



PREEMPTIVE ANALGESIA FOR POSTOPERATIVE PAIN RELIEF IN LAPAROSCOPIC CHOLECYSTECTOMY; COMPARISON OF ROPIVACAINE VS PLACEBO

Anaesthesiology

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ABSTRACT

The aim of preemptive analgesia is Prevention of transmission of nerve signals from the trauma site to the spinal cord and reduction of neurogenic local inflammation at the trauma site, infiltration of local anesthetics reduce the incidence of pain, various studies have shown the positive role of intra-peritoneal instillation of the Ropivacaine and similar local anesthetics. Patients undergoing laparoscopic cholecystectomy were randomized into two groups of 30 patients each, who were administered the study drug intraperitoneally before creation of pneumoperitoneum. Group R received ropivacaine (0.25% 40cc), whereas group P received normal saline. Postoperatively, the degree of pain assessed using visual analogue scale, time of request for first analgesic, total opioid consumption, and postoperative nausea and vomiting were recorded in postanesthesia care unit for 24 h. Ropivacaine group had better postoperative analgesia. Number of opioid consumption in postoperative period was lower with Ropivacaine group. The mean time for rescue analgesia was high in Ropivacaine group and both the groups didn't have shoulder tip pain. Intraperitoneal instillation of ropivacaine significantly decreases postoperative pain score and opioid consumption without evidence of adverse effects compared to normal saline solution instillation.

KEYWORDS

Preemptive Analgesia, Laparoscopic Cholecystectomy, Ropivacaine

INTRODUCTION:

Laparoscopic Cholecystectomy is one of the most frequently performed elective day care procedures. Provision of adequate postoperative pain relief is of considerable importance to enhance the recovery^[1]. Pain after laparoscopic cholecystectomy is generally lesser than open cholecystectomy; however postoperative shoulder and abdominal pain still cause considerable distress. Patients often suffer from visceral pain during coughing, respiration and mobilisation which can lengthen hospital stay, increase morbidity and cost of treatment. The pain after laparoscopic cholecystectomy may be generated by stretching of the abdominal wall during the pneumoperitoneum and release of inflammatory mediators, local dissection and irritation of the peritoneum due to blood, bile spillage or CO₂ used for pneumoperitoneum^[1]. Pain may be transient and most of the time lasts for 24 hours and sometimes even up to 3 days. Intensity of pain is more immediately after surgery and less after 24 hours. There are certain more complications like postoperative nausea and vomiting which are more in first 24 hours^[2].

Prevention of transmission of nerve signals from the trauma site to the spinal cord and reduction of neurogenic local inflammation at the trauma site has been reported with the use of local anaesthetics. As large volumes are required in these techniques, cardiovascular toxicity needs special attention^[3]. The use of NSAIDs for peritoneal inflammation after CO₂ pneumoperitoneum is rational but the preoperative administration of NSAID is questionable because of the pathophysiologic changes of renal blood flow induced by pneumoperitoneum^[4]. In order to further reduce the incidence of pain, various studies have shown the positive role of intra-peritoneal instillation of the Ropivacaine and similar local anaesthetics^[5]. Different modalities have been proposed to relieve postoperative pain after laparoscopy. These include parenteral NSAIDs, opioids, preemptive and post-operative intra peritoneal local anaesthetic instillation, port site infiltration of local anaesthetic, intra peritoneal saline, removal of insufflation gas/ gas drains, low pressure abdominal insufflations, Acetazolamide administration, use of N₂O in place of CO₂ etc.^[6].

Ropivacaine is a newer amide, it is preferred as a local anesthetic for instillation due to less risk of cardiovascular toxicity and central nervous system side effects. Accordingly a study was designed using Ropivacaine for postoperative pain relief in laparoscopic cholecystectomy as against placebo. The supremacy analgesic effect of preemptive analgesia with Ropivacaine verses over administration of 'on demand' analgesia - a conventional technique was assessed in this study.

MATERIALS AND METHOD:

After approval from hospital ethical committee, informed written

consent was taken from patients for participation in the study.

Subjects were randomized into 2 groups with 1:1 allocation ratio. The chief investigator, medical and nursing personnel were not blinded as it was an open-label trial. Subjects were followed from point of randomization till complete recovery. Patients were randomly allocated into 2 groups with 30 patients in each group with allocation ratio 1:1. Group 'R' were given Ropivacaine intra-peritoneal (0.25% 40ml). Group 'P' were given Placebo intra-peritoneal (40 ml).

