

Original Research Article

## EVALUATION OF EFFECT OF INTRAPERITONEAL INSTILLATION OF DEXMEDETOMIDINE FOR POSTOPERATIVE ANALGESIA IN LAPAROSCOPIC CHOLECYSTECTOMY

Dr. Dinesh Patidar<sup>1</sup> Dr Avtar Singh Yadav<sup>2</sup>, Dr. Hansraj Baghel<sup>3\*</sup>, Dr. Abhay Raj  
Yadav<sup>4</sup>, Dr. Sudhakar Dwivedi<sup>5</sup>

Resident Department of Anesthesiology, Shyam Shah Medical College Rewa (M.P.)<sup>1</sup>

Professor, Department of Anesthesiology, Shyam Shah Medical College Rewa (M.P.)<sup>2</sup>

Associate Professor, Department of Anesthesiology, Shyam Shah Medical College Rewa  
(M.P.)<sup>3</sup>

Associate Professor, Department of Anesthesiology, Shyam Shah Medical College Rewa  
(M.P.)<sup>4</sup>

Professor, Department of Anesthesiology, Shyam Shah Medical College Rewa (M.P.)<sup>5</sup>

\*Corresponding Author: Dr, Hansraj Baghel

### ABSTRACT

**Introduction:** Dexmedetomidine can decrease the duration and intensity of postoperative pain due to their anti-nociceptive effects. Dexmedetomidine acts on dorsal root neurons to block the pain pathway.

**Aim:** To compare the analgesic efficacy and duration of postoperative analgesia after intraperitoneal instillation of bupivacaine with dexmedetomidine to bupivacaine alone in laparoscopic cholecystectomy.

**Materials and Methods:** The present study was a randomized controlled study, in which 60 patients of age 18-60 years, belonging to American Society of Anesthesiologists (ASA) grade I or II were randomly selected and divided in two groups. Patients of Group D received dexmedetomidine 1 µg/kg with 0.25% bupivacaine 30 mL, and patients of Group B received 0.25% of plain bupivacaine 30 mL. Postoperative pain was assessed using Visual Analog Scale (VAS) score as primary outcome. Time to rescue analgesia (VAS ≥4 or on demand) and patients satisfaction score were the secondary outcomes. All recorded data were analyzed by statistical tests (Analysis of Variance (ANOVA), posthoc Tukey's HSD (Honest Significant Difference) test and Chi-square test).

**Results:** Time to first rescue analgesia was highest in Group D as compared to Group B. The mean VAS score was 2.57±0.78 and 2.88±0.92 Group D and Group B, respectively (<0.05). Total analgesic requirement (Paracetamol) in first 24 Hrs postoperatively was lower in Group D (2.17±0.53 gm) as compared to Group B (2.87±0.47 gm). Highly satisfied patients in group D was 03 none in Group B. There were 18 dissatisfied and highly

dissatisfied patients in group B as compared to 07 in Group D. This difference in patients satisfaction score was statistically significant ( $P= 0.0002$ ).

**Conclusion:** intraperitoneal instillation of dexmedetomidine was found to be superior for postoperative analgesia in first 24 hours after laparoscopic cholecystectomy as reflected by a lower vas score, longer duration of analgesia and low total analgesic requirement.

## 1. INTRODUCTION

Laparoscopic cholecystectomy is a common day care procedure. The pain after open cholecystectomy is mostly parietal whereas it is more of visceral following laparoscopic cholecystectomy [1]. The pain occurs due to stretching of the abdominal wall during the pneumoperitoneum and release of inflammatory mediators, local dissection and irritation of the peritoneum, or CO<sub>2</sub> used for pneumoperitoneum [2]. The pain can be prevented or reduced by blocking the nociceptor before their stimulation via use of local anaesthetics [3].

Many studies have demonstrated the effectiveness of local anaesthetics instilled intraperitoneal, alone or mixed with other drugs for postoperative analgesia in laparoscopic cholecystectomy but there is no consensus regarding the dose, concentration, site and manner of administration [4-6] Dexmedetomidine used in combination with local anaesthetic, is associated with prolonged analgesic effects.

Studies on the role of intraperitoneal instillation of dexmedetomidine for postoperative analgesia, suggest its role in prolonging the duration of analgesia in Transversus Abdominis Plane (TAP) block in various surgeries [7,8].

This study was designed to compare duration of analgesia and total analgesic requirement after intraperitoneal instillation of dexmedetomidine with bupivacaine and bupivacaine alone. Primary outcome was VAS score at different time intervals, and secondary outcomes were time to first rescue analgesia, patient's satisfaction score and side effect (if any).

