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Comparative study of analgesic efficacy of levobupivacaine alone and levobupivacaine plus dexmedetomidine in patients undergoing laparoscopic cholecystectomy

Neha Pareek[1], Nikita Badmaliya[2], Sweta Bharadiya[3], Pramila Soni[4]

[1]Assistant Professor, [2]Senior Resident, Department of Anaesthesia, Dr. M. K. Shah Medical College and Research Center, Ahmedabad, Gujarat, [3,4]Assistant Professor, Department of Anaesthesia, Government Medical College, Pali, Rajasthan, India

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ABSTRACT

Background: Instillation of intraperitoneal lignocaine, bupivacaine, levobupivacaine, and ropivacaine has been used, following laparoscopic gynecological and general surgical procedures, to reduce postoperative pain through randomized trials for many years. **Aims and Objectives:** Intraperitoneal instillation of 0.25% levobupivacaine provides effective analgesia, and we have added dexmedetomidine 1 mcg/kg to compare the analgesic efficacy of levobupivacaine alone and levobupivacaine plus dexmedetomidine in patients undergoing laparoscopic cholecystectomy (LC). **Materials and Methods:** A total of 120 patients of either sex were included in the study. The age range of the included patients was 25–70 years. All the included patients had the American Society of Anesthesiologists physical status I and II and had to undergo LC surgeries. All patients were randomly divided into two groups of 60 patients each. **Results:** The mean visual analog scale (VAS) score readings at 4 and 8 h in group A were 21.48 ± 1.80 and 25.41 ± 2.50, respectively, and in group B were 18.14 ± 0.90 and 20.95 ± 1.78, respectively. At 4, 8, and 12 h postoperatively, the mean VAS readings for group B were statistically significantly lower in comparison to the mean VAS readings for group A ($P < 0.05$). Among the A group and B group, the number of patients requiring rescue analgesia was lower in group B in comparison to group A ($P < 0.05$). **Conclusion:** It was concluded that intraperitoneal instillation of local anesthetic is an easy, cheap, and noninvasive method, which provides good analgesia in the immediate postoperative period after laparoscopic surgery. Adding dexmedetomidine 1 μg/kg to intraperitoneal levobupivacaine 0.25% in LC decreases the postoperative analgesic needs in the postoperative period compared to levobupivacaine 0.25% alone and improves the quality and duration of analgesia.

Key words: Dexmedetomidine; Intraperitoneal injection; Levobupivacaine; Pain; Laparoscopic cholecystectomy

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INTRODUCTION

Laparoscopy has been a boon to the field of surgery for its different advantages over open surgery like a smaller and more cosmetic incision, reduced blood loss, reduced post-operative pain, faster recovery, faster discharge, and a subsequent decrease in health-care cost.[1] Early post-operative pain is the most common complication associated with laparoscopic surgeries. Pain after laparoscopy is due to stretching and inflammation of the peritoneum, irritation of the phrenic nerve, and residual carbon dioxide in the peritoneal cavity.[2]

Pain after laparoscopic cholecystectomy (LC) is a common complaint that prolongs the duration of hospital stay and

Address for Correspondence:
Dr. Pramila Soni, Assistant Professor, Department of Anaesthesia, Government Medical College, Pali, Rajasthan, India.
Mobile: +91-95888 58931. **E-mail:** drpramilasoni22@gmail.com

thus increases morbidity. This is especially concerning for centers that are performing LC as a day care procedure.[3] Postoperative visceral and shoulder pain occurring after LC results from peritoneal and diaphragmatic stretching and irritation of nerves, changes in intra-abdominal pH, release of inflammatory mediators, and retention of the insufflated gas in the abdominal cavity.[3,4]

Instillation of intraperitoneal lignocaine, bupivacaine, levobupivacaine, and ropivacaine has been used, following laparoscopic gynecological and general surgical procedures, to reduce postoperative pain through randomized trials for many years. The use of adjuvant drugs in combination with intraperitoneal instillation of local anesthetic has been found to reduce post-operative pain following LC more effectively.[5] A noteworthy prolongation of the time length of analgesia had been stated when dexmedetomidine was supplemented in epidural blockades LA, caudal blocks, subarachnoid blocks, paravertebral blocks, brachial plexus blocks, ulnar nerve blocks, and greater palatine nerve blocks.[6,7]

Levobupivacaine is advantageous for intraperitoneal use as it is a long-acting local anesthetic with less cardiovascular and neurological toxicity.[8] Dexmedetomidine is a selective alpha-2 agonists with both analgesic and sedative properties. Its use in combination with levobupivacaine is associated with the prolongation of local anesthetic effect either epidurally, intrathecally, or intraperitoneally.[7,9]

Intraperitoneal instillation of 0.25% levobupivacaine provides effective analgesia, and we have added dexmedetomidine 1 mcg/kg to compare the analgesic efficacy of levobupivacaine alone and levobupivacaine plus dexmedetomidine in patients undergoing LC.

