Original Research Article

A comparative study on intraperitoneal bupivacaine alone or with dexmedetomidine for post-operative analgesia following laparoscopic cholecystectomy

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Abstract

Background: Intraperitoneal instillations of local anaesthetic agents alone or in combination dexmedetomidine have been found to reduce post-operative pain following laparoscopic cholecystectomy.

Aim: Comparing antinociceptive effects of intraperitoneal instillation of bupivacaine plain and bupivacaine with dexmedetomidine in patients undergoing laparoscopic cholecystectomy.

Materials and methods: Study was conducted on 100 adult patients of ASA physical status 1 and 2 in the age group of 18 years to 60 years, posted for elective laparoscopic cholecystectomy under general anaesthesia. Patients were randomly divided on an alternate basis into two groups of 50 each. Group B: (n=50) patients received Intraperitoneal bupivacaine 50 ml 0.25% + 5 ml normal saline. Group DB: (n=50) Intraperitoneal bupivacaine 50 ml 0.25% + dexmedetomidine 1 μg/kg with normal saline 5 ml.

Results: Mean pain scores were significantly lower in the group BD when compared to group B during the entire duration of the study. There was statistically significant difference in VAS pain score at 6, 8, 12, 18, 24 hours after surgery. Mean pain scores were significantly lower in the group BD

when compared to group B during the entire duration of the study. There was statistically significant difference in VAS pain score at 6, 8, 12, 18, 24 hours after surgery. There was statistically significant difference between two groups of patients in terms of heart rate, systolic and diastolic blood pressure from 1 hour to 12 hours. 4 patients (8%) of group B and only 5 (10%) patients of groups B + D had postoperative nausea/vomiting, and 7 (14%) patients of group B and 2 (4%) patients of groups B+D had postoperative shoulder pain.

Conclusion: Intraperitoneal instillation of dexmedetomidine with bupivacaine prolongs the duration of postoperative analgesia as compared to that with bupivacaine alone.

Key words

Bupivacaine, Dexmedetomidine, Laparoscopic cholecystectomy.

Introduction

Laparoscopic cholecystectomy has rapidly become the procedure of choice for routine gallbladder removal and is currently the most commonly performed major abdominal procedure in Western countries [1]. A National Institutes of Health consensus statement in 1992 stated that laparoscopic cholecystectomy provides a safe and effective treatment for most patients with symptomatic gallstones and has become the treatment of choice for many patients [2]. This procedure has more or less ended attempts at non-invasive management of gallstones.

Laparoscopic procedures have many advantages over open procedures such as lesser haemorrhage, better cosmetic results, lesser post-operative pain, and shorter recovery time, leading to shorter hospital stay and less expenditure. Pain results from stretching of the intra-abdominal cavity [3], peritoneal inflammation, and diaphragmatic irritation caused by residual carbon-dioxide in the peritoneal cavity [4].

Many methods have been used to decrease post-operative pain including NSAID's, opioids and intraperitoneal local anesthetics with variable success. A combined approach using intra-peritoneal and peri-portal infiltration of local anesthetic solution may be more beneficial than intra-peritoneal infiltration alone. A literature search revealed limited studies examining the combined effect of somato-visceral blockade for pain relief during laparoscopic cholecystectomy [5]. Significant analgesic effect with intra-peritoneal buupivacaine has been described [6, 7].

The aim of this study was to compare the antinociceptive effects of intraperitoneal instillation of bupivacaine plain and bupivacaine with dexmedetomidine in patients undergoing laparoscopic cholecystectomy.

Materials and methods

This clinical study was conducted on 100 adult patients of ASA physical status 1 and 2 in the age group of 18 years to 60 years, posted for elective laparoscopic cholecystectomy under general anaesthesia after taking informed consent over a period of 12 months. After approval from the hospital ethical committee, a comparative study was carried out on 100 adult patients.

Patients were randomly divided on an alternate basis into two groups of 50 each.

Group B: (n=50) patients received Intraperitoneal bupivacaine 50 ml 0.25% + 5 ml normal saline.

