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Research Article

Comparative Evaluation of Analgesic Efficacy of Intraperitoneal Ropivacaine with and Without Dexmedetomidine for Postoperative Pain Relief Following Laparoscopic Cholecystectomy

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ABSTRACT

Aim: The aim of the present study was to compare analgesic efficacy and safety of intraperitoneal instillation of ropivacaine with or without dexmedetomidine for post operative analgesia after laparoscopic cholecystectomy.
Methods: The study was conducted at the OT complex of the Department of General Surgery as well as the department of Anaesthesiology of the North Bengal Medical College and Hospital, a tertiary care teaching institute of Darjeeling, India from December 2022 to November 2023.The study population consisted of adult patients of either sex admitted to the study institution to undergo elective laparoscopic cholecystectomy.
Results: It was observed that the mean age of the participants receiving ropivacaine only was 40.4±3.7 years, and that receiving ropivacaine and dexmedetomidine was 42.8±4.2 years. It was observed that 54.5% of the participants in group R and 57.6% of the participants in group RD were men.It was observed that all of the participants from either study groups had a ASA physical status of grade I.It was observed that the mean duration of surgery for group R participants was 59.5±8.1 mins, while that for group RD patients was 57.9±7.2 mins.It was observed that the total duration of anesthesia in the group R participants was 69.7±12.4 mins, while that for group RD participants was 68.1±9.7 mins.
Conclusion: The study concluded that the combination of ropivacaine and dexmedetomidine provided superior postoperative analgesia compared to ropivacaine alone in patients undergoing elective laparoscopic cholecystectomy. Participants in group RD, who received the combination therapy, reported significantly lower pain scores at 1, 2, 4, 8, and 12 hours postoperatively. Additionally, group RD patients required rescue analgesia significantly later time period and analgesic dose required is also lower than in group R.

Keywords: *Analgesic efficacy, intraperitoneal instillation, ropivacaine, dexmedetomidine, laparoscopic cholecystectomy.*

INTRODUCTION

Pain management is critical aspect of surgical care; and anaesthesia plays a central role in ensuring that patients are comfortable and pain free during and after surgery. Anaesthesia involves the use of medications and techniques to induce reversible loss of consciousness/sensation; allowing surgeons to perform procedures without causing undue pain or distress to the patient. The role anaesthesia in surgery is multifaceted. It involves not only inducing and maintaining a state of unconsciousness but also ensuring effective pain management before, during and after the surgical procedure.[1]

Laparoscopy is a type of surgical procedure that allows surgeon to access the inside of abdomen and pelvis with minimal incisions over the skin. Large incisions can be avoided during laparoscopy by using an instrument with a light source and

a camera, which relays image of the inside of the abdomen or pelvis to television monitor. The advent of laparoscopy procedures has revolutionized and have almost replaced the traditional open procedures. Faster wound healing gives cosmetic benefit to the patient and it is associated with lesser intraoperative blood loss, faster recovery time, reduced postoperative complications, early enteral feed, reduced hospital stay[2] and also making cost effective, thus laparoscopic approach has almost replaced open cholecystectomies.[3] These days almost all cholecystectomies worldwide, including developing countries such as India performed by the laparoscopic method, and the procedure has proven its efficacy, safety, and excellent outcomes.[4]