Group R: Received Inj. Ropivacaine 0.25% (40ml) Preemptive as intra-peritoneal instillation in the below mentioned sites

1st in right sub diaphragmatic region 10ml

2nd in gall bladder bed 10ml

3rd in left sub diaphragmatic region 10ml

4th All entry ports – total 10 ml

Group P: Received normal saline 40 ml as intra-peritoneal instillation at above mentioned sites.

After instillation of the above two drugs patient were maintained in reverse trendelenburg with right side down position for 15mins. Hemodynamic parameters: heart rate, systolic blood pressure, diastolic blood pressure, ECG, SpO₂, ETCO₂ were monitored throughout the procedure.

- Heart rate < 60beats per minute was managed with Inj. Glycopyrrrolate 0.2mg IV,
- Hypotension was managed with specific intra venous fluids and vasopressors.
- Post-operative pain was assessed with visual analogue scale.
- Postoperative monitoring chart was done up to 24hrs for pain and hemodynamic changes and adverse effects of study drugs.
- Rescue analgesia in post-operative period:
- Inj. Tramadol 1mg/kg I.V (if patients develops nausea and/or vomiting because of Inj. Tramadol, Inj. Ondansetron 0.07mg/kg will be repeated).
- Inj. diclofenac 75mg IV repeated if necessary to maintain VAS score of <5.

Statistical Analysis Details. :

Data was collected and Appropriate Bio – Statistical analytical test was applied. Sample size was calculated after taking a thorough literature review in which we found that a study titled Evaluation of postoperative analgesia with intra-peritoneal Ropivacaine instillation in video laparoscopic cholecystectomy by Thiago Lucena Cesar de Albuquerque et al year 2016 concluded that the mean analgesic effect of Ropivacaine was 23.67±20.66 and the mean analgesic effect of

placebo was 7.32±9.34 34 by putting these values in open epi software with 80% power and 95% confidence interval the sample size in each group came out to be 16 but in my study total sample size is 60, in each group 30 samples so as to assess better efficacy of the study drugs. All the data was entered in Microsoft excel. % proportions frequency was calculated "t" test was applied for quantitative data. SPS SPSS trial version 20 was used to apply test & Data represented in tabular and graphical format.

RESULT:

The demographic profile was found to be comparable with no statistically significant difference between the groups. The preop and intraoperative haemodynamics were not statistically significant.

Table No- 1 Postoperative Pain Monitoring (visual Analogue Scale) In Both The Groups

Postoperative pain monitoring (VAS scale)	Ropivacaine		Placebo		T value	P value
	Mean	SD	Mean	SD		
1 st hr	1.14	0.34	1.4	0.49	2.04	<0.05(significant)
15 min	1.2	0.40	1.4	0.50	2.24	<0.05(significant)
30 min	1.3	0.49	1.6	0.49	2.1	<0.05(significant)
45 min	1.6	0.56	1.9	0.55	2.53	<0.05(significant)
60 min	2.03	0.61	2.5	0.86	2.41	<0.05(significant)
2 nd hr	2.2	0.61	3.0	1.06	3.71	<0.05(significant)
3 rd hr	3.1	0.88	4.0	0.73	4.59	<0.05(significant)
4 th hr	3.7	0.86	4.6	0.49	4.74	<0.05(significant)
8 th hr	4.7	0.50	5	0	2.53	<0.05(significant)
12 th hr	5.0	0.25	5.1	0.30	0.46	0.64(not significant)
16 th hr	5.0	0.25	5.0	0.25	0	1(not significant)
20 th hr	5.0	0.25	5.0	0.25	0	1(not significant)
24 th hr	5.0	0.25	5.0	0.25	0	1(not significant)

In the above table we compared Postoperative pain relief in both the groups by using visual analogue scale. We applied student unpaired "t" test. In the above comparison 1st 8hrs of postoperative pain score shows p-value <0.05 which is statistically significant. Comparison of the postoperative pain score in both the groups after 8hrs shows p-value >0.05 which is statistically not significant.

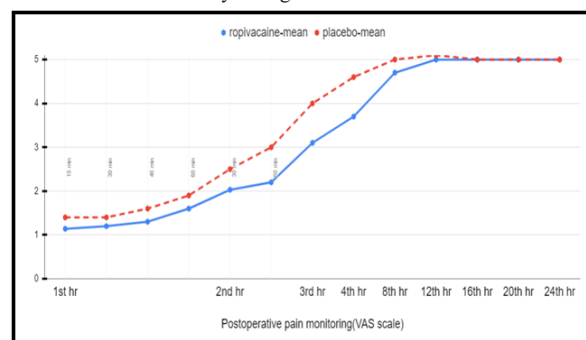


Chart number:1 This Chart Depicts-postoperative Pain Monitoring By VAS Score Up To 24hrs

Table No-2 Mean Time Of Rescue Analgesia In Postoperative Period:

Rescue analgesia time	Ropivacaine		Placebo		T value	P value
	mean	SD	Mean	SD		
1.	8.6	2.4	5.3	2.2	5.42	<0.05

In the above table we compared mean time of rescue analgesia in postoperative period, Ropivacaine group shows mean rescue analgesia time 8.6 with SD±2.4, placebo group shows mean rescue analgesia time 5.3 with SD±2.2. We applied student unpaired "t" test. The rescue analgesia time in postoperative period between both the groups are comparable and the p-value is <0.05 which is statistically significant.