Group DB: (n=50) Intraperitoneal bupivacaine 50 ml 0.25% + dexmedetomidine1 μg/kg with normal saline 5 ml.

Inclusion criteria

- ASA grade 1 and 2 female patients
- Age group of 18 –60 years
- Patients giving valid informed consent

- Those patients scheduled to laparoscopic cholecystectomy under general anesthesia

Exclusion criteria

- Patient refusal
- Patients belonging to ASA grade 3 and grade 4
- Patients physically dependent on narcotics
- Patients with history of drug allergy
- Patients with gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis or neurological involvement/ diseases
- Head injury cases
- Patients with cardiac, pulmonary, hepatic or renal disorders
- Patients with peripheral neuropathy

Pre anesthetic check-up was carried out pre operatively with a detailed history, general physical examination and systemic examination. Airway assessment examination was done.

The following laboratory examinations were done in all the subjects in study – Hemoglobin, Urine analysis, Blood sugar, Blood urea, Serum creatinine, Coagulation profile, Blood grouping and Rh typing, ECG-for patients over 40 years of age and Chest X- ray.

Patient's informed consent was taken. Nil per oral status was confirmed. They were premedicated with tablet diazepam 10 mg and tablet ranitidine 150 mg orally 10:00 pm at night before surgery and at 7:00 am on the morning of surgery.

All patients were transported to the operating room without premedication. On arrival to operating room, an 18-gauge intravenous (IV) catheter was inserted and 6 ml/kg/h crystalloid was infused intra-operatively monitoring of electrocardiography, non-invasive blood pressure, oxygen saturation (SpO_2) was started and baseline values were recorded. Pre-oxygenation with 100% oxygen (O_2) was done for 3 min. General anaesthesia was induced with IV fentanyl 1.5 μg/kg, propofol 2.0-2.5 mg/kg followed by succinyl choline 2 mg/kg to facilitate orotracheal intubation. The trachea was intubated with a cuffed orotracheal tube of appropriate size, lubricated with lidocaine jelly 2%. Anaesthesia was maintained with 60% N_2O in oxygen with 0.5-1% isoflurane. Intermittent boluses of vecuronium bromide were used to achieve muscle relaxation. Minute ventilation was adjusted to maintain normocapnia (end tidal carbon-dioxide - $EtCO_2$ between 34 and 38 mm Hg) and $EtCO_2$ was monitored. Nasogastric tube of appropriate size was inserted.

Hypotension/hypertension was defined as fall/rise in systolic blood pressure of >20% from the baseline values and bradycardia/tachycardia was defined as fall/rise in pulse rate of >20% from the baseline values. Hemodynamic fluctuations were to be managed accordingly. Patients were placed in 15-20° reverse Trendelenberg′s position with the left side tilt position. During laparoscopy, intra-abdominal pressure was maintained 12-14 mm Hg. The CO_2 was removed carefully by manual compression of the abdomen at the end of the procedure with open trocar.

Study drugs were prepared by an anaesthesiologist not involved in the study. Anaesthesiologist who observed the patient and surgeon were unaware of the study group until the end of the study. At the end of the surgery, the study solution was given intraperitoneally before removal of trocar in Trendelenberg′s position, into the hepato-diaphragmatic space, on gall bladder bed and near and above hepatoduodenal ligament. The neuro-muscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg and trachea was extubated. The nasogastric tube was removed, and the patient was shifted to post-anaesthesia care unit (PACU).

