



COMPARISON BETWEEN INTRAPERITONEAL INSTILLATION OF BUPIVACAINE HCL AND BUPIVACAINE HCL PLUS TRAMADOL FOR PAIN RELIEF AFTER LAPAROSCOPIC SURGERIES.

Anaesthesiology

Chavda Dhaval K	Resident Doctor, Department of Anaesthesiology, Gujarat Cancer And Research Institute, Ahmedabad, Gujarat, India.
Solanki Rekha N*	Assistant Professor, Department of Anaesthesiology, Gujarat Cancer And Research Institute, Ahmedabad, Gujarat, India. *Corresponding Author
Fefar Suman A	Resident Doctor, Department of Anaesthesiology, Gujarat Cancer And Research Institute, Ahmedabad, Gujarat, India.
Thakkar Jayshree M	Professor And Head of Department of Anaesthesiology, Gujarat Cancer And Research Institute, Ahmedabad, Gujarat, India.

ABSTRACT

BACKGROUND AND AIMS: Acute postoperative pain is associated with increased morbidity, prolonged hospital stay. Our study was designed to evaluate the analgesic efficacy of intraperitoneal instillation of Bupivacaine HCL and Bupivacaine HCL plus Tramadol for postoperative analgesia in laparoscopic surgeries. **METHODS:** 60 patients were randomised into 2 groups. Intraperitoneal instillation of Bupivacaine HCL in group B and Bupivacaine HCL plus Tramadol in group BT was done. The primary outcome variable was to compare pain score. Time to first rescue analgesia and total analgesic doses were recorded and patients were monitored for VAS score, hemodynamic parameters, and adverse effects. Student's t test and chi square tests were used. $P < 0.05$ was considered significant. **RESULTS:** In postoperative period of 24hrs VAS score (at rest and on movement) was significantly lower in group BT compared to group B. Time to first rescue analgesia was prolonged and total dose of rescue analgesic was less in group BT with better hemodynamic stability. **CONCLUSION:** Intra-peritoneal instillation of Tramadol as adjuvant to Bupivacaine HCL in laparoscopic surgeries significantly reduces the pain scores and the analgesic requirement in post-operative period as compared to Bupivacaine HCL alone with safety profile.

KEYWORDS

Intraperitoneal instillation, Laparoscopic surgeries, Postoperative pain.

INTRODUCTION

Acute postoperative pain is associated with increased morbidity, functional and quality of life impairment, delayed recovery time, prolonged hospital stay and results in harmful effects on various organ systems. (1)

The main aim of effective pain management is to provide adequate pain relief at the appropriate time, even post-operatively.

Postoperative discomfort after laparoscopic surgeries is more of visceral origin than somatic. (2)

Several clinical studies have reported intraperitoneal instillation with local anaesthetic drugs (Lignocaine, Bupivacaine, Levobupivacaine, Tramadol and Ropivacaine) alone or in combination as safe and effective method for postoperative analgesia with minimal systemic side effects in various laparoscopic surgeries. (3,4,5,6).

Thus, the study was designed to evaluate the analgesic efficacy of intraperitoneal instillation of Bupivacaine alone and Bupivacaine plus Tramadol for postoperative analgesia in patients undergoing laparoscopic surgeries.

MATERIALS AND METHODOLOGY-

After obtaining institutional ethical committee approval and written informed consent, this prospective, double blind randomized study was conducted on 60 patients of either sex belonging to ASA (American Society of Anaesthesiologist) grade I and II, age ranging from 18 to 65 yrs, scheduled for laparoscopic surgeries like Diagnostic laparoscopy, lap. cholecystectomy, hemicolectomy, pancreatectomy etc. in our institute over a period of 4 months.

Patients dependant on narcotics, history of drug allergy, having hemorrhagic diathesis and coagulopathy or neurological diseases were excluded from study.

Prior to the procedure pre-anesthetic evaluation was done including detailed history, thorough clinical examination and routine investigation. All patients were explained about the procedure. Computerized generation of random number was done. The patients were allocated by closed envelope method into two groups.

