower (P<0.05) in the RD group (82.4±15 mg) compared to the RN group (158.5±16 mg).

None of the patients in our study had hypotension, bradycardia, itching, shoulder tip pain, and respiratory

Table 1: Demographic characteristics of study patients in two groups

Parameter	Group RD (n=50) (%)	Group RN (n=50) (%)	P-value
Age (years)	35.4±7.83	34.7±8.13	0.662
Gender			
Male	27 (54)	29 (58)	0.687
Female	23 (46)	21 (42)	
ASA			
ASA I	38 (76)	41 (82)	0.461
ASA II	12 (24)	9 (18)	
Weight (kg)	65.1±8.91	63.5±7.54	0.335
BMI (kg/m²)	23.2±3.43	22.8±3.15	0.545
Duration of surgery (minutes)	68.4±10.71	70.3±9.42	0.349

Data are expressed as mean±SD. ASA: American Society of Anesthesiologists, BMI: Body mass index, RD: Ropivacaine+Dexmedetomidine, RN: Ropivacaine+Nalbuphine

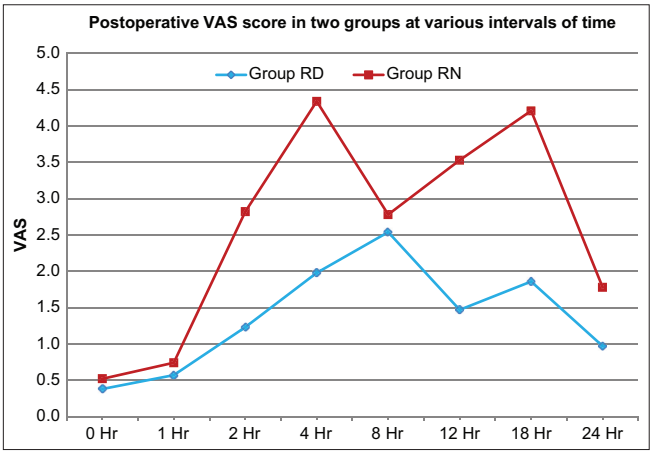

Figure 1: Post-operative visual analog scale scores were lower in the ropivacaine-dexmedetomidine group

Table 2: Post-operative overall VAS score and analgesic requirements in two groups

Parameter	Group RD		Group RN		P-value
	Mean	SD	Mean	SD	
Overall VAS (24 h)	1.38	0.78	2.59	1.15	<0.001*
Time to first request of analgesia (hours)	7.3	3.74	4.2	2.71	<0.001*
Total dose of diclofenac (mg) in 24 h	82.4	15.34	158.5	16.19	<0.001*

*Statistically significant difference (P<0.05). RD: Ropivacaine+Dexmedetomidine, RN: Ropivacaine+Nalbuphine, VAS: Visual Analog Scale

depression in the post-operative period. Only five patients (10%) in the RN group experienced drowsiness. The sedation level of the patients was assessed based on the Ramsay Sedation Scale. However, a higher incidence of emesis was reported in the RN group (8 patients, 16%), which was statistically significant compared to the RD group (Table 3).

Table 3: Post-operative side effects in two groups

Side effects	Group RD		Group RN		P-value
	No.	% age	No.	% age	
PONV	1	2	8	16	0.036*
Sedation	0	0	5	10	0.118
Shoulder tip pain	0	0	0	0	-

PONV: Post-operative nausea and vomiting, *Statistically significant difference (P<0.05). RD: Ropivacaine+Dexmedetomidine, RN: Ropivacaine+Nalbuphine

DISCUSSION

Although LC is a minimally invasive procedure, it may be associated with significant post-operative pain.[11] Pain after LC is multifactorial and should be managed in multimodal fashion. LA techniques are part of multimodal approach for post-operative pain management after LC. IPI of LA is used as a method to provide effective pain relief while minimizing the adverse effects of systemic analgesics, including non-steroidal anti-inflammatory drugs and opioids. The rationale for this route of administration is that the LA will block the visceral nociceptive conduction from the peritoneum. In addition, systemic absorption from the large peritoneal surface may occur, providing an additional mechanism of analgesia.[12] Ropivacaine is a new long-acting amide LA that is formulated as a pure S-enantiomer and is chemically related to bupivacaine, with less toxic cardiac and central nervous system side effects.[13] This drug possesses anti-inflammatory activity that may further reduce pain when administered locally.[14] The antinociceptive effect of dexmedetomidine is seen at dorsal root neuron level, where it blocks the release of substance P in the nociceptive pathway, through action on inhibitory G protein, which increases the conductance through potassium channels.[15] IPI of opioids added to LA, in an attempt to enhance and prolong post-operative analgesia, has shown good results. Peripheral antinociceptive effect of opioids occurs owing to interaction with opioid receptors, which are located on peripheral intact perineurium on sensory nerves. Lipophilic opioids, such as nalbuphine, can diffuse easily across the intact perineural barrier, resulting in better analgesia on IPI.[16]

