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Original Article

Comparative Study of Intraperitoneal Instillation of Levobupivacaine (0.25%) Plus Dexmedetomidine Versus Ropivacaine (0.25%) Plus Dexmedetomidine for Post-operative Analgesia in Patients Undergoing Laparoscopic Cholecystectomy

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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 post-operative pain through randomized trials for many years. Hence, the present study was undertaken for assessing and comparing the efficacy of intraperitoneal instillation of levobupivacaine (0.25%) and ropivacaine (0.25%) for post-operative analgesia in patients undergoing laparoscopic cholecystectomy (LC).

Materials and Methods: Ninety patients were enrolled and were randomly divided into three groups of 30 each. Group L: Patients were given 20 ml of 0.5% levobupivacaine plus dexmedetomidine at 1 μg per kg body weight and making total volume 40 ml by adding normal saline (NS), intraperitoneally after gallbladder removal. Group R: Patients were given 20 ml of 0.5% ropivacaine plus dexmedetomidine at 1 μg per kg body weight and making total volume 40ml by adding NS, intraperitoneally after gallbladder removal. Group C: Patients were given 40 ml of NS. Postoperatively, the patients were assessed for pain utilizing visual analog scale (VAS). The results were statistically analyzed using latest software.

Results: The mean VAS score reading was lower in Group L and Group R in comparison to Group C at all the time intervals. The number of patients requiring rescue analgesia was significantly higher in Group C in comparison to other study groups. Among the L group and R group, the number of patients requiring rescue analgesia was lower in Group L in comparison to Group R.

Conclusion: Intraperitoneal instillation of local anesthetic solution in LC provided effective post-operative analgesia, but analgesia provided by levobupivacaine plus dexmedetomidine was significantly better than ropivacaine plus dexmedetomidine.

Key words: Dexmedetomidine, Intraperitoneal instillation, Laparoscopic cholecystectomy, Levobupivacaine, Ropivacaine

INTRODUCTION

Gallstones are hardened deposits of the digestive fluid bile that can form within the gallbladder. Laparoscopic removal is now the procedure of choice when cholecystectomy is indicated. Pain after laparoscopic surgery has a visceral component, as a result of surgical handling and diaphragmatic irritation by dissolved carbon dioxide and a somatic component due to the holes made in the abdominal wall for the trocars.[1-3]

Instillation of intraperitoneal local anesthetics has been used following laparoscopic surgical procedures to reduce postoperative pain through randomized trials for many years. The use of adjuvants with of local anesthetic has been found to reduce post-operative pain following laparoscopic

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cholecystectomy (LC) more effectively. Prolongation of time length of analgesia had been stated when dexmedetomidine was supplemented with local anesthetics in epidural blockades, caudal blocks, subarachnoid blocks, paravertebral blocks, brachial plexus blocks, ulnar nerve blocks, and greater palatine nerve blocks.[4-7] Hence, the present study was undertaken for assessing and comparing the efficacy of intraperitoneal instillation of levobupivacaine (0.25%) plus dexmedetomidine and ropivacaine (0.25%) plus dexmedetomidine for post-operative analgesia in patients undergoing LC.

MATERIALS AND METHODS

It was prospective, randomized, double-blind study comprising of 90 patients of American Society of Anesthesiologists (ASA) Grades I and II of age group 18–65 years of either sex, scheduled to undergo LC surgery under general anesthesia. All patients were randomly divided into three groups of 30 each. A double-blind study was done using sealed envelopes which were randomly selected and opened by an assistant, with instruction to instil the relevant drug. The syringe was labeled with the patient's name and was given to the investigator. An independent observer observed the onset of analgesia.

Group L: Patients were given 20 ml of 0.5% levobupivacaine plus dexmedetomidine at 1 μg/kg and making total volume 40 ml by adding normal saline (NS), intraperitoneally after gallbladder removal.

Group R: Patients were given 20 ml of 0.5% ropivacaine instead of levobupivacaine, keeping volume, concentration, and rest of the things similar.

Group C: Patients were given 40 ml of NS.

Pre-anesthetic check-up including detailed history and physical examination of the patient selected for study was carried out a day before surgery and was recorded as per pro forma. General physical examination along with examination of cardiovascular and respiratory system was done. Respiratory rate, pulse rate, and blood pressure were recorded preoperatively.

Patients were kept nil per orally for at least 6 h before operation. The patients were assured, the procedure was explained and a written informed consent was obtained in patient's vernacular language. Postoperatively, the patients were assessed for pain utilizing visual analog scale (VAS). The patients were enquired about nausea, vomiting, confusion, dizziness, number of times, and dose of rescue analgesia using a predesigned pro forma, which were assessed at 0, 0.5, 1, 2, 4, 6, 8, 12, and 24 h.

