International Journal of Clinical Trials
Katoch ML et al. Int J Clin Trials. 2020 Feb;7(1):28-31
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: http://dx.doi.org/10.18203/2349-3259.ijct20200203

Original Research Article

Comparative evaluation of post-operative analgesic effects of intraperitoneal levobupivacaine plus fentanyl and levobupivacaine plus tramadol in patients undergoing laparoscopic cholecystectomy

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Received: 20 October 2019
Revised: 25 November 2019
Accepted: 28 November 2019

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ABSTRACT

Background: Laparoscopic cholecystectomy is commonly performed as a day care procedure for treating symptomatic gallstones. Suitability of patient discharge from the inpatient facility depends upon adequacy of postoperative pain control. Among the various modalities for pain relief, intraperitoneal local anaesthetic has become an important approach. In this study we aimed at comparing the post-operative analgesic effects of intraperitoneal levobupivacaine plus fentanyl and levobupivacaine plus tramadol in patients after laparoscopic cholecystectomy. The objective of this study was to determine which adjuvant drug was superior to the other in terms of prolonging the analgesic effects of levobupivacaine in post-operative period of laparoscopic cholecystectomy.
Methods: A total of 90 patients undergoing laparoscopic cholecystectomy were selected. They were divided into three groups: Group L- received 50 ml of 0.25% levobupivacaine; Group LT- received 0.25% of levobupivacaine and tramadol 2 ml (50 ml total); group LF- received 0.25% levobupivacaine plus fentanyl 2 ml (50 ml total). Postoperative pain was assessed using visual analogue scale.
Results: The combination of levobupivacaine fentanyl and levobupivacaine tramadol was superior to plain levobupivacaine for reducing postoperative pain. No significant difference was found between Group LT and LF with respect to first analgesic and total analgesic requirement. However significant difference was found between LF and L; and between LT and L.
Conclusions: Levobupivacaine should be used along with adjuncts either tramadol or fentanyl.

Keywords: Levobupivacaine, Fentanyl, Tramadol, Laparoscopic cholecystectomy

INTRODUCTION

Pain has been defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Unrelieved postoperative pain may result in clinical and psychological changes that increase morbidity and decrease the quality of life.[1]

Besides the distress caused, severe postoperative pain increases the work of breathing as it limits full chest expansion and impairs patient's ability to cough effectively.[2] Many interventions have been tried to reduce such severe pain; including epidural analgesia, patient controlled analgesia, transversus abdominis plane block and local wound infiltration.

Laparoscopic cholecystectomy is commonly performed procedure for treating symptomatic gallstones. The benefits of laparoscopic surgery include reduced haemmorhage, smaller and more cosmetic incision and shorter hospital stay. Pain after laparoscopy results from

the stretching of intra- abdominal cavity, peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity.[3]

Intraperitoneal local anaesthetic has become an important modality for pain control in laparoscopic surgeries. The rationale of choosing intraperitoneal route is to block the visceral afferent signals and potentially modifying visceral nociceptor which provides analgesia.[4] Systemic absorption of local anaesthetic from the peritoneal cavity may also play in reducing nociceptor.[5] Combination of local anaesthetic with opioids having a synergistic effect and it reduces the total doses of analgesic requirement in the post-operative period.[6]

In our study we observed the effect of combining levobupivacaine and opioids to significantly reduce pain outcomes in patients undergoing laparoscopic cholecystectomy.

METHODS

This study was carried out in the Department of Anaesthesia and Intensive care Government Medical College, Jammu between December 2015 and September 2016. Approval was obtained from the hospital ethical committee.

Inclusion criteria

Patients in age group 18-60 years, American Society of Anesthesiologists (ASA) 1 and 2 patients scheduled for laparoscopic cholecystectomy.

Exclusion criteria

Patients with BMI <18 and >35 kg/m^2, acute cholecystitis, local anaesthetic allergy and chronic pain syndrome.

All the 90 patients were equally divided into 3 groups: group L- received 50 ml of 0.25% of levobupivacaine; group LT received 0.25% of levobupivacaine 48 ml and tramadol 2 ml (total 50 ml); group LF received 0.25% levobupivacaine 48 ml and fentanyl 2 ml (total 50 ml).

