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ORIGINAL RESEARCH ANESTHESIOLOGY

Intraperitoneal bupivacaine alone or with dexmedetomidine for post-operative analgesia following laparoscopic cholecystectomy: A prospective randomized comparative study

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Abstract

Background & objetives: Laparoscopic procedures are usually followed by postoperative pain of variable intensity. The pain occurs due to streching of the visceral organs and peritoneum. We compared the antinociceptive effect of intraperitoneal instillation of bupivacaine with a combination of bupivacaine and dexmedetomidine in laparoscopic surgery. We assessed the quality of analgesia, time to the first request of rescue analgesia and total analgesics required in the first 24 h.

Methodology: After institutional ethical committee approval a total of 162 patients were selected, out of which 81 patients were allocated into two groups using table of randomization. Group B received 0.25 % bupivacaine 50 ml with 5 ml normal saline and Group BD received 0.25 % bupivacaine 50 ml plus dexmedetomidine 1 µg/kg diluted in 5 ml of normal saline intraperitoneally.

Results: We found a significant difference between mean VAS scores of the two groups in all time points ($p < 0.05$). There was significant difference between mean time to the first request for analgesia and the mean total dose for analgesic required ($p < 0.05$) in between both groups.

Conclusion: We conclude that intraperitoneal instillation of dexmedetomidine 1 µg kg in combination with bupivacaine 0.25% in elective laparoscopic cholecystectomy significantly reduces the postoperative pain and analgesic requirement in postoperative period when compared to bupivacaine 0.25% alone.

Abbreviations: VAS – Visual analog scale; NS - Normal saline; PACU - post-anesthesia care unit; HR – Heart rate;

Key words: Anesthetics, Local / administration & dosage; Bupivacaine / administration & dosage; Cholecystectomy, Laparoscopic / adverse effects; Dexmedetomidine, Intraperitoneal; Bupivacaine; Visual analogue scale; Pain Measurement; Pain, Postoperative / diagnosis; Pain, Postoperative / etiology; Pain, Postoperative / prevention & control

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1. Introduction

Laparoscopic surgery has many advantages over open surgical procedures, such as lesser hemorrhage, better cosmetic results, lesser post-operative pain and reduced use of analgesics and shorter recovery time, which lead to shorter hospital stay and less expenditure. [1] For some patients the severity of the pain may be mild to moderate, but many patients experience considerably severe pain in the first 24 h. Pain results from stretching of the intra-abdominal cavity, [2] peritoneal inflammation, and diaphragmatic irritation caused by residual carbon dioxide in the peritoneal cavity. [3]

To relieve post-operative pain following laparoscopic cholecystectomy, many methods have been tried, e.g., intraperitoneal instillation of local anesthetics, opioids, α_2 agonists. All have shown good effect on duration and quality of analgesia. [4, 5, 6, 7] Dexmedetomidine is highly selective α_2 agonist like clonidine with more effect on α_2 receptors, provides sedation, anxiolysis, analgesia and sympatholysis. Due to its favorable hemodynamic, [8] neuroprotective and anesthetic sparing effect, dexmedetomidine is frequently being used in operating rooms and in critical care units. It has been used in regional anesthesia practice for its high selectivity to α_2 receptors. [9] This study compared the antinociceptive effect of intraperitoneal instillation of bupivacaine alone and in combination with dexmedetomidine in laparoscopic surgery, and to find out which method offers better analgesic properties.

2. Methodology

After the approval of the hospital ethical committee, patients of the age group of 18-60 y, of either sex, belonging to ASA-I and II, were included in this prospective, randomized-controlled, double blind study. Informed consent was obtained from all the patients who fulfilled the inclusion criteria. Patients allergic to local anesthetics or dexmedetomidine, with cardiopulmonary or renal disease or a history of any prior laparotomy were excluded from the study.

Total 162 patients were selected under convenient sampling technique and randomly assigned in one of the two equal group; Group B (n = 81) to receive 50 ml of bupivacaine 0.25% and 5 ml of normal saline (NS) intraperitoneally. Group BD (n = 81) were to receive 50 ml bupivacaine 0.25% and dexmedetomidine 1 µg/kg (diluted in 5 ml NS) intraperitoneally.

