

Comparative Study Of Intravenous Paracetamol And Dexmedetomidine On Perioperative Hemodynamics And Postoperative Pain Relief For Laparoscopic Cholecystectomy

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Abstract

Background: Unrelieved post-operative pain may bring about physical suffering as well as a couple of physiological and mental effects, which may adversely affect the peri-operative outcome and make contributions to growth during the period of stay in the health center. **Aim and objective:** The study aimed to assess the comparative evaluation of dexmedetomidine and paracetamol on preoperative and postoperative hemodynamics and analgesia for patients undergoing laparoscopic cholecystectomy. **Material and methods:** 50 consenting, American society of Anesthesiologist-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 IV 1g Paracetamol infusion over 10 min pre-operatively and 6 hourly thereafter and group D (n = 25) received IV Dexmedetomidine 1 µg/kg bolus over 10 min pre-operatively and 0.2-0.4 µg/kg/hr thereafter for 24 hrs. Preoperative hemodynamic variables, postoperative pain scores, and the needs for rescue analgesics have been recorded and compared. **Results:** Profiles of intra-operative hemodynamic changes had been similar in each group regarding heart rate (HR), diastolic blood pressure (DBP), and mean arterial pressure (MAP) except within the systolic blood pressure (SBP) where Dexmedetomidine significantly decreased it compared to Paracetamol (P = 0.014). Postoperatively 4th hrs and 24th hrs 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 hrs (P < 0.001). Sedation scores have been statistically better inside group D compared with group P at postoperative 4th, 8th, 16th, and 24th hrs (P < 0.006). **Conclusion:** Paracetamol is superior to Dexmedetomidine for analgesia in short surgical procedures and should form a part of multi-modal analgesia. The use of paracetamol provides multimodal analgesia with minimum sedation in short surgical procedures and dexmedetomidine provides analgesia and cooperative sedation

Keywords: Dexmedetomidine, Laparoscopic Cholecystectomy, Multi modal Analgesia, Paracetamol, Heart Rate

Introduction

Laparoscopic cholecystectomy is a minimally invasive surgical procedure for the removal of a diseased gallbladder. 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 preoperative setting is defined as pain that is present in the surgical patient due to per-current disease, surgical procedure, or an aggregate of those which is detrimental to post-operative final results. It will increase the sympathetic response of the body with a subsequent rise in oxygen consumption of the body, 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 illness, nausea, vomiting, and urinary retention.[3] As a result, adequate pain comfort receives translated to better preoperative outcomes, early recovery, and reduced periods 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, the strength of the opioid used, and worry approximately respiratory depression, vomiting, sedation, and dependence. [4,5]

Dexmedetomidine is an incredibly selective α_2 adrenoceptor agonist that provides sedation, analgesia, and sympatholytic 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 effect of Dexmedetomidine and Paracetamol on postoperative pain relief, adverse effects, and hemodynamics in patients undergoing laparoscopic surgical procedures under general anesthesia.

Materials and Methods

The study was conducted in NCMC and Hospital, Department of Anesthesiology and Critical Care. Ethical clearances were obtained from the Institutional Ethical Committee and written informed consent was taken, before carrying out the study, 50 female patients aged 20-60 years, ASA-ps-I scheduled for laparoscopic cholecystectomy were taken for those randomized study. Patients with body weight >80kg, cardiovascular disorder, broncho-pulmonary disorder, renal, neurologic, gastrointestinal, and hepatic dysfunction, records of allergy, long-time period use of medicinal drugs which includes beta-blocker and different anti-hypertensives, antipsychotics, analgesics, alcohol, sedative, TCA, etc., Patients with psychiatric illness, patient refusal had been excluded from this study patients have been randomly assigned to one of the following groups: group P (n = 25) obtained IV 1g Paracetamol infusion over 10min pre-operatively and 6 hourly thereafter and group D (n = 25) received IV Dexmedetomidine 1 $\mu\text{g}/\text{kg}$ bolus over 10 min per-operatively and 0.2-0.4 $\mu\text{g}/\text{kg}/\text{hr}$ thereafter for 24 hrs using a computer-generated random-number table. Within the pre-operative holding area, the patients found out and familiarized about 10 points 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 2mg, Ondansetron 4mg, and Glycopyrrolate 0.2 mg IV. Intra-operative monitoring devices included pulse-oximetry, noninvasive blood pressure, ECG, and capnography.

After acquiring bottom-line measurement of the heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure (DBP), and mean arterial pressure (MAP), infusion of Paracetamol 1g turned into given over 10 min for group P and infusion Dexmedetomidine turned into given 1 $\mu\text{g}/\text{kg}$ (diluting in normal saline making a 50 ml solution) over 10 min and 0.2-0.4 $\mu\text{g}/\text{kg}/\text{hr}$ thereafter for 24 hrs for group D.

