

COMPARISON OF EFFICACY OF INTRAPERITONEALLY ADMINISTERED LOCAL ANAESTHETICS WITH ADJUVANTS FOR POST-OPERATIVE ANALGESIA AFTER LAPAROSCOPIC CHOLECYSTECTOMY

T. D. P. Subbalakshmi¹, A. Satyanarayana², Krishna Chaitanya B³

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ABSTRACT: CONTEXT: Post-operative pain after laparoscopic cholecystectomy is less than open cholecystectomy, but many patients require strong analgesia postoperatively. Intraperitoneal administration of local anaesthetics alone or in combination with various adjuvants can control post-operative pain. **AIM:** To compare the analgesic effect of the intraperitoneal administration of Bupivacaine, Bupivacaine plus Tramadol and Bupivacaine plus Dexmedetomidine. **SETTINGS AND DESIGN:** 80 patients undergoing laparoscopic cholecystectomy were randomly allocated to one of four groups: Group C; Group B, Group T and Group D. **METHODS AND MATERIAL:** 80 patients undergoing laparoscopic cholecystectomy were randomly allocated to one of four groups: Group C received 20 ml of saline; Group B received 20 ml of 0.25% Bupivacaine. Group T received 20 ml of 0.25% Bupivacaine with 100 mg Tramadol and patients allocated to Group D received 20 ml of 0.25% Bupivacaine with 1µg/kg of Dexmedetomidine intraperitoneally post-operatively. Faces pain scale was recorded at 0.5, 1, 2, 4, 6 and 24 hours postoperatively. Time of requirement of rescue analgesia was calculated. Level of sedation postoperatively was assessed. Incidence of postoperative nausea and vomiting (PONV) was also recorded. **STATISTICAL ANALYSIS:** Data was analyzed by two-way analysis of variance, Student's t-test, Kruskal-Wallis and Mann-Whitney U-test. **RESULTS:** Pain intensity, time of requirement of rescue analgesia, sedation score, as well as PONV were significantly lower in Group D, Group T and Group B than in Group C. Duration of post-operative analgesia was highest with Bupivacaine plus Dexmedetomidine. There were no differences between the three groups receiving Bupivacaine and Bupivacaine with Tramadol and Bupivacaine with Dexmedetomidine in FPS score, incidence of PONV and postoperative analgesic and antiemetic consumption. **CONCLUSIONS:** Bupivacaine with or without adjuvants provides significant pain relief when administered intraperitoneally after laparoscopic cholecystectomy. Bupivacaine with Dexmedetomidine is superior to plain Bupivacaine or Bupivacaine with Tramadol in providing analgesia for greater duration. No side effects were noticed with instillation of local anaesthetic with or without adjuvants. It significantly reduced the need for antiemetic medication.

KEYWORDS: Laparoscopic Cholecystectomy, Intra-Peritoneal, Local Anaesthetics, Adjuvants, Post-Operative Analgesia.

KEY MESSAGES:

1. Laparoscopic cholecystectomy is not completely devoid of pain. Pain is of visceral type.
2. Bupivacaine when administered intraperitoneally can provide significant postoperative analgesia, this effect can be enhanced by the addition of adjuvants.
3. Bupivacaine along with an Alfa-2 agonist like Dexmedetomidine can provide prolonged analgesia to the patient in the postoperative period.

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INTRODUCTION: Laparoscopic cholecystectomy has become the surgery of choice in recent times for chronic cholecystitis. Though it requires considerable expertise on the part of surgeons, it is being increasingly performed as an elective surgery with the introduction of advanced equipment and increasing training of the budding surgeons. Patients are showing preference to laparoscopic procedures because of lesser post-operative pain, greater cosmetic value, and lesser duration of post-operative hospital stay and an overall reduced financial burden,^[1,2] when compared to open cholecystectomy. However laparoscopic cholecystectomy is not completely devoid of post-operative pain. Besides the effects of the peritoneal stretching and post-operative nausea and vomiting, pain at the operated site is of definite concern for the patient and the anaesthesiologist. Intrapleural instillation of local anaesthetics for post-operative pain relief in case of thoracotomies, upper abdominal surgeries in children and even laparoscopic cholecystectomy.^[3,4,5] have been tried recently, but with no definitive conclusion of value as of now. Aim of this study was to study and compare the efficacy of intraperitoneal instillation of Bupivacaine vs. Bupivacaine plus Tramadol vs. Bupivacaine plus Dexmedetomidine for post-operative analgesia after laparoscopic cholecystectomy.

The Objectives were:

1. Compare the quality of analgesia with regard to Faces pain scale for pain.
2. To compare the duration of post-operative analgesia after intra peritoneal instillation of Bupivacaine, Bupivacaine plus Tramadol and Bupivacaine plus Dexmedetomidine.
3. Assess and compare the level of sedation post operatively.
4. To compare the changes in mean arterial pressure after the administration of the drugs.