However, the early postoperative pain experienced by patients is a hindrance and may negate all the advantages of laparoscopic procedures, from the perspective of patients, it manifests as postoperative pain. In the immediate postoperative period, patients have reported to experiencing significant amount of pain.[5] The origin of this pain after laparoscopic cholecystectomy is multifactorial, which may be due to increased pressure of carbon dioxide in the abdomen during the insufflation procedure as well as diaphragmatic inflammation during the surgery.[6] It has also been observed that a sustained intraoperative pressure on the capillary beds in the abdominal viscera can also lead to increase in the duration as well as the intensity of the pain felt by the patients in the postoperative period.[5] Postoperative period pain can affect all organ systems, and can lead to dysfunctions in the respiratory (atelectasis, tachypnea, hypoxemia etc.), cardiovascular (tachycardia, increase in BP, increased oxygen demand), gastrointestinal (decreased emptying, and reduced motility), genitourinary (retention of urine), musculoskeletal (reduced mobility and increased risk of DVT), and can also affect the patient psychologically.[7] Following laparoscopic cholecystectomy, postoperative pain has been observed to be of the visceral type, located in the upper abdominal, lower abdominal, or shoulder region.[8] Post cholecystectomy pain usually lasts for 24 hours, but it has been reported that this pain remain up to 3 days postoperatively.[9]

Ropivacaine is a long-acting, amide local anesthetic agent which is similar to Bupivacaine in its structure and pharmacodynamics.[10] It reversibly blocks the entry of sodium into the nerve cell membranes, leading to decreased membrane permeability to sodium and raises the threshold for nerve excitability. Ropivacaine slows the nerve conduction and reduces the rate of rise of the action potential, thus providing analgesia.[11] The intraperitoneal infiltration of ropivacaine is a widely-used method for postoperative pain management following laparoscopic cholecystectomy, owing to is excellent analgesic and good safety profile.[12] In the recent years, it has been observed that the analgesic effects of ropivacaine, especially in the context of intraperitoneal instillation, can be significantly prolonged with the addition of an adjuvant drug.[13] One such drug that has seen growing interest is dexmedetomidine.It has been observed that Ropivacaine with Dexmedetomidine as an adjuvant is associated with prolongations of local anesthetic(LA) effect.[14]There are benefits of adding alpha adrenergic agonists such as dexmedetomidine to ropivacaine in the context of post-laparoscopy pain management,but as there are comparatively fewer studies done previously for this purpose.[15,16]

The aim of the present study was to compare analgesic efficacy and safety of intraperitoneal instillation of ropivacaine with or without dexmedetomidine for post operative analgesia after laparoscopic cholecystectomy.

MATERIALS AND METHODS

The study was conducted at the OT complex of the Department of General Surgery as well as the department of Anaesthesiology of the North Bengal Medical College and Hospital, a tertiary care teaching institute of Darjeeling, India from December 2022 to November 2023.The study population consisted of adult patients of either sex admitted to the study institution to undergo elective laparoscopic cholecystectomy.

Inclusion criteria

The inclusion criteria for the study population were –

1. Patients aged 18-60 years
2. Patients of either sex
3. Patients admitted to the study institution to undergo elective laparoscopic cholecystectomy
4. Patients providing written informed consent to take part in the present study
5. Patients with American Society of Anesthesiologists (ASA) physical status of I or II.

Exclusion criteria

The exclusion criteria for the participants that were considered for the current study were as follows

1. Patient's refusal to participate in the study.
2. Patients with known sensitivity to study drugs.
3. Patients with renal and hepatic insufficiency.
4. Patients with obesity (body mass index > 35/kg/m).
5. Pregnant and lactating women.

Study tools
The following tools were used in the present study:
1.Proforma for written informed consent.
2.Proforma for data collection.
3.Pre anaesthetic checkup questionnaires.
4.Inj. dexmedetomidine.
5.VAS score sheet
6.Inj. 0.20% Ropivacaine.
7.Inj. Diclofenac sodium.
8.Emergency drugs for resuscitation like inj. Adrenaline, inj. Atropine etc.
9.Multichannel Monitor

Study variables
The study variables included in the current study were as follows
A. Quality of analgesia determined by 10 cm LINEAR VAS SCORE for 24 hours.
B. Time to first request of rescue analgesic.
C. Total dose of rescue analgesic required in the first 24 hours postoperatively.
D. Total number of patients requiring rescue analgesic.

ETHICAL CONSIDERSATIONS
The Institutional Ethics Committee of North Bengal Medical College & hospital, Darjeeling, reviewed and approved the project before it was carried out.