## 2. MATERIALS AND METHODS

This randomized controlled study was carried out in the Department of Anaesthesia, Government Medical College, Rewa, Madhya Pradesh, India, from April 2018 to March 2019. After getting clearance from Institutional Ethics Committee (IEC) (91/19) and informed consent from every patient, this study was carried out on 60 patients.

**Inclusion criteria:** Patients between 18-60 years of age, ASA grade I and II, of either sex, posted for laparoscopic cholecystectomy under general anaesthesia.

**Exclusion criteria:** Patients with allergy to study drugs, chronic alcoholism, systemic diseases like severe heart disease, lung disease, diabetes mellitus etc., renal dysfunction, and patients who refused to consent

**Sample size calculation:** After considering power of study by 90% and level of significance with 5%, calculated sample size came out 28 patients in each group, so decided to select total 60 patients after randomization ( $n=30$ ) using computer based randomization software,

“Random Allocation Software 1.0” (Copyright © 2017 Informer Technologies, INC) as under [Table/Fig-1].

**Group D-** Patients received intraperitoneal instillation of 30 mL, inj. bupivacaine 0.25% and inj. dexmedetomidine 1 µg/kg b.w.

**Group B-** Patients received intraperitoneal instillation of 30 mL of inj. bupivacaine 0.25% .

All patients were kept nil by mouth for at least six hours prior to surgery. After shifting them to the operating theatre, monitors were attached and baseline parameters (heart rate, non invasive blood pressure, and SpO<sub>2</sub> and ETCO<sub>2</sub> values) were recorded. Intravenous access secured with 18 G IV (intravenous) cannula. All the patients were premedicated with Inj. glycopyrrolate 0.01 mg/kg, Inj. midazolam 0.03 mg/kg and Inj. fentanyl 2 µg/kg. After preoxygenation for 3 minutes, patients were induced with Inj. propofol 2.5 mg/kg and Inj. succinylcholine 1.5 mg/ kg, laryngoscopy was performed and orotracheal intubation was done. The correct placement of endotracheal tube was confirmed by 5 point auscultation and ETCO<sub>2</sub> . Anaesthesia was maintained with O<sub>2</sub> 40%, N<sub>2</sub> O 60%, isoflurane and intermittent Inj. atracurium IV. After cholecystectomy and achievement of haemostasis, abdomen was thoroughly washed to remove the blood clots and debris. The surgeon instilled 10 mL of study solution in the subdiaphragmatic space and 10 mL at suprahepatic surface of liver and remaining drug in the gallbladder fossa under vision, which was prepared by investigator. Patients who required intraperitoneal drain after surgery were excluded from this study. All the patients received inj. diclofenac 75 mg IV at the end of surgery and same dose was repeated after 12 hours, as per institutional protocol. All the patients were reversed with Inj. neostimine 0.05 mg/kg and Inj. glycopyrrolate 0.01 mg/kg. Patients were extubated after absence of residual neuromuscular deficit. After surgery, patients were transferred to the postanaesthesia care unit. Pain severity was assessed using a VAS at 0, 2, 4, 6, 8, 10, 12 and 24 hours after surgery. When patients complained of pain or VAS  $\geq 4$  for first time in postoperative period, paracetamol 1 gm IV infusion (max 4 gm in 24 hours) was given as rescue analgesic. The duration of analgesia and total paracetamol consumption in first 24 hours were duly noted. Patient’s satisfaction score was assessed and noted at 24 hours after surgery, using a 5-point patient’s satisfaction score to evaluate the level of postoperative analgesic satisfaction.

### STATISTICAL ANALYSIS

All recorded data were tabulated and statistically analysed by appropriate statistical test (ANOVA, post-hoc tukey’s HSD test and Chi-square test). Mean values were compared for normally distributed parameters by using ANOVA. Post-hoc (tukey’s HSD) test was used if statistically significant difference was found with ANOVA to asses’ pair wise comparisons. Categorical outcomes were compared using Chi-square test between study groups. The p-value

### 3. RESULTS

All the groups were comparable with respect to demographic profiles and there was no statistically significant difference found in between the groups [Table - 1].

**Table:- 1 Demographic Characteristics**

PARAMETER	GROUP D	GROUP B	P-VALUE D VS B
Age (years)	38.53±10.29	37.6±11.8	0.9474
Height ( cm)	161.6±7.92	162.5±7.41	0.8914
Weight (kg)	62.3±9.43	60.0±9.23	0.6138
Sex (F:M)	25 F 5 M	23 F 7 M	0.5186

The duration of analgesia was significantly longer in patients of Group D (7.60 ±1.22) as compare to patients of Group B (4.93±1.14 hrs). Total analgesic requirement in first 24 Hrs( Paracetamol) requirement was lower in Group D ( 2.17 ±0.53gm) as compare to Group B (2.87±0.47) [Table-2].