Aims and objectives

Present study was done with an aim to compare the analgesic efficacy of levo-bupivacaine alone and levo-bupivacaine plus Dexmedetomidine in patients undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS

This was a prospective, randomized, and blind study. A total of 120 patients of either sex were included in the study. The age range of the included patients was 25–70 years. All the included patients had the American Society of Anesthesiologists (ASA) physical status I and II and had to undergo LC surgeries. We found that approximately 60 patients in each group are enough to get a power of 0.8 to detect a 15% or more decrease in pain intensity and an increase in the duration of postoperative analgesia in the dexmedetomidine group.

The included patients were explained in detail about the purpose of the study and surgical procedure. Only those patients who provided the written informed consent were included in the study. The study drugs were prepared by an anesthesiologist not involved in the study. The anesthesiologists, who observed the patients and the surgeons, were unaware of the study group until the end of the study.

All patients were randomly divided into two groups of 60 patients each. The syringe was labeled with the patient's name and was given to the investigator. Patients were randomly allocated to one of the groups using the sealed envelope method of randomization:

- Group A: Patients who were given intraperitoneal instillation of 40 mL of 0.25% levobupivacaine
- Group B: Intraperitoneal instillation of 40 mL of 0.25% levobupivacaine plus 1 mcg/kg dexmedetomidine.

Inclusion criteria

- ASA grade I and II patients
- Age group of 25–70 years
- Patients giving informed consent.

Exclusion criteria

Patient's refusal, patients belonging to ASA grade III and grade IV, patients physically dependent on narcotics, patients with a history of drug allergy, patients with sepsis, hemorrhagic diathesis, or neurological diseases, head injury cases, and patients with cardiac, pulmonary, and hepatorenal disorders were excluded from the study.

All the patients underwent pre-anesthetic examination the day before surgery, and all routine and specific investigations were noted. The patients were nil per orally for 8 h. The patients were transported to the operating room, an 18-gauge intravenous catheter was inserted, and 6–8 mL/kg/h crystalloid was infused. General physical examinations with an examination of the cardiovascular and respiratory systems were done.

Postoperatively, the patients were assessed for pain utilizing a visual analog scale (VAS). The patient was also enquired about nausea-vomiting, confusion, dizziness, and number of times and dose of rescue analgesia using a predesigned pro forma, which was assessed at 0, 1, 4, 8, 12, and 24 h.

A rescue analgesic was injection diclofenac 75 mg, slow intravenously (in 100 mL normal saline). It was given when the VAS is more than 3, and injection dexmedetomidine 1 mcg/kg per kg intravenously (in 100 mL normal saline) for any patient who still demanded more analgesia. The data from the present study were statistically analyzed to draw relevant conclusions.

RESULTS

The age of the patients in both groups varied from 25 to 70 years. The mean age in group A was 39.9±15.22 years and in group B was 46.9±10.4 years. The mean duration of surgery in group A was 58.82±10.22 min and in group B was 63.32±8.65 min (Table 1). The difference in the duration of surgery in all the groups was statistically significant (P<0.05).

The mean VAS score readings were recorded postoperatively in both groups at 0, 1, 4, 8, 12, and 24 h. 0 time was the time of the end of surgery. The mean VAS score reading was lower in comparison to group B at different time intervals. The mean VAS score readings at 4 and 8 h in group A were 21.48±1.80 and 25.41±2.50, respectively, and in group B were 18.14±0.90 and 20.95±1.78, respectively. At 4, 8, and 12 h postoperatively, the mean VAS readings for group B were statistically significantly lower in comparison to the mean VAS readings for group A (P<0.05) (Table 2).

Among the A group and B group, the number of patients requiring rescue analgesia was lower in group B in comparison to group A (P<0.05) (Table 3).