MATERIAL AND METHODS: This randomised, double blinded, prospective interventional study was approved by the Ethical Committee of the institution. 80 patients of age group 18-60 years of either sex and of American Society of Anaesthesiologists physical status 1 or 2, posted for laparoscopic cholecystectomy in the Department of Surgery, King George hospital, Visakhapatnam were included in this study after obtaining written informed consent from all subjects, The study was not registered.

Patients with ASA grade 3 and 4, patients with chronic pain syndrome, those allergic to protocol drug, those with history of previous abdominal surgery, with history of CNS or CVS abnormalities and those patients in whom conversion to open cholecystectomy was done for any reason were excluded from the study. A detailed history was taken and complete clinical examination was done. Routine investigations like blood grouping, hemoglobin, blood urea and blood sugar were done. ECG was taken to rule out the presence of any cardiac disease. Pre-operative vitals, respiratory rate, blood pressure and conditions of heart and lungs and patients' weights were recorded. The patients were divided into 4 groups of 20 each by computer based randomisation:

1. Group C- who received 20 ml of Normal Saline.
2. Group B- who received 20 ml of 0.25% BUPIVACAINE.
3. Group T- who received 20ml of 0.25% BUPIVACAINE PLUS 100mg TRAMADOL.
4. Group D- who received 20ml of 0.25% BUPIVACAINE plus 1µg/kg. DEXMEDETOMIDINE.

Pre-medication consisted of Midazolam 1mg I.V, Glycopyrrolate (0.2mg) and Fentanyl I.V. 2mic/kg body weight. Induction was done with intravenous Propofol (2.5mg/kg body weight). Orotracheal intubation was facilitated by I.V. Vecuronium (0.1mg/kg body weight). Ventilation with intermittent positive-pressure ventilation with 5:3 ratio N₂O:O₂ was done.

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Fifteen minutes before the end of the surgery, the respective drug mixture was administered by an anesthetist who was unaware of the composition of the mixture into the hepatodiaphragmatic space, near and above the hepato-duodenal ligament and above the gall bladder bed under direct vision via a 23G Quinke spinal needle, placing the patient in 20° Trendelenburg position. The entry point was 5mm port in the right hypochondriac space. All patients stayed in PACU after surgery for two hours:

1. Intensity of the pain- Faces Pain Scale (Wong – Baker) at 0.5, 1, 2, 4, 6 and 24 hours after surgery.
2. Time of requirement of rescue analgesia was calculated.
3. Rescue analgesia requirements were recorded. If the FPS>3, the patient received opioid (pentazocine 30mg I.V). If the FPS<3, the patient received nonsteroidal anti-inflammatory drugs like Diclofenac 75mg I.V.
4. Level of sedation assessed using Ramsay sedation score.^[6] at 0.5,1,2,4,6 and 24 hours.
5. Occurrence of postoperative nausea and vomiting if any were noted. In case of PONV, patients received Metoclopramide (10mg) intravenously.
6. Pulse rate, blood pressure were monitored at 0.5, 1, 2, 4, 6 and 24 hours.

Results are reported as mean±SD. Data were analyzed by two-way analysis of variance. Demographic data were studied using Student's t-test. Pain score for both groups were compared using the Kruscal-Walis and Mann-Whitney U-test. Results were considered statistically significant at the 5% critical level (p<0.05). SPSS® software (IBM) - Version 20 was used to analyze the data.

RESULTS AND DISCUSSION: Over a few years, clinical trials were conducted to assess the advantage of local anaesthetics with or without adjuvants like opioids, administered intraperitoneally for post-operative analgesia after laparoscopic cholecystectomy. The results have been variable. Jiranantar V et al.^[7] in their study on 80 patients found that intraperitoneal instillation of Bupivacaine does not have any added advantage for post-operative analgesia after laparoscopic cholecystectomy. Bharadwaj N et al.^[8] studied the characteristics of pain after laparoscopic cholecystectomy and the effect of intraperitoneal instillation of 20ml of 0.25% Bupivacaine with 1:200000 Adrenaline and found that there was significant difference in pain scores at 1st and 4th post-operative hours when Group B was compared to the control group. This is in support to the results of our study, probably due to the placement of the patient in 20° Trendelenburg position at the time of instillation of the analgesic, helping in its accumulation in the gallbladder bed.

