

## Comparison of administration of intraperitoneal bupivacaine and intraperitoneal bupivacaine with dexmedetomidine in post laparoscopic cholecystectomy patients for post operative pain relief

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### Abstract

**Introduction:** Intraperitoneal administration of local anesthetic found to be effective in controlling postoperative pain in laparoscopic surgeries. So, this prospective study was conducted to compare antinociceptive effect of intraperitoneal administration of bupivacaine and bupivacaine with dexmedetomidine in patients after undergoing Laparoscopic Cholecystectomy.

**Materials and Methods:** A total of 60 patients of either sex undergoing laparoscopic cholecystectomy were randomly divided into two groups 30 patients in each. Group B received intraperitoneal 50ml bupivacaine 0.25 % (125mg). Group BD received intraperitoneal 50ml bupivacaine 0.25 % (125mg) and 50µg dexmedetomidine before removal of trocar at end of the surgery. Post op analgesia (VAS Score), sedation, Vitals was assessed at different time intervals. Time to first rescue analgesia, total dose of analgesic and adverse effect were noted.

**Results:** We observed significant difference in mean VAS score at 8hr, 12hr, 16hr and 20hr between two group with 2.27±0.74, 3.03±0.67, 3.5±0.63, 4.03±0.72 in group B and 1.7±1.36, 2.1±1.09, 2.6±1.22, 3.03±1.09 in group BD respectively. The mean time to first rescue analgesia in group B was 8.86± 4.13hrs and 11.64± 3.95hrs in group BD. Total analgesic consumption was less in Group BD.

**Conclusion:** Intraperitoneal instillation of bupivacaine with dexmedetomidine is superior to bupivacaine alone in terms of duration of post operative analgesia, total analgesic consumption in the post laparoscopic cholecystectomy patients.

**Keywords:** Laparoscopic cholecystectomy, Intraperitoneal instillation, Bupivacaine, Dexmedetomidine.

### Introduction

In modern era of surgery, laparoscopic cholecystectomy is preferred technique over open cholecystectomy whenever possible for cholelithiasis because of less complications rate and various advantages. Despite of minimal incision, there is postoperative pain due to various reasons such as diaphragmatic irritation, peritoneal inflammation and stretching of abdominal cavity. There are three main components of pain described till date which are parietal, visceral and referred shoulder pain.<sup>1,2</sup>

Different modalities are currently used for post operative pain relief after laparoscopic cholecystectomy such as parental analgesic, infiltration of local anesthetics, intraperitoneal administration of local anesthetic alone and or in combination with other drugs like opioids or  $\alpha$  2 agonist.<sup>3-5</sup>

Intraperitoneal administration of local anesthetic is simple, and can be effective for reducing the pain after laparoscopic surgery.

The aim of our prospective study is to compare postoperative pain relief after intraperitoneal administration of bupivacaine alone and in combination with dexmedetomidine in patients planned for laparoscopic cholecystectomy.

### Materials and Methods

A prospective, randomized, double blind study conducted between August 2016 to October 2017 in our Government Medical College Kota, Rajasthan which is a tertiary care and teaching hospital. After approval from Institutional Ethical Committee, sixty patients of ASA I and II, aged between 25 and 60 years posted for elective laparoscopic cholecystectomy included in the study. Patients who refused for surgery, history of allergy to study drugs, patient with co-morbidities, patients left with abdominal drain at end of surgery were excluded. Sample size calculation was based on previous studies.

Pre anesthetic checkup was carried out of all the patients and were admitted one day before surgery and taught how to evaluate their pain intensity using visual analogue scale scored from 0 to 10 (where 0= No pain and 10=worst pain).