The codes were kept under sealed envelopes by a person who was not involved in study. Pre-anesthetic evaluation was done and premedication was given a night before and in the morning of the surgery with oral tablet alprazolam 0.25 mg and tab ranitidine 150 mg.

Study drugs were prepared by an anesthesiologist not involved in the study. All the study patients were instructed about the use of the VAS scoring before induction of anesthesia. Vital signs e.g., non-invasive blood pressure (NIBP), heart rate (HR) and SpO_2 were registered and monitoring continued till the completion of 24 h after the surgery. Routine general anesthesia was used for every patient with relaxants and intubation and IPPV. At the end of the surgery, the study solution was injected intraperitoneally in Trendelenburg position, into the hepato-diaphragmatic space, at gall bladder bed and near and above hepatoduodenal ligament. The neuro-muscular blockade was antagonized with neostigmine and glycopyrrolate and trachea was extubated. The nasogastric tube was removed, and the patient shifted to post-anesthesia care unit (PACU). All patients were kept in PACU for 2 h after the surgery. The primary outcome measure was postoperative pain measured in terms of the VAS score using VAS scores at

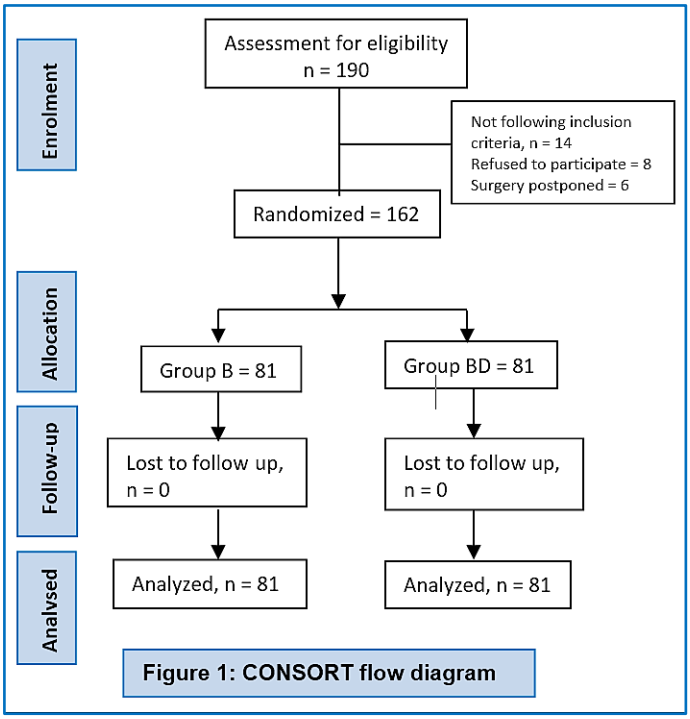

Figure 1: CONSORT flow diagram

Table 1: Comparative data regarding VAS scores, time to first analgesic request and total diclofenac sodium consumption during 24 h

Parameter	Group B	Group BD	t value	p value
VAS Score	4.16 ± 0.39	2.70 ± 0.27	27.700	0.010
Time to first request for analgesia (h)	1.54 ± .526	3.12 ± .781	-15.111	0.000
Total diclofenac sodium in 24 h (mg)	192.59 ± 45.319	79.01 ± 35.676	17.723	0.000

VAS-visual analogue score, Group B-bupivacaine group; Group BD-bupivacaine + dexmedetomidine group; Data presented as mean ± SD; p ≤ 0.05 is significant

0.5, 1, 2, 4, 6, 12, and 24 h after surgery. Patients with VAS ≥ 3 were given inj. diclofenac 50 mg intramuscularly as rescue analgesia. The secondary outcome measures included the time to the first request of analgesia in the postoperative period, and the total dose of analgesic required in 24 h postoperative period.

