

Comparison of Postoperative Analgesia by Intraperitoneal Infiltration of Bupivacaine versus Bupivacaine with Dexmedetomidine in Laparoscopic Surgeries

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Abstract

The primary aim is to compare postoperative analgesia by intraperitoneal infiltration of bupivacaine *versus* bupivacaine with dexmedetomidine in laparoscopic surgery. The secondary objective to assess postoperative pain relief, rescue analgesic drug requirement and side-effects in both groups. The study was approved by the University's institutional ethics committee (Reg No. ECR 518/Inst/MH/2014/RR-17) and written informed consent was obtained from all subjects participating in the trial. The study was conducted prior to patient enrollment at Bharati Vidyapeeth Medical College institutional ethics committee (REF: BVDUMC/IEC/62, Principal investigator: Hemadip Tavethiya, Date of registration: 7th September, 2018). This prospective comparative study enrolled a sample of 52 patients, 26 in each group. Group B received only Bupivacaine intraperitoneally and Group BD received Bupivacaine with adjuvant Dexmedetomidine intraperitoneally. VAS score was seen at 1, 2, 4, 6, 12, 24 hours postsurgery and VAS score > 3 was given IV paracetamol or IV diclofenac sodium as rescue drug. *Results*: VAS at different time intervals, overall VAS in 24 h was significantly lower (2.34 ± 0.84 , 3.65 ± 0.47), total analgesic consumption was low in Group BD than Group B. *Conclusion*: Intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is superior to bupivacaine alone.

Keywords: Laparoscopic surgery; Bupivacaine hydrochloride; Dexmedetomidine hydrochloride; Intraperitoneal injection; Postoperative pain.

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Introduction

Surgery using minimal laparoscopic approach are now a days common with the benefits of less discomfort, shorter hospitalization and earlier return to normal activity.^{7,17} Main disadvantage of such Surgery is post operative pain at incisional site, during coughing and respiratory movement and handling during first hour after surgery.⁷

Hence, pain management remains the mainstay for anesthesiologist.

Use of Local anesthetic agents into the intraperitoneal space is one of the effective way of the postoperative pain relief.⁸ It suppresses many of the pain mediated stress responses due to stretching of peritoneum, irritation due to residual carbon dioxide after laparoscopic surgery and inflammation of peritoneum.^{8,17}

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Intraperitoneal instillation of local anesthetic agents alone or in combination with adjuvant such as α_2 agonists like clonidine and dexmedetomidine has been found to reduce postoperative pain following laparoscopic surgery.¹⁷

Materials and Methods

This prospective, randomized study was carried out on 52 patients after getting approval from ethical committee and written informed consent. Patients were divided into 2 groups by simple randomization, Group B & Group BD (26 patients each). Study was conducted between October 2018 and September 2019.

Group B received only Bupivacaine intraperitoneally;

Group BD received Bupivacaine with adjuvant Dexmedetomidine intraperitoneally.

Patients of ASA Grade I/II between 18 and 60 years of age posted for all elective laparoscopic abdominal surgery in which Bupivacaine can be used were included. Patients with cardiopulmonary systemic illness, emergency surgeries or patients on enzyme inducer drugs (Isoniazid, Phenytoin, Rifampicin, etc.), allergic to Bupivacaine or Dexmedetomidine, patient may require postoperative intraabdominal drain were excluded from the study.

All patients were transported to the operating room without premedication. On arrival to operating room, a 20-gauge intravenous (IV) catheter was inserted and 6 ml/kg/h crystalloid was infused intraoperatively monitoring of electrocardiography, noninvasive blood pressure, oxygen saturation (SpO₂) was started and baseline values were recorded. Preoxygenation with 100% oxygen (O₂) was done for 3 min. General anesthesia was induced with IV Midazolam 1mg, IV Fentanyl 2 μ g/kg, IV propofol 2.0–2.5 mg/kg followed by Succinylcholine 2 mg/kg to facilitate orotracheal intubation.

The trachea was intubated with a cuffed orotracheal tube of appropriate size. Anesthesia was maintained with 50% air in oxygen with 0.2–2% sevoflurane. Intermittent boluses of vecuronium bromide were used to achieve muscle relaxation. Minute ventilation was adjusted to maintain normocapnia (end tidal carbon-dioxide [EtCO₂] between 34 and 38 mm Hg) and EtCO₂ was monitored. Nasogastric tube of appropriate size was inserted.