Group B received intraperitoneal instillation of 0.125% Bupivacaine (30ml)

Group BT received intraperitoneal instillation of 2mg/kg Tramadol plus 0.125% Bupivacaine (total 30ml).

Preoperatively all patients were familiarized with a 11 points visual analogue scale (VAS) where score 0 is no pain and score 10 is worst possible pain. (7)

Patients were nil per orally for 8 hours. Upon arrival in the operating room, standard monitors were attached and baseline vitals were recorded. 18 G intravenous cannula was inserted in a peripheral vein and Ringer lactate solution was started and premedicated with Inj. Ondansetron 0.1mg/kg i.v., Inj. Glycopyrrolate (0.004mg/kg) i.v. and Inj. Fentanyl citrate (2mcg/kg) i.v.

After 3 mins of preoxygenation, anesthesia was induced with Inj. Thiopentone sodium (5mg/kg) i.v and Inj. Succinylcholine bromide (2mg/kg) i.v. to facilitate endotracheal intubation with proper sized cuffed portex endotracheal tube. Nasogastric tube of proper size was inserted and foley's catheterization done.

Intraoperative anesthesia was maintained with 50% N₂O:50% O₂ plus Sevoflurane. Intermittent boluses Atracurium of 0.1 mg/kg were used to achieve muscle relaxation. Minute ventilation was adjusted to maintain ETCO₂ between 30 and 35 mm Hg.

Patients were randomized into B and BT groups which included Bupivacaine alone and combination of Bupivacaine and Tramadol respectively.

The study drugs were prepared by an anesthesiologist not involved in the study. The surgeons were unaware of the study group until the end of the study.

Intraoperatively Inj. Fentanyl 0.25mcg/kg IV bolus given to all patients to maintain vitals within range of 20% of baseline.

Inj. Paracetamol 15mg/kg IV given just before peritoneal exsufflation.

At the end of the surgery after thorough intraperitoneal suction and before removal of trocars, the study solution was given through intra peritoneal route into the right sub-diaphragmatic and iliac regions of the abdomen. The time of instillation was noted. In patients when surgical drain was needed, it was clamped for 30 mins after drug instillation.

The neuromuscular blockade was antagonized with Neostigmine 0.05mg/kg i.v. and Glycopyrrolate 0.01mg per kg i.v. and trachea was extubated. Patient was shifted to post anaesthesia care unit. No other analgesics were used other than the study drug until the patient complained of pain.

All patients stayed in post anesthesia care unit (PACU) for 24 hours after the end of surgery. The primary outcome variable was to compare pain score. The secondary outcome included time to first request of analgesia in the post-operative period, total dose of analgesic used, hemodynamics and adverse effects during 24hrs post operatively.

The intensity of postoperative pain was recorded for all the patients using VAS score at rest and on movement at 0,1,2,4,6,8,12 & 24 hours after the surgery.

Patients who reported VAS more than 4 were given injection Diclofenac 75mg intravenously as rescue analgesic. Time to the first request of analgesia (considering time immediately after extubation as time 0), total number of doses of analgesic over 24 h post-operatively were noted.

Patients were also observed for postoperative nausea and vomiting. Those who suffered were given Ondansetron 0.1mg/kg iv.

STATISTICAL ANALYSIS AND SAMPLE SIZE:

We calculated sample size on base of a pilot study. We required 25 patients in each group for significance level of 0.05 and power of 0.8. To compensate for drop outs 30 patients were included in each group.

Statistical analysis was carried out using student's t test and chi square tests. All tests were evaluated for 95% confidence limit. P value <0.05 was considered as significant.

Table. 1 Demographic Data in Both Groups

	GROUP B (n=30)	GROUP BT (n=30)	P VALUE
Age(years)	50.93 ± 15.59	49.33 ± 13.01	0.66
Gender (M/F)	17/13	13/17	0.66
Height(cm)	158.16 ± 6.46	160.83 ± 5.47	0.089
Weight(kg)	58.03 ± 8.1	60.03 ± 9.84	0.39
ASA(I/II)	18/12	20/10	0.78
Duration of surgery (hours)	2.75 ± 2.01	2.98 ± 1.73	0.63
Type of surgery			
Diagnostic laparoscopy	6(20%)	5 (16.6%)	0.73
Laparoscopic cholecystectomy	12 (40%)	13 (43.3%)	0.79
Laparoscopic hemicolectomy	7 (23.3%)	6 (20%)	0.75
Others	5 (16.6%)	6 (20%)	0.73

Data expressed as Mean± SD

Table 1 shows that both the groups were comparable with respect to age, gender, height, weight, ASA grade and mean duration of surgery with no statistical difference between them (P>0.05).

