Original Article

Indian Journal of Anesthesia and Analgesia
Volume 9 Number 2 March-April 2022
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.9222.10

Intraperitoneal Instillation of Ropivacaine 0.375% with Dexmedetomidine vs Ropivacaine 0.375% with Clonidine for Postoperative Analgesia in Laproscopic Cholecystectomy: A Comparative Study

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Abstract

Introduction: Laproscopic Cholecystectomy is a standard technique for symptomatic cholelithiasis. It is most commonly performed day care surgery. On the day of surgery pt experiences vague abdominal and shoulder pain. As the discharge is delayed due to lack of adequate analgesia, provision of adequate analgesia is of utmost importance.

Objective: To compare the efficacy of postoperative analgesia after intraperitoneal instillation of 0.375% Ropivacaine with Dexmedetomidine vs 0.375% Ropivacaine with Clonidine

Materials and Methods: 40 patients posted for laproscopic cholecystectomy were randomly divided into two groups A and B. Group A received 20 ml of 0.375% Ropivacaine with 1mcg/kg of Dexmedetomididne and Group B received 0.375% Ropivacaine with 1mcg/Kg Clonidine intraperitoneally through the 10mm supraumbilical port before closure. Pain was recorded on Visual Analog Scale at frequent intervals for 24 hrs postoperatively and categorised as either mild, moderate or severe. Inj. Diclofenac 75mg iv was administered as rescue analgesic in pts with moderate to severe pain.

Results: PostoperativeVAS score showed a statistically significant difference between both groups with lower values in Group A compared to Group B. ($P < 0.05$). The amount of rescue analgesia used was also less with dexmedetomidine as adjuvant.

Conclusion: Ropivacaine 0.375% with 1mcg/kg Dexmedetomidine provided better postoperative analgesia and significantly less requirement of rescue analgesia as compared to 0.375% Ropivacaine with 1mcg/kg clonidine.

Keywords: Ropivacaine; Intraperitoneal instillation; Laproscopic cholecystectomy; Dexmedetomidine; Clonidine.

How to cite this article:

Nazma Jabeen, K Yugandhar, S Kiran kumar / Intraperitoneal Instillation of Ropivacaine 0.375% with Dexmedetomidine vs Ropivacaine 0.375% with Clonidine for Postoperative Analgesia in Laproscopic Cholecystectomy: A Comparative Study / Indian J Anesth Analg. 2022; 9(2): 75-79.

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Email: nazmajabeen440@gmail.com, **Received on:** 13.01.2022, **Accepted on:** 22.01.2022

Introduction

Laparoscopic cholecystectomy is a treatment of choice in treating Gall Bladder disease. It has improved surgical outcomes in reduced pain, recovery duration, morbidity, better cosmetic results, and shorter hospitalization. However, it is a minimally invasive procedure; the pain has been mentioned as a major complaint and a reason for delayed postoperative recovery. The origin of pain after laparoscopic cholecystectomy is multifactorial with different pain components secondary to different pain mechanisms: Somatic Pain - Pain from the incisional site, Visceral Pain - pain from abdominal trauma due to gall bladder removal and referred shoulder pain - due to diaphragmatic irritation caused by residual CO_2 in the peritoneal cavity.[1]

Recently the use of local anesthetics for postoperative pain relief after laproscopic cholecystectomy has become a popular technique, and it is part of a multimodal approach to postoperative pain management.[2] The main advantage of using local anaesthetics is that it provides adequate analgesia without any considerable side effects, unlike opioids which may delay recovery.[3]

Intraperitoneal (IP) instillation of local anaesthetic agents alone or in combination with opioids [(4)] and α-2 agonists such as clonidine and dexmedetomidine has been found to reduce postoperative pain following laparoscopic surgeries.[5] The present study was carried out to compare the efficacy of postoperative analgesia after intraperitoneal instillation of 0.375% Ropivacaine with Dexmedetomidine vs 0.375% Ropivacaine with Clonidine in patients undergoing laparoscopic cholecystectomy.