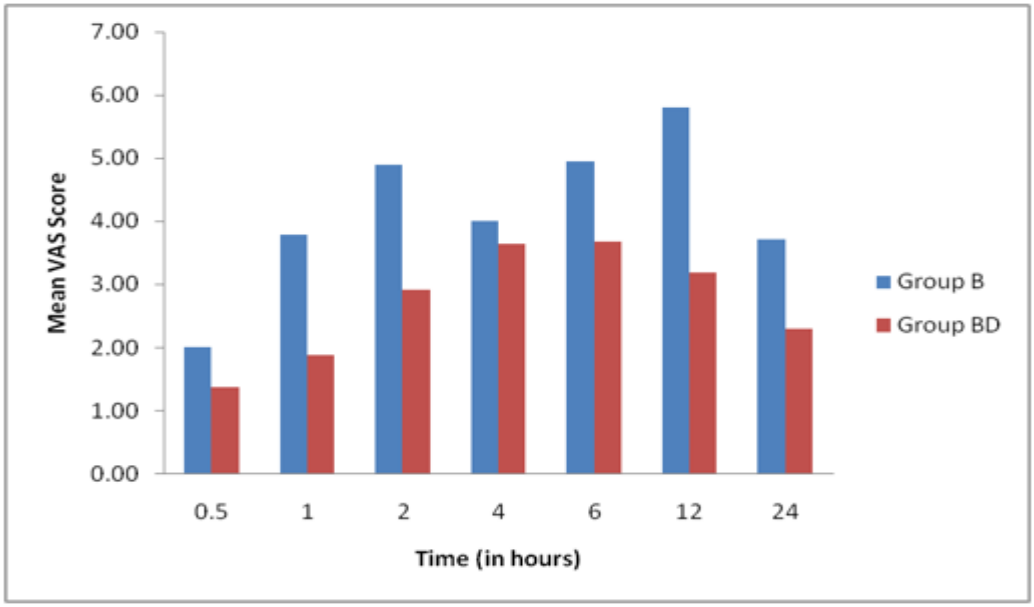

Figure 2: Comparative VAS score between the groups at each time point

Statistical analysis: The data was entered in Win Pepi computer software and Microsoft (MS) Office Excel software and was analyzed using post hoc analysis method to assess the outcome of study. Demographic data was analyzed using unpaired Student's t-test (for comparison of parameters among groups). Comparison was carried out using Chi-square ($\chi 2$) test with a P value reported at 95% confidence level. Level of significance was used as P = 0.05 assuming equal variance for both the study groups. The means of all VAS scores were analyzed (Figures 1).

3. Results

In this study 46 male and 116 female patients were enrolled. The mean age of the participants in Group B was 38.32 ± 11.28 y, and in Group BD was 36.37 ± 12.06 y. Out of 162 patients, 136 patients were ASA-I and 26 patients were ASA-II. Out of 162 patients, 161 were diagnosed with cholelithiasis and one patient with gall bladder sludge. Vital parameters, including HR and NIBP are important indicators of patient's comfort and the findings correlated well with the VAS scores.

The mean VAS score of the study subjects in Group B, initially showed increasing trend up to 12th hour and later it decreased up to 24th hour. The mean VAS score in Group BD showed increasing trend up to 6th hour, later it decreased. Statistically significant difference was observed in VAS of both groups at all points of time (Figure 2). The overall mean VAS score of the study subjects in Group BD was lower than that of Group B, e.g., 2.70 vs. 4.16 (P < 0.05) (Table 1).The mean time of first request for analgesia in Group B was earlier than that of Group BD (1.54 vs. 3.12 h). The table also shows that there was significant difference between mean time to first request for analgesia in groups (P < 0.05) (Table 1). The mean dose for analgesic requirement (inj. diclofenac sodium 50 mg) in Group B was higher as compared to Group BD (292.59 vs. 179.01 mg). The difference was significant between the groups (P < 0.05) (Table 1).