Figure 1: Comparison of VAS score (at rest and on movement) at different time interval.

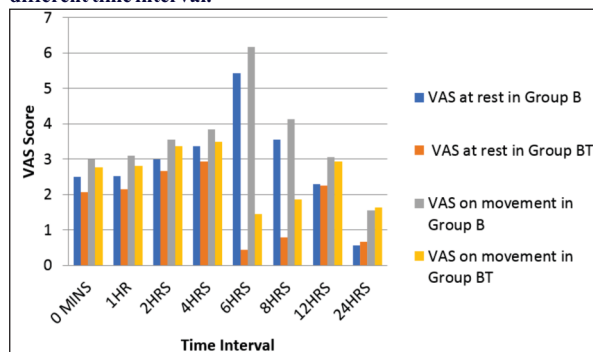


Figure 1 shows during 0, 1hr, 2 hrs, and 4hrs there was no significant difference in VAS score (at rest and on movement) between both the groups. VAS was significantly higher at 6th and 8th hrs in group B than

group BT (P<0.05). At 12th hrs and 24th hrs there were no significant differences in VAS scores.

Table 2. Comparison of requirement of rescue analgesia:

Parameters	Group B	Group BT	P value
Time of first rescue analgesia	4.88 ± 1.97 hr	11 ± 5.72 hr	<0.0001
Total no. of dose of Diclofenac/patient	1.33 ± 0.711	0.51 ± 0.50	<0.0001
Total patients required Diclofenac	27(90%)	16(53.3%)	0.0016

Data expressed as Mean± SD

Table 2 shows that in group B patients required rescue analgesic earlier compared to group BT. It is suggestive of prolonged duration of post op analgesia in group BT. There was increased demand of rescue analgesia in Group B compared to Group BT. Total dose of Diclofenac (75mg) consumed and total number of patients required Diclofenac was higher in Group B than in Group BT.

Incidence of side effects like nausea and vomiting was 40% (12pts) in group B and 20% (6 pts) in group BT which were statistically not significant. There was no report of other adverse effects like dyspepsia, allergic reactions and diarrhea.

Statistically nonsignificant higher incidence of nausea and vomiting in group B was due to greater requirement of Inj. Diclofenac sodium and those patients were treated with Inj. Ondansetron 1mg/kg iv.

DISCUSSION-

Pain after laparoscopic surgeries remains a major problem in postoperative period.

Postoperative discomfort after laparoscopic surgeries is more of visceral origin than somatic and is due to stretching and inflammation of peritoneum, irritation of the phrenic nerve, residual carbon dioxide in peritoneal cavity. (2)

Postoperative pain is multi factorial in origin, and therefore multimodal therapy may be needed to optimize pain relief.

Local anesthetic techniques are part of the multimodal approach to postoperative pain management.

We compared the effects of intraperitoneal instillation of Bupivacaine alone and Bupivacaine plus Tramadol after laparoscopic surgeries.

In our study we observed that VAS (at rest & on movement) at 6th hour and 8th hour postoperatively was less in group BT as compared to group B which is statistically significant. While at 1st, 2nd, 4th, 12th and 24th hours difference in VAS score was not significant. Whereas the time to first demand of rescue analgesia was prolonged in group BT compared to group B and analgesic requirement in group-BT were significantly lower than those in group-B during the first 24 hours after surgery.