Table 1: Duration of surgery in minutes in all the groups

Duration	Group A	Group B	P-value
Mean±SD	58.82±10.22	63.32±8.65	0.03*

*Indicates statistical significance at P≤0.05. SD: Standard deviation

Table 2: Mean VAS score in all the groups

Time	Group A	Group B	P-value
0 h	11.92±0.56	12.20±0.50	0.89
1 h	14.80±1.40	14.21±2.22	0.74
4 h	21.48±1.80	18.14±0.90	0.002*
8 h	25.41±2.50	20.95±1.78	0.05*
12 h	33.35±2.54	27.75±4.32	0.001*
24 h	29.36±3.20	28.84±4.64	0.07

*Indicates statistical significance at P≤0.05. VAS: Visual analog scale

Table 3: Time to first rescue analgesic

Variable	Group A	Group B	P-value
Time to 1st rescue analgesic (h)	12.01±3.80	15.90±4.21	0.001*

*Indicates statistical significance at P≤0.05

DISCUSSION

Post cholecystectomy pain includes three types, visceral, parietal, and shoulder pain with varying degrees in intensity, latency, and duration. Previous studies suggested that parietal pain is predominant; other studies reported that visceral pain is predominant due to small incisions and surgical trauma and tissue destruction in the viscera are more.[10] Opioid drugs, nonsteroidal anti-inflammatory drugs, or local anesthetics were used to reduce pain after laparoscopic surgeries with its adverse effects such as respiratory depression and nausea. Intraperitoneal application of local anesthetic drugs becomes an important way to decrease postoperative pain, nausea, vomiting, and decreased cost.[11]

Various adjuvants, including opioids, were added in the past to augment the efficacy of local anesthetic instillation intraperitoneally; however, no studies were conducted with clonidine added intraperitoneally. In this study, we evaluated the effect of adding clonidine to levobupivacaine for intraperitoneal instillation at the end of gallbladder dissection under the two domes of the diaphragm and gallbladder bed for postoperative pain relief; pain was assessed using VAS score for pain.[12]

Although there was a considerable difference in the duration of surgery between the two groups, it can be considered an incidental finding in a small sample. The mean VAS score reading was lower in group B in comparison to group A at different time intervals. The mean VAS values for group B were statistically significantly lower than the mean VAS readings for group A at 4, 8, and 12 h postoperatively. In a study conducted by Sharan et al.,[13] authors compared adding dexmedetomidine to intraperitoneal levobupivacaine in patients undergoing LC and found similar results to the present study. Our study is in concordance with those of Bakhamees et al., Narchi et al., and Upadya et al., who found that intraperitoneal local anesthetic (IPLA) is more effective in reducing pain up to 48 h and had lower VAS scores up to 4 h in the postoperative period.[14-16]

Among the A group and B group, the number of patients requiring rescue analgesia was lower in group B in comparison to group A. In a study conducted by Sharan et al.,[13] analogous findings were observed, and it was found that the instillation of bupivacaine and ropivacaine intraperitoneally was an effective method of postoperative pain relief in LC. Shukla et al.[17] added dexmedetomidine or tramadol to intraperitoneal bupivacaine 0.25% in elective LC with a better analgesic result with respect to VAS score over 24 h and overall analgesic requirement. This finding collaborated with this study also where the VAS score was significantly lower up to 24 h in Group II.

Limitations of the study

The limitations of the study include not measuring the plasma concentration of the study drugs after administration,the effects of these drugs were observed only in healthy ASA-I, II group of patients and assessment of

post-operative pain was based upon subjective experience of the patients which is difficult to quantify objectively.

CONCLUSION

The findings in our study indicate that intraperitoneal instillation of dexmedetomidine in combination with levobupivacaine in LC significantly reduces the post-operative pain and the analgesic requirement in the post-operative period compared to levobupivacaine alone and is associated with lesser side effects and better hemodynamics.

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Authors Contribution:
NP- Concept and design of the study, and prepared the first draft of the manuscript; **NB-** Interpreted the results; reviewed the literature and manuscript preparation; **SB-** Concept, coordination, and preparation of the manuscript; **PS-** Statistical analysis and interpretation.

Work attributed to:
Department of Anesthesia, Dr. M. K. Shah Medical College and Research Center, Ahmedabad, Gujarat, India.

Orcid ID:
Dr. Neha Pareek - https://orcid.org/0009-0007-3316-6110
Dr. Nikita Badmaliya - https://orcid.org/0009-0007-1665-1915
Dr. Sweta Bharadiya - https://orcid.org/0000-0002-8189-5875
Dr. Pramila Soni - https://orcid.org/0000-0003-1002-5255

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