Our study showed that the addition of dexmedetomidine with ropivacaine administered via IPI and periportal infiltration provided better post-operative analgesia than that obtained with combination of ropivacaine and nalbuphine. This effective pain relief observed in the RD group was reflected by lower VAS scores than that of the RN group, longer time to first analgesic request, and lower total consumption of rescue analgesics. VAS values were lower in the RD group than their corresponding values in the RN group at all points of time except at 0, 1, and 8 h postoperatively. This may be explained by analgesic effect of intraoperatively administered analgesics at 0 and 1 h and that of rescue analgesics at the 8th h which were administered earlier in the RN group owing to shorter time for first analgesic demand. Praveena et al.[17] observed the effect of IPI of 0.2% ropivacaine combined with dexmedetomidine (1 μg/kg) or fentanyl in 80 patients undergoing LC. They observed lower 24-h post-operative VAS scores, longer time to first request for rescue analgesia, and lower total analgesia consumption with ropivacaine and dexmedetomidine combination, as observed in our study. Modir et al.[18] concluded that VAS scores at different time intervals, pain, and total opioid consumption in post-operative 24 h were significantly lower in the ropivacaine plus dexmedetomidine group and higher in the ropivacaine group. Chiruvella and Nallam[19] studied the post-operative pain relief provided by the IPI of ropivacaine alone versus ropivacaine with dexmedetomidine in patients undergoing LA under GA. These studies supported our findings of better post-operative pain control with IPI of dexmedetomidine in combination with LA such as ropivacaine in various laparoscopic surgeries.

PONV was a significant finding in the RN group compared to the RD group. Injection ondansetron 4 mg was administered iv to relieve PONV. Mahajan et al.[20] concluded a higher incidence of PONV in the group receiving IPI of ropivacaine 0.2% with nalbuphine compared to ropivacaine alone and ropivacaine with butorphanol. In another study, the incidence of PONV was greater in patients with IPI

of nalbuphine or saline than in patients given IPI of ropivacaine alone.[9] Morsy and Abdalla[21] found a higher incidence of PONV with IPI of nalbuphine and lidocaine. This finding of nausea and vomiting seen in our study with the ropivacaine-nalbuphine group can be attributed to the pharmacodynamic effect of nalbuphine on the chemoreceptor trigger zone and due to its direct effect on the gastrointestinal tract.[22] Sedation was seen in 5 patients in Group RN, and no sedation was seen in Group RD. The level of sedation observed was 2 (patient being co-operative, oriented, and tranquil). This observation was in concordance with the study conducted by Mahajan et al.[20] and Singh et al.[9]

The limitation of the present study is the post-operative pain, which is a subjective experience and can be difficult to quantify objectively and compare when comparing various treatment options. As there are very few studies in the past on the addition of dexmedetomidine and nalbuphine to IP ropivacaine, further studies with different doses of dexmedetomidine and nalbuphine, timing, concentrations of LA, and routes of administration are needed to provide maximal benefit in terms of post-operative pain relief with minimal adverse effects after laparoscopic surgeries. Sample size was also small in our study and large multicenter trials are required to reproduce the findings of our study.

Limitations of the study

The pain perception varies from patient to patient and depends on the pain threshold, emotional and psychological well being of patient. The test used to quantify pain was subjective.Our sample size was also small, so for a better assessment more large sample trials are required to reproduce the findings of our study.

CONCLUSION

The addition of dexmedetomidine or nalbuphine to ropivacaine provides excellent post-operative analgesia when administered at the end of LC. Both the drugs in combination with ropivacaine were effective in providing adequate post-operative pain relief. However, dexmedetomidine appears to be superior to nalbuphine in terms of prolonged post-operative analgesia, lesser requirement of rescue analgesia, and less complications.

ACKNOWLEDGMENT

None.

