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The study of comparative evaluation of dexmedetomidine and paracetamol on perioperative and postoperative hemodynamic analgesia for patients undergoing laparoscopic cholecystectomy

Dr. **Sonal Bajpayee[1], Dr. Abhinav Shukla[2], Dr. Prafulla Agnihotri[3]**

1. Dr. Sonal Bajpayee, Associate Professor, Department of Anesthesiology, Shri Balaji Institute of Medical Sciences, Mowa, Raipur, CG, India
2. Dr. Abhinav Shukla, Assistant Professor, Department of Anesthesiology, Shri Rawatpura Sarkar Institute of Medical Sciences and Research Centre, Pacheda, Nava Raipur, Raipur, CG, India
3. Dr. Prafulla Agnihotri, senior consultant and executive director, Department of Anesthesiology and Critical Care Medicine, Shri Balaji Institute of Medical Sciences, Mowa, Raipur, CG, India

Corresponding Author:

Dr. Sonal Bajpayee, Associate Professor, Department of Anesthesiology, Shri Balaji Institute of Medical Sciences, Mowa, Raipur, CG, India

Abstract

Background: With the increase in incidence of gallbladder stone disease, laparoscopic cholecystectomy is the most preferred surgical technique. Laryngoscopy and peritoneal gas insufflation lead to hemodynamic stress response and pain during and after the procedure. Multimodal analgesia is recommended to reduce the stress response and prevent the post-laparoscopic pain. Intravenous paracetamol and intravenous dexmedetomidine are both effective components in respect of multimodal analgesia. **Aim and objective:**The study aimed to assess the comparative evaluation of dexmedetomidine and paracetamol on perioperative and postoperative hemodynamic analgesia for patients undergoing laparoscopic cholecystectomy. **Material and methods:** 50 consenting American Society of Anesthesiologists-Physical Status-I (ASA-ps-I), female patients, aged 20-60 yr, become randomly assigned to one of the following groups: group P (n = 25) received an IV 1 g Paracetamol infusion over 10 min pre-operatively and 6 hourly thereafter, and group D (n = 25) received an IV Dexmedetomidine 1 μg/kg bolus over 10 min pre-operatively and 0.2-0.4 μg/kg/h thereafter for 24 h. Perioperative hemodynamic variables, postoperative pain scores, and the desire for rescue analgesics have been recorded and compared. **Results**: Profiles of intraoperative hemodynamic changes had been similar in each group regarding heart rate (HR), diastolic blood pressure, and mean arterial pressure except within the systolic blood pressure, where Dexmedetomidine significantly decreased it compared to Paracetamol ($P = 0.014$). Postoperatively, at 4th h and 24th h, changes in mean HR between the two groups changed into a statistically significant ($P < 0.05$). Visual analog scale scores have been significantly lower inside group P than in group D at 8th, 16th, and 24th h ($P < 0.001$). Sedation scores have been statistically better inside group D compared with group P at postoperative 4th, 8th, 16th, and 24th h ($P < 0.006$). **Conclusion:**

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Adjunctive use of each paracetamol and dexmedetomidine infusion reduced opioid use. But paracetamol perioperatively offers adequate analgesia with less sedation, while dexmedetomidine provides analgesia and cooperative sedation.

Key words: Dexmedetomidine, laparoscopic cholecystectomy, multimodal analgesia, Paracetamol