Before surgery written informed consent was taken from all the patients. In operating room nil per oral status confirmed. Intravenous line secured with 18-gauge cannula and Ringer lactate infusion started at the rate of 8ml/kg. Monitoring of electrocardiography (ECG), non-invasive blood pressure (NIBP), oxygen saturation (SpO<sub>2</sub>) and temperature was started and baseline values of pulse, Systolic BP, Diastolic BP, heart rate were noted. Pre-anaesthetic medication Inj. glycopyrrolate 4 µg/kg i.v., Inj. midazolam 30 µg /kg

i.v. was given. All the patients had received fentanyl in dose of 1.5 µg/kg i.v. Anaesthesia was induced with Inj. Propofol 1.5-2 mg/kg and Inj. succinylcholine 1.5-2 mg/kg i.v was given to facilitate intubation. Trachea was intubated with appropriate sized cuffed endotracheal tube. Anaesthesia was maintained with nitrous oxide and oxygen mixture (50:50) with Isoflurane 1%-1.5%. Controlled ventilation was adjusted to maintain end tidal carbon dioxide (EtCO<sub>2</sub>) between 35 and 40 mm of Hg and vecuronium 0.08mg/kg was used to maintain intraoperative neuromuscular blockade. Intraoperative pulse rate, NIBP, SpO<sub>2</sub> and EtCO<sub>2</sub> were monitored. A pneumoperitoneum was created by insufflations of CO<sub>2</sub> and the operation table was tilted to approximately 15° in the reversed Trendelenberg position. Intra-abdominal pressure was maintained <12 mm Hg. Hemodynamic fluctuations were managed accordingly.

Patients were randomized into two groups of equal size (n=30) using a computer generated table of random numbers. Intraperitoneal 50 mL inj. bupivacaine hydrochloride 0.25% (125 mg) [Group B] and Intraperitoneal 50 mL inj. bupivacaine hydrochloride 0.25% (125 mg) + 50 µg inj. dexmedetomidine [Group BD]. We took these doses to confirm our findings with previous studies as they have taken the same amount of drug. Bupivacaine 125 mg is less than the toxic doses in all patients (weight >50kg) in whom we have included in study. Study drugs were prepared and filled in precoded (red sticker for Group B and green sticker for Group BD) 50 ml syringes by an anesthesiologist who was not involved in the study. Observation made by another anesthesiologist who was unaware of the study group.

At the end of surgery, after removal of gall bladder and achieving proper haemostasis, in both the study groups, intraperitoneal instillations of study drugs according to group allocated was done by surgeon who is unaware of study, under the guidance by the camera on the surgical site and under both the copulae of the diaphragm through trocar. The CO<sub>2</sub> was carefully evacuated at the end of surgery by manual compression of abdomen with open trocars. At the end of the operation the neuro-muscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. Patients were extubated after attaining of adequate recovery which is assessed by clinical signs (hand grip, sustained head lift etc.). Patients were transferred to the post-operative ward for 24 hours and were monitored for vital signs. Postoperative data were collected by a blind observer.

In post operative period Pain assessment was done by using VAS, sedation by Modified Observer Assessment Alertness/Sedation scale and were monitored along with vitals (Heart rate, Systolic BP, Diastolic BP) at regular intervals (at 15 minute, 30 min., 45 min, 1 hour, 2 hour, 4 hour, 8 hour, 12 hour, 16 hour, 20 hour, 24 hour after the surgery). Rescue

analgesia Diclofenac sodium aqueous 75 mg i.v. was given when VAS ≥4. Time to first rescue analgesia, total no. of rescue analgesia any complications were also assessed.

All the data variables were expressed as mean±standard deviation or number or percentage. Statistical analysis was done by using Microsoft office Excel 2000. Categorical variable were analyzed by using Chi-square test and continuous data were compared by unpaired student's t test. P value <0.05 was considered statistically significant.

## Results

Both the groups were comparable with regard to demographic data. (Table 1)

As shown in Table 2 mean VAS score were comparable in both groups till 6 hours in post operative period. However from 8 hours to 20 hours of postoperative period the mean pain score significantly lower in group BD as compared to group B.

As compared to group B, in group BD less number of patient required rescue analgesics, however difference was insignificant. But duration of analgesia was significant lower in group BD as compared to group B (P<0.05) also total number of dose require in post operative period was significantly lower in group BD (P<0.01). (Table 3)

Sedation score were significantly lower in group BD as compared to group B up to 4 hours in postoperative period and thereafter up to 24 hours sedation score were comparable in both groups. (Table 4)

Post operatively up to 6 hours heart rate was significantly less in group BD as compared to group B, after that change in heart rate were comparable in both the groups (Fig. 1). None of the patient had to be administered anticholinergics.