REFERENCES

1. Gharaibeh KI and Al-Jaberi TM. Bupivacaine instillation into gallbladder bed after laparoscopic cholecystectomy: Does it decrease shoulder pain. J Laparoendosc Adv Surg Tech A. 2000;10(3):137-141.
https://doi.org/10.1089/lap.2000.10.137
2. Bisgaard T, Kehlet H and Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. Eur J Surg. 2001; 167(2):84-96.
https://doi.org/10.1080/110241501750070510
3. Barczynski M, Konturek A and Herman RM. Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of pneumoperitoneum for laparoscopic cholecystectomy: A randomized, double-blind, placebo controlled study. Surg Endosc. 2006;20(7):1088-1093.
https://doi.org/10.1007/s00464-005-0458-1
4. Wills VL and Hunt DR. Pain after laparoscopic cholecystectomy. Br J Surg. 2000;87(3):273-284.
https://doi.org/10.1046/j.1365-2168.2000.01374.x
5. Verma GR, Lyngdoh TS, Kaman L and Bala I. Placement of 0.5% bupivacaine-soaked surgicel in the gallbladder bed is effective for pain after laparoscopic cholecystectomy. Surg Endosc. 2006;20(10):1560-1564.
https://doi.org/10.1007/s00464-005-0284-5
6. Pasqualucci A, Contardo R, Da Brol U, Colo F, Terrosu G, Donini A, et al. The effects of intraperitoneal local anesthetic on analgesic requirements and endocrine response after laparoscopic cholecystectomy: A randomized double-blind controlled study. J Laparoendosc Surg. 1994;4(6):405-412.
https://doi.org/10.1089/lps.1994.4.405
7. Singh A, Mathur S and Shukla V. Postoperative analgesia with intraperitoneal ropivacaine with and without fentanyl after laparoscopic cholecystectomy: A randomized double-blind controlled trial. OA Anaesth. 2013;1:9.
https://doi.org/10.13172/2052-7853-1-1-719
8. Khurana S, Garg K, Grewal A, Kaul TK and Bose A. A comparative study on postoperative pain relief in laparoscopic cholecystectomy: Intraperitoneal bupivacaine versus combination of bupivacaine and buprenorphine. Anesth Essays Res. 2016;10(1):23-28.
https://doi.org/10.4103/0259-1162.164731
9. Singh S, Giri MK, Sing M and Giri NK. A clinical comparative study of intraperitoneal instillation of ropivacaine alone or ropivacaine with nalbuphine for postoperative analgesia in laparoscopic cholecystectomy. Anesth Pain Intensive Care. 2017;21(3):335-339.
10. Shukla U, Prabhakar T, Malhotra K, Srivastava D and 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):234-239.
https://doi.org/10.4103/0019-5049.155001
11. Labille T, Mazoit JX, Paqueron X, Franco D and Benhamou D. The clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. Anesth Analg. 2002;94(1):100-105.
https://doi.org/10.1213/00000539-200201000-00019
12. Ng A and Smith G. Intraperitoneal administration of analgesia: Is this practice of any utility? Br J Anaesth. 2002;89(4):535-537.
https://doi.org/10.1093/bja/aef219
13. Moller R and Covino BG. Cardiac electrophysiologic properties of bupivacaine and lidocaine compared with those of ropivacaine, a new amide local anesthetic. Anesthesiology. 1990; 72(2):322-329.
https://doi.org/10.1097/00000542-199002000-00019

14. Karamanlioglu B, Turan A, Memis D, Kaya G, Ozata S and Ture M. Infiltration with ropivacaine plus lornoxicam reduces postoperative pain and opioid consumption. Can J Anaesth. 2005;52(10):1047-1053.
https://doi.org/10.1007/bf03021603
15. Kamibayashi T and Maze M. Clinical uses of alpha2-adrenergic agonists. Anesthesiology. 2000;93:1345-1349.
https://doi.org/10.1097/00000542-200011000-00030
16. Jairath A, Gupta S, Singh K and Katyal S. Can intraperitoneal tramadol decrease pain in patients undergoing laparoscopic cholecystectomy in postoperative period? A randomized controlled trial. World J Lap Surg. 2017;10(1):26-29.
https://doi.org/10.5005/jp-journals-10007-1297
17. Praveena BL, Bharathi B and Sahana VR. Intraperitoneal ropivacaine with dexmedetomidine or fentanyl for postoperative analgesia following laparoscopic cholecystectomy: A comparative randomized trial. Anesth Essays Res. 2019;13(1):169-173.
https://doi.org/10.4103/aer.aer_191_18
18. Modir H, Yazdi B, Piri M and 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):88-93.
https://doi.org/10.4103/2045-9912.314327
19. Chiruvella S and Nallam SR. Intraperitoneal instillation of ropivacaine plus dexmedetomidine for pain relief after laparoscopic hysterectomy: A comparison with ropivacaine alone. J NTR Univ Health Sci. 2016;5:93-7.
https://doi.org/10.4103/2277-8632.185432
20. Mahajan L, Singh AP, Kaur SS and Kumari A. Comparison of the efficacy of intraperitoneal instillation of butorphanol versus nalbuphine as adjuvants to ropivacaine for postoperative pain relief in patients undergoing laparoscopic cholecystectomy under general anesthesia: A randomized, double-blind placebo-controlled study. Anesth Essays Res. 2022;16(2):191.
https://doi.org/10.4103/aer.aer_74_22
21. Morsy KM and Abdalla EE. Postoperative pain relief after laparoscopic cholecystectomy: Intraperitoneal lidocaine versus nalbuphine. Ains Shams J Anesthesiol. 2014;7:40-44.
https://doi.org/10.4103/1687-7934.128402
22. Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MK, Ortega MC, et al. Opioids. In: South Asian Edition of Clinical Anesthesia. 8th ed., Ch. 20. New Delhi: Wolters Kluwer; 2017. p. 505-526.

Authors Contribution:
SB - Definition of intellectual content, prepared first draft of manuscript, data collection, data analysis, manuscript preparation, and implementation of study protocol; **TAS -** Concept, design, clinical protocol, literature survey, and manuscript preparation; **RA -** Concept, clinical protocol, design of study, data collection, manuscript preparation, editing, manuscript revision, and submission of article; **HS -** Design of study, revision of manuscript, literature survey, and preparation of figures; **AMC -** Coordination and manuscript revision.

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Source of Funding: Nil, **Conflicts of Interest:** None declared.