Rescue analgesics were inj. diclofenac 75 mg slow intravenously (in 100 ml NS) given when VAS was > 3 and injection dexmedetomidine 1 μg/kg intravenously (in 100 ml NS) for any patient who still demanded more analgesia. The data were systematically collected, compiled, and statistically analyzed using latest software (IBM SPSS 21 version). The results were compared to the previous studies.

RESULTS

With respect to the distribution of mean age, sex, difference in occupation, mean weight, ASA grading, and duration of surgery, the difference in the three groups was statistically non-significant ($P > 0.05$); hence, the three groups were comparable with respect to all these parameters [Table 1].

The mean pre-operative systolic blood pressure in Group L, Group R, and Group C was 112.72 ± 10.52 mmHg, 114.23 ± 7.22 mmHg, and 118.51 ± 9.56 mmHg, respectively. The mean systolic blood pressure at 1 h post-operative in Group L, Group R, and Group C was 121.19 ± 9.66 mmHg, 122.29 ± 9.71 mmHg, and 126.86 ± 7.85 mmHg, respectively. The mean pre-operative diastolic blood pressure in Group L, Group R, and Group C was 72.72 ± 5.78 mmHg, 70.12 ± 5.24 mmHg, and 68.56 ± 5.12 mmHg, respectively. The mean diastolic blood pressure at post-operative 1 hour in Group L, Group R, and Group C was 72.91 ± 10.56 mmHg, 73.21 ± 7.94 mmHg, and 80.88 ± 7.27 mmHg, respectively. The mean pre-operative heart rate was 78.42 ± 6.61 per minute in Group L, 76.56 ± 7.07 per minute in Group R, and 77.95 ± 7.45 per minute in Group C. The mean post-operative SpO_2 at baseline was 99.88 ± 0.09% in Group L, 99.71 ± 0.32 % in Group R, and 99.49 ± 0.15% in Group

Table 1: Demographic profile

Variables	Group L (Mean±SD)	Group R (Mean±SD)	Group C (Mean±SD)
Age group (years)	41.7±10.3	43.8±13.8	42.8±14.1
Weight (KG)	67.15±6.81	69.27±7.28	67.64±7.29
Mean duration of surgery (minutes)	60.44±5.61	61.05±4.55	61.67±5.28
Gender			
Male	5	4	7
Female	25	26	23

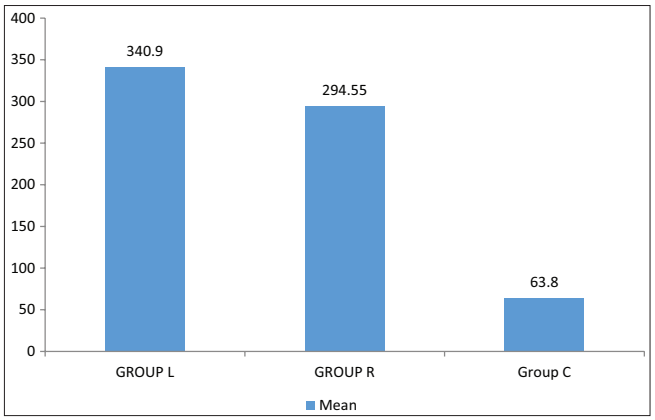
Table 2: Mean VAS score

Time (h)	Group L		Group R		Group C		Group L versus Group R	Group R versus Group C	Group L versus Group C
	Mean	SD	Mean	SD	Mean	SD			
0	1.53	0.51	1.73	0.45	2.19	0.65	0.18	0.02 (S)	0.01 (S)
0.5	1.87	0.57	2.07	0.69	2.32	0.79	0.19	0.03 (S)	0.00 (S)
1.0	2.23	0.68	2.13	0.78	4.46	1.01	0.75	0.01 (S)	0.02 (S)
2.0	2.60	0.77	2.83	0.65	2.91	1.02	0.19	0.00 (S)	0.01 (S)
4.0	2.47	0.78	4.37	0.78	2.75	1.12	0.02(S)	0.03 (S)	0.01 (S)
6.0	3.74	0.93	2.85	1.25	2.18	1.28	0.02(S)	0.02 (S)	0.01 (S)
8.0	2.57	0.93	2.68	0.87	3.92	1.50	0.92	0.01 (S)	0.00 (S)
12.0	1.94	0.76	2.87	0.87	2.03	0.91	0.42	0.02 (S)	0.01 (S)
24.0	1.10	0.71	1.23	0.77	1.26	0.68	0.77	0.81	0.44

VAS: Visual analog scale

Table 3: Number of patients requiring rescue analgesia

Time (h)	Group L		Group R		Group C	
	n	%	*n*	%	*n*	%
0	0	0	0	0	0	0
0.5	0	0	2	6.67	10	33.33
1.0	1	3.33	2	6.67	18	60
2.0	2	6.67	3	10	5	16.67
4.0	2	6.67	13	43.33	6	23.33
6.0	12	40	9	30	5	36.67
8.0	5	16.67	6	20	10	33.33
12.0	0	0	1	3.33	4	13.33
24.0	0	0	0	0	0	0



Graph 1: Mean time to first analgesic requirement

C, respectively. The mean post-operative readings of all the above-mentioned parameters were recorded in all the groups at 0, 0.5, 1, 2, 4, 6, 8, 12, and 24 h intervals. Zero time was the time of end of surgery.