In a study done by Memis et al evaluated the effects of intraperitoneal instillation of Bupivacaine and the combinations of Bupivacaine plus Tramadol and Bupivacaine plus Clonidine for postoperative pain control in total abdominal hysterectomy. They observed that VAS values for groups which received combination of drugs were lower than Bupivacaine alone (p<0.05). In Bupivacaine alone group time for first rescue analgesia was earlier and also mean dose of rescue analgesic was high which was found to be statistically significant. Whereas better hemodynamic stability was observed in combination of drugs. (8)

Study of khaled et al for laparoscopic colorectal cancer surgery with intraperitoneal instillation of placebo (group1), Bupivacaine (group2) and Bupivacaine with Dexmedetomidine (group3) shows significant decrease in VAS with prolonged time for 1st rescue analgesia and less total analgesic requirement in patients of group 3 compared to others. (9)

Vrinda et al observed less number of patients required rescue analgesic when Dexmedetomidine was added to Bupivacaine in intraperitoneal instillation after laparoscopic surgeries which was found to be statistically significant. (10)

In a study done by Neha T. Et al evaluated the effects of intra-peritoneal

Bupivacaine and Ropivacaine versus Placebo on postoperative pain after Laparoscopic cholecystectomy. The duration of analgesia was highest in Ropivacaine group followed by Bupivacaine and placebo. (11)

There are other studies demonstrating combination of Bupivacaine plus Tramadol intraperitoneal instillation more efficacious than Bupivacaine when used for postoperative analgesia following laparoscopic surgeries. Our study findings are in accordance with above mentioned studies which have reported good postoperative analgesia with better hemodynamic stability with use of Bupivacaine with adjuvant drugs in laparoscopic surgeries. (12,13,14)

Golubovic et al observed that intraperitoneal instillation of Bupivacaine or Bupivacaine plus Tramadol significantly reduced VAS score compared to normal saline in laparoscopic surgeries, but found no significant difference between Bupivacaine and Bupivacaine plus Tramadol. (15)

A study by Anshu kumari concluded that Intraperitoneal instillation of Ropivacaine with Tramadol reduces the post-operative pain and analgesic requirement in laparoscopic cholecystectomy as compared to Ropivacaine alone. (16)

In a study by Vrinda there was decrease in heart rate in Bupivacaine plus Dexmedetomidine group due to effect of Dexmedetomidine on heart. Memis et al compared mean arterial pressure and heart rate between Bupivacaine and Bupivacaine plus Tramadol where lesser MAP and HR observed in Bupivacaine plus Tramadol group at 30min, 2hrs, 4hrs and 6hrs. In our study hemodynamic stability in terms of MAP and HR changes were comparable in both groups except at 6th, 8th hrs and 12th hrs where hemodynamic stability was better in group BT compared to group B. (8,10)

A study done by Jamal A et al found that there was a lower incidence of nausea and vomiting in patients receiving combination of Bupivacaine plus Tramadol due to less requirement of rescue analgesia. In our study we found no statistical difference in side effects between both the groups. (10)

Randomised, double blind design was strength of our study but small sample size and no long term follow up were limitations.

CONCLUSION

Intra-peritoneal instillation of Bupivacaine in combination with Tramadol in laparoscopic surgeries significantly reduces the post-operative pain and the analgesic requirement in post-operative period as compared to Bupivacaine alone and is associated with lesser side effects and better hemodynamics.

REFERENCES:

1. Perla Ekstein, Amir Szold, Boaz Sagie, Nachum Werbin, Joseph M. Klausner, and Avi A. Weinbroum. Laparoscopic Surgery May Be Associated with Severe Pain and High Analgesia Requirements in the Immediate Postoperative Period, *Ann Surg.* 2006; 243(1):41-6.
2. J.Joris, E. Thiry, P. Paris, J. Weerts and M. Lamy, —Pain after Laparoscopic Cholecystectomy: Characteristics and Effect of Intraperitoneal Bupivacaine, *Anesthesia & Analgesia*, 1995; 81(2):379-84.
3. Kim TH, Kang H, Park JS, Chang IT, Park SG. Intraperitoneal Ropivacaine Instillation for Postoperative Pain Relief after Laparoscopic Cholecystectomy. *J Korean Surg Soc.* 2010; 79(2):130-6.
4. Jung-Kyu Park, Soon Ho Cheong, Kun Moo Lee. Does Dexmedetomidine reduce postoperative pain after laparoscopic Cholecystectomy with multimodal analgesia *Korean J Anesthesiol.* 2012; 63(5):436-40.
5. Rakesh Babu, Prithi Jain, Lulu Sherif. Intraperitoneal Instillation: Ropivacaine Vs Bupivacaine For Postoperative Pain Relief In Laparoscopic Cholecystectomy. *IJHSR.* 2013; 3(12):42-7.
6. Dr. Sulekha. The Effect Of Intraperitoneal Bupivacaine For Post Operative Pain Management In Patients Undergoing Laparoscopic Cholecystectomy. A Prospective Double-Blind Randomized Control Study *IOSR Journal of Dental and Medical Sciences, IOSR-JDMS.* 2013; 4(5):64-9.
7. Srinivasa N Raja, Daniel B Carr, Milton Cohen, Nanna B Finnerup, Herta Flor, Stephen Gibson, Francis J Keefe, Jeffrey S Mogil, Matthias Ringkamp, Kathleen A Sluka, Xue-Jun Song, Bonnie Stevens, Mark D Sullivan, Perri R Tutelman, Takahiro Ushida, Kyle Vader. IASP Taxonomy, international association for the study of pain Definition of pain. *Pain.* 2020; 161(9).
8. Memis D, Turan A, Karamanlioglu B, Tükenmez B, Pamukcu Z. The effect of tramadol or clonidine added to intraperitoneal bupivacaine on postoperative pain in total abdominal hysterectomy. *J Opioid Manag* 2005; 1:77-82.
9. Fares KM, Mohamed SAE, Rahman AMAE, Mohamed AA, Amin ATE. Efficacy and safety of intraperitoneal dexmedetomidine with bupivacaine in laparoscopic colorectal cancer surgery, a randomized trial. *Pain Medicine: the Official Journal of the American Academy of Pain Medicine* 2015; 16(6):1186-94.
10. Oza VP, Parmar V, Badheka J, Nanavati DS, Taur P, Rajyaguru AM. Comparative study of postoperative analgesic effect of Intraperitoneal instillation of dexmedetomidine with bupivacaine and bupivacaine alone after laparoscopic surgery. *J Min Access Surg* 2016; 12:260-4.
11. Das NT, Deshpande C. Effects of Intraperitoneal Local Anaesthetics Bupivacaine and Ropivacaine versus Placebo on Postoperative Pain after Laparoscopic Cholecystectomy: A Randomised Double Blind Study. *J Clin Diagn Res.* 2017; 08-12.
12. Aslam Jamal, Hammadusmani, Mohd Mozaffarkhan, Amjad Ali Rizvi, Mohammadaslam. Intraperitoneal pre-insufflation of 0.125% bupivacaine with tramadol for postoperative pain relief following laparoscopic cholecystectomy. *Journal of anesthesiology and clinical pharmacology.* 2016; 32(2):257-60.
13. Shukla U, Prabhakar T, Malhotra K, Srivastava D, Malhotra K. Intraperitoneal bupivacaine alone or with dexmedetomidine or Tramadol for post-operative analgesia following laparoscopic cholecystectomy: A comparative evaluation. *Indian J Anaesth* 2015; 59:234-9.
14. Dr. M. Prakash, Dr. M. Rajaram. Comparison of Effects of Adding Dexmedetomidine or Tramadol to Intraperitoneal Bupivacaine in Postoperative Analgesia in Patients Undergoing Laparoscopic Cholecystectomy. *IOSR-JDMS.* 2016; 15(2):35-9.
15. Golubović S, Golubović V, Cindrić-Stancin M, Tokmadžić VS. Intraperitoneal analgesia for laparoscopic cholecystectomy: bupivacaine versus bupivacaine with tramadol. *Coll Antropol.* 2009; 33(1):299-302.
16. Kumari A, Acharya B, Ghimire B, Shrestha A. Post-operative analgesic effect of intraperitoneal ropivacaine with or without tramadol in laparoscopic cholecystectomy. *Indian J Anaesth.* 2020; 64(1):43-8.