**Table 2 :- Duration Of Analgesia And Total Analgesic Requirement**

PARAMETER	GROUP D	GROUP B	P-VALUE
Duration of Analgesia (Hrs)	7.60 ±1.22	4.93±1.14	<0.0001
Total Paracetamole requirement in 24 hrs (gm)	2.17 ±0.53	2.87±0.47	0.0006

Immediately after surgery, VAS was zero in all patients. After 2 hours and 4 hours of surgery, no statistical difference was noted between group D and group B. After 6 hours of surgery, VAS was significantly lower (p-value 0.05) between patients of all the two groups. The patients of Group D received rescue analgesia at mean time 7.60±1.22 hours which led to decreased VAS at subsequent point of times [Table-3]. According to patients' satisfaction score, Group D patients were highly satisfied (33.33%) by pain relief procedure than patients of Group B at any point of time. Group B patients were highly dissatisfied patients (46.67%). The difference in the patient satisfaction score between groups was statistically significant [Table -4]

**Table 3 :- Vas Score At Different Time Intervals**

Vas score	GROUP D	GROUP B	P-VALUE D VS B
Immediately after Surgery	0	0	-
2 Hrs postoperatively	1.57±0.82	1.97±1.07	0.1714
4 Hrs postoperatively	1.93±0.58	3.07±1.11	0.0001
6 Hrs postoperatively	3.00±0.95	3.53±0.90	0.0338

8 Hrs postoperatively	3.57±0.86	3.00±0.00	0.0805
10 Hrs postoperatively	2.93±0.87	2.93±0.87	0.9898
12 Hrs postoperatively	2.50±0.78	2.97±0.96	0.0937
24 Hrs postoperatively	2.47±0.68	2.70±0.75	0.4091

**TABLE 4:- Patient Satisfaction Score**

PATIENTS SATISFACTION SCORE	GROUP D	GROUP B	P-VALUE D VS B
	N(%)	N(%)	N(%)
Highly satisfied	03 (10)	0	0.0001
Satisfied	14(46,67)	06(20)	0.0004
Neither satisfied nor dissatisfied	06(20)	06(20)	0.0111
Dissatisfied	07 (23.33)	14(46.67)	0.0194
Highly dissatisfied	0	4(13.33)	0.0004
<b>TOTAL</b>	30	30	

**ADVERSE EFFECTS**

Bradycardia (Heart Rate) was seen in six patients of Group D. The incidence of nausea was seen four patients of group D and six patients of group B. Vomiting was not seen in any of the patients of all the two groups. No incidence of sedation, hypotension or hypertension was seen in any of the group in first 24 hours postoperatively [Table-5].

**Table 5 :- Adverse Events**

Adverse effects	Group D	Group B
None	20	25
Bradycardia (heart Rate <60/min)	06	0
Nausea	04	06
Vomiting	0	0
<b>Total</b>	30	30

**4. DISCUSSION**

Intraperitoneal instillation of analgesics drugs is a single-shot technique and provides a substantial period of postoperative analgesia with negligible side-effects. The present randomized and controlled study shows that intraperitoneal instillation of dexmedetomidine

provides postoperative analgesia after laparoscopic cholecystectomy. Rapolu S et al., evaluated the intraperitoneal instillation of dexmedetomidine adjuvant with bupivacaine for postoperative analgesia in 100 patients in two groups following laparoscopic cholecystectomy [9]. Similarly, they found the mean duration of analgesia was more in dexmedetomidine group as compared to control group. Ali U et al., compared the intraperitoneal instillation of bupivacaine alone with dexmedetomidine or tramadol for postoperative analgesia following laparoscopic cholecystectomy [7]. They concluded that intraperitoneal instillation of dexmedetomidine 1 mcg/kg in combination with bupivacaine after laparoscopic cholecystectomy significantly increases the duration of postoperative analgesia and significantly reduces the analgesic requirement in postoperative period, as compared to bupivacaine alone and may be better than bupivacaine combined with tramadol. Present study also found long duration of analgesia as previous studies but it was lower than magnesium sulphate [9, 10]. The total analgesic requirements (paracetamol) in first 24 hours postoperatively were lower in Group D than Group B which was statistically significant, and the results were in concordance with a study done by Yadava A et al., where they have compared magnesium sulphate with tramadol [11]. Pati BK, observed the total analgesic consumption was lower in Group BD (Bupivacaine with Dexmedetomidine) compared to Group B (Bupivacaine), which was statistically significant [10]. Mean VAS score increased till 8 hours in group D in present study.