The difference in the three groups was statistically non-significant ($P > 0.05$), with respect to mean pre-operative readings as well as intraoperative and post-operative readings of mean systolic blood pressure, diastolic blood pressure, heart rate, and SpO_2 at various intervals; hence, the three groups were comparable with respect to all these parameters.

The mean VAS scores readings in all the three groups were noted at 0, 0.5, 1, 2, 4, 6, 8, 12, and 24 h. Zero time was the time of end of surgery. The mean VAS score reading was lower in Group L and Group R in comparison to Group C at all the time intervals. The mean VAS score reading at 4 h in Group L and in Group R was 2.47 ± 0.78 and 4.37 ± 0.78, respectively. The mean VAS score for Group L was statistically significantly lower in comparison to the mean VAS score for Group R ($P < 0.05$) at 4 h postoperatively [Table 2].

The number of patients requiring rescue analgesia was significantly higher in Group C (58) in comparison to other study groups. Among Group L and Group R, the number of patients requiring rescue analgesia was lower in Group L (22) in comparison to Group R (36) [Table 3]. While comparing between Group L and Group R, it was found that mean time to first analgesic requirement among Group L (340.90 ± 119.12 min) was significantly higher in comparison to Group R (294.55 ± 123.11 min.). However, mean time of first analgesic requirement among Group C (63.8 ± 135.4 min) patients was significantly lower in comparison to Group L and Group R [Table 4]. Complications were noted in <10% of the patients in both the groups. Nausea and vomiting were seen in two patients in Group L, three patients of Group R, and two patients in Group B. All the readings were comparable and the difference was found to be non-significant in the two groups ($P > 0.05$).

DISCUSSION

Reduced post-operative pain is one of the biggest advantages of laparoscopy compared with open surgery. Pain can increase morbidity and is the primary reason for prolonged hospitalization after LC. Patients frequently complain of back, shoulder region pains, and discomfort of port site incisions. Shoulder and sub-diaphragmatic pain occurs in about 12–60% of patients. Peak of pain intensity is during the first few post-operative hours and usually

Table 4: Mean time to first analgesic requirement

Time (min)	Group L	Group R	Group C	Group L versus Group R	Group R versus Group C	Group L versus Group C
Mean	340.90±119.12	294.55±123.11	63.8±135.4	0.00 (S)	0.000 (S)	0.001 (S)

declines after 2 or 3 days.[8] The etiology of pain after LC is multifactorial. One cause of pain after laparoscopy is the peritoneal insufflation with CO_2 and phrenic nerve irritation in the peritoneal cavity. In fact, the dissolution of CO_2 gas causes peritoneal irritation and phrenic nerve damage in LC. Additional contributing factors include sociocultural status and individual factors.[9-12]

Effective pain control is essential for optimum care of patients in the post-operative period. However, despite advances in the knowledge of pathophysiology of pain, the pharmacology of analgesics, and the development of more effective techniques, patients continue to experience considerable pain after surgery. If we can provide post-operative analgesia in a simple and inexpensive manner, it may go a long way in alleviation of pain and suffering.[9-12] The improved understanding of origin of abdominal and shoulder pain after laparoscopic procedures led to the use of intraperitoneal and port site instillation of local anesthetic to reduce post-operative pain. The ease of use and safety of local anesthetics are well recognized and collectively they serve as one of the most important classes of drugs in perioperative care. The main advantage of local anesthetic agents is that they do not have the adverse effects of systemically administered opioids, such as post-operative sedation, nausea, gastrointestinal paralysis, and respiratory suppression, and they act directly on the tissue that they are applied to. Local anesthetics are commonly administered in abdominal surgery by skin infiltration or epidural administration, blocking somatic afferents and providing significant benefits in reducing post-operative pain, and improving recovery.[9-12]

The present study was conducted to compare the post-operative analgesic effect of 0.25% levobupivacaine plus dexmedetomidine with 0.25% ropivacaine plus dexmedetomidine with NS (control group) following intraperitoneal instillation in LC.