Fig. 2 & 3; Trend shows that there is lower systolic BP and diastolic BP in group BD as compared to group B throughout the study but statistically significant difference was found from one hour to sixteen hours postoperatively. Although there was no evidence of hypotension in any patient was found.

In our study, 5(16.67%) out of 30 cases in group B and 3(10%) out of 30 cases in group BD had postoperative nausea and vomiting. There was no other complications occur during the study period in both the groups.

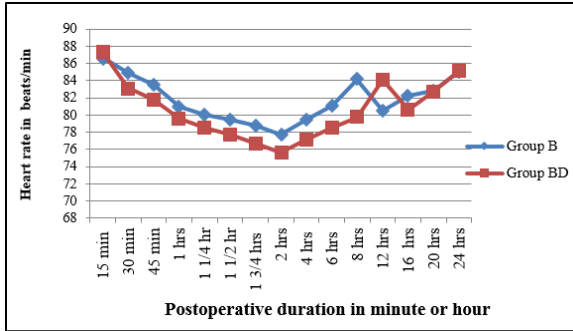


Fig. 1: Changes in heart rate postoperatively

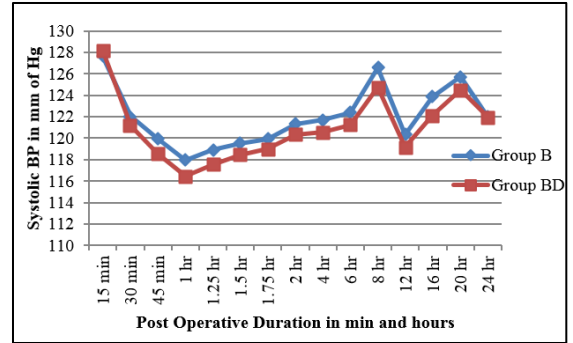


Fig. 2: Systolic BP changes postoperatively

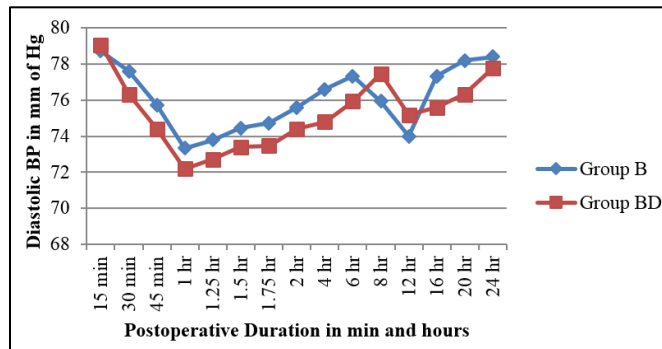


Fig. 3: Diastolic BP changes postoperatively

Table 1: Demographic distribution in study

Variables	Group B (n=30)	Group BD (n=30)
Age (years)	41.63±10.39	40.03±10.53
Sex (Male/Female)	10/20	7/23
Weight in kg	52.95±6.01	53.97±7.1

Data presented as mean ± standard deviation or Number.

Table 2: Mean pain scores

Post op assessment time	Group B	Group BD
6 hr	1.7±0.75	1.6±1.35
8 hr	2.27±0.74	1.7±1.36*
12 hr	3.03±0.67	2.1±1.09**
16 hr	3.5±0.63	2.6±1.22**
20 hr	4.03±0.72	3.03±1.09*
24 hr	3.03±0.67	2.6±1.22

(\* P value <0.05, \*\* P value <0.01)

Table 3: Analgesic requirement

Analgesic requirement	Group B	Group BD
No. of patients given rescue analgesic	21(70%)	17(56%)
Duration of analgesia (hours)	8.86±4.13	11.647±3.95*
Mean total no. of dose	1.7±1.20	0.86±0.93**

(\* P value <0.05, \*\* P value <0.01)

