

A PROSPECTIVE COMPARATIVE STUDY OF INTRAPERITONEAL INSTILLATION OF BUPIVACAINE WITH TRAMADOL OR DEXMEDETOMIDINE TO ASSESS POSTOPERATIVE ANALGESIA AFTER LAPAROSCOPIC CHOLECYSTECTOMY



Anaesthesiology

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ABSTRACT

Background: In laparoscopic surgeries, intraperitoneal (IP) instillation of local anaesthetics, opioids, alpha-2 agonists is gaining popularity for better pain relief. This study compared the quality and duration of post-operative analgesia using IP bupivacaine combined with dexmedetomidine (BD) with that of IP bupivacaine combined with tramadol (BT) in the patients undergoing laparoscopic cholecystectomy.

Materials and Methods: A total of 60 patients were included in this prospective, double-blind, randomized study done during the period January 2019 to January 2020 at Alluri Sitarama Raju Academy of Medical Sciences, Eluru. Patients were randomly divided into two equally (n = 30) study groups. Patients received intraperitoneal bupivacaine 40 ml 0.25% + dexmedetomidine 1 µg/kg in Group BD and bupivacaine 40 ml 0.25% + tramadol 1 mg/kg in Group BT before removal of trocar at the end of surgery. The quality of analgesia was assessed by visual analogue scale score (VAS). Time to the first request of analgesia, total number of doses of analgesic in the first 24 h and adverse effects if any were noted. Statistical analysis was performed using Microsoft (MS) Office Excel Software with the Student's t-test and Chi-square test (level of significance P = 0.05).

Results: VAS at different time intervals, overall VAS in 24 h was significantly lower (1.16 ± 0.57 , 2.09 ± 0.63), total no. of doses of analgesic consumption (mg) was lowest (1.33 ± 0.5 , 2.06 ± 0.5) and time to first request of analgesia (min) was longest (312.7 ± 30.3 , 213.5 ± 23.5) in Group BD than Group BT. There were no statistically significant differences in the adverse effects.

Conclusion: Intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is superior to bupivacaine with tramadol.

KEYWORDS

Bupivacaine hydrochloride, dexmedetomidine hydrochloride, intraperitoneal injection, pain, post-operative, tramadol hydrochloride.

INTRODUCTION:

PAIN-is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (IASP 1979)⁽¹⁾.

Laparoscopic cholecystectomy is currently the most accepted surgical technique for cholelithiasis as opposed to open cholecystectomy. Laparoscopic operative procedures revolutionized surgery with many advantages such as smaller and more cosmetic incision, reduced blood loss, decreased postoperative stay and pain, which cut down on the hospital cost.⁽²⁾ Post-operative pain after laparoscopic cholecystectomy consists of three components, visceral, parietal⁽³⁾ and referred shoulder pain distinguishable from each other in the intensity, latency and duration.

Patients after laparoscopic cholecystectomy complain more of visceral pain that results from stretching of intra-abdominal cavity, peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity⁽⁴⁾. Pain intensity which is influenced by several factors usually peaks during the initial postoperative period and usually declines over the next 2-3 days⁽⁵⁾.

Many methods have been proposed to relieve post-operative pain following laparoscopic Cholecystectomy to discharge the patient early. Recently Intraperitoneal injections of local anaesthetic have been proposed to minimize postoperative pain after laparoscopic surgery⁽⁶⁾. Peritoneal origin of pain suggests that analgesia delivered locally to the peritoneal cavity may be beneficial postoperatively.

Hence, we chose intraperitoneal route because it blocks the visceral afferent signals and modifies visceral nociception. The local anaesthetic agents provide antinociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins which stimulates the nociceptors and cause inflammation.

As pain after laparoscopic surgery is multifactorial, multimodal

analgesia can counter this pain and enables early discharge of the patient. Adjuvants like dexmedetomidine and tramadol were added to bupivacaine to see if there is a better relief of post-operative pain.