Authors did not find other side-effects like sedation or hypotension in any of the study group in first 24 hours postoperatively; similar results were concluded in study conducted by Rapolu S et al., and Oza VP et al. [9, 12]. This was due to intraperitoneal instillation of drugs not by intravenous route. Present study showed the superiority of intraperitoneal instillation of bupivacaine with dexmedetomidine then bupivacaine alone in providing analgesia in first 24 postoperative hours, as evident by longer duration of analgesia along with lesser consumption of paracetamol and lower VAS score.

### **LIMITATION(S)**

Postoperative pain is a subjective experience and can be difficult to quantify and compare objectively. As it was a single centre study so there is a need for multicentric studies for more conclusive results.

### **5. CONCLUSION(S)**

It can be concluded that intraperitoneal instillation of magnesium sulphate was found to be superior for postoperative analgesia in first 24 hours after laparoscopic cholecystectomy as reflected by a lower VAS score and longer duration of analgesia along with lesser consumption of paracetamol. Intraperitoneal instillation can be considered as a part of multimodal analgesia technique for laparoscopic surgeries in future. An optimal dose finding study is also the need of hour with using large number of patients.

## 6. REFERENCES

1. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: A critical assessment of the evidence. *Anesthesiology*. 2006;104:835-46.
2. Pasqualucci A, de Angelis V, Contardo R, Colò F, Terrosu G, Donini A, et al. Preemptive analgesia: Intraperitoneal local anesthetic in laparoscopic cholecystectomy. A randomised, double-blind, placebo-controlled study. *Anesthesiology*. 1996;85:11-20.
3. Babu R, Jain P, Sherif L. Intraperitoneal instillation: ropivacaine vs bupivacaine for postoperative pain relief in laparoscopic cholecystectomy. *Int J Health Sci Res*. 2013;3(12):42-47.
4. Sharan R, Singh M, Kataria AP, Jyoti K, Jarewal V, Kadian R. Intraperitoneal instillation of bupivacaine and ropivacaine for postoperative analgesia in laparoscopic cholecystectomy. *Anesth Essays Res*. 2018;12(2):377-80.
5. Goldstein A, Grimault P, Henique A, Keller M, Fortin A, Darai E. Preventing postoperative pain by local anesthetic instillation after laparoscopic gynecologic surgery: A placebo-controlled comparison of bupivacaine and ropivacaine. *AnesthAnalg*. 2000;91(2):403-07.
6. Sharma CS, Singh M, Rautela RS, Kochhar A, Adlakha N. Comparison of intraperitoneal and periportal bupivacaine and ropivacaine for postoperative pain relief in laparoscopic cholecystectomy; a randomised prospective study. *AnesthPain & Intensive Care*. 2014;18(4):350-54.
7. Ali U, Ommid M, Alamgir NS, Nazir S, Lone S, Taj A, et al. Intraperitoneal bupivacaine alone with dexmedetomidine or tramadol for postoperative analgesia following laparoscopic cholecystectomy- a comparative evaluation. *J Evolution Med Dent Sci*. 2017;6(90):6373-80.
8. Elnabtity AM, Ibrahim M. Intraperitoneal dexmedetomidine as an adjuvant to bupivacaine for postoperative pain management in children undergoing laparoscopic appendectomy: A prospective randomised trial. *Saudi J Anaesth*. 2018;12(3):399-405.
9. Rapolu S, Anil Kumar K, Aasim SA. A comparative study on intraperitoneal bupivacaine alone or with dexmedetomidine for postoperative analgesia following laparoscopic cholecystectomy. *IAIM*. 2016;3(12):33-40.
10. Pati BK. Intraperitoneal analgesia for postoperative pain relief after laparoscopic gynaecological surgeries. *Int J Reprod Contracept Obstet Gynecol*. 2017;6:5099-102.
11. Yadava A, Rajput SK, Katiyar S, Jain RK. A comparison of intraperitoneal bupivacaine-tramadol with bupivacaine-magnesium sulphate for pain relief after laparoscopic cholecystectomy: A prospective, randomised study. *Indian J Anaesth*. 2016;60(10):757-62.
12. Oza VP, Parmar V, Badheka J, Nanavati DS, Taur P, Rajyaguru AM. Comparative study of postoperative analgesic effect of intraperitoneal instillation of dexmedetomidine with bupivacaine and bupivacaine alone after laparoscopic surgery. *J Minim Access Surg*. 2016;12(3):260-64