ORIGINAL ARTICLE

Can Intraperitoneal Tramadol decrease Pain in Patients undergoing Laparoscopic Cholecystectomy in the Postoperative Period? A Randomized controlled Trial

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ABSTRACT

Aim: To evaluate the analgesic effect of intraperitoneal tramadol in patients undergoing laparoscopic cholecystectomy.

Settings and design: Prospective, double blind, randomized study

Materials and methods: A total of 100 patients undergoing laparoscopic cholecystectomy were randomized into two groups I and II of 50 patients each: Group I received intraperitoneal tramadol 100 mg (diluted in 20 ml of distilled water) immediately after induction of pneumoperitoneum and just before removal of trocars. Similarly, Group II received 20 ml of intraperitoneal normal saline. All patients had a standard anesthetic. Rescue analgesia was with diclofenac sodium. Postoperatively, visual analog scale scores, 1 and 24 hours diclofenac consumption, postoperative hospital course, and adverse effects were recorded.

Statistical analysis used: Student's t test and Epi Info statistical software.

Results: Pain intensity is significantly less in group I than in group II in the first 4 hours, while requirement of analgesic postoperatively is significantly less in group I than in group II in the first 8 hours except at 30 and 60 minutes. Better control of blood pressure and respiratory rate was seen in group I in the first 4 hours. There was no significant difference between the two groups regarding postoperative hospital course and incidence of adverse effect.

Conclusion: Intraperitoneal tramadol provides superior postoperative analgesia in the early postoperative period after laparoscopic cholecystectomy compared with normal saline in patients undergoing laparoscopic cholecystectomy.

Keywords: Intraperitoneal tramadol, Laparoscopic cholecystectomy, Pain, Visual analog scale.

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INTRODUCTION

Laparoscopic cholecystectomy has become the treatment of choice for gallbladder stone disease[1] as it offers many advantages compared with the open cholecystectomy, the major advantage being shorter duration of hospital stay and early convalescence,[2] but some patients still experience considerable pain in the postoperative period. The site of most severe pain is in the right upper quadrant and port site during first 24 hours,[3] which can be due to traumatic traction on the nerves, release of inflammatory molecules, trauma to the abdominal wall, maintenance of high abdominal pressure, and irritation of the phrenic nerve.[4,5] While laparotomy results mainly in parietal pain, laparoscopy has a visceral component, a somatic component, and shoulder pain secondary to diaphragmatic irritation.[6] In laparoscopic cholecystectomy, visceral pain predominates in first 24 hours, whereas shoulder pain, less on the 1st day, increases and becomes significant on the following days.[7] The degree of pain after laparoscopic procedure is influenced by factors, such as the volume of residual gas, the type and temperature of gas used for pneumoperitoneum, and the pressure created by pneumoperitoneum.[8] The peritoneal origin of the pain suggests that analgesia delivered locally to the peritoneal cavity may be of benefit postoperatively.[9] While some studies show that intraperitoneal instillation of drugs for pain relief is more effective if used before creation of pneumoperitoneum,[10] others suggest it to be more effective at the end of the surgery.[11] So, considering these facts, the present study was undertaken to evaluate analgesic effect of intraperitoneal tramadol in patients undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS

After approval from the ethical committee, the study was conducted on 100 patients scheduled for elective laparoscopic cholecystectomy under a standardized general anesthesia technique after informed consent. Uncooperative and unwilling patients, those with history of anaphylaxis to opioids, drug abuse, narcotic use or previous abdominal surgery, American Society of Anesthesiologists grade III, IV, V, or any other significant

comorbidity, and those needing conversion to open cholecystectomy were excluded from the study.

After preoxygenation with 100% oxygen for 3 minutes, induction of anesthesia was achieved with thiopentone sodium (2.5%) 4 to 6 mg/kg intravenous (IV) slowly (till the abolition of eye lash reflex) along with injection of fentanyl 1.5 μg/kg IV. Intubation is with an appropriate sized endotracheal cuffed tube, that is, facilitated by neuromuscular blocker suxamethonium 1.5 mg/kg IV.

