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Intraperitoneal Analgesia for Laparoscopic Cholecystectomy: Use of Bupivacaine with and Without Dexmedetomidine as Adjuvant

Dr. Mohamad Ommid*, Ummer Ali, Shahzada Gani, Shaheeda Akhter, Nuzhat ul Islam, Saba Ahad, Anka Amin, Humera Manzoor
Department of Anaesthesiology, Government Medical College Srinagar, J&K-190010, India

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***Corresponding author**
Dr. Mohamad Ommid
Assistant Professor

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Abstract: Intraperitoneal instillation of local anaesthetic agents alone or in combination with opioids, ∝-2 agonists such as dexmedetomidine have been found to reduce post operative pain following laparoscopic cholecystectomy. The purpose of this study was to assess the analgesic effect of the intraperitoneal administration of intraperitoneal dexmedetomidine combined with bupivacaine and intraperitoneal bupivacaine alone in patients undergoing laparoscopic cholecystectomy. One hundred patients of (ASA) physical status I-II of both sexes, aged between 18 to 60 years, equally divided in to two groups, randomly allocated to one of the groups using table of randomization, Group B (n = 50): Intraperitoneal bupivacaine 30 ml 0.25% +5 ml normal saline (NS), Group BD (n = 50): Intraperitoneal bupivacaine 30 ml 0.25% + dexmedetomidine1u g/kg (diluted in 5 ml NS). Visual analogue scale was recorded half and hours, 1, 2, 4, 6 and 24 hours postoperatively. Incidence of postoperative nausea and vomiting (PONV) was also recorded. In addition, supplementary analgesic and antiemetic consumption were assessed. 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). Pain intensity, as well as postoperative supplementary medications were significantly lower in Group BD,(2.12±0.91) as compared to Group B(4.21±1.15). Time to first request of analgesia (min) was longest (132±20),(60±19) and total analgesic consumption (mg) was lowest (48 ± 18), (182 ± 80) in Group BD than Group B. Intraperitoneal instillation of dexmedetomidine in combination with bupivacaine is an effective method for management of postoperative pain after laparoscopic cholecystectomy. It significantly reduced supplementary postoperative analgesic and antiemetic medication.

Keywords: Bupivacaine, Dexmedetomidine, Laparoscopic cholecystectomy, intraperitoneal injection, post operative pain.

INTRODUCTION

Surgical procedures are characterized by incisional damage to skin and various other tissues, application of thermal and chemical stimuli to wound and often prolonged traction and manipulation of somatic and visceral structures. Nociceptive pain is often regarded as the key feature of acute post operative pain. Besides inflammatory, visceral and neuropathic pain mechanisms may contribute to the pain occurring during the post-operative period [1].

The economic and health impact of cholelithiasis is significant due to high morbidity. Since the introduction of laparoscopic cholecystectomy in early 90s ,which is considered a safe treatment for cholelithiasis, many studies have demonstrated safety ,feasibility and cost effectiveness of laparoscopic cholecystectomy as a day care procedure[2].

Currently, the standard treatment for acute post-operative pain is the use of systemic opioids. Opioids bind to specific receptors located throughout the central nervous system and other tissues. Unfortunately, opioids are not without complications. Drowsiness, nausea, vomiting, ileus, urinary retention and pruritus, are all side effects of opioids. These side effects can lead to longer lengths of stays and poor patient outcomes [3,4].

Another approach to control post-operative pain and limit post-operative opioid usage is local anesthetic wound infiltration prior to wound closure. Injecting local anesthetics prior to surgical incision into the surgical wound has been more extensively studied. The results in this area are mixed with several studies showing significant pain reduction [5-7].

Intraperitoneal instillation of local anesthetic agents alone or in combination with opioids, ∝-2

agonists such as clonidine and dexmedetomidine have been found to reduce postoperative pain following laparoscopic cholecystectomy [8-11]. After laparoscopic cholecystectomy patients complain more of visceral pain as a result of stretching of the intraabdominal cavity, peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity, whereas after open cholecystectomy the type of pain results mostly in parietal pain [12]. Postoperative abdominal pain usually occurs during the first 24 hours, while shoulder pain most commonly appears the second day after laparoscopic cholecystectomy. Intraperitoneal (IP) administration of some aroscopic surgery. Some authors suggest that intraperitoneal instillation of drugs for pain relief is effective if used before creation of pneumoperitoneum [13]. While others conclude that intraperitoneal drug administration is effective at the end of the surgery applied through a trocar [14].