The aim of the study was to compare the antinociceptive effects of intraperitoneal bupivacaine with dexmedetomidine (alpha 2 agonist) to intraperitoneal bupivacaine combined with tramadol (a weak opioid) in prospective randomized manner in patients undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS:

This was a prospective randomized double-blind study done during the period January 2019 to January 2020 at Alluri Sitarama Raju Academy of Medical Sciences, Eluru. It compares the antinociceptive effects of intraperitoneal bupivacaine combined with dexmedetomidine to bupivacaine combined with tramadol in laparoscopic cholecystectomy patients for postoperative analgesia.

This study included 60 patients of ASA class 1 or 2 of either sex aged from 18 to 60 years scheduled for laparoscopic cholecystectomies. A written informed consent was obtained to participate in the study.

60 patients of both genders were randomly allocated into two equal groups of 30 each.

Group-BD: Patients of this group received 40ml 0.25% bupivacaine with 1 µg/kg dexmedetomidine

Group-BT: - Patients of this group received 40ml 0.25% bupivacaine with 1mg/kg tramadol

INCLUSION CRITERIA:

- ASA I-II adult subjects
- Age 18-60 years of either sex
- Laparoscopic cholecystectomies
- Written informed consent

EXCLUSION CRITERIA:

- Patients who were allergic to local anaesthetic and study drugs
- Patients with acute cholecystitis
- Patients with severe cardiac, pulmonary and neurological diseases ASA 3,4,5
- Patients with chronic pain syndrome Pregnancy

Preoperative assessment was done and patients with hypertension, heart disease, diabetes mellitus were excluded from the study. Hematological parameters including hemoglobin level, clotting time, bleeding time and biochemical parameters like blood sugar, blood urea, serum creatinine were noted and were within the normal limits.

PROCEDURE

All the patients were explained the procedure of the technique and written informed consent was obtained. The patients were thoroughly evaluated and examined. Pulse rate and Blood pressure were recorded before providing anesthesia. Pre-oxygenation with 100% oxygen (O₂) was done for 3 min.

General anaesthesia was induced with IV fentanyl 2 µg/kg, propofol 2.0–2.5 mg/kg followed by Atracurium 0.5 mg/kg to facilitate orotracheal intubation. Anaesthesia was maintained with 60% air +40% oxygen with Et sevoflurane of 2%. Intermittent boluses of Atracurium was used to achieve muscle relaxation. Minute ventilation was adjusted to maintain normocapnia (end tidal carbon-dioxide [EtCO₂] between 34 and 38mm Hg) and EtCO₂ was monitored. Nasogastric tube of appropriate size was inserted. Intraoperative analgesia is given with Inj paracetamol and Inj fentanyl. At the end of the surgery, surgeon was requested to instill the drug intraperitoneally before removal of trocar in Trendelenburg's position, into the hepatodiaphragmatic space (10ml), sub hepatic area (10ml) on gall bladder bed (10ml) and near and above hepatoduodenal ligament(10ml). For postoperative pain diclofenac sodium is used.

Patients were monitored continuously using NIBP, Pulse oximeter and ECG.

PARAMETERS OBSERVED:

1. Pain (visual analogue scale [VAS]) score.
2. Time of first request of analgesia in the post-operative period
3. Total dose (Number) of rescue analgesics
4. Adverse effects.

RESULTS:

The demographic profile of our patients is comparable with respect to mean age, body weight, height, sex distribution, and types of surgeries.

Table 1: Comparison of VAS Score over 24hrs

Time(hrs)	Group BD	Group BT	p-value
1	0.5 ± 0.5	1.5±0.5	0.0001
2	0.93±0.64	1.8±0.48	0.0001
4	1.4±0.6	2.5±0.6	0.0001
6	1.6±0.4	2.3±0.8	0.0001
12	1±0.5	2.4±0.6	0.0001
24	1.13±0.6	1.93±0.7	0.0001

The VAS score was taken regularly for the first 24 hours at 1hr, 2hr, 4hr, 6hr, 12hr, 24hrs. Visual analogue scale at different time intervals were statistically significantly lower at all times in Group BD than Group BT.