All of the participants were informed in their own language about the study and their rights for participation before providing data for the researcher-administered questionnaire. They were informed about the participant's role and rights, to clarify that their participation was voluntary, the information was treated confidentially, and they could withdraw from the study at any time.

After the collection of data, the data was cleaned, anonymised and stored in a password protected spreadsheet for data analysis.

DATA ANALYSIS
The collected data were checked for consistency, completeness and entered into Microsoft Excel (MS-EXCEL, Microsoft Corp.) data sheet. Analyzed with the statistical program Statistical Package for the Social Sciences (IBM SPSS, version 22). Data were organized and presented using the principles of descriptive and inferential statistics. The data were categorized and expressed in proportions. The continuous data were expressed as mean±SD. The data were graphically presented in the form of tables, vertical bars, horizontal bar, pie diagram. Where analytical statistics were performed, a p-value of <0.05 was considered to be statistically significant for the purpose of the study.

RESULTS

Table 1: Distribution of study participants according to their mean age

Age (years)	**group R**	**group RD**	**p-value**
Mean	40.4	42.8	0.842
SD	3.7	4.2	
Total	**42.6±3.8 years**		

It was observed that the mean age of the participants receiving ropivacaine only was 40.4±3.7 years, and that receiving ropivacaine and dexmedetomidine was 42.8±4.2 years. The difference between the two groups was not found to be statistically significant on analysis.

Table 2: Distribution of study participants according to their sex, ASA status, Duration of surgery (mins) and Duration of anaesthesia (min)

Sex	**group R (%)**	**group RD (%)**	**p-value**
Male	18 (54.5)	19 (57.6)	0.822
Female	15 (45.5)	14 (42.4)	
Total	**33 (100)**	**33 (100)**	
ASA status			
Grade I	33 (100)	33 (100)	-
Grade II	0 (0)	0 (0)	
Total	**33 (100)**	**33 (100)**	

Duration of surgery (mins)			
Mean	59.5	57.9	0.331
SD	8.1	7.2	
Total	**58.8±9.6 mins**		
Duration of anaesthesia (min)			
Mean	69.7	68.1	0.277
SD	12.4	9.7	
Total	**68.9±9.9**		

It was observed that 54.5% of the participants in group R and 57.6% of the participants in group RD were men. The difference between the two study groups was not found to be statistically significant on analysis.It was observed that all of the participants from either study groups had a ASA physical status of grade I.It was observed that the mean duration of surgery for group R participants was 59.5±8.1 mins, while that for group RD patients was 57.9±7.2 mins. The difference between the two groups was not found to be statistically significant on analysis (0.331).It was observed that the total duration of anesthesia in the group R participants was 69.7±12.4 mins, while that for group RD participants was 68.1±9.7 mins. The difference between the two study groups was not found to be statistically significant (p-value 0.277).

Table 3: distribution of study participants according to their preoperative hemodynamic parameters

Hemodynamic parameters (mean ± SD)	group R	group RD	p-value
Pulse rate	84.6±12.1	86.1±8.8	0.544
Systolic blood pressure	134.4±22.1	131.6±9.9	0.422
Diastolic blood pressure	84.4±6.1	82.9±8.4	0.389
SpO2	98.3±1.1	97.9±1.3	0.188

It was observed that the there was no statistically significant difference between the two study groups with respect to their hemodynamic parameters in the preoperative period.