Table No 3-comparison Of Mean Analgesic Consumption Between The Groups In Postoperative Period:

Mean analgesic consumption	Ropivacaine		Placebo		"t" value	"p" value
	Mean	SD	Mean	SD		
	1.53	0.50	1.8	0.40	2.2	0.02

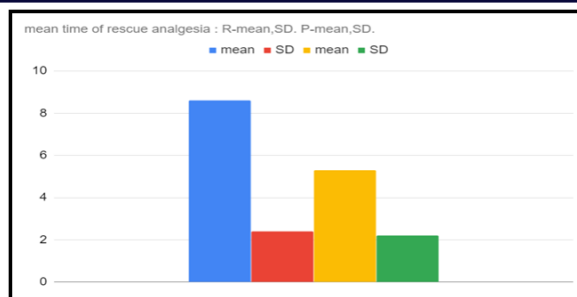


Chart No:2 Mean Time Of Rescue Analgesia In Postoperative Period

Mean analgesic consumption of both the groups are comparable .mean analgesic consumption of Ropivacaine group is 1.53, mean analgesic consumption of placebo group is 1.8 and "p" value is <0.05 statistically significant.

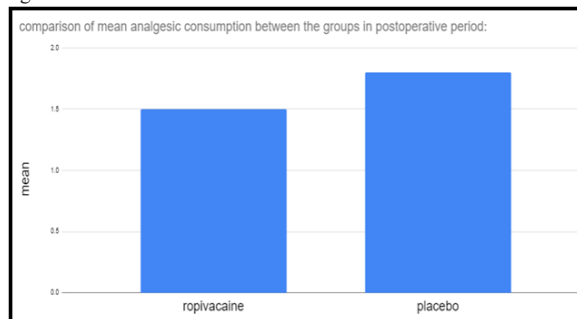


Chart No:3 Comparison Of Mean Analgesic Consumption Between The Groups In Postoperative Period

In our study, Group R received intra peritoneal instillation of Ropivacaine 0.25% while Group P received intra peritoneal instillation of normal saline (0.9%) before creation of pneumoperitoneum. VAS score for postoperative pain was recorded at various time intervals up to 24hrs. Out of the total 60 study subjects, the entire subjects were comparable in demographic characteristics like age, gender and weight and ASA grade.

DISCUSSION:

Intraoperative Hemodynamic Parameters- Heart Rate, Systolic Blood Pressure And Diastolic Blood Pressure.

In our study intraoperative hemodynamic parameters like heart rate, systolic blood pressure and diastolic blood pressure were not significantly different between both the groups in preoperative and intra-operative period. Our study findings are similar with **MONIKA GUPTA^[12] et al** 2016 in which they concluded that there was no intergroup variations in heart rate, systolic blood pressure, diastolic blood pressure in both the groups at different time intervals intra operatively (p>0.05) along with no significant change from the baseline.

Normal saline (0.9%) versus Ropivacaine 0.25% for postoperative pain relief.

Many studies have concluded that normal saline instillation also provides analgesia, thus we compared the effect of intra peritoneal local anesthetic drugs with normal saline^[14]. Intra peritoneal instillation has been evaluated previously for providing postoperative analgesia after laparoscopic cholecystectomy using Ropivacaine, Bupivacaine, levo-Bupivacaine, lignocaine with positive outcomes^[12]. In our study VAS score for postoperative pain was recorded up to 24hrs at various time intervals which showed significant pain relief in Ropivacaine group up to first 8 postoperative hours.

B.M.P RADEMAKER^[1] et al used normal saline (0.9%) intra-peritoneal at the end of surgery to compare the postoperative pain relief with the groups of lignocaine and Bupivacaine. In our study also we used normal saline (0.9%) intra-peritoneal before starting the procedure to compare the postoperative pain relief with the Ropivacaine group. In their study they concluded that there was no significant difference in analgesic requirement between the groups. It may be due to the small sample size, less volume of drug they used. We used Ropivacaine because of its lower toxicity and longer duration of

action. When Ropivacaine is given intra-peritoneal it starts acting within 10-20min and duration of action lasts for 4-6hrs.