During laparoscopy, intraabdominal pressure was maintained 12–14 mm Hg. At the end of surgery the CO₂ was removed carefully by manual compression of the abdomen at the end of the procedure with open trocar.

Patients were randomly allocated to one of the groups using table of randomization, Group B ($n = 26$): Intraperitoneal bupivacaine (2 mg/kg) 0.25% + 5 ml normal saline (NS), Group BD ($n = 26$): Intraperitoneal bupivacaine (2 mg/kg) 0.25% + dexmedetomidine 1 μ g/kg (diluted in 5 ml NS). Drug was given to patient intraperitoneally before trocar removed at the end of surgery.

All patients stayed in PACU for 2 h after the end of surgery. The primary outcome variable was to compare pain (visual analog scale [VAS]) score. The secondary outcome included time to the first request of analgesia in the postoperative period, total dose of rescue analgesic used in 24 h period (postoperative) and any adverse/side-effects.

The intensity of postoperative pain was recorded for all the patients using VAS score at 1, 2, 4, 6, 12, 24 hour 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 (VAS score 0 - no pain, VAS score 10 - worst possible pain). Patients who reported VAS > 3 were given Diclofenac 75 mg intravenous or Paracetamol 1 gm intravenous as rescue analgesia. Patients were also observed for postoperative nausea and vomiting. Patients who suffered nausea or vomiting were given ondansetron 4 mg IV. Time to the first request of analgesia (considering the extubation as time 0), total dose of analgesia and adverse or side-effects over 24 h postoperatively were noted.

Statistical analysis was performed using SPSS ver. 20. Results were expressed as mean \pm standard deviation, number and percentage (%). Data were analyzed normally distributed data were assessed using independent sample *t*-test (for comparison of parameters among groups). Comparison was carried out using Chi-square (χ^2) Fisher exact test with a *p* - value reported at 95% confidence level. *p* - value < 0.05 considered as statistically significant.

Results

There was no significant difference with respect to age, sex, weight and ASA physical status, duration of surgery and anesthesia time, (Table 1).

Table 1: Demographic characteristics of patients, operative data in studied groups

| Variable | Mean \pm SD | | p^* | Statistical Significance |
|---------------------------|-------------------------|--------------------------|-------|--------------------------|
| | Group B ($n = 26$) | Group BD ($n = 26$) | | |
| Age (years) | 39.0 \pm 14.29 | 34.08 \pm 12.38 | 0.19 | NS |
| Sex | | | | |
| Males | 7 (58.3) | 5 (41.7) | 0.510 | NS |
| Females | 19 (47.5) | 21 (52.5) | | |
| ASA | | | | |
| I | 16 (48.5) | 17 (51.5) | 0.773 | NS |
| II | 10 (52.6) | 9 (47.4) | | |
| Duration of surgery (min) | 95.58 \pm 55.16 | 123.46 \pm 67.92 | 0.11 | NS |

ASA: American Society of Anesthesiologists, SD: Standard Deviation, Group B: Bupivacaine only, Group BD: Bupivacaine with dexmedetomidine; $p^* < 0.05$ considered as statistically significant. p^* value > 0.05 by independent sample t -test.

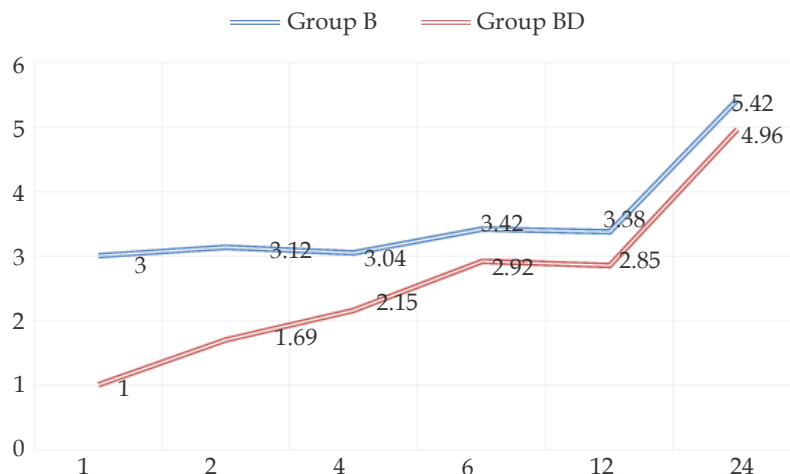
So, there was no significant difference with respect to age, sex, weight and ASA physical status, duration of surgery. Visual analog scale at different

time intervals were statistically significantly lower at all times in Group BD than Group B, (Table 2 and Fig. 1).