Anesthetic induction turned into finished with pre-oxygenation with 100% O₂ injection of Fentanyl 1µg/kg IV, and injection of Propofol 2 mg/kg IV followed by using an injection of Succinylcholine 1.5 mg/kg IV to facilitate tracheal intubation. Anesthesia become maintained with nitrous oxide (N₂O) 50% and oxygen (O₂) 50% the mixture in combination with 0.5-1% Isoflurane, and injection Atracurium dose 0.5mg/kg IV. The end-tidal carbon dioxide was maintained inside 35-40 mmHg. The HR, SBP, DBP, and MAP were recorded intra-operatively at 5 min, 15 min, 30 min, 45 min, and 60 min starting from the completion of bolus dose to infusion of the study drug and HR, SBP, DBP and MAP were recorded post-operatively at 1st, 4th, 8th, 16th, and 24th hrs. MAP has been maintained within \pm 25% of the baseline values through various the stimulated Isoflurane concentration. Hypotension[7] (defined as MAP value <25% of the baseline value on 2 consecutive readings within 2-3 min) not responding to a reduction in inspired Isoflurane concentration and 200 ml fluid bolus was treated with injection Mephenteramine 5 mg. The infusion of study medication was discontinued if the hypotension persisted >2 min after those interventions. Upon return of the MAP \pm 25% of the baseline values, we take a look at remedy infusion became resumed at 50% of the initial infusion rate. In the presence of high blood pressure[6] (defined as MAP value >25% of the baseline values on two consecutive readings within 2-3 min) and or tachycardia[6] (described as HR value >25% of the baseline value on 2 consecutive readings within 2-3 min) inspired concentration of Isoflurane and study medication became increased. Bradycardia[6] (defined as HR <45/min) persisting for >2 min become treated with an injection of Atropine. Post-operative pain and sedation score were recorded at 1st, 4th, 8th, 16th, and 24th hrs.

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 \pm SD was 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 16. Wilks' Lambda test was used to analyze the parametric data. P-values considered significant were as follows: – P < 0.05– a Significant and P > 0.001 –a highly Significant.

Results and Observations

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

Table 1 shows there were no significant differences between the two groups concerning age, weight, and height (P > 0.05).

Table 1: Baseline demographic data

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

Intra-operative hemodynamic parameters were recorded at 5, 15, 30, 45, and 60 min after the completion of bolus dose infusion of study medication. Table 2 shows profiles of hemodynamic changes, which were similar in both groups in respect to HR, DBP, MAP except in SBP where Dexmedetomidine significantly reduced it in compare 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±6.86	90.72±6.90	125.08±8.95	124.84±7.49	84.48±5.12	84.44±4.68	91.96±5.85	94.72±6.14
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 hrs. No significant differences in the post-operative hemodynamic parameters were seen in MAP, as shown in Table 3. Mean HR ranges from (84.48±5.12) to (85.24±4.94) for the Group P whereas, it ranges between (82.44±5.78) to (85.76±3.90) in Group D. Post-operatively 4th h and 24th hrs changes in mean HR between two groups was statistically significant ($P < 0.05$).

Table 3: Post-Operative Hemodynamic Parameters

Time (hr)	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

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

Table 4: Post-Operative Analgesia and Sedation Score

Pain scale	Group P	Group D	Sedation 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

Note:VAS = Visual analog scale

Discussion

During laparoscopic surgical procedures changes 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 50 adult patients belonging to ASA-PS -I to evaluate the effect of IV Paracetamol and Dexmedetomidine infusion on peri-operative hemodynamic response and postoperative analgesia in 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 hrs in 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 peri-operative baseline analgesia.[10] Paracetamol enhances analgesic efficacy when introduced to NSAIDs as compared to NSAIDs alone. Dexmedetomidine and α -2 adrenoceptor agonist is approved for sedation of initially with intubated and mechanically ventilated patients using non-stop infusion for most effective in less than 24 hrs in an intensive care setting. α -2 adrenoceptor agonists are being increasingly used in anesthesia and critical care as they not only decrease sympathetic tone and attenuating the stress responses to anesthesia and surgery; however also cause sedation, analgesia, and anxiolysis. The bolus of 1 μ g/kg Dexmedetomidine initially results in a transient increase in the blood pressure and a reflex fall in HR, mainly in younger, healthful patients.[11] Given the propensity of the drug to produce hypotension and or bradycardia when it is administered to volunteers or patients, it become 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 μ g/kg bolus followed by 0.2-0.7 μ g/kg/hrs infusion for 24 hrs.[12] It is a safe sedative opportunity for benzodiazepine/opioid aggregate in patients undergoing monitored anesthesia takes care for 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 μ g/kg infusion had significant hemodynamic stability over post-operative hrs, which corroborates with the study done by Jung et al. in a prospective randomized double-blind study comparing the consequences of Dexmedetomidine and remifentanyl on hemodynamic stability, sedation, and submit-operative pain control in Paracetamol with the Dexmedetomidine at a dose of 1 μ g/kg IV over 10 min observed by 0.2-0.7 μ g/kg/hr non-stop IV infusions had a significant benefit in terms of postoperative hemodynamic stability.[13]

Talke et al. in 1995 of their study showed that both HR and SBP reduced in response to the 1 hrs Dexmedetomidine infusion to the centered plasma conc. of 0.45 ng/ml, which appears to be advantageous peri-operative 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 supports our finding Adjunctive use of both Paracetamol and Dexmedetomidine infusion reduced opioid use. However, Paracetamol peri-operatively provides adequate analgesia with less sedation whereas Dexmedetomidine provides analgesia and co-operative sedation.[16]

In our study, we found postoperative pain and sedation score 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 1g of Paracetamol pre-medication and highlighted the reality that Paracetamol has a good analgesic motion by using studying the 1st 30 hours- 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, post-operative 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 analgesia.[17]

Overall, Dexmedetomidine provided similar pain relief in our study but cautions use is advocated due to higher incidence of bradycardia and Hypotension

Conclusion:

Paracetamol is superior to Dexmedetomidine for analgesia in short surgical procedures and should form a part of multi-modal analgesia. The use of paracetamol provides multimodal analgesia with minimum sedation in short surgical procedures and dexmetetomidine provides analgesia and cooperative sedation

Strength and Limitations of the Present Study

There are a few drawbacks to the study. In the present study, only 20–60 years ages subjects participated in the research as well a reduced sample size. Hence, in the feature, we would like to include an increase in the number of participants to reach a concrete conclusion, Our results cannot be applied to major extensive surgeries in which effect of Dexmedetomidine need to be studied. Further use of intraoperative fentanyl may have also contributed better VAS score in immediate post operative period.

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