TRIPAT KAUR BINDRA^[13] et al used 3mg/kg of Ropivacaine intra peritoneal instillation in 100ml normal saline before creating pneumoperitoneum and 3mg/kg of Ropivacaine intra peritoneal instillation in 100ml normal saline after completion of surgery .Postoperative pain was assessed with VAS(visual analogue scale) Score and they concluded that group “A” who received intra-peritoneal infiltration of Ropivacaine before creating pneumoperitoneum had lesser pain in postoperative period than group “B” who received Ropivacaine after completion of the procedure indicating the timing of intra-peritoneal instillation also plays a major role in postoperative analgesia ,thus we used Ropivacaine pre-emptively.

THIAGO LUCENA^[12] et al compared intra-peritoneal instillation of Ropivacaine and normal saline at completion of surgery in laparoscopic cholecystectomy patients for postoperative analgesia. They used Ropivacaine 0.5% 30ml, in their study and concluded that postoperative pain relief was more in patients who received Ropivacaine compared to patients who received normal saline. Ropivacaine group has statistically significant postoperative pain relief up to 8hrs .This prolonged analgesic effect may be due to instillation of Ropivacaine before starting the procedure.

TRIPAT KAUR^[13], DAVINDER CHAWLA et al compared intra-peritoneal instillation of Ropivacaine (0.5% 3mg/kg diluted to 100ml with normal saline (0.9%) and saline (0.9%) before creation of pneumoperitoneum. Pain score was calculated up to 24hrs postoperatively. Ropivacaine group had statistically significant pain relief more than saline group more than 24hrs. Results are comparable with our study, in our study Ropivacaine group had statistically significant postoperative pain relief up to 8hrs. Less duration of postoperative analgesia in our study may be due to less volume of total drug we used.

Postoperative opioid consumption between Ropivacaine and placebo group:

In our study Ropivacaine group has consumed less opioids in the first 24hrs of postoperative period compared to placebo group.

TRIPATKAUR^[13] et al also concluded in their study that intra peritoneal instillation of Ropivacaine causes less opioid consumption in the first 24hrs of postoperative period compared to placebo group.

THIAGO LUCENA^[12] et al concluded that postoperative opioid consumption was significant only for initial 2 postoperative hours in Ropivacaine group 0.5% verses placebo group. This finding may be due to instillation of Ropivacaine after completion of surgery in their study.

TAE HAN KIM et al^[7] concluded that postoperative opioid consumption in Ropivacaine group was less up to 48hrs compared to normal saline group. This prolonged analgesic effect may be due to more volume of drug they used in their study.

DR. DEEPALI VALESCHA et al^[9] conducted a study with Bupivacaine 0.25% as intra peritoneal instillation compared with normal saline group and concluded that Bupivacaine group received less postoperative analgesics and that was statistically significant only up to 4hrs.

NEERAJA BHARDWAJ et al^[4] also concluded that intra peritoneal Bupivacaine produces more analgesia compared to normal saline group; rescue analgesia requirement was also less in Bupivacaine group.

Mean time of rescue analgesia in postoperative period:

In our study mean time of rescue analgesia in postoperative period for Ropivacaine group was 8.6 with standard deviation 2.4, whereas for placebo group mean time was 5.3 with standard deviation of 2.2 which was statistically significant ($p < 0.5\%$).

NEERJA BHARDWAJ et al^[4] observed in their study that the mean time for the first dose of postoperative analgesia for Bupivacaine group was 5.23hrs compared to placebo group which was 1.25hrs.

TRIPATKAUR BINDRA et al^[13] also observed in his study that the

mean time of postoperative analgesia was 472 mints as they received inj.Ropivacaine before creation of pneumoperitoneum when compared to a group who received Ropivacaine after completion of surgery had mean time of rescue analgesia as 189 minutes. Ropivacaine group results are similar to our study.

THIAGO LUCENA et al^[12] conducted a similar study with Ropivacaine (0.5%-30 ml) showed mean time of rescue analgesia in Ropivacaine group was 23.67mins and in placebo group it was 7.32 minutes. This reduced the mean time for first rescue analgesia may be due to instillation of local anesthetics after dissection of gallbladder before its removal.

In our study no incidence of shoulder tip pain was noticed. The Ropivacaine and placebo groups had stable hemodynamics throughout intra operative period. Adverse effects associated with the use of local anesthesia such as allergic reactions and systemic toxicity were not observed in our study .No patients from entire study population had any complications.

This shows that intra peritoneal Instillation of Ropivacaine in the volume and dose used in our study is not associated with any adverse effects. Limitations of this study may be lack of measurement of Ropivacaine plasma concentration.

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