Anesthesia was maintained using controlled ventilation with isoflurane (0.5–1.5%) and nitrous oxide (N_2O) 66% + oxygen (02) 33% using Bain's circuit. Neuromuscular blockade was achieved with atracurium besylate. All patients were given metoclopramide 0.5 mg/kg IV injection intraoperatively at the end of procedure. Patients were randomly allocated in a double blind manner using computer-generated random numbers to one of the two groups comprising 50 patients each and use of coded syringe which is prepared by anesthesiologist not involved in study. Patients with group I labeled syringe (Study group) received intraperitoneal tramadol 100 mg (diluted in 20 ml of distilled water), while patients in group II coded syringe (control group) received 20 ml of intraperitoneal normal saline. In both groups, 10 ml of the study drug was injected into the hepatodiaphragmatic space, 5 ml into the area of the gallbladder, and 5 ml into the space between the liver and the kidney under direct vision by the surgeon immediately after induction of pneumoperitoneum and just before removal of trocars; so in both groups a total of 40 ml drug was instilled. Postoperatively patients were extubated and shifted to recovery room where observations were made, recorded, and analyzed, such as postoperative pain scores at 0, 15, 30, 60 minutes, 4, 8, 12, 24 hours, cumulative 1 and 24-hour analgesic consumption, postoperative hospital course (monitoring of heart rate (HR), blood pressure (BP), respiratory rate (RR), arterial oxygen saturation (SpO_2), temperature at 0, 4, 8, 16, and 24 hours), and incidence of adverse effect (nausea, vomiting, shoulder pain, itching, and shivering) at 0, 4, 8, 16, and 24 hours.

Intensity of pain was measured by visual analog scale (VAS).[12] Patients showing a VAS ≥ 3 or patients who request for analgesia were administered a supplemental dose of an analgesic (diclofenac sodium; 3 ml, 75 mg). Results were reported as mean ± standard deviation. The sample size has been calculated based on a study[13] where mean pain score of the normal saline (3.9 ± 2.7) has been consulted. The sample size per group has been calculated to be 50 with 5% level of significance. The 20% reduction in pain at 0 minute has been assumed to be significant reduction. This sample size will maintain at least 89% power of the study. Data were collected and analyzed using Student's t test. Epi Info statistical software was used for all analyses.

RESULTS

For this study, 100 patients were recruited. There were no significant differences between two groups according to age, sex, and body weight (Table 1).

The mean intensity of postoperative pain was significantly lower in group I than in group II ($p < 0.05$) at 0, 15, 30 minutes, 1, and 4 hours after the operation. There was no statistical difference between the two groups thereafter (Graph 1).

The supplementary mean dose of rescue analgesic (diclofenac sodium, 3 ml, 75 mg) in the 1 and 24 hours was significantly higher in group II (76.47 ± 10.39 and 213 ± 41.11 mg) as compared with group I (0 and 84 ± 59.92 mg) respectively (Graph 2).

There is no significant difference between mean HR, SpO_2, and temperature between the two groups at any point of time during our study. Mean systolic BP (Table 2) and RR (Table 3) were lower in group I than in group II at all time intervals but the difference is significant statistically at 0 and 4 hours attributed to better pain control in the early postoperative period.

There was no significant difference in the incidence of shoulder pain, nausea, vomiting sensation, itching, and shivering in the two groups (Graph 3). No patient experienced muscle rigidity.

Table 1: Data from 100 patients who received intraperitoneal saline (group II), tramadol (group I), during laparoscopic surgery

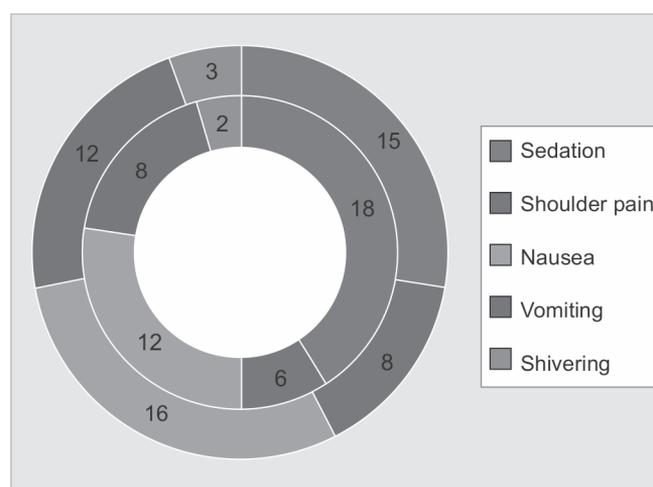| Parameter	Group I	Group II
Age (years)	39.20 ± 11.53	42.04 ± 13.14
Sex ratio (F:M)	34:16	34:16
Body weight (kg)	68.98 ± 11.96	69.72 ± 11.39