Materials and Methods

After taking approval from the Institutional Ethical Committee and informed consent from the patient and their close relatives; This Comparative prospective randomised controlled double-blind hospital-based study was conducted on 40 patients of ASA grade I & II, 18 to 65 years of age & both sexes undergoing elective laparoscopic cholecystectomy. Patients with any chronic medical illness, allergic to study drugs, pregnant and lactating women are excluded from the study.

The patients were randomly allocated to two groups by a computer generated random number table and group assigned by sealed opaque envelope technique. Blinding was ensured by having an independent anesthesiologist not participating in the study to prepare the study drug in a ready to inject form for a total volume of 20 mL.

Group A received 20 ml of 0.375% Ropivacaine with 1mcg/kg of Dexmedetomidine, and Group B received 0.375% Ropivacaine with 1mcg/Kg Clonidine intraperitoneal through the 10mm supraumbilical port before closure.

General anaesthesia was administered to all patients. Inj. Glycopyrrolate (0.2 mg) and Inj. midazolam (0.03 mg/kg) were given as premedication. General anaesthesia was induced with Inj. Propofol and Inj. Fentanyl (2 μg/kg). Tracheal intubation was facilitated with Inj. Vecuronium (0.06 mg/kg). Anaesthesia was maintained with O_2 and air (50-50%) and isoflurane at 1 Minimum Alveolar Concentration (MAC).

Muscle relaxation was maintained by additional doses of Inj. Vecuronium as and when required. All patients received Inj. Ranitidine and Inj. Ondansetron as antiemetics. Monitoring included heart rate, respiratory rate, continuous ECG, NIBP, SpO_2, and $EtCO_2$. All surgeries were performed in Trendelenburg position. Intra-abdominal pressure of CO_2 was kept stable at 10-12 mmHg in all cases. A volume of 20 ml drug solution was given as an Intraperitoneal instillation site through the umbilical port.

The quality of analgesia was determined by a visual analogue scale (VAS) for 24 hrs. Postoperative pain scores were recorded by independent resident doctors at ½ hr, 1 hr, 2 hrs, 4 hrs, 8 hrs, 12 hrs, and 24 hrs. Postoperative analgesia was standard in all groups. When VAS score was >4, patients were given Diclofenac sodium (75 mg IV). Time to first request of analgesia, the total dose of analgesic required in the first 24 hrs, and any adverse effects such as nausea and vomiting and shoulder tip pain were noted.

Statistical analysis was performed using SPSS software version 12. Continuous data were described as mean±standard deviation (SD), and Categorical data were presented as absolute numbers or percentages. Continuous variables were compared using Student's independent t-test. Chi-square tests were used to match the demographic data of two groups. All data were presented as mean±SD, percentage (%), or number.

Results

There were no significant differences among the two groups regarding patient demographics and operative data (Table 1).

Table 1: Demographics and clinical characteristics of study participants.

Variable	Group A (n=20)	Group B (n=20)	P-value
Age (years)	44.7±11.4	41.0±12.1	0.242
Sex (Male/Female) (n)	12/8	13/7	0.419
Weight (kg)	64.2±12.9	61.0±12.1	0.185
BMI (kg/m2)	26.4±2.8	26.4±4.2	0.746
ASA PS (I/II) (n)	11/9	14/6	0.428
Duration of surgery (min)	70.6±23.7	76.2±32.3	0.296
Duration of anaesthesia (min)	99.8±27.0	106.4±36.9	0.158

Heart rate

In this study there was no significant difference in the heart between the groups at various time intervals. The results were shown in table 2.

Table 2: Comparison of heart rate between the groups.

