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ORIGINAL ARTICLE

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

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ABSTRACT

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

Settings and design: Prospective, double blind, randomized study.

Materials and methods: Hundred patients undergoing laparoscopic cholecystectomy were randomized into two groups, I and II, of 50 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, 1 and 24 hours diclofenac consumption, postoperative hospital course, and adverse effects were recorded.

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

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

Conclusion: Intraperitoneally, 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 score.

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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 being shorter duration of hospital stay and early convalescence,[2] but some patients still experience considerable pain in 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, 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 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 a history of anaphylaxis to opioids, drug abuse, narcotic use, or previous

abdominal surgery; American Society for 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 fentanyl 1.5 µg/kg IV. Intubation with an appropriate-sized endotracheal cuffed tube, i.e., 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 (O_2) 33% using Bain's circuit. Neuromuscular blockade achieved with atracurium besylate. All patients were given injection metoclopramide 0.5 mg/kg IV intraoperatively at the end of procedure. Patients were randomly allocated in 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 with 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 was injected 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, patient was extubated and shifted to recovery room where observations were made, recorded, and analyzed, such as postoperative pain scores at 0, 15, 30, and 60 minutes; 4, 8, 12, 24, and 24 hours; cumulative 1 and 24 hours analgesic consumption, postoperative hospital course [monitoring of heart rate (HR), blood pressure (BP), respiratory rate (RR), SPO_2, temperature at 0, 4, 8, 16, and 24 hours, and incidence of adverse effect (nausea, vomiting, shoulder pain, itching, 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 ± SD. The sample size has been calculated based on the 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 was collected and analyzed using Student's t-test. Epi Info statistical software was used for all analyses.

RESULTS

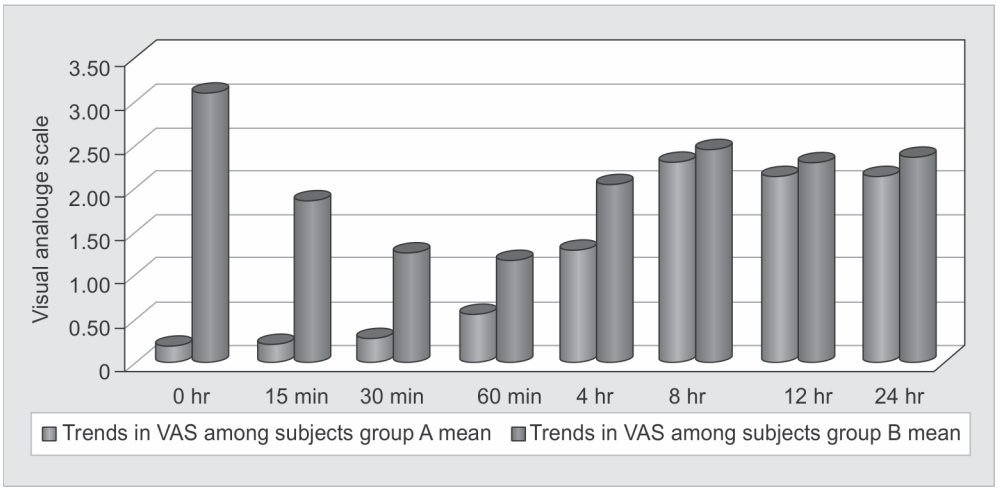
For this study, 100 patients were recruited. There were no significant differences between two groups according to age, sex, and body weight (Table 1).

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

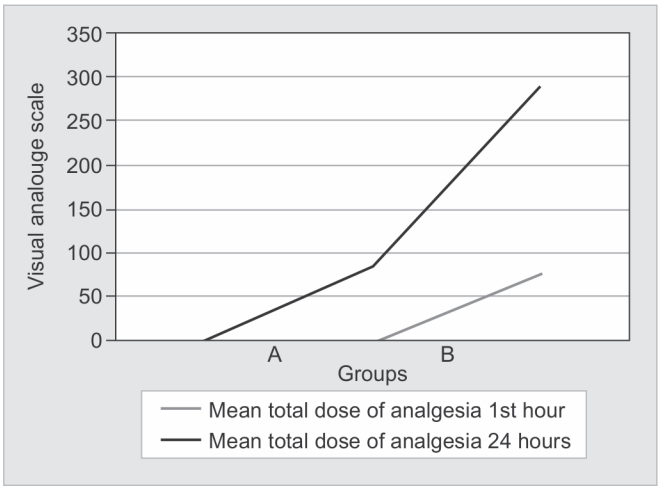
Table 1: Data from 100 patients who received IP saline (group II), tramadol (group I), during laparoscopic surgery

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

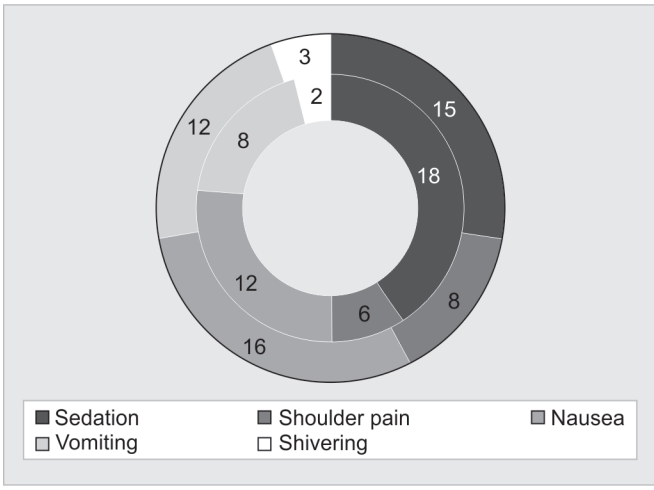
Values are mean ± SD. *p < 0.05 was considered statistically significant



Graph 1: Trends in VAS among subjects



Graph 2: Cumulative requirement of analgesic



Graph 3: Trends in incidence of adverse effects

Table 2: Trends in systolic BP

Time	Group I		Group II		
(hours)	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 RR

Time	Group I		Group II		
(hours)	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

The supplementary mean dose of rescue analgesic (diclofenac sodium, 3 mL, 75 mg) in first hour and 24 hours were significantly higher in group II, being 76.47 ± 10.39 mg and 213 ± 41.11 mg as compared to group I of 0 and 84 ± 59.92 mg respectively (Graph 2).

There is no significant difference between mean HR, SPO_2, 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 early postoperative period.

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

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 low in first 4 hours postoperatively than in group II due to the effect of Tramadol given intraperitoneally. The maximum mean VAS score was observed at 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 findings of Golubovic et al[14] who showed this significant reduction for first 6 hours.

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

Peripheral antinociceptive effect of opioids occurs due to interaction of opioids with opioid receptor located on peripheral intact perineurium that prevent entry of hydrophilic opioid molecule, such as morphine while lipophilic opioids, such as tramadol, buprenorphine can diffuse across the intact perineural barrier, which results in better analgesia on intraperitoneal administration. Secondly, as duration of action of parenterally administered tramadol is 6 to 8 hours, so this explains low VAS scores and less need for rescue analgesic in 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 early postoperative period. As there was no differences in the incidence of adverse effect, so

tramadol can be used safely at doses as in our study intraperitoneally, which can be correlated with 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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