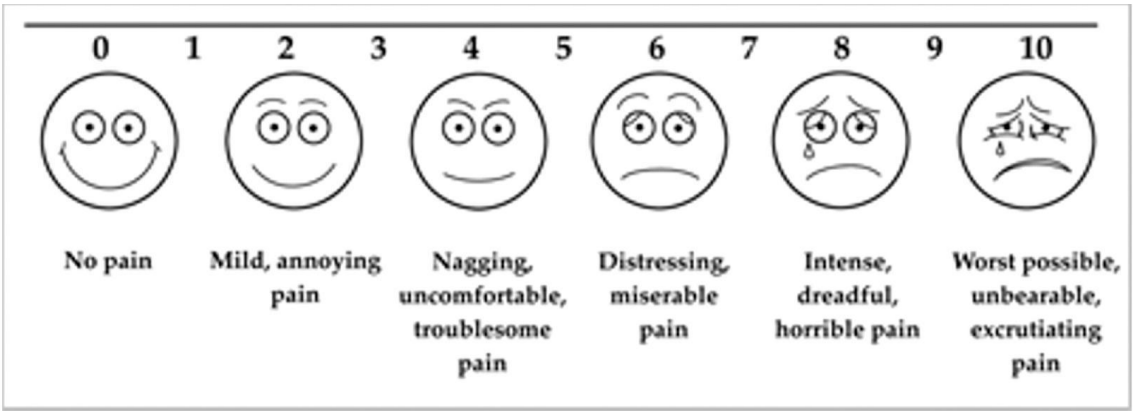
All patients stayed in PACU for 2 h after the end of surgery. The primary outcome variable was to

compare pain (visual analogue scale - VAS) score. The secondary outcome included time to the first request of analgesia in the post-operative period, total dose of analgesic used in 24 h period (post-operative) and any adverse/side effects.

The intensity of post-operative pain was recorded for all the patients using VAS score at 0.5, 1, 2, 4, 6, 12, 24 h after surgery and over all VAS score (mean of all VAS scores). All the study patients were instructed about the use of the VAS score before induction of anesthesia (**Photo – 1**).

The following parameters were evaluated in all study groups: (1) Time to first request of analgesia (time elapsed between extubation and first request for analgesic dose), (2) The incidence and severity of postoperative pain for 24 h (the severity of postoperative pain measured at 1, 2, 4, 6, 8, 12, 16, 20 and 24 hrs. postoperatively, using VAS pain score, (3) total dose of analgesia (4) Postoperative complications (5) Postoperative hemodynamics (pulse, blood pressure) (6) Comparative sedation score.

Photo – 1: Vas score.



Results

Demographic distribution was as per **Table – 1**. Mean pain scores were significantly lower in the group BD when compared to group B during the entire duration of the study. There was statistically significant difference in VAS pain score at 6, 8, 12, 18, 24 hours after surgery in group BD (3.21±0.83) compared to group B (2.81±0.91) up to 24 hours (**Table – 2**).

Time to requirement of first dose rescue analgesia was prolong in the group BD (7.61 hours) compared to group B (5.81 hours), indicating better and longer pain relief in the group BD compared to groups B. Total analgesic consumption was more in group B (2.12) compared to group BD (1.93) as per **Table - 3**.

There was statistically significant difference between two groups of patients in terms of pulse rate all the time (**Figure – 1**). There was statistically significant difference between two groups of patients in terms of systolic blood pressure from 1 hour to 12 hours (**Figure – 2**).
There was statistically significant difference between two groups of patients in terms of diastolic blood pressure from 1 hour to 12 hours (**Figure – 3**).

In our study, only 4 patients (8%) of group B and only 5 (10%) patients of groups B + D had postoperative nausea/vomiting, and 7 (14%) patients of group B and 2 (4%) patients of groups B+D had postoperative shoulder pain. However, hypotension, bradycardia and sedation were not seen in either group (**Table – 4**).

Discussion

Mean pain scores were significantly lower in the group BD when compared to group B during the entire duration of the study. There was statistically significant difference in VAS pain

score at 6, 8, 12, 18, 24 hours after surgery in group BD (3.21±0.83) compared to group B (2.81±0.91) up to 24 hours. Similar results were observed with study done by Ahmed, et al. [8] who compared the antinociceptive effect of dexmedetomidine or meperidine with bupivacaine to bupivacaine alone intraperitoneally after the laparoscopic gynaecological surgery found that intraperitoneal instillation of meperidine or dexmedetomidine in combination with bupivacaine significantly decreases VAS score.

Table - 1: Demographic distribution in study.