Introduction

Laparoscopic cholecystectomy, being a minimally invasive procedure, has become the standard technique to remove the gallbladder in symptomatic gallbladder illnesses. This technique essentially has replaced the open technique for routine cholecystectomies since the early 1990s [1]. At this time, laparoscopic cholecystectomy is indicated for the treatment of cholecystitis (acute/chronic), symptomatic cholelithiasis, biliary dyskinesia, acalculous cholecystitis, gallstone pancreatitis, and gallbladder masses/polyps. [2]. The International Association for the Study of Pain (IASP) is the global professional forum for science, practice, and education in the field of pain. IASP brings together scientists, clinicians, healthcare providers, and policymakers to stimulate and support the study of pain and to translate that knowledge into improved pain relief worldwide. Acute pain inside the perioperative setting is defined as pain that is present in the surgical patient due to a pre-current disease, surgical procedure, or the aggregate of those that is detrimental to postoperative final results. It will increase the sympathetic response of the body with a subsequent rise in oxygen consumption of the body and the chance of deep vein thrombosis due to immobility and consequent pulmonary embolism. Similarly, there may be sizable effects on the gut and urinary tract motility, which may lead, in turn, to postoperative ileus, nausea, vomiting, and urinary retention. [3] As an end result, adequate pain comfort is translated to a better perioperative outcome, early recovery, and a reduced period of living in the health center. Routine use of strong opioids is unwanted due to adverse consequences including nausea, vomiting, pruritus, and sedation. Studies have shown that under-treatment of acute postoperative pain occurs due to the fact there may be an overestimation of the duration of action, strength of the opioid used, and worry approximately respiratory depression, vomiting, sedation, and dependence. [4,5]

Dexmedetomidine is an incredibly selective α2 adrenoceptor agonist that provides sedation, analgesia, and sympatholysis without causing respiratory depression. Previous studies document that intravenous dexmedetomidine has a definitive role in postoperative analgesia through the reduction of opioid consumption. [6]Paracetamol is an extensively used and popular analgesic and antipyretic. So, we have planned this study to see the impact of Dexmedetomidine and Paracetamol on postoperative pain comfort, adverse effects, and hemodynamics in patients undergoing laparoscopic surgical procedures under general anesthesia.

Materials and Methods

The study was conducted in Shri Rawatpura Sarkar Institute of Medical Sciences and Research Center, Nava Raipur, Raipur, Department of Anesthesiology and Critical Care. Ethical clearances were obtained from the Institutional Ethical Committee, and written informed consent was obtained. Before carrying out the study, 50 female

patients aged 20-60 years, ASA PS-I scheduled for laparoscopic cholecystectomy had been taken for those randomized studies. Patients with body weight >80 kg, cardiovascular disorder, broncho-pulmonary disorder, renal, neurologic, gastrointestinal, and hepatic dysfunction, records of allergies, long-term use of medicinal drugs, which include beta-blockers and different anti-hypertensives, antipsychotics, analgesics, alcohol, sedatives, TCA, etc., patients with psychiatric illness, and patient refusal had been excluded from this study.

Patients have been randomly assigned to one of the following groups: group P (n = 30) obtained an IV 1 g Paracetamol infusion over 10 min pre-operatively and 6 hourly thereafter, and group D (n = 30) received an IV Dexmedetomidine 1 μg/kg bolus over 10 min pre-operatively and 0.2-0.4 μg/kg/h thereafter for 24 h using a computer-generated random-number table. Within the pre-operative holding area, the patients found out and familiarized themselves with about 10 points of the visible analog scale (VAS) to assess their baseline pain, with 0 = none to 10 = maximum. Without delay, earlier than entering the operating room, patients were pre-medicated with Midazolam 2 mg, Ondansetron 4 mg, and Glycopyrrolate 0.2 mg IV. Intra-operative monitoring devices included pulse-oximetry, non-invasive blood pressure, ECG, and capnography.