Table 2: Postoperative VAS[#] score (mean \pm SD) in studied groups

| Time (in hrs) | Group B ($n = 26$) | Group BD ($n = 26$) | p^* | Statistical Significance |
|---------------|----------------------|-----------------------|--------|--------------------------|
| 1 | 3.0 \pm 0.00 | 1.0 \pm 0.00 | 0.99 | NS |
| 2 | 3.12 \pm 1.21 | 1.69 \pm 0.47 | 0.0001 | S |
| 4 | 3.04 \pm 1.14 | 2.15 \pm 0.67 | 0.001 | S |
| 6 | 3.42 \pm 1.47 | 2.92 \pm 1.35 | 0.209 | NS |
| 12 | 3.38 \pm 1.35 | 2.85 \pm 1.34 | 0.158 | NS |
| 24 | 5.42 \pm 0.50 | 4.96 \pm 1.18 | 0.076 | NS |

p^* : Level of significance between Group B and Group BD; VAS[#]: Visual Analog Scale; SD: Standard Deviation; $p^* < 0.05$ Considered as statistically significant.

**Fig. 1:** Postoperative VAS comparison.

Furthermore, overall VAS in 24 h was also significantly lower in Group BD (2.34 \pm 0.84) than

Group B (3.65 \pm 0.47), (Table 3 and Fig. 2).

Table 3: Overall Postoperative VAS[#] score (mean ± SD) in studied groups

| Variable | Group B (n = 26) | Group BD (n = 26) | p* | Statistical Significance |
|------------------------------------|------------------|-------------------|--------|--------------------------|
| Overall VAS 24 hrs postoperatively | 3.65 ± 0.47 | 2.34 ± 0.84 | 0.0001 | S |

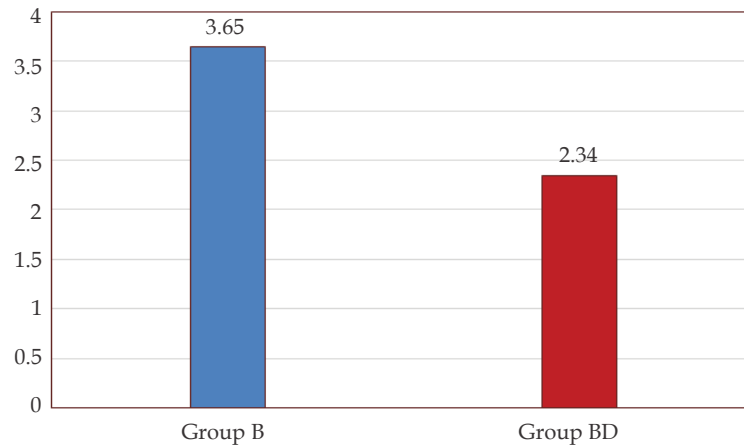


Fig. 2: VAS score comparison in 24 hours.

Table 4: Hourly consumption of rescue analgesic drug is also significantly low

| Drug used in 2 hrs | Group | | p* | Significance |
|----------------------------|-------|----|--------|--------------|
| | B | BD | | |
| Not used | 20 | 26 | 0.009 | S |
| Diclofenac | 4 | 0 | | |
| PCM | 2 | 0 | | |
| Total | 26 | 26 | | |
| Drug used in 4 hrs | | | | |
| Not used | 18 | 26 | 0.014 | S |
| Diclofenac | 3 | 0 | | |
| PCM | 5 | 0 | | |
| Total | 26 | 26 | | |
| Drug used in 6 hrs | | | | |
| Not used | 13 | 18 | 0.010 | S |
| Diclofenac | 3 | 7 | | |
| PCM | 9 | 1 | | |
| PCM + Diclophenac | 1 | 0 | | |
| Total | 26 | 26 | | |
| Drug used in 12 hrs | | | | |
| Not used | 8 | 20 | 0.0001 | S |
| Diclofenac | 8 | 2 | | |
| PCM | 10 | 4 | | |
| Total | 26 | 26 | | |
| Drug used in 24 hrs | | | | |
| Not used | 0 | 16 | 0.0001 | S |
| Diclofenac | 13 | 3 | | |
| PCM | 13 | 10 | | |
| Total | 26 | 26 | | |

p*: Level of significance between Group B and Group BD;

p* value < 0.05 by Fisher Exact test

Discussion

Laparoscopic surgery is the most effective in all the day care surgery. But pain management is also important in laparoscopic surgery. Effects of insufflation during laparoscopic surgery are *via* two mechanism.