Patients Characteristic	Group B (N=50)	Group-BD(N=50)	p value
Age in years	34.10±10.44	35.8±10.14	0.59
sex	21/29	19/31	0.812
Body weight in kgs	52.95+6.01	53.97+7.1	0.2
ASA* I/II	30/20	24/25	0.421
Duration of surgery(min)	46.9+12.98	47.3+11.34	0.64

Data presented as mean ± standard deviation or Number: *P value < 0.05 was considered significant.

Table - 2: VAS post-operative period up to 24 hrs.

VAS score	Group B (N=50)	Group-BD(N=50)	p value
1st hr	0.6±0.55	0.69±0.45	>0.05
4th hr	1.17±0.43	1.28±0.73	>0.05
6th hr	3.21±0.83	2.81±0.91	<0.05
8th hr	2.91±0.57	2.01±0.59	<0.05
12th hr	3.81±0.40	3.01±10.48	<0.05
18th hr	3.50±0.72	2.91±0.81	<0.05
24th hr	6.25±0.63	5.15±0.99	<0.05

*P value < 0.05 was considered significant

Table - 3: Analgesic requirement.

Analgesic profile	Group B (N=50)	Group-BD (N=50)	P- value
Number of patients given rescue analgesia	27(54%)	23(46%)	0.043*
Mean time for first dose(hours)	5.81±0.71	7.61±0.56	0.0001*
Mean total dose	2.12±0.53	1.93±0.32	0.0001*

Bakhamees, et al. [9] evaluated the patients who received dexmedetomidine and found that they had less VAS score as compared to placebo in the postoperative period. Ahmed Mostafa, et al. [10] observed that the patients who received intraperitoneal levobupivacaine instillation had profound postoperative analgesia. Usha Shukla, et al. [11]. Intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is superior to bupivacaine alone and may be better than bupivacaine with tramadol.

Time to requirement of first dose rescue analgesia was prolong in the group BD (7.61 hours) compared to group B (5.81 hours), indicating better and longer pain relief in the group BD compared to groups B. Total analgesic consumption was more in group B (2.12) compared to group BD (1.93). Our study results

also show that the duration of analgesia was higher and had less need of rescue analgesia in bupivacaine and dexmedetomidine group as compared to bupivacaine alone which were statistically significant. Also Ahmed, et al. [8] observed that intraperitoneal instillation of meperidine or dexmedetomidine in combination with bupivacaine significantly decreases total rescue analgesia requirement in postoperative period. Rajni Gupta, et al. [12] compared postoperative analgesia with intraperitoneal bupivacaine and fentanyl with bupivacaine after laparoscopic surgery and observed that there is decrease total analgesics consumption in fentanyl with bupivacaine group.

Figure - 1: Heart rate in the study for different time intervals.