After acquiring bottom-line measurements of the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), an infusion of Paracetamol (1 g) was given over 10 min for group P, and an infusion of Dexmedetomidine was given at 1 μg/kg (diluting in normal saline to make a 50 ml solution) over 10 min and 0.2-0.4 μg/kg/h thereafter for 24 h for group D. Anesthetic induction turned into finished with pre-oxygenation, injection of fentanyl 1 μg/kg, and injection of propofol 2 mg/kg IV, followed by using injection of succinylcholine 1.5 mg/kg IV to facilitate tracheal intubation. Anesthesia is maintained with nitrous oxide (N2O) (66%) and oxygen (O2) 34% of the mixture in combination with 0.5-1 vol% isoflurane and injection atracurium. The end-tidal carbon dioxide was maintained inside 35-40 mmHg. The HR, SBP, DBP, and MAP were recorded intraoperatively at 5 min, 15 min, 30 min, 45 min, and 60 min starting from the completion of bolus dose infusion of the study drug and HR and MAP postoperatively at 1st, 4th, 8th, 16th, and 24th h. MAP has been maintained within ± 25% of the baseline values through various stimulated isoflurane concentrations. Hypotension [7] (defined as MAP value <25% of the baseline value on 2 consecutive readings within 2-3 min) was not responding to a reduction in inspired isoflurane concentration, and a 200-ml fluid bolus was treated with injection phenylephrine. The infusion of study medication was discontinued if the hypotension persisted >2 min after those interventions. Upon return of the MAP ± 25% of the baseline values, they take a look at remedy infusion, which was resumed at 50% of the initial infusion rate. In the presence of high blood pressure [6] (defined as MAP value >25% of the baseline value on two consecutive readings within 2-3 min) and/or tachycardia [6] (described as HR value >25% of the baseline value on two consecutive readings within 2-3 min), the concentration of isoflurane and study medication increased. Bradycardia [6] (defined as HR <45/min) persisting for >2 min becomes treated with injection atropine. post-operative pain and sedation score were recorded at 1st, 4th, 8th, 16th, and 24th h.

During the operation, patients obtained similar quantities of IV crystalloid solutions. The residual neuromuscular block becomes reversed with Neostigmine 40 μg/kg and

Glycopyrrolate 5 μg/kg IV after the end of the operation. post-operatively injection Tramadol changed into given as a rescue analgesic at a dose of 100 mg IV when VAS > 5.

Statistics Analysis

Mean ± SD were calculated for all the parameters to examine and were differentiated by (ANOVA), and repeated measures of ANOVA were used to evaluate the changes among the groups using SPSS 23. Wilks' Lambda test was used to analyze the parametric data. *P*-values considered significant were as follows: $P < 0.05$ was considered significant, and $P > 0.001$ was considered highly significant.

Observation and Result

A total of 50 patients were enrolled and divided into two groups ($n = 25$). Two patients were excluded from final analysis due to repeated hypotension and bradycardia.

Table 1 shows there were no significant differences among the two groups with respect to age, weight, and height ($P > 0.05$).

Table 1: Baseline demographic data

	Group P(N=25)	**Group D(N=25)**
Age (year)	41.6 ± 9.99	43.56 ± 8.24
Hight (cm)	151.84 ± 8.38	154.44 ± 7.134
Weight (kg)	54.68 ± 5.99	55.64 ± 6.50

Intra-operative hemodynamic parameters were recorded at 5, 15, 30, 45, and 60 min after the completion of a bolus dose infusion of study medication. Table 2 shows profiles of hemodynamic changes, which were similar in both groups with respect to HR, DBP, and MAP except in SBP, where dexmedetomidine significantly reduced it in comparison to paracetamol ($P = 0.015$).

Table 2: Intra-operative hemodynamic parameters

Time (min)	**HR (min)**		**SBP (mmHg)**		**DBP (mmHg)**		**MAP (mmHg)**	
	Group P	**Group D**	**Group P**	**Group D**	**Group P**	**Group D**	**Group P**	**Group D**
5	101.28±8.48	92.4±8.49	116.96±10.41	129±7.86	82.84±5.80	83.24±5.10	86.8±5.83	94.44±6.60
15	100.32±7.44	96.88±22.49	120.72±18.34	116.96±8.31	79.48±4.0	77.6±3.21	87.32±5.80	87.68±6.06
30	102.44±6	90.72±6.	125.08±8.	124.84±7	84.48±5.	84.44±4.	91.96±5.	94.72±6.