METHODS

The present study was conducted at the SMHS Hospital which is one of the associated hospitals of Government Medical College Srinagar. After obtaining approval from competent authorities of the government medical college Srinagar, One hundred patients of (ASA) physical status I-II of both sexes, aged between 18 to 60 years, equally divided in to two groups, Group B (n=50), and group BD (n=50), undergoing laparoscopic cholecystectomies were included in this prospective double blinded study. Patient who were allergic to local anesthetic and study drugs, patients with acute cholecystitis, patients with severe cardiac, pulmonary, and neurological diseases, those in whom procedure had to be converted to open cholecystectomy were excluded from the study. After getting approval from Institutional Ethical Committee, written informed consent was obtained from all the patients before surgery.

Patients were randomly divided into two groups of 50 patients each by computer generated random table number. Group B (n = 50): Intraperitoneal bupivacaine 30 ml 0.25% +5 ml normal saline (NS), and Group BD (n = 50): Intraperitoneal bupivacaine 30 ml 0.25% + dexmedetomidine1u g/kg (diluted in 5 ml NS). The study drug solution was prepared by an anesthesiologist who was blinded to study protocol and was not involved for intra operative data collection. The surgeon and resident anesthetist were also be blinded to the treatment regimen. All patients were admitted prior to the day of the surgery, and fasting of 6 hour was ensured. On arrival to the operation theatre, the baseline systemic blood pressure, heart rate, peripheral oxygen saturation (SpO_2) and ECG were recorded. After establishing the intravenous line, lactate Ringer solution was started and they were pre medicated with ondansetron (0.1-0.3mg/kg), glycopyrrolate (10 µg/kg), 15 min before induction of anesthesia.

After pre oxygenation for 3 min, anesthesia was induced with propofol (2 mg/kg) till loss of verbal command and tracheal intubation was facilitated with vecuronium 0.1 mg/kg. Anaesthesia was maintained with 60% nitrous oxide in oxygen and isoflurane dial concentration was titrated to achieve a systolic blood pressure 30% below the baseline values. Patients were mechanically ventilated to maintain the end tidal concentration ($EtCO_2$) between 30 and 35 mm Hg. Intra operatively, the heart rate, arterial blood pressure, ECG, $EtCO_2$ and peripheral pulse oximetry (SpO2) were monitored and recorded at 5 min intervals till end of surgery.

Hypotension/hypertension was defined as fall/rise in systolic blood pressure of >20% from the baseline values and bradycardia/tachycardia was defined as fall/rise in pulse rate of >20% from the baseline values. Haemodynamic fluctuations were to be managed accordingly. Patients were placed in 15-20° reverse rendelenberg's position with the left side tilt position. During laparoscopy, intra-abdominal pressure was maintained 12-14 mm Hg. The CO_2 was removed carefully by annual compression of the abdomen at the end of the procedure with open trocar.

At the end of the surgery, the study solution was given intraperitoneally before removal of trocar in Trendelenberg's position, into the hepato-diaphragmatic pace, on gall bladder bed and near and above hepatoduodenal ligament. The neuro-muscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg and trachea was extubated. The nasogastric tube was removed, and the patient was shifted to post-anesthesia care unit (PACU).

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

The intensity of post-operative pain was recorded for all the patients using VAS score at 0.5, 1, 2, 4, 6, 12, 24 h 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 or >3 were given diclofenac 75 mg intramuscularly as rescue analgesia. Patients were also observed for post-operative 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

A total sample size of 100 patients (n = 50 each for two groups) was calculated using Power and Sample size calculator (PS version 3.0.0.34), assuming 30% improvement in pain scores with error of 0.05 and power of 80%. To obtain a 100 study sample size, a total of 115 patients were included; but 15 patients were excluded on the basis of exclusion criteria.