Values are mean ± SD. *$p < 0.05$ was considered statistically significant; SD: Standard deviation
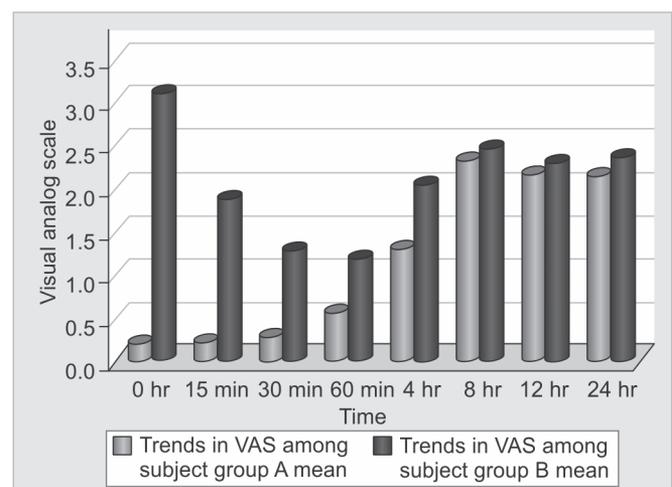
Graph 1: Trends in visual analog scale among subjects
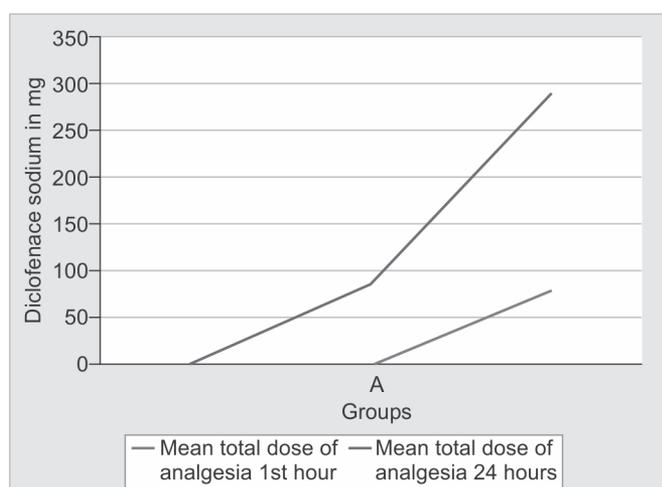
Graph 2: Cumulative requirement of analgesic

Graph 3: Trend in incidence of adverse effect

Table 2: Trends in systolic blood pressure

Time (hours)	Group I		Group II		
	Mean	SD	Mean	SD	p-value
0	131.44	16.54	146.08	18.02	0.0001
4	125.00	11.86	132.16	11.84	0.003
8	124.44	10.93	124.52	10.03	0.970
16	121.48	9.96	125.24	11.71	0.087
24	122.44	8.83	124.28	11.49	0.371

SD: Standard deviation

Table 3: Trends in respiratory rate

Time (hours)	Group I		Group II		
	Mean	SD	Mean	SD	p-value
0	21.56	1.42	22.88	1.35	0.0001
4	20.88	1.15	21.84	1.06	0.0001
8	21.12	1.67	21.64	1.05	0.065
16	20.48	1.49	20.56	1.28	0.774
24	20.24	1.70	20.32	1.58	0.808

SD: Standard deviation

DISCUSSION

In our study, we showed that intraperitoneal administration of tramadol resulted in much lower postoperative pain scores, cumulative postoperative analgesic consumption without significant increase in incidence of adverse effect, or adverse hemodynamic changes in patients undergoing laparoscopic cholecystectomy.

In our study, the mean VAS scores in group I were significantly lower in the first 4 hours postoperatively than in group II due to effect of tramadol given intraperitoneally. The maximum mean VAS score was observed at the 8th hour (2.32 ± 0.96 cm). Administration of rescue analgesic thereafter leads to downward trend in subsequent pain scores. The results are consistent with the findings of Golubovic et al[14] who showed this significant reduction for the first 6 hours.

Our study also showed significant reductions in cumulative postoperative analgesic requirement in group I than in group II in 0 and 24 hours, which is consistent with the study done by Golubovic et al[14] and Golubovic et al[15] who demonstrated that intraperitoneal administration of tramadol had valuable implication in reducing VAS score/pain in patients undergoing laparoscopic cholecystectomy.

Peripheral antinocicepive effect of opioids occurs due to interaction of opioids with opioid receptor which are located on peripheral intact perineurium. While hydrophilic opioid molecules (i.e., morphine) does not diffuse across perineural barrier, lipophilic opioids, such as tramadol, buprenorphine can diffuse freely across the intact perineural barrier resulting in better analgesia on intraperitoneal administration. Secondly, duration of action of parenterally administered tramadol is 6 to 8 hours and this explains low VAS scores and less need for rescue analgesic in the early postoperative period.[16]

Mean systolic BP and RR were lower in group I than in group II at all time intervals, but the difference is significant statistically at 0 and 4 hours attributed to better pain control in the early postoperative period. As there were no differences in the incidence of adverse effect, tramadol can be used safely at doses as in our study intraperitoneally, which can be correlated with the study done by Akinci et al.[13]

CONCLUSION

Intraperitoneal tramadol significantly reduces pain scores in early postoperative period (4 hours in our study) and requirement of rescue analgesic for first 8 hours without significantly increasing incidence of adverse effect or hemodynamic complications. So, it can be safely introduced for control of postoperative pain in patients undergoing laparoscopic cholecystectomy.

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