The aim was accomplished by carrying out the study in 90 patients randomly divided into three groups of 30 each in the age group of 18–65 years, of either sex, of ASA Grades I and II selected for LC after proper pre-anesthetic check-up. Patients in Group L received 40 ml of 0.25% levobupivacaine plus dexmedetomidine (at 1 μg/kg) while patients in Group R received 40 ml of 0.25% ropivacaine plus dexmedetomidine (at 1 μg/Kg). Group C included patients that received 40 ml of NS. Three groups were compared with respect to hemodynamics, effectiveness, and duration of post-operative analgesia with the help of visual linear analog scale, side effects, and complications. Then, data were compiled, tabulated, and statistically analyzed.

With regard to mean age, sex ratio, occupation, weight, distribution as per ASA grading, duration of surgery, mean intraoperative and post-operative: Systolic B.P., diastolic B.P., heart rate, and SPO_2, the differences in all the three groups were statistically non-significant ($P > 0.05$). Hence, the three groups were comparable with respect to the above variables.

The mean VAS score reading was lower in Group L and Group R in comparison to Group C at all the time intervals. The mean VAS score reading at 4 h in Group L and in Group R was 2.47 ± 0.78 and 4.37 ± 0.78, respectively. At 4 h postoperatively, the mean VAS readings for Group L were statistically significantly lower in comparison to the mean VAS reading for Group R ($P < 0.05$).

The number of patients requiring rescue analgesia was significantly higher in the control group in comparison to other study groups. Among L group and R group, the number of patients requiring rescue analgesia was lower in Group L in comparison to Group R. While comparing between Group L and Group R, it was found that mean time to first analgesic requirement among Group L was significantly higher in comparison to Group R. However, mean time of first analgesic requirement among Group C patients was significantly lower in comparison to Group L and Group R.

Complications were noted in <10% of the patients in both the groups. Nausea and vomiting were seen in two patients in Group L, three patients of Group R, and two patients in Group B. All the readings were comparable and the difference was found to be non-significant in the two groups ($P > 0.05$).

In a study conducted by Beder *et al.*, they compared adding dexmedetomidine to intraperitoneal levobupivacaine in patients undergoing LC. Group C patients received intraperitoneal 40 ml NS as controlled group. Group L was given 40 ml 0.25% levobupivacaine. Group LD received 40 ml 0.25% levobupivacaine + dexmedetomidine 1 μg/kg. Post-operative VAS at different time intervals was significantly lower, time to the first demand of painkiller was longer (30.2 ± 14.4, 45.9 ± 20.1, and 56.5 ± 13.2 min),

and total painkiller consumption was lower (203.5 ± 42.9, 117.8 ± 63.7, and 46.3 ± 41.3 mg) in Group LD than Group L than Group C.[13]

In a study conducted by Bindra *et al.*, they assessed efficacy of pre-emptive analgesia with intraperitoneal instillation of ropivacaine in LC. In Group A, patients received 3 mg/kg of ropivacaine intraperitoneal instillation in 100 ml NS before creation of pneumoperitoneum and in Group B patients received 3 mg/kg of ropivacaine intraperitoneal instillation in 100 ml NS after completion of surgery. Significantly lower visual analog scores for pain were observed in Group A versus Group B. Group A reported significantly lower pain at 0 h ($P < 0.001$), 1 h ($P = 0.003$), 3 h ($P = 0.006$), 6 h ($P = 0.003$), and 12 h ($P = 0.001$) postoperatively, but the difference was not statistically significant after 12 h. The mean time of first rescue analgesic was 472.8 ± 26.32 min in Group A, as compared with 189 ± 11.87 min in Group B. A significantly lower analgesic requirement was observed in Group A versus Group B throughout the entire study period ($P < 0.05$).[14]

In a study conducted by Sharan *et al.*, they compared intraperitoneal instillation of bupivacaine and ropivacaine for post-operative analgesia in patients undergoing LC. Group A patients received 20 mL of 0.5% bupivacaine intraperitoneally after cholecystectomy and Group B patients received 20 mL of 0.5% ropivacaine intraperitoneally after cholecystectomy. The VAS score was significantly lower in Group B. Rescue analgesic requirement was also less in Group B. The instillation of bupivacaine and ropivacaine intraperitoneally was an effective method of post-operative pain relief in LC.[15]

In a study conducted by Karaman *et al.*, they assessed the effects of pre-incisional infiltration and intraperitoneal levobupivacaine 0.25% on pain control in patients undergoing LC. They reported that there were no intraoperative and post-operative complications related to levobupivacaine use.[16]

Our results were comparable to results obtained by above-mentioned studies.

CONCLUSION

Intraperitoneal instillation of local anesthetic solution in LC provides effective post-operative analgesia, and analgesia provided by levobupivacaine plus dexmedetomidine is significantly better than ropivacaine plus dexmedetomidine.

Limitation

The study population as calculated at the start of our project was based on the previous studies. We could have drawn that more positive results had the power of study been increased by inclusion of more number of patients but were avoided as it would have increased the inclusion of population at risk.

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