Statistical analysis was performed using Microsoft (MS) Office Excel Software (Microsoft Microsoft Excel, Redmond, Washington: Microsoft 2003, Computer software). Results were expressed as mean ± standard deviation, number and percentage (%). Data were analyzed using *post hoc* analysis method. Normally distributed data were assessed using unpaired Student's *t*-test (for comparison of parameters among groups). Comparison was carried out using Chi-square test with a P value reported at 95% confidence level. Level of significance used was P = 0.05.

RESULTS

There was no significant difference with respect to age, sex, weight, height, ASA physical status, duration of surgery and anaesthesia time [Table 1].

Table-1: Demographic characteristic of patients in study groups (Mean±SD)

VARIABLES	GROUP B (N=45)	GROUP BD (N=45)	P
Age (years)	42.5±16.259	49.8±14.896	0.649*
SEX MALE/FEMALES	41/9	38/12	0.83*
WEIGHT (KG)	61.50±8.87	62.50±10.99	0.82*
HEIGHT	166.3±4.610	166.1±4.407	0.264*
ASA I/II	42/08	39/11	0.23*
DURATION OF SURGERY (min)	62.55±12.927	55.69±10.049	0.562*
Duration of anaesthesia (min)	74±10.30	70±11.05	0.685*

ASA American society of Anaesthesilogy, SD standard deviation, * Level of significance

Visual analogue scale at different time intervals were statistically significantly lower at all times in Group BD than Group B fig. 1. Furthermore, overall VAS in 24 h was also significantly lower in Group BD (1.80 ± 0.36) than Group B (3.01 ± 0.48) [Table 2].

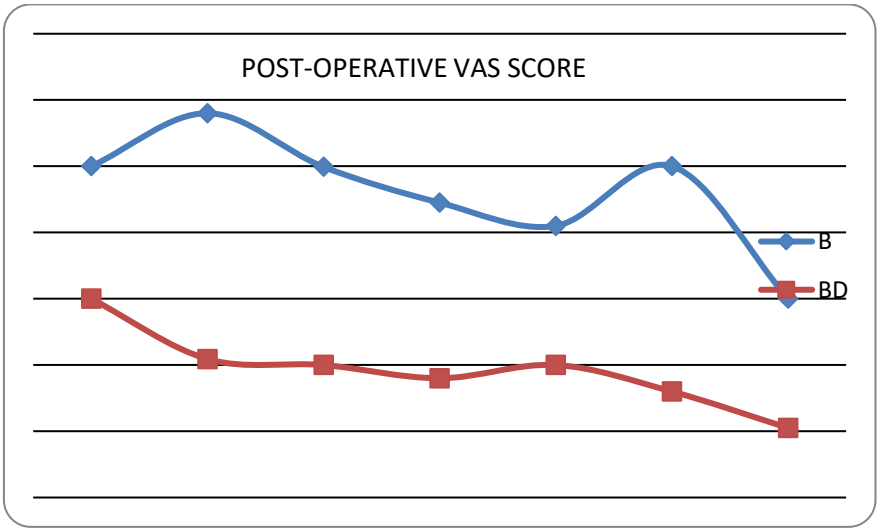

Fig-1: Post-operative VAS score (mean±SD) in studied groups

Table-2: Post-operative over all VAS score & analgesic requirements (Mean±SD)

variable	GROUP B (N=50)	GROUP BD (N=50)	P
Over all VAS over 24h post operatively	4.50±1.50	1.75±0.83	0.003
Time to request for first analgesia in post operative period (min)	60±3.54	132±7.6	0.0030
Total dose of analgesia in 24 h (mg)	182±8.34	48±2.97	0.0021

Time to first request of analgesia was longest in Group BD (128 ± 20 min) as compared to Group B (118 ± 22 min). Total diclofenac consumption was also lowest in Group BD (45 ± 15 mg) than Group B (85 ± 35) [Table 2].

Table-3: Post-operative adverse/side effects in the study group

Variable	GROUP B (N=50)	GROUP BD (N=50)
Nausea	05	02
Vomiting	06	02
Shoulder pain	30	
Pruritis	0	0

Regarding the adverse/side effects the analysis showed that adverse events were not statistically significantly different in all the two study groups (*P* = 0.3013) [Table 3].