Heart rate (BPM)	Group A(n=20)	Group B (n=20)	P value
½ hr	88.4±17.7	86.5±16.1	0.56^{NS}
1 hr	68.8±16.3	70.1±15.8	0.87^{NS}
2 hr	75.1±17.8	73.6±16.5	0.92^{NS}
4 hrs	74.7±16.8	72.5±15.1	0.75^{NS}
8 hrs	70.5±12.4	71.7±14.2	0.65^{NS}
12 hrs	72.1±11.2	73.4±10.2	0.34^{NS}
24 hours	75.7±9.1	76.3±8.8	0.45^{NS}

The data are represented as mean ± SD.* denotes p value < 0.05. NS- Non-significant

Systolic blood pressure (SBP)

There was no significant difference in the baseline systolic blood pressure between the groups (p=0.65). Further, the SBP was significantly lower at 1 hour (p=0.005), 2 hour (p=0.002) in group A as compared to the group B. Meanwhile, at 4 and 8 hours there was no significant change in SBP between the groups. The results were shown in table 3.

Table 3: Comparison of Systolic blood pressure (SBP) between the groups.

SBP	Group A(n=20)	Group B (n=20)	P value
½ hr	135.3±18.0	133.3±15.4	0.65^{NS}
1 hr	128.2±14.7	134.3±20.6	0.005*
2 hr	124.1±18.5	130.6±13.6	0.002*
4 hrs	122.0±19.2 8	125.6±15.	0.08^{NS}
8 hrs	121.0±18.56	123.6±12.76	0.12^{NS}
12 hrs	128.2±14.7	134.3±20.6	0.005*
24 hours	121.7±11.6	130.6±10.12	0.001*

The data are represented as mean ± SD.* denotes p value <0.05. NS-Non-significant.

Diastolic blood pressure (DBP)

There was no significant difference in the systolic blood pressure between the groups at various time intervals. The results were shown in table 4.

Table 4: Comparison of Diastolic blood pressure (DBP) between the groups.

DBP	Group A(n=20)	Group B (n=20)	P value
½ hr	80.8±14.6	79.2±11.0	0.65^{NS}
1 hr	78.2±14.8	77.2±11.1	0.78^{NS}
2 hr	77.2±15.7	76.4±11.3	0.62^{NS}
4 hrs	79.4±13.7	80.9±13.3	0.71^{NS}
8 hrs	80.5±14.65	80.2±15.25	0.76^{NS}
12 hrs	81.2±12.12	83.7±15.6	0.61^{NS}
24 hours	82.6±11.45	84.6±16.12	0.54^{NS}

The data are represented as mean ± SD.* denotes p value < 0.05. NS-Non-significant.

The mean VAS scores of group A were significantly lower at all time intervals except till the 2nd hr postoperatively when compared to group B (p<0.05) (Table 2). At 24th hr, the difference between VAS scores of the two groups was statistically significant (p<0.05) (Table 5).

Table 5: Comparison of postoperative VAS scores at various time intervals between the groups.

VAS score	Group A (n=20)	Group B (n=20)	P-value
½ hr	0.25±0.44	0.33±0.47	0.465^{NS}
1 hr	1.58±0.59	1.83±0.54	0.054^{NS}
2 hr	2.10±0.67	2.23±0.66	0.404^{NS}
4 hrs	1.48±0.71	4.13±0.72	0.000*
8 hrs	1.75±0.87	2.35±0.74	0.012*
12 hrs	1.98± 0.76	4.25±1.12	0.001*
24 hours	1.67±0.54	2.86±0.98	0.001*

The values are expressed as mean ± SD. * p-value <0.05, NS-Non-significant

The time to requirement of the first rescue analgesia was 487.7±40.96 minutes in group A as compared to 242.5±19.84 minutes in group B (p<0.05) (Table 6). The mean total consumption of Inj. Diclofenac in group A was at an average of 61.88±37.55 mg, while in group B, it was 183.75±44.78 mg, which was statistically significantly high (p=0.00) (Table 6). All patients received rescue analgesia in group B at various time intervals, whereas only 60% of the patients in group A received rescue analgesia.

Table 6: Comparison of rescue analgesic requirements.

Variable	Group A (n=20)	Group B (n=20)	P-value
Number of patients given rescue analgesia (%)	12 (60%)	20 (100%)	0.001*
Meantime for the first dose (minutes)	487.7±40.96	242.5±19.84	0.001*
Mean total dose (mg) in 24 hrs	61.88±37.55	183.75±44.78	0.001*

The values are expressed as mean ± SD. * p-value <0.05, NS-Non- significant.