Pre anaesthetic checkup was done one day prior to surgery which included detailed history and physical examination. Patients were kept fasting overnight and received pantoprazole 40 mg and alprazolam 0.5 mg night prior to surgery. On the morning of surgery IV line was secured and patients were premedicated with iv glycopyrrolate .005 mg/kg, ondansetron 0.1 mg/kg and diclofenac 75 mg in 30 minutes prior to surgery.

In the operation theatre, routine monitors such as electrocardiography (ECG), non-invasive blood pressure (NIBP), peripheral capillary oxygen saturation (SpO2) were attached. Patients were preoxygenated for 3 min and anaesthesia was induced with propofol 2-2.5 mg/kg iv and intubated after 3 min of giving vecuronium 0.1 mg/kg. Anaesthesia was maintained with 33% O_2, 66% N_2O and 0.5% halothane. End-tidal CO_2 ($EtCO_2$) was maintained at 35-40 mmHg. Intraabdominal pressure was maintained at 12 mmHg.

After removal of gall bladder, intraperitoneal instillation of total volume 50 ml of prepared drug according to the study group was given into hepatodiaphragmatic space near and above the hepatoduodenal ligament and in the gall bladder fossa under direct vision and patients were kept in trendelenburg position till end of procedure (10-15 minutes). After skin closure local infiltration of each port site with 3 ml of levobupivacaine 0.25% was done.

Reversal of neuromuscular block was done with neostigmine and glycopyrrolate. Patients were given 100% O_2 during emergence. Post-operative pain was assessed using visual analogue score. If VAS score was more than 3. patients were prescribed diclofenac sodium 75 mg im.

Parameters assessed were (1) time to first request of analgesia, (2) total number of analgesic doses of opoid or nonsteroidal anti-inflammatory drug (NSAID) in 24 hours, (3) incidence of postoperative nausea and vomiting, (4) incidence of postoperative shoulder and arm pain for 24 hours, (5) Sedation was evaluated using Ramsay sedation score.

Data so collected will be analyzed, compared and subjected to statistical analysis using student t test and chi square test.

RESULTS

Among all 90 patients who were enrolled in the study, no difference was observed between the two groups with respect to gender, age, height and weight (Table 1).

Table 1: Demographics.

Variable	Group L	Group LF	Group LT	P value
Age (yrs)	46.33	45.30	46.50	0.724
Weight	75.83	72.81	74.33	0.657
BMI	24.84	23.75	23.61	0.634
Sex (F/M)	16/14	14/16	17/13	0.352

The three groups remained statistically comparable with respect to intraoperative heart rate, NIBP and SPO_2. Post operatively heart rates and NIBP remained comparable at 6, 8, 10, 12, 18 and 24 hours. However, there was a significant difference between the three groups at 0 min, 30 min, 1 hr, 2 hr and 4 hr postoperatively with LF showing lowest heart rate and NIBP (Table 2). 6% patients in group LF developed hypotension whereas no patient in group L and LT experienced hypotension.

The VAS scores were significantly less in groups LT and LF as compared to Group L. However, the VAS scores of LT and LF were statistically comparable. The time to first analgesic requirement was significantly longer in Group LT and LF than Group L. However, the difference between Group LT and LF was not significant (Table 3).

Table 2: Heart rate comparison.

Time	Group L	Group LF	Group LT	P value
0 min	84.63	80.90	86.83	0.01
30 min	67.07	60	73.90	0.01
1 hour	67.57	66.83	76.27	0.02
2 hour	69.03	66.20	74.03	0.01
4 hour	77.80	75	79.50	0.03
8 hour	77.63	75.83	78	0.29
10 hour	76.97	78.20	76.70	0.52
12 hour	77.83	77	78.43	0.64

Table 3: VAS scores.

Time	Group L	Group LF	Group LT	P value
0 min	2.87	2.60	2.57	0.023
30 min	3.17	2.43	2.37	0.011
1 hour	3.63	2.40	2.37	0.001
2 hour	3.37	2.37	2.30	0.001
4 hour	2.43	2.43	2.40	0.983
8 hour	2.30	2.43	3.77	0.001
10 hour	2.43	3.93	3.90	0.001
12 hour	2.13	3.63	1.90	0.001

Ramsay sedation score was significantly highest in group LF upto 30 min postoperatively, after which the sedation scores became comparable for all the groups.