DISCUSSION

Post-operative pain after laparoscopic cholecystectomy consists of three components, visceral, parietal and referred shoulder pain distinguishable from each other in the intensity, latency and duration[15]. Previous studies [16] suggest that predominant cause of pain is parietal but in contrast many other studies emphasized that in early convalescent period, major portion is occupied by visceral pain because as compared to small incisions and limited trauma to the abdominal wall, the surgical manipulation and tissue destruction in visceral organs is much more [17].

Mean pain scores were significantly lower in the group BD when compared to group B during the entire duration of the study. There was statistically significant difference in VAS pain score at 6, 8, 12, 18, 24 hours after surgery in group BD (2.12±0.93) compared to group B (4.21±1.66) up to 24 hours. Similar results were observed with study done by Ahmed, *et al*. [18] who compared the antinociceptive effect of dexmedetomidine or mepiridine with bupivacaine to bupivacaine alone intraperitoneally after the laparoscopic gynecological surgery found that intraperitoneal instillation of mepiridine or dexmedetomidine in combination with bupivacaine significantly decreases VAS score.

Bakhamees, *et al*.[19] evaluated the patients who received dexmedetomidine and found that they had less VAS score as compared to placebo in the postoperative period. Ahmed Mostafa, *et al*.[20] observed that the patients who received intraperitoneal levobupivacaine instillation had profound postoperative analgesia. Usha Shukla, *et al*.[21]. Intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is superior to bupivacaine alone and may be better than bupivacaine with tramadol.

Time to requirement of first dose rescue analgesia was prolong in the group BD (132±7.6 min) compared to group B (60±3.54 min), indicating better and longer pain relief in the group BD compared to groups B. Total analgesic consumption was more in group B (182±8.34 mg) compared to group BD (48±2.97 mg). Our study results also show that the duration of analgesia was higher and had less need of rescue analgesia in bupivacaine and dexmedetomidine group as compared to bupivacaine alone which were statistically significant. Also Ahmed, et al.[18] observed that intraperitoneal instillation of meperidine or dexmedetomidine in combination with bupivacaine significantly decreases total rescue analgesia requirement in postoperative period.

Arain *et al*.[22] studied the efficacy of dexmedetomidine and morphine for postoperative analgesia after a major surgery. Bhattacharjee *et al*.[23] concluded that dexmedetomidine improves intra and post operative hemodynamic stability during laparoscopic surgeries without prolongation of recovery and similar results were obtained by Bakhamees *et al*.[19].

In our study, among group B patients, nausea/vomiting was found in 11 patients out of 50 patients and 4 patients out of 50 patients in groups BD that is comparable to a study done by Bhakhamees *et al.* [19].

In our study, the incidence of shoulder pain was significantly low in groups BD compared to group B. We found that in group B 30 patients out of 50 patients and in groups BD, 4 patients out of 50 patients had postoperative shoulder pain that is comparable to the study done by Ahmed *et al*.[18].

CONCLUSION

We concluded that intraperitoneal instillation of dexmedetomidine with bupivacaine provides prolonged duration of analgesia and require less number of rescue analgesic doses compared to bupivacaine alone in patients undergoing laparoscopic surgery without any significant side effects.

REFERENCES

1. Jorgen BD, Kehlet H. postoperative pain and its management: Mc Mohan SB, Koltezenburg M, editors. Wall and Melzack textbook of pain. 5th edition. Elsevier Churchill livingstone: Philadelphia; 2006; p. 635.
2. Dr Ayaz Gul, Dr Ahmad Fayaz. Laparosc cholecystectomy: Effect of intraperitoneal