Table 2: Comparison of time of 1st request of analgesics

Time of first dose of analgesics(min)	Group BD	Group BT	p Value
	Mean ± SD	Mean ± SD	
	312.7±30.3	213.5±23.5	0.0001

Time of 1st request of analgesics in group BD is 312.7 ± 30.3 min and in group BT is 213.5 ± 23.5min and this difference was statistically significant as p value is 0.0001.

Table 3: Comparison of analgesics doses in 24hrs

Total no. of doses in 24hrs (1 dose of diclofenac=75mg)	Group BD	Group BT	p Value
	Mean ± SD	Mean ± SD	
	1.33±0.5	2.06±0.6	0.0001

Duration in group BD (1.33±0.5) and in group BT (1.33±0.6) and this

difference was statistically significant as p value is 0.0001.

Table 4: Comparison of adverse effects noted in two groups

Groups	ADVERSE EFFECTS		
	Nausea	Nausea,	Nil
Group BD(n=30)	2	1	27
Group BT(n=30)	4	3	23
P Value	0.171		

The values showed that adverse events (nausea, vomiting) were not statistically significantly in all the two study groups ($P = 0.171$). Two patients in group BD and four patients in group BT complained of nausea. One patient in BD group and three patients in BT group complained of vomiting. There was no incidence of significant side effects like pruritus, excessive sedation, drowsiness, or dryness of mouth in both the groups.

DISCUSSION:

In our study, postoperative VAS score was observed up to 24 h. The VAS score in Bupivacaine-Dexmedetomidine group is 1.16 ± 0.57 and in group Bupivacaine-Tramadol is 2.09 ± 0.63 . In a study conducted by **Mukkavilli Lakshmi Narasimham et al⁽⁸⁾** found that VAS scores in dexmedetomidine group (0.98 ± 0.35) than tramadol group (2.11 ± 1.34). Results of our study showing mean VAS score in BD group lesser than BT group correlates with the above study.

Time to first request of analgesia in post-operative period was significantly delayed in Group BD (312.7 ± 30.3) as compared to Group BT (213.5 ± 23.5) in our study. Similar results were seen in the study done by **Shukla et al⁽⁷⁾** who compared the antinociceptive effect of dexmedetomidine or tramadol with bupivacaine to bupivacaine alone intraperitoneally after the laparoscopic cholecystectomy in which time to first request of analgesia was longest in Group BD (128 ± 20 min) as compared to BT (118 ± 22 min). Therefore, these results are comparable with our study.

Dose of diclofenac required in post-operative period, statistically significant higher doses are required in Group BT (2.06 ± 0.5) as compared to Group BD (1.33 ± 0.5) which was in agreement with the study done by **Shukla et al⁽⁷⁾** which has shown the total diclofenac consumption was also lowest in Group BD (45 ± 15 mg) than Group BT (85 ± 35).

There were few complications like nausea and vomiting post-surgery among the groups, out of which, group BT had more incidence than group BD which is statistically insignificant ($P = 0.171$). Two patients in BD group and 4 patients in BT group complained of nausea. One patient in BD group and 3 patients in BT group complained of vomiting. There was no incidence of Significant side effects like pruritus, excessive sedation, drowsiness, or dryness of mouth in both the groups. **Mohamad ommid et al⁽⁹⁾** in their study reported that 6 patients complained nausea, 6 patients complained vomiting and 16 patients complained of shoulder pain in tramadol group when compared to 4 patients complained of nausea and 5 patients shoulder pain and 0 patients vomiting. The authors thus concluded that there is statistically significant difference among the 2 groups and this is comparable with our study.

CONCLUSION:

We conclude that intraperitoneal instillation of dexmedetomidine 1 µg/kg in combination with 40ml of 0.25% bupivacaine in elective laparoscopic cholecystectomy significantly reduces the post-operative pain and significantly reduces the analgesic requirement in post-operative period as compared to 40ml of 0.25% bupivacaine combined with tramadol. This was also, simple to use with minimal side effects and discomfort to the patient and hence it is suggested for routine use.

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