	.86	90	95	.49	12	68	85	14
45	102±4.76	87.2±5.67	123.36±8.64	121.68±8.38	81.44±5.24	81.44±5.24	93.2±6.30	88.64±5.0
60	99.12±4.17	88.32±6.04	123.56±8.83	119.28±6.66	79.44±6.26	82.52±5.88	93.84±5.57	88.48±6.10

Note: HR = heart rate, SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP = mean arterial pressure.

Post-operative hemodynamic parameters were recorded at 4th, 8th, 16th, and 24th h. No significant differences in the post-operative hemodynamic parameters were seen in MAP, as shown in Table 3. The mean HR ranges from (84.48±5.12) to (85.24±4.94) for Group P, whereas it ranges from (82.44±5.78) to (85.76±3.90) in Group D. Post-operatively, 4th h and 24th h changes in mean HR between two groups were statistically significant ($P < 0.05$).

Table 3: Post-operative hemodynamic parameters

Time (h)	HR		MAP	
	Group P	Group D	Group P	Group D
4	84.48±5.12	78.36±4.72	88.56±6.31	83.12±4.40
8	85.24±4.94	78.44±4.59	93.04±5.15	93.04±5.15
16	86.52±3.90	85.76±3.90	90.04±5.74	90.04±5.74
24	89.12±4.94	82.44±5.78	88.04±4.42	88.04±4.42

Note: HR = heart rate, MAP = mean arterial pressure.

The VAS score for postoperative pain was measured on a scale of 10, where 0 = no pain and 10 = maximum pain at 4th, 8th, 16th, and 24th h. Sedation was measured according to the Ramsay sedation scale. VAS scores were significantly lower in Group P compared with Group D at 8th, 16th, and 24th h ($P < 0.001$). Sedation scores were statistically higher in Group D compared with Group P at 4th, 8th, 16th, and 24th h ($P < 0.005$), as shown in Table 4.

Table 4: Post-operative analgesia and sedation score

Pain			**Sedation**		
scale	**Group P**	**Group D**	**scale**	**Group P**	**Group D**
VAS 4	2.56±0.40	2.26±0.42	SS 4	1.96±0.39	2.51±0.34
VAS 8	1.71±0.46	2.33±0.35	SS 8	2.21±0.40	2.33±0.35
VAS 16	1.75±0.42	2.17±0.39	SS 16	2.03±0.44	2.3±0.33
VAS 24	1.89±0.36	2.17±0.39	SS 24	1.91±0.38	2.21±0.33

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Note: VAS = Visual analog scale

Discussion

During laparoscopic surgical procedures, changes in the inpatient's position and the surgical pressure, especially following pneumoperitoneum, cause labile hemodynamics. The selection of anesthetic technique for upper abdominal laparoscopic surgical operation is mostly associated with general anesthesia with muscle rest, tracheal intubation, and intermittent positive pressure ventilation. [7] This study was conducted on 80 adult patients belonging to ASA-PS-I toevaluate the effect of IV Paracetamol and dexmedetomidine infusion on perioperative hemodynamic response and the postoperative analgesia in the laparoscopic cholecystectomy.

According to the New South Wales Therapeutic Advisory Group's current opinion in October 2005, the recommended dose of paracetamol is 1 g IV up to 4 times each day with a minimum interval among every dose as a minimum of 4 hin adults.[8] At recommended dosages, paracetamol is no longer associated with the increased incidence of nausea, vomiting, and respiratory depression observed with opioids. Furthermore, Paracetamol, due to its different action mechanisms, interferes neither with platelet nor kidney function. Its analgesic action isn't clean, even though its significant movement level has been hypothesized. [9] Because of the decrease in adverse events compared to NSAIDs, paracetamol is the desired choice for perioperative baseline analgesia. [10] Paracetamol enhances analgesic efficacy when introduced to NSAIDs as compared to NSAIDs alone.