instillationof bupivacaine on mean post operativeImtiyaz Khan opic scores. Professional med j 2014;21(4):593-600
3. Brennan TJ. Postoperative models of nociception. ILAR journal. 1999 Jan 1;40(3):129-36.
4. Sherwinter DA, Ghaznavi AM, Spinner D, Savel RH, Macura JM, Adler H. Continuous infusion of intraperitoneal bupivacaine after laparoscopic surgery: a randomized controlled trial. Obesity surgery. 2008 Dec 1;18(12):1581.
5. Hilvering B, Draaisma WA, van der Bilt JD, Valk RM, Kofman KE, & Consten E. C.post operative abdominal pain (2011Br J Surg, 98(6), 784-789.
6. Lohsiriwat V, Lert-akyamanee N, Rushatamukayanunt W. Efficacy of pre-incisional bupivacaine infiltration on postoperative pain relief after appendectomy: prospective double-blind randomized trial. World journal of surgery. 2004 Oct 1;28(10):947-50.
7. Sihoe AD, Manlulu AV, Lee TW, Thung KH, Yim AP. Pre-emptive local anesthesia for needlescopic video-assisted thoracic surgery: a randomized controlled trial. European journal of cardio-thoracic surgery. 2007 Jan 1;31(1):103-8.
8. El-Labban GM, Hokkam EN, El-Labban MA, Morsy K, Saadl S, Heissam KS. Intraincisional vs intraperitoneal infiltration of local anaesthetic for controlling early post-laparoscopic cholecystectomy pain. J Minim Access Surg. 2011;7:173–7.
9. Ahmed B, Elmawgoud AA, Dosa R. Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy J Med Sci. 2008;8:400–4.
10. Golubovic S, Golubovic V, Cindric-Stancin M, Tokmadzic VSColl Antropol. Intraperitoneal use of local anesthetic in laparoscopic cholecystectomy: 2009;33:299–302.
11. Memis D, Turan A, Karamanlioglu B, Tükenmez B, Pamukçu ZJ Opioid Manag. The effect of tramadol or clonidine added to intraperitoneal bupivacaine on postoperative pain in total abdominal hysterectomy. 2005;1:77–82.
12. Fredman B, Jedeikin R, Olsfanger D, Flor P, Gruzman A. Residual pneumoperitoneum: a cause of postoperative pain after laparoscopic cholecystectomy. Anesthesia and analgesia. 1994 Jul;79(1):152-4.
13. Pappas-Gogos G, Tsimogiannis KE, Zikos N, Nikas K, Manataki A, Tsimoyiannis EC. Preincisional and intraperitoneal ropivacaine plus normal saline infusion for postoperative pain relief after laparoscopic cholecystectomy: a randomized double-blind controlled trial. Surgical endoscopy. 2008 Sep 1;22(9):2036-45.
14. Shukla U, Prabhakar T, Malhotra K, Srivastava D, Malhotra K. Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy: A comparative evaluation. Indian journal of anaesthesia. 2015 Apr;59(4):234.
15. Moharari RS, Hadavi M, Pourfakhr P, Najafi A, Etezadi F, Khajavi MR. Evaluation of the postoperative analgesic efficacy of intraperitoneal ketamine compared with bupivacaine in laparoscopic cholecystectomy. Archives of Anesthesiology and Critical Care. 2016 Apr 17;2(1):146-9.
16. Verma GR, Lyngdoh TS, Kaman L, Bala I. Placement of 0.5% bupivacaine-soaked Surgicel in the gallbladder bed is effective for pain after laparoscopic cholecystectomy. Surg Endosc 2006;20:1560-4.
17. Karaaslan D, Sivaci RG, Akbulut G, Dilek Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy: ON. Pain Pract 2006;6:237-41.
18. Ahmed B, Elmawgoud AA, Dosa R. Antinociceptive effect of (ά-2 adrenoceptor agonist) dexmedetomidine vs meperidine, topically, after laproscopic gynecologic surgery. J Med Sci., 2008; 8: 400–4.
19. Bakhamees HS, El-Halafawy YM, El-Kerdawy HM, Gouda NM, Altemyatt SU. Effects of dexmedetomidine in morbidly obese patients undergoing laparoscopic gastric bypass. Middle East J Anesthesiol. 2007 Oct;19(3):537-51.
20. Hamid AM. Intraperitoneal levobupivacaine instillation improves outcome of laparoscopic cholecystectomy: A comparative study of preemptive versus postoperative instillation. ASJA. 2009;2:53-63.
21. Shukla U, Prabhakar T, Malhotra K, Srivastava D, Malhotra K. Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol for post-operative analgesia following laparoscopic cholecystectomy: A comparative evaluation. Indian journal of anaesthesia. 2015 Apr;59(4):234.
22. Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesthesia & Analgesia. 2004 Jan 1;98(1):153-8.
23. Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K. Effects of dexmedetomidine on haemodynamics in patients undergoing laparoscopic cholecystectomy-a comparative study. Journal of Anaesthesiology Clinical Pharmacology. 2010 Jan 1;26(1):45.