1. Mechanical effect due to increase intraperitoneal pressure (e.g., Decrease venous return; Decrease cardiac output; Decrease blood pressure; etc.)
2. Chemical effects due to CO₂ absorption and its inflammatory effect on peritoneum (e.g., Hypoxia; Acidosis; Cardiac arrhythmias; etc.)

Due to inflammation and irritation of peritoneum pain scale is increase which is already present due to surgery. Pain have three component in laparoscopic surgery visceral, parietal and referred pain.¹⁶ The major portion of pain is parietal but may studies showed that in early postoperative time major portion is occupied by visceral pain due to small incision and less tissue trauma to abdominal wall.¹⁶

For this multi factorial pain stimulus requirement of pain management also multimodal. For this intraperitoneal local anesthetic agent give some additive effect of analgesia. Which is further give more analgesic effect with some adjuvant added with it. But analgesic effects are different according to various study by intraperitoneal instillation of local anesthetic agents.

BMP Rademaker³ shown that 20 ml of local analgesic agent is not effective for postoperative pain management, it is may because of low amount of agents.

This justification is covered by our study and adequate amount of drug with adequate concentration is used. They also shown some argument about position of patient during instillation, gravity is also a factor to act the drug on specific nerve ending sites.

A Ng, G Smith¹ shown that intraperitoneal instillation of anesthetic appear to demonstrate more effective in elective gynecological laparoscopic surgery because of it is less traumatic surgery than other laparoscopic surgery like laparoscopic cholecystectomy or laparoscopic hernia repair.

Usha Shukla, T Prabhakar¹⁷ assessed effect of dexmedetomidine is *via* dorsal root neuron level, where they release substance P and through the action on G protein. They also assessed dexmedetomidine is give better analgesia effect

with bupivacaine as compared to bupivacaine alone or bupivacaine with tramadol.

Khaled Mohamed Fares, Sahar Abd Elbaky Mohmed⁹ give conclusion that for postoperative pain management in laparoscopic colorectal carcinoma surgery 50 ml of 0.25% bupivacaine with dexmedetomidine 1 mcg/kg is effective as compare to 50 ml of 0.25% bupivacaine alone.

Our study results correlates with study done by Usha Shukla¹⁷ and Khaled Mohamed Fares⁹ which have shown that intraperitoneal instillation of 50 ml of Bupivacaine with 1 mcg/kg dexmedetomidine was effectively reduce postoperative pain as compare to 50 ml bupivacaine alone in laparoscopic cholecystectomy¹⁷ and laparoscopic colorectal surgery⁹ respectively. Our study show no significant difference with respect to Age, Sex, ASA status and Duration of surgery (Table 1).

In our study VAS score was below 3 in both group in first two hour but patient was more comfortable in Group BD as compare to Group B and no rescue analgesic drug used in first hour postoperatively in both group so, in First hour study is not significant statically ($p = 0.99$) but mean VAS was as low as 1.0 ± 0.00 in Group BD as compare to Group B which has mean VAS score 3.0 ± 0.00 (Table 2).

But in second and fourth hour VAS score was increase in both Group BD and B (mean VAS 1.69 ± 0.47 and 3.12 ± 1.21 respectively in second hour and mean VAS 2.15 ± 0.67 and 3.04 ± 1.14 respectively, shown in Table 2 but during this time period rescue drug used only in Group B and significantly analgesia maintain in Group BD ($p < 0.05$), (Table 4).

After fourth hour VAS score was above 3 in both group and rescue analgesia was used in both Group BD and B so, test is not significant statistically after fourth hour postoperative but number of patient required rescue analgesia was significantly low in BD all the time in 24 hour duration, (Table 2 and 4).

Overall low VAS score and patient's comfortability was in Group BD in 24 hour time interval with mean VAS 2.34 ± 0.84 as compare to Group B with mean VAS 3.65 ± 0.47 so, test show significant in overall VAS score in 24 hour with significantly low p - value ($p = .0001$), (Table 3).

Limitation

Our study is postoperative VAS which is subjective entity and difficult to quantify.

Conclusion

We conclude that intraperitoneal instillation of 0.25% bupivacaine in adequate volume (2 mg/kg) with adjuvant dexmedetomidine 1 mcg/kg reduce pain and analgesia requirement in postoperatively in elective laparoscopic surgery as compare to 0.25% bupivacaine (2 mg/kg) alone.

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