Dexmedetomidine and α-2 adrenoreceptor agonists are approved for sedation to start with intubated and mechanically ventilated patients by means of a non-stop infusion that is most effective in less than 24 h in an intensive care setting. α-2 adrenoceptor agonists are being increasingly used in anesthesia and critical care as they are not the most effective decrease sympathetic tone and attenuate the strain responses to anesthesia and surgery; however, they also cause sedation, analgesia, and anxiolysis. The bolus of 1 μg/kg Dexmedetomidine initially results in a transient increase in the blood strain and a reflex fall in HR, mainly in younger, healthful patients.[11] Given the propensity of the drug to produce hypotension and/or bradycardia while it is administered to volunteers or patients, it becomes important to determine an infusion rate that would maximize the anesthetic and analgesic sparing impact even though minimizing the occurrence of unfavorable cardiovascular side effects requiring therapeutic intervention. Jung et al., in their comparative study, showed a significant gain of Dexmedetomidine at a dose of 1 μg/kg bolus followed by a 0.2-0.7 μg/kg/h infusion for 24 h. [12] It is a safe sedative opportunity to benzodiazepine/opioid aggregate in patients undergoing monitored anesthesia and take care of a large number of procedures due to its analgesic, "co-operative sedation," and shortage of respiration depression properties. [10] Numerous findings lead to the conclusion that the principal sedative and antinociceptive effects of dexmedetomidine are due to its stimulation of the α-2 adrenoceptors in the locus coeruleus.

In our study at a dose of 0.2-0.4 μg/kg, infusion had a significant hemodynamic stability over post-operative h, which corroborates with the study done by Jung et al.

in a prospective randomized double-blind study comparing the consequences of Dexmedetomidine and remifentanil on hemodynamic stability, sedation, and post-operative pain control in % with the Dexmedetomidine at a dose of 1 μg/kg IV over 10 min observed by 0.2-0.7 μg/kg/h non-stop IV infusion had a significant benefit in terms of post-operative hemodynamic stability. [13]

Talke et al.'s 1995 study showed that both HR and SBP reduced in response to the 1 h Dexmedetomidine infusion to the centered plasma concentration of 0.45 ng/ml, which appears to be advantageous perioperative hemodynamic control in patients undergoing vascular surgery. [14] In another study, Talke et al. administered Dexmedetomidine infusion for its ability to reduce pressure responses all through emergence from anesthesia after the major vascular operation and found that Dexmedetomidine attenuates the increase in HR and plasma noradrenaline concentration during emergence from anesthesia, which is helping the hemodynamic finding in our study [15]. Sarbari Swaika et al. study also strongly supporting our finding. Adjunctive use of both paracetamol and dexmedetomidine infusions reduced opioid use. However, paracetamol perioperatively provides adequate analgesia with less sedation, whereas dexmedetomidine provides analgesia and cooperative sedation. [16]

In our study, we found postoperative pain and sedation scores in group D remained significantly in an acceptable range. Our study is also supported by Jung, who found that the hemodynamic stability remained normal in post-operative duration and demonstrated good pain control with patient awareness. Cattabriga et al. administered 1 g of Paracetamol pre-medication and highlighted the reality that Paracetamol has a good analgesic motion by studying the 1st 30 h-deep breathe VAS scores, which were significantly lower. With this idea, in our study, we used 1 g paracetamol and determined that the VAS score was significantly lower in group P than in group D at the 8th, 16th, and 24th postoperative hours. [10] Salihoglu described that there may be superior pain control and a significant reduction of time to 1st rescue medication and additionally the total consumption of rescue medicinal drugs with fewer side effects. In addition, in our study, we observed that there was a significantly lower VAS score in group P than in group D, and there was a minimal requirement for rescue analgesic. [17]

Conclusion

According to the findings of the current research, IV paracetamol, when administered 30 min before surgery, was successful in reducing the post-operative VAS score and the analgesic demand and can be considered an effective and safe alternative for post-operative analgesia. In addition, it helps to attenuate the hemodynamic changes that are involved with having an upper limb procedure done. Hence, IV paracetamol can be used as an effective method for postoperative analgesia with the least possible side effects

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