4. Discussion

Pain after laparoscopic surgery is due to skin incision, creation of pneumoperitoneum, and tissue trauma created by surgical procedure. [10] Postoperative pain after laparoscopic surgery is mainly due to expansion of intraabdominal cavity (visceral pain), phrenic nerve irritation by residual carbon dioxide in the peritoneal cavity (shoulder pain) and surgical incision (parietal pain). [3] The gas insufflation and raised intra peritoneal pressure causes peritoneal inflammation and neuronal rupture with a linear relationship between abdominal compliance and resultant severity of the postoperative pain.[10] Intra peritoneal route can be chosen for drug instillation to block the visceral afferent signals and modify visceral nociception. The local anesthetic agents provide antinociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins which stimulates the nociceptors and causes inflammation. [11] As pain after laparoscopic surgery is multifactorial, thus multimodal analgesia is necessary to counter this pain. Dexmedetomidine is a potent and more selective alpha-2 agonist and reduces pain scores after laparoscopic cholecystectomy with multimodal analgesia. [12] The antinociceptive effect of dexmedetomidine occurs at dorsal root neuron level, where it blocks the release of substance P in the nociceptive pathway and through action on inhibitory G protein, which increases the conductance through potassium channels. [13]

In our study, the mean VAS score of the study subjects in Group B, initially was increased up to 12th hour and later it decreased in 24th hour. But in Group BD, receiving bupivacaine plus dexmedetomidine, the mean VAS score increased initially up to 6th hour later it decreased till the end of the study. The pain score was less in the group who received bupivacaine plus dexmedetomidine than the subjects who received bupivacaine alone. Some researchers used plain bupivacaine or bupivacaine plus magnesium in laparoscopic cholecystectomy and they found less VAS scores in the study group patients. [10, 15] The mean time of first request for analgesia in the patients who received bupivacaine alone was lower when compared with the patients who received bupivacaine plus dexmedetomidine in the postoperative period. Our results correlate with study done by Ahmed et al. which has shown that intraperitoneal instillation of meperidine or dexmedetomidine in combination with bupivacaine 0.25% significantly decreased the post-operative analgesic requirements and decreased incidence of shoulder pain in patients undergoing laparoscopic gynecological surgeries. [6] Another researcher, however, found no difference between tramadol or clonidine groups and in present study, the time gap for the requirement of first dose of rescue analgesia was significantly shorter in bupivacaine group than dexmedetomidine group (P = 0.00). [8]

In our study, the mean total dose of analgesic requirement in 24 hours was higher in Group B i.e. bupivacaine alone when compared with the Group BD i.e. the combination of bupivacaine and dexmedetomidine, which was in agreement with studies by Ahmed et al and Memis et al. [6, 8] Time for the first analgesic dose was significantly prolonged and total analgesic doses required was significantly less in Group BD compared to Group B. This clearly shows that the application of bupivacaine in combination of dexmedetomidine reduces the requirement of analgesia during the postoperative period.

All our study findings fulfilled the study objectives and proved the antinociceptive effect of intraperitoneal instillation of bupivacaine plus dexmedetomidine in laparoscopic surgery showed better results than the bupivacaine alone with quality VAS score, better hemodynamic values, less doses of analgesic requirement during postoperative period with minimal adverse events.

5. Limitations

Postoperative pain is a subjective experience and can be difficult to quantify. As there are very few studies in the past on addition of dexmedetomidine to intraperitoneal bupivacaine, further studies with different doses of dexmedetomidine, timing, concentration and volume of local anesthetics and routes of administration are required to provide maximal benefit in terms of postoperative pain relief with minimal adverse effects after laparoscopic surgeries.

6. Conclusion

Laparoscopic surgeries by using two or more ports produces significant surgical trauma and moderate to severe pain. From the findings of our study, we conclude that intraperitoneal instillation of dexmedetomidine (1 µg/kg) in combination with bupivacaine 0.25% produces prolonged duration of analgesia and reduces the number of analgesic doses required when compared to bupivacaine 0.25% alone in patients undergoing laparoscopic cholecystectomies.

7. Conflict of interests

The authors declare no conflict.

8. Funding

No external or internal funding was provided to complete this study.

9. Data availability

The study data is available with the authors on a reasonable request.

10. Authors' contribution

SS−Conduction of the study

BKG−Supervision of the study

MKS, SS−Literature search

ARP−Manuscript writing and editing

VD−Statistical analysis

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