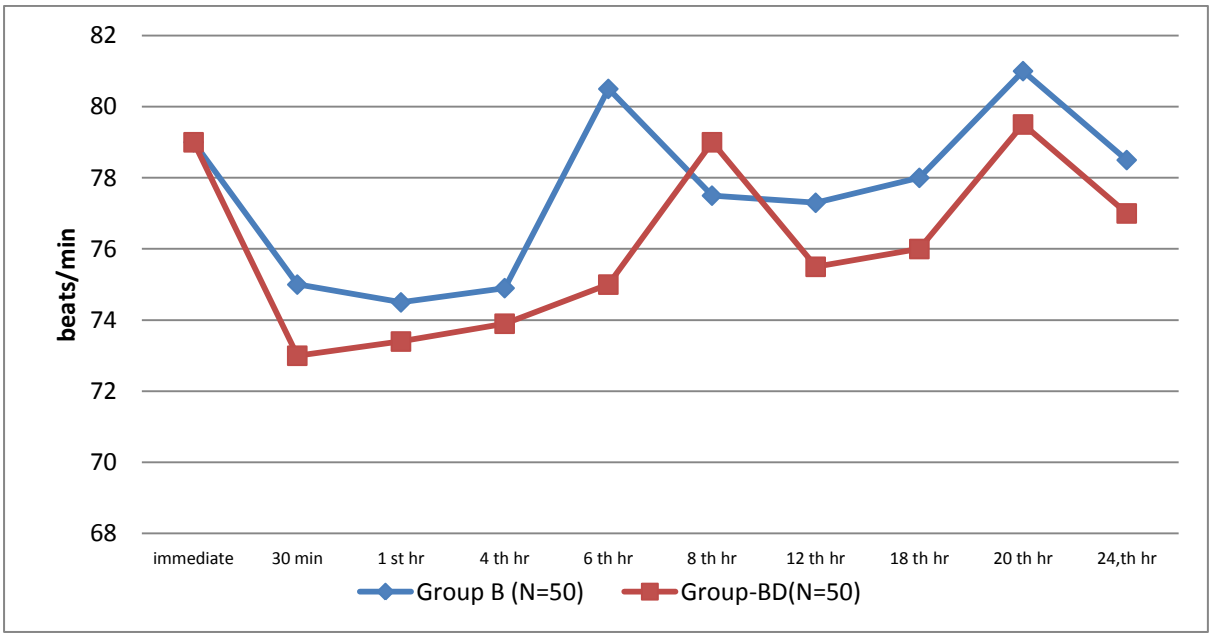


Figure - 2: Systolic blood pressure in the study for different time intervals.

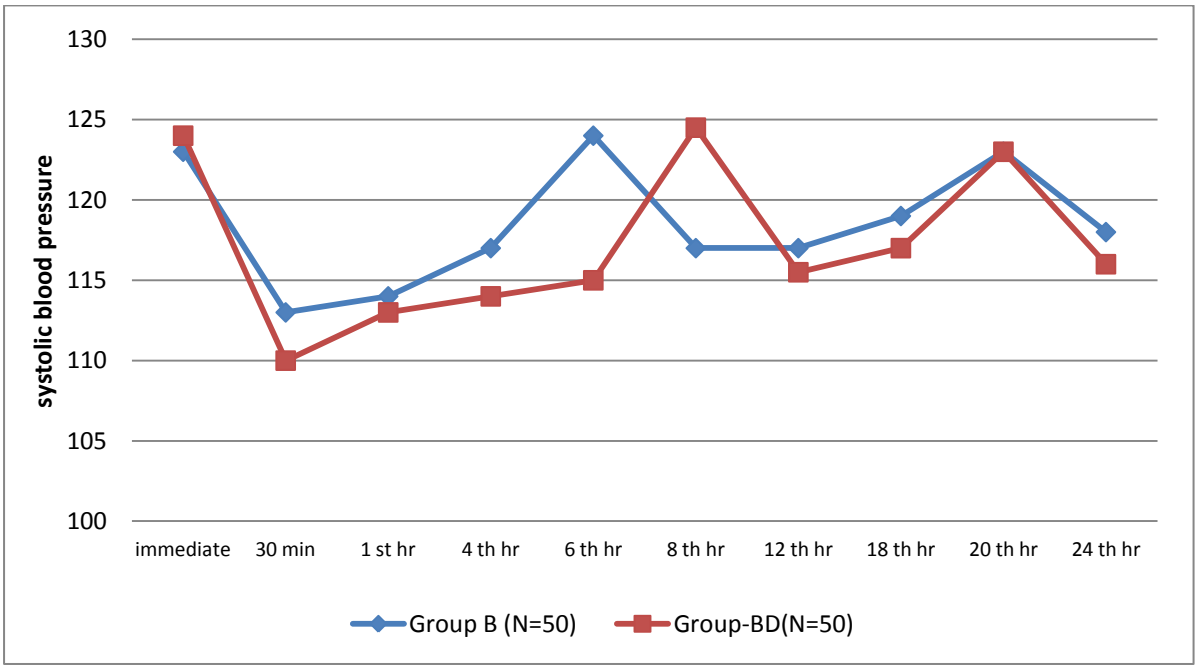


Figure - 3: Diastolic blood pressure in the study for different time intervals.