This study showed that there was a statistically significant difference in the pain scores in Group B,T,D from Group C at 1, 2, 4, 6 and 24hours after the surgery(p<0.05). Akinci et al.^[9] showed that I.V tramadol produced superior post-operative analgesia compared with equivalent dose of Tramadol. On the contrary, Memis et al.^[10] found that intraperitoneal Tramadol and Bupivacaine are very effective for post-operative analgesia in patients undergoing Laparoscopic tubal ligation. These results were in support of this study. Snjeana Golubovic et al.^[11] in their study, showed that intraperitoneal Tramadol with Bupivacaine provided superior post-operative analgesia compared to control group. Although in our study, lesser volume of analgesic (20ml of 0.25% Bupivacaine with or without additives) was used in contrast to 50 ml of 0.25% Bupivacaine in the above said study, the quality and duration of analgesia were the same as in the above study.

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There were no pharmacological side effects of either the local anaesthetic used in large volume or due to any other analgesic used post operatively in our study. The prolonged post-operative analgesia leading to less analgesic consumption also contributed to its cost effectiveness.

In the present study, we compared the changes in post-operative haemodynamics and the incidence of PONV, which was not done in previous studies. Our study showed that there was statistically significant rise in MAP in Group C, probably due to the post-operative pain and anxiety.

There was a statistically significant fall in MAP in Group D; the fall in MAP in Group D may be attributed to the absence of post-operative pain, enhanced patient comfort, reduced anxiety, apart from the inherent hypotensive property of Dexmedetomidine. There were no untoward effects like excessive sedation and PONV.

Table 1: Sex ratio and duration of the surgery in each group .There was no significant difference in the sex ratio and duration of the operation in the four groups ($p>0.05$).

	GROUP C	GROUP B	GROUP T	GROUP D
Sex Ratio (F:M)	10:10	13:7	13:7	11:9
Duration of operation(Min)	72.8±16.5	74.6±22	75.5±18	73.3±21.1

Table 1

Table 2: Duration of Analgesia- The duration of analgesia in the post-operative period was on an average 12hrs in Group B, even more prolonged when additives like Tramadol (Group T) and Dexmedetomidine (Group D), were added to 0.25% Bupivacaine, as the analgesic solution.

GROUP	Time (hours) (MEAN±SD)
C	0.50± 0
B	12.9± 2.6
T	16.5± 0.9
D	26.4± 1.3

Table 2

Table 3: There was significant change in mean arterial pressure in the Groups C and D. In our study, there was a rise in M.A.P in Group C probably due to the post-operative pain and anxiety and a statistically significant fall in MAP in Group D probably due to good post-operative analgesia and reduced patient anxiety.

GROUP	CHANGE IN M.A.P(mm of Hg) (MEAN±S.D)	p value
C	3.9± 2.2	<0.05*
B	2.4± 10.1	>0.05
T	5.7±1.9	>0.05
D	2.4±3.8	<0.05*

Table 3

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Figure 1. COMPARISON OF FACES PAIN SCALE: The mean intensity of postoperative pain was significantly lower in Group B, Group T and Group D than - Group C at 1, 2, 4, 6 and 24 hours after the operation ($p < 0.05$). The pain was more in the group C and required rescue analgesia even before 30 minutes. Patients in group B and group T showed increase in pain scales at approximately 12 and 16 hours at which they required rescue analgesia leading to lowered pain scores subsequently. However, Group D patients showed consistently lower pain scores for about 26 hours without the need for rescue analgesia.

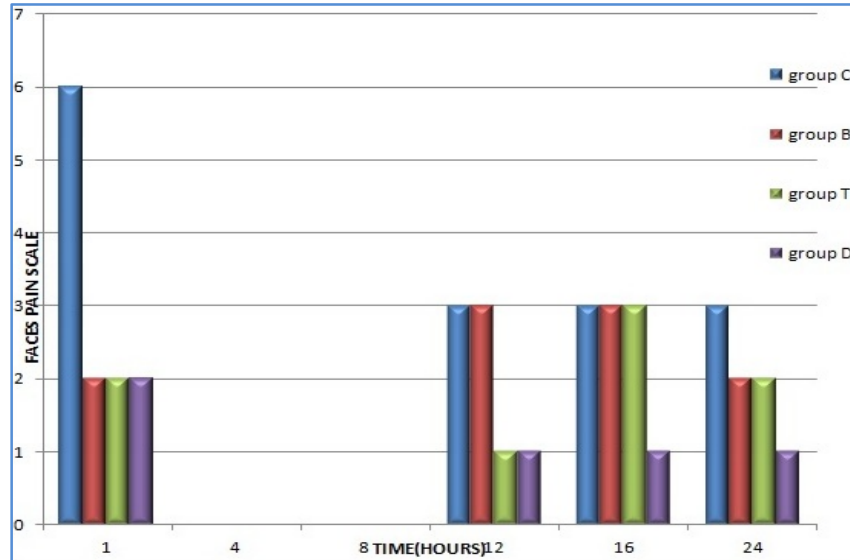


Fig. 1: Comparison of faces pain scale

Figure 2. SEDATION SCORES: All the patients receiving Bupivacaine with or without adjuvants showed equal scores of sedation (RSS-2) in contrast to the control group, which showed minimal scores of sedation (RSS-1). Thus no unwanted side effects of over sedation were noticed in Group B, T or D nor did Tramadol or Dexmedetomidine contribute to sedation apparently. The mild degree of sedation might be attributed to the superior analgesia leading to patient's comfort.