No patient in any group developed respiratory depression. Incidence of nausea was 1% in all three groups. The incidence of pruritis was 14% in group LF and 0% in group L and LT.

Incidence of shoulder pain at 10 and 12 hours was 16.67% in group LF, 50% in group LT and 10% in Group L.

DISCUSSION

Post-operative pain after laparoscopic cholecystectomy consists of three components- visceral, parietal and referred shoulder pain. Previous studies suggest that predominant cause of pain is parietal, but many other studies showed that major portion of early convalescent period is occupied by visceral pain. This is because as compared to limited trauma to abdominal wall, the surgical manipulation and tissue destruction in visceral organs is much more.[7]

In laparoscopic surgeries because of gas insufflations and raised intraperitoneal pressure, there is peritoneal inflammation and neuronal rupture with a linear relationship between abdominal compliance and resultant severity of post-operative pain.[8] Hence, we chose intraperitoneal route because it blocks the visceral afferent signals and modifies visceral nociception. The local anaesthetic agents provide antinociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins which cause pain.[9] Intraperitoneal instillations of 0.5% levobupivacaine provides effective analgesia; we added fentanyl, tramadol to levobupivacaine to compare antinociceptive efficacy.

Preoperative and intraoperative haemodynamics were comparable in all three groups. Post-operative heart rates and NIBP were lowest in Group LF. This is probably due to more dense and prolonged analgesia and systemic absorption of fentanyl from peritoneal cavity. Fentanyl being an opioid show fall in heart rate and heart rate. Our results are similar to Gupta et al, Singh et al and Goldstein et al.[10-12]

VAS scores were significantly higher in Group L than in Group LT and LF. The VAS scores in Group LT and LF were comparable though. Our results are similar to Singh et al which showed that intraperitoneal instillation of fentanyl along with bupivacaine significantly reduces immediate post-operative pain.[11] VAS scores were significantly lower in the early post-operative period in Group LT and LF than in Group L. Similar results were seen by Memis et al.[13]

However, our results were in contrast to Rademaker et al, Ali et al.[14,15] This could be explained by lesser dose, instillation of drug in supine position which prevented its flow over coeliac plaexus and phrenic nerve endings.[16]

The time to first analgesic requirement was shortest in Group L and longest in Group LF. The total analgesic dose consumption was highest in Group L and lowest in Group LF. This shows levobupivacaine along with fentanyl reduces not only intensity of pain but also total dose of analgesia consumed. Similar findings were seen by Gupta et al and Memis et al.[10,13] On the other hand, contrary results were seen by Rademaker and Ali et al.[14,15]

The sedation scores were monitored post operatively in all three groups using Ramsay sedation score. Group L and LT showed low sedation scores, however Group LF showed highest sedation score for first 30 min post operatively. The high sedation score is due to fentanyl.

The incidence of pruritis was highest in group LF, which was probably due to absorption of fentanyl. Incidence of emesis was similar in all three groups. Incidence of hypotension was highest in patients receiving levobupivacaine with fentanyl than in those who received

levobupivacaine alone or levobupivacaine plus tramadol. Similar results were seen by Gupta et al, Goldstein et al and Kim et al.[17]

Incidence of bradycardia was highest in patients receiving fentanyl. Increased incidence of bradycardia was due to fentanyl absorption, which is known to cause bradycardia as a side effect. Shoulder pain was not observed in group LT in the first 6 and in group LF in first 8 hours post operatively and the patients observed shoulder pain after 30 min in group L post operatively. The reason could be the blocking of nociceptive inputs generated by inflamed diaphragm peritoneum caused by instillation of levobupivacaine.

CONCLUSION

The combination of intraperitoneal levobupivacaine and fentanyl; levobupivacaine and tramadol were superior to plain levobupivacaine for reducing postoperative pain in patients who underwent laparoscopic cholecystectomy. The total analgesic requirement was reduced and time to rescue analgesia was prolonged by the addition of fentanyl and tramadol.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Katoch ML, Kour L. Comparative evaluation of post-operative analgesic effects of intraperitoneal levobupivacaine plus fentanyl and levobupivacaine plus tramadol in patients undergoing laparoscopic cholecystectomy. Int J Clin Trials 2020;7(1):28-31.