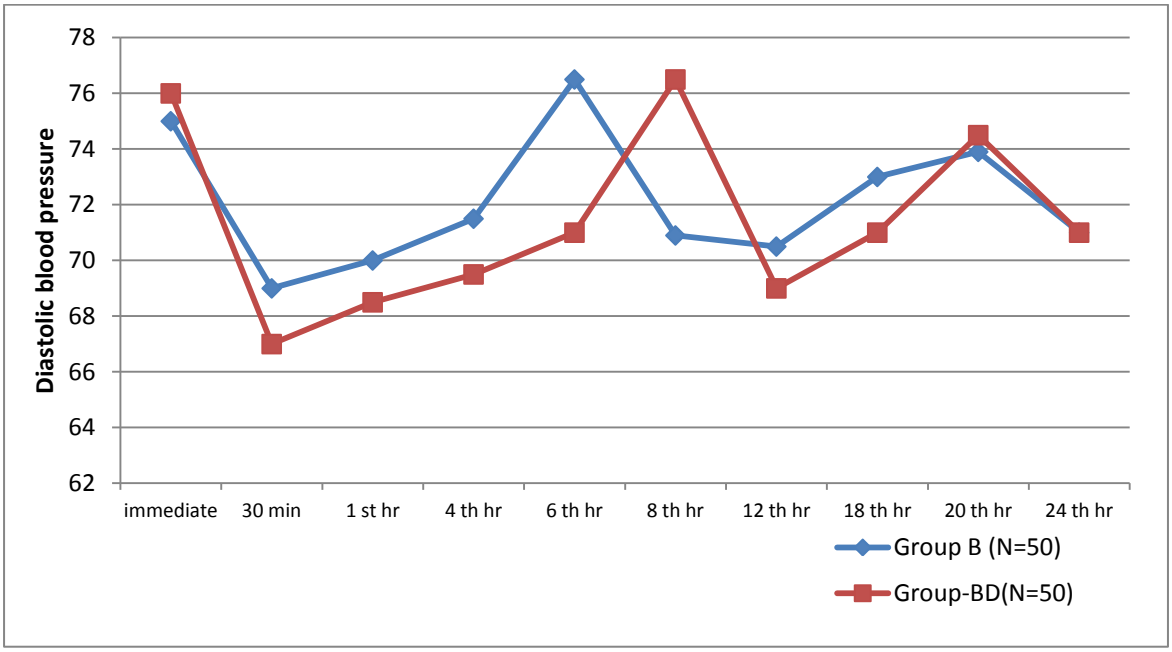


Table - 4: Adverse effects.

Side effects	Group B (N=50)	Group-BD (N=50)
Sedation	0	0
vomiting/ Nausea	4(8%)	5(10%)
Diarrhoea	0	0
Pruritus	0	0
Urinary retention	0	0
Constipation	0	0
Shivering	0	0
Shoulder pain	7(14%)	2(4%)

Vital parameters like heart rate, blood pressure are important indicators of patients comfort as the values correlated well with high VAS scores.

Arain, et al. [13] studied the efficacy of dexmedetomidine and morphine for postoperative analgesia after a major surgery. Bhattacharjee, et al. [14] concluded that dexmetedomedine improves intra and post operative hemodynamic stability during laproscopic surgeries without prolongation of recovery and similar results were obtained by Bakhamees, et al. [9].

In our study, among group B patients, nausea/vomiting was found in 4 patients out of 50 patients and 5 patients out of 50 patients in groups B+D that is comparable to a study done by Bhakhamees, et al. [9].

In our study, the incidence of shoulder pain was significantly low in groups B+D compared to group B. We found that in group B 7 patients out of 50 patients and in groups B+D, 2 patients out of 50 patients had postoperative shoulder pain that is comparable to the study done by Ahmed, et al. [8].

Conclusion

We concluded that intraperitoneal instillation of dexmedetomidine with bupivacaine produces prolonged duration of analgesia and require less number of analgesic doses compared to bupivacaine alone in patients undergoing laparoscopic surgery without any significant side effects.

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