Table 4: Distribution of study participants according to their mean VAS score at 24 hours

Mean VAS score	group R	group RD	p-value
30 mins	0.35±0.48	0.25±0.44	0.403
1 hour	1.81±0.52	1.42±0.5	0.004*
2 hours	2.21±0.62	1.64±0.66	0.001*
4 hours	4.2±0.88	1.5±0.79	<0.001*
8 hours	3.34±1.43	1.88±1.17	<0.001*
12 hours	4.22±1.54	2.33±1.29	<0.001*
24 hours	2.27±0.67	1.89±0.88	0.064

It was seen that the mean VAS score of the two groups of participants was not statistically significant at 30 mins of observation (0.35±0.48 in group R and 0.25±0.44 in group RD, p-value 0.403). However, on subsequent observations at 1 hour, 2 hours, 4 hours, 8 hours, and 12 hours, group R patients (1.81±0.52, 2.21±0.62, 4.2±0.88, 3.34±1.43 and 4.22±1.54 respectively) had statistically significantly higher VAS scores as compared to group RD patients (1.42±0.5, 1.64±0.66, 1.5±0.79, 1.88±1.17, and 2.33±1.29 respectively. At the end of 24 hours, however, the difference between the mean pain scores of the two groups was found not to be statistically significantly different (2.27±0.67 in group R vs 1.89±0.88 in group RD, p-value 0.064).

Table 4: Distribution of study participants according to number of patients requiring rescue analgesia in 24 hours

Rescue analgesia required	group R (%)	group RD (%)	p-value
Yes	33 (100)	21 (63.6)	0.003*
No	0	12 (36.4)	
Total	**33 (100)**	**33 (100)**	

It was observed that all of the participants receiving ropivacaine alone required rescue analgesia in 24 hours, while 21 (63.6%) of the participants required it in the ropivacaine+ dexmedetomidine group. The difference between the two was found to be statistically significant on analysis (p-value 0.003<0.05).

Table 5: Distribution of study participants according to incidence of adverse events

Adverse events	group R (%)	group RD (%)	p-value
Bradycardia	0 (0)	2 (6.1)	0.472
Nausea	8 (24.2)	1 (3)	0.031*
Vomiting	2 (6.1)	0 (0)	0.472
Shoulder tip pain	1 (3)	0 (0)	0.998

It was seen that group R patients had significantly higher incidence of nausea as compared to group RD patients (24.2% vs 3%, p-value 0.031). On the other hand, the groups were not statistically significantly different with respect to the incidence of bradycardia, vomiting and shoulder tip pain among them.

DISCUSSION

The literature supports that ropivacaine is a well-established local anesthetic commonly used for postoperative analgesia due to its long-acting effects and lower cardiotoxicity compared to bupivacaine.[17] Dexmedetomidine, a selective alpha-2 adrenergic agonist, has been shown to enhance the analgesic effects of local anesthetics like ropivacaine when used in combination, potentially due to its sedative and analgesic properties that modulate pain pathways and reduce inflammatory responses.[18]

The mean age of participants in the ropivacaine-only group was 40.4±3.7 years, while those in the combined treatment group had a mean age of 42.8±4.2 years. The p-value of 0.842(i.e.>0.05) indicates no statistically significant difference in age between the two groups, suggesting that age is not a confounding factor in the comparison of analgesic efficacy and safety between the two groups. Furthermore, 54.5% of the participants in group R and 57.6% of the participants in group RD were men. The mean age of the patients in the present study is similar to that reported by authors such as Chiruvella et al[13] (40.1±2.0 years) and Praveena et al[14] (44.6±6.9 years).

In this study, all participants from both study groups had an American Society of Anesthesiologists (ASA) physical status of grade I, indicating they were all considered healthy with no systemic disease. This uniformity in ASA status helps ensure that the participants' baseline health conditions did not bias the outcomes related to the analgesic efficacy and safety of the interventions. The mean duration of surgery for participants in group R (ropivacaine only) was 59.5±8.1 minutes, while for group RD (ropivacaine and dexmedetomidine), it was 57.9±7.2 minutes. The p-value of 0.331 (i.e.>0.05)suggests that there was no statistically significant difference in the duration of surgery between the two groups. The average surgical time reported in the present study is consistent with findings in existing literature. For instance, a study by Simopoulos et al. reported an average operative time of 60.2±15.3 minutes, indicating similar efficiency in surgical procedures.[19] Additionally, a meta-analysis by Keus et al. found that the mean duration of laparoscopic cholecystectomy ranged between 45 to 90 minutes, further supporting the present study's results.[20] However, some studies have reported slightly longer operative times. For example, a comprehensive review by Shea et al. noted an average surgical time of 70±20 minutes.[21]