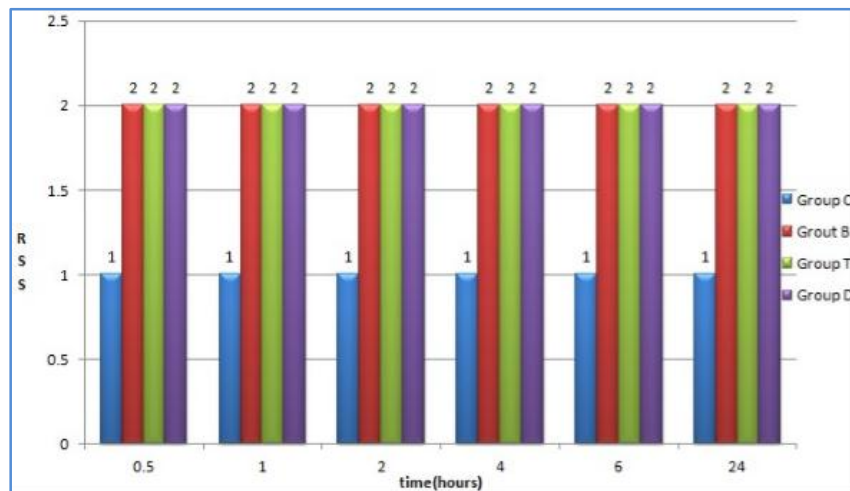


Fig. 2: Sedation scores

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Figure 3. Approximate time of requirement of rescue analgesia: The time of requirement of post-operative analgesia is the greatest in the Group D (26.4 ± 1.3 hrs) followed by Groups T (16.5 ± 0.9 hrs), B (12.9 ± 2.6 hrs) and C (≤ 0.5 hrs.), indicating the superior quality and duration of analgesia with Dexmedetomidine as adjuvant.

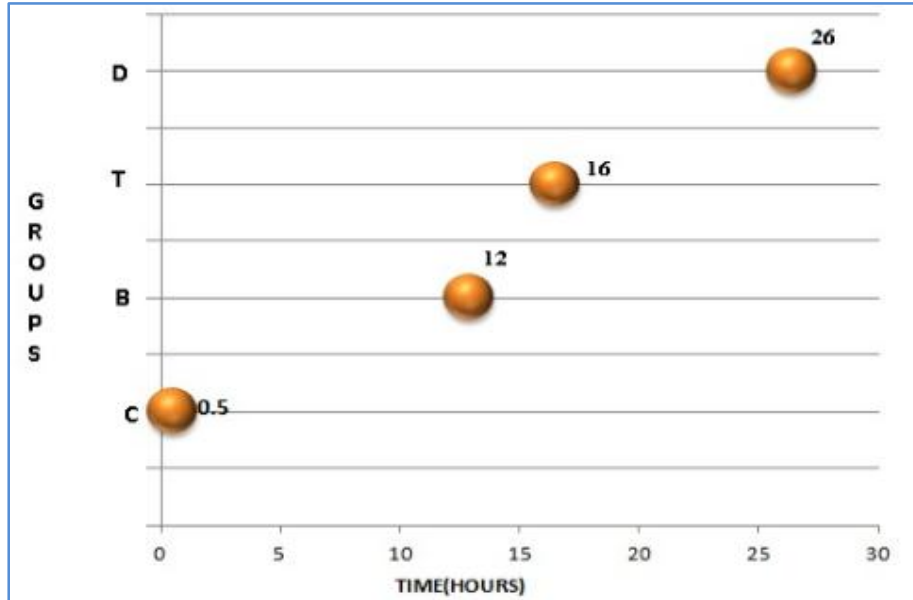


Fig. 3: Approximate time of requirement of rescue analgesia

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AUTHORS:

1. T. D. P. Subbalakshmi
2. A. Satyanarayana
3. Krishna Chaitanya B.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesiology, King George Hospital,
2. Professor and HOD, Department of Anaesthesiology, King George Hospital.
3. Post Graduate, Department of Anaesthesiology, King George Hospital.

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NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Krishna Chaitanya B,
H. No. 2-3-416, Plot No. 6, Road No. 4,
Department of Anesthesiology,
King George Hospital, Maharani-peta,
Visakhapatnam-530002.
E-mail: krrish22002@gmail.com

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