Discussion

Laparoscopy is a minimally invasive procedure; a certain degree of pain is still experienced by patients. Pain can be multifactorial, arising from the incision site (somatic pain), from the surgical site (visceral pain), and due to pneumoperitoneum (referred pain).[6] Out of the different regimens proposed for postoperative pain, such as intravenous NSAIDS, opioids, and local infiltration, Intraperitoneal infiltration of local anaesthetic has been chosen by many surgeons as an effective modality. The rationale for this route is that visceral nociceptive conduction is blocked.

The local anaesthetic inhibits nociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins and other agents that sensitise the nociceptors and contribute to inflammation. However, absorption from a large peritoneal surface may also occur, and this may be a further mechanism of analgesia. Local anaesthetics have been administered into the peritoneal cavity during laparoscopic cholecystectomy[6], and the main advantage of using local anaesthetics is that they do not have the adverse effect of opioids, which may delay recovery and discharge from the hospital.

Bupivacaine has been used most widely for treating postoperative analgesia after laparoscopic cholecystectomy. Ropivacaine, a new long-acting amide local anaesthetic, is chemically related to bupivacaine, but it has been shown to be less toxic to cardiac and central nervous systems.[8]

Dexmedetomidine is a highly lipophilic α2 agonist. Its antinociceptive effect occurs at the dorsal root neuron level. Here, it blocks the release of substance P in the nociceptive pathway through the action of inhibitory G protein, which increases the conductance through K+ channels.[9] Dexmedetomidine enhances both central and peripheral neural blockade by local anaesthetics.[10] Its peripheral neural blockade is due to its binding to α2a-AR antibody. Because of the high lipophilic nature of dexmedetomidine, it acts over the peritoneal neural receptors and blocks the nociceptive stimuli.

Memis et al.[11] in 2005, studied the effects of tramadol and clonidine added to Intraperitoneal bupivacaine on postoperative pain in total abdominal hysterectomy and found it to be better than bupivacaine alone. Only few studies in literature have examined the analgesic effect of Intraperitoneal dexmedetomidine.

Ahmed et al.[12] compared meperidine or dexmedetomidine in combination with bupivacaine (0.25%) in gynecological laparoscopic surgery and concluded that dexmedetomidine group significantly decreased postoperative analgesic requirement. Results of our study correlate with the above study.

On analysis of mean scores, it was observed that group 1 had better pain relief till 24 hrs postoperatively and this was statistically significant (P=0.05), except at ½ hr, at 1 hr, and 2 hrs postoperatively when pain scores were not statistically different.

Shukla et al. had done the same study in laparoscopic cholecystectomy and concluded that Intraperitoneal instillation of dexmedetomidine in combination with bupivacaine gives better pain relief and reduces analgesic requirement as compared to bupivacaine alone [13].

Table 3 shows that in group 2, patients required the first dose of rescue analgesia by 242.5±19.84 minutes, whereas in group 1, analgesia stayed for nearly 487.7±40.96 minutes. However, the VAS score in group 2 was low after 4th hr; this may be due to the administration of diclofenac to these patients after 4th hr postoperatively.

In patients receiving ropivacaine and dexmedetomidine, only few patients required the second dose of rescue analgesia. The mean dose of Diclofenac consumption was significantly higher in group 2 (183.75±44.78 mg) than in group 1 (61.88±37.55 mg). These findings suggest that adding dexmedetomidine to ropivacaine intraperitoneal significantly decreases analgesic requirement. The above results were in agreement with that of Memis et al.[14] and Ahmed et al.[15] but on contrast, Memis et al.[14] in their study found higher doses in clonidine group than tramadol group. In the present study, dexmedetomidine shows better results which might be due to its high selectivity than clonidine

Conclusion

Intraperitoneal instillation of ropivacaine and dexmedetomidine combination is an easy and

effective mode of providing postoperative analgesia in laparoscopic cholecystectomy for a longer period and is superior to ropivacaine with clonidine without any significant increase in adverse events.

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