The Visual Analog Scale (VAS) scores observed in this study provide significant insights into the analgesic efficacy of group R (ropivacaine alone) versus group RD (ropivacaine with dexmedetomidine) for postoperative pain management following laparoscopic cholecystectomy. At 30 minutes postoperatively, there was no statistically significant difference between the two groups, with mean VAS scores of 0.35±0.48 in the group R and 0.25±0.44 in the group RD, as indicated by a p-value of 0.403(i.e.>0.05). However, significant differences emerged in subsequent observations. At 1 hour, 2 hours, 4 hours, 8 hours, and 12 hours postoperatively, group R reported higher mean VAS scores (1.81±0.52, 2.21±0.62, 4.2±0.88, 3.34±1.43, and 4.22±1.54 respectively) compared to group RD (1.42±0.5, 1.64±0.66, 1.5±0.79, 1.88±1.17, and 2.33±1.29 respectively). These differences were statistically significant(p value <0.05), highlighting the superior analgesic effect of the combination therapy over ropivacaine alone during these time points. More or less same result has been reported by Yu et al[16] and Chiruvella et al.[13]The study's findings on the need for rescue analgesia highlight the superior analgesic efficacy of combining ropivacaine with dexmedetomidine compared to using ropivacaine alone. All participants in the group R (ropivacaine -only) required rescue analgesia within 24 hours, whereas only 63.6% of those in the group RD(ropivacaine plus dexmedetomidine) needed additional pain relief. This difference was statistically significant, with a p-value of 0.003(i.e<0.05). Furthermore, participants in the group RD required rescue analgesia significantly later than those in the group R, with a highly significant p-value of <0.001. Additionally, patients receiving only ropivacaine needed significantly higher doses of rescue analgesia compared to those receiving the combination therapy. Zhu et al. in their study reported that when added to ropivacaine, dexmedetomidine led to significantly reduced requirement for rescue analgesia as well as a significantly reduced dosage for the same.[22]

One notable observation in the present study was the significantly higher incidence of nausea in the group R compared to the group RD, with incidences of 24.2% and 3%, respectively. This difference was statistically significant, with a p-value of 0.031(i.e<0.05). However, the incidence of other postoperative complications such as bradycardia, vomiting, and shoulder tip pain did not differ significantly between the two groups. The significantly lower incidence of nausea in the

combination group suggests an additional benefit of using dexmedetomidine as an adjuvant. Nausea and vomiting are common postoperative complications that can significantly impact patient comfort and recovery. The antiemetic properties of dexmedetomidine, potentially mediated through its central sedative effects and reduction in opioid requirements, may contribute to the observed reduction in nausea.[23]

CONCLUSION

The study concluded that the combination of ropivacaine and dexmedetomidine provided superior postoperative analgesia compared to ropivacaine alone in patients undergoing elective laparoscopic cholecystectomy. Participants in group RD, who received the combination therapy, reported significantly lower pain scores at 1, 2, 4, 8, and 12 hours postoperatively. Additionally, group RD patients required rescue analgesia significantly later time period and analgesic dose required is also lower than in group R. The number of patients required rescue analgesia was lesser in group RD as compared to group R, So notable difference in the number of patients not requiring additional pain relief in group RD. Moreover, the incidence of adverse events such as nausea was significantly lower in the combination therapy group. These findings suggest that the addition of dexmedetomidine to ropivacaine enhances the quality of postoperative pain management, leading to better patient outcomes and potentially reducing the overall need for postoperative analgesics.

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