Table 4: Sedation score

Post op assessment time	Group B	Group BD
15 min	3.6±0.53	3.233±0.52*
1 hr	4.56±0.81	4.166±0.89*
2 hr	4.8±0.961	4.533±1.38*
4 hr	4.867±0.79	4.566±1.422*

(\* P value <0.05)

## Discussion

In modern era, anesthesiology is an emerging specialty in pain control and management either pre or postoperatively. This is because of better acceptance of evidence based medicine and patient directed approach. Thorough knowledge of various parameters of drugs linked with anesthesiology has been revolutionized the anesthesia speciality.<sup>6,7</sup> Various clinical trials had been undertaken with one or multiple analgesics with different groups for postoperative pain relief with minimal side effects.

Though laparoscopic cholecystectomy is advantageous as compared to open cholecystectomy in cholelithiasis but pain is still there and is the main complain on day of surgery and also first reason for prolonged hospital stay and recovery time. So postoperatively pain relief becomes necessary. Recent evidences suggest intraperitoneal instillation of multimodal and opioid sparing analgesics to hasten recovery and avoid side effects.

The rationale of our double blind prospective study was to compare intraperitoneal instillation of bupivacaine alone and with combination of dexmedetomidine as antinociceptive agent in terms of VAS scale, total number of analgesic dose required, and time to first rescue analgesia.

In our study, we found that intraperitoneal bupivacaine alone (group B) and with dexmedetomidine (group BD) are very effective in controlling post operative pain after laparoscopic cholecystectomy. Intraperitoneal local anesthetic seems to block free nerve endings in peritoneum along with systemic absorption from peritoneal cavity may play role to control of pain after intraperitoneal administration.<sup>4</sup>

There was statistically significant difference in VAS pain score in both groups. There was less VAS scale and prolonged duration of analgesia, with less number of does as compared to group B due to highly selectivity on  $\alpha_2$  receptor of dexmedetomidine for analgesia. (Table 2,3) Ahmed et al<sup>4</sup> 2008 studied antinociceptive effect of dexmedetomidine vs. meperidine, topically, after laparoscopic gynecological surgery and concluded that intraperitoneal instillation of dexmedetomidine or meperidine in combination with bupivacaine significantly reduces intravenous morphine requirement as post operative analgesics as compared to bupivacaine alone. Shukla et al<sup>8</sup> 2016 found that intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is better than bupivacaine or tramadol and bupivacaine mixture as regard to post operative analgesia following laparoscopic cholecystectomy. Similar study done by Srinivas Ropul et al<sup>9</sup> 2016 and concluded that bupivacaine- dexmedetomidine combination is superior than bupivacaine alone in terms of long duration of

analgesia, less number of analgesic dose required and minimal side effects following laparoscopic surgery.

First dose of rescue analgesia required late (11.64±3.95 hours) in group BD as compared to Group B (8.86±4.13 hours) indicating better and longer pain relief in group BD. Total number of analgesic consumption (0.86) was less in group BD as compared to group B (1.7±1.20). These observations are comparable to the studies of Usha Shukla et al,<sup>8</sup> Srinivas Rapoluet et al,<sup>9</sup> Oza, et al.<sup>10</sup>

In our study, there was decrease in heart rate, systolic BP and diastolic BP in group BD due to effect of dexmedetomidine on heart. However, all patients were clinically stable throughout the study period. The study of Bhattacharjee et al<sup>11</sup> and Arain et al<sup>12</sup> had similar observation which in agreement with our study.

In our study, we encounter nausea and vomiting (16.67% in group B and 10% in group BD) as side effect but there was no significant difference in both groups. We did not encounter any complications in our study.

## Conclusion

Based on our results, we concluded that intraperitoneal bupivacaine 50 ml of 0.25% in combination with dexmedetomidine 50 µg provided prolong duration of analgesia and required less number of analgesic doses as compared to bupivacaine alone without significant side effects. So, we recommend routine use of intraperitoneal bupivacaine with dexmedetomidine for postoperative analgesia in laparoscopic cholecystectomy patients.

**Conflict of Interest:** None

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