



ANALGESIC EFFICACY OF INTRAPERITONEAL BUPIVACAINE VS ROPIVACAINE VS PLACEBO AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Introduction: The cause of pain in abdominal surgeries, is Somatic and Visceral. Out of many ways to reduce Post laparoscopic pain one way is Intra peritoneal instillation of local anaesthesia. Intra peritoneal instillation of local anaesthesia is a simple, cheap and safe method of providing post operative analgesia after laparoscopic cholecystectomy. Aim of this study was to compare the analgesic efficacy of intraperitoneally instilled bupivacaine and ropivacaine and Placebo (Normal saline) in relieving postoperative pain after laparoscopic cholecystectomy. **Methods and methodology:** Prospective Randomized Open Label study was conducted in 90 patients posted for laparoscopic cholecystectomy divided into three groups each containing 30 patients according to computer generated numbers: Group Saline (S) received 35 ml of 0.9% normal saline, Group Bupivacaine (B) received 35 ml of 0.25% bupivacaine (87.5 mg), Group ropivacaine (R) received 35 ml of 0.375% ropivacaine (131.25 mg). Post operative pain and analgesia, Time until use of first rescue analgesic and its total dose, Post operative hemodynamic changes like pulse rate, Blood pressure (Systolic BP, Diastolic BP, Mean BP), Post operative nausea and vomiting and post operative complication if any was studied. **Results:** VAS Score in different time interval of Bupivacaine and Ropivacaine group was lower than saline group with $p < 0.0001$, a significant fall in rescue analgesia dose with p value < 0.05 . **Conclusion:** Intra Peritoneal Instillation of Local Anaesthetic Drug is useful for Post operative Pain relief and better control of postoperative Nausea and Vomiting for Patients undergoing Laparoscopic Cholecystectomy.

KEYWORDS :

INTRODUCTION:

In this Advanced Era of medical Science Laparoscopic Cholecystectomy is most frequently performed elective day care surgery done⁽¹⁾. The cause of pain in abdominal surgeries, is Somatic And Visceral⁽²⁾. Somatic pain is because of skin incision and the visceral pain is because of handling of the intestine and peritoneal inflammation. Laparoscopic surgeries Cause less somatic pain due to a small skin incision⁽³⁾. Post laparoscopic pain can be minimized by following ways: creating the pneumoperitoneum slowly, aspiration of gas under the diaphragm which lets out the residual CO₂, keeping gas drain, using low pressure and heated gas, using nitrous oxide pneumoperitoneum, instillation of local anaesthetics under the diaphragm, rectus sheath block, surgery under subarachnoid block, peri-operative NSAID'S and opioids⁽⁴⁾. Out of many ways to reduce Post laparoscopic pain one way is Intra peritoneal instillation of local anaesthesia. Intra peritoneal local anaesthesia is a simple, cheap and safe method of providing post operative analgesia. Visceral nociceptors blocked by Intraperitoneal instillation of local anaesthetic so that visceral pain is decreased in laparoscopic surgeries. Also The anti inflammatory action of local anaesthetic prevents peritonitis and bowel adhesion. drugs :

1. **Bupivacaine**⁽⁴⁾ - is 1-butyl pipecoloxylidide. Clinically used as a racemic mixture containing both 'R' and 'S' form. (table 1)

Table 1: Physical Property Of Bupivacaine

Molecular weight	288
Protein binding	95%
Lipid solubility	28
Pka	8.1
Elimination half life	210 minutes
Toxic plasma concentration	5 to 10µg/ml

2. **Ropivacaine**⁽⁴⁾ - is 1-propyl,2,6- pipecoloxylidide available as S-enantiomer.(table 2)

Table 2: Physical Property Of Ropivacaine

Molecular weight	274
Protein binding	94 %
Lipid solubility	Less
Pka	8.1
Elimination half life	less than bupivacaine

Aim of this study was to compare the analgesic efficacy of intraperitoneally instilled bupivacaine and ropivacaine and Placebo

(Normal saline) in relieving postoperative pain after laparoscopic cholecystectomy when used as a part of multimodal analgesia. The Objective of this study is Post operative pain (fig 1) and analgesia, Time until use of first rescue analgesic and its total dose, Post operative hemodynamic changes like pulse rate, Blood pressure (Systolic BP, Diastolic BP, Mean BP), Post operative nausea and vomiting, To assess post operative complication if any.

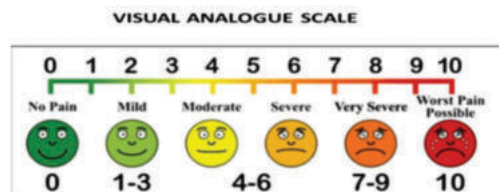


Fig 1: Postoperative Pain

MATERIALS AND METHODS:

Prospective Randomized Open Label study was in Department of Anaesthesiology, where 90 patients of either sex scheduled to undergo laparoscopic cholecystectomy, aged 18-60 years belonging to American society of anaesthesiologist (ASA) physical status I and II, body mass index (BMI) 18-29 kg/m². we excluded Patients not giving consent, Age less than 18 and more than 60 years, Patients needing bile duct exploration, insertion of a T-drain or patients with acute cholecystitis, Surgery related complication eg. bile spillage or conversion to open cholecystectomy or if the surgery exceeded 120 minutes, Patients with severe systemic disease, patients on analgesics for any reason, patients with difficult airway, cases of emergency surgery, patients with any psychiatric illness or substance abuse and patients with history of allergy to local anaesthetics. Patients were randomly divided into three groups each containing 30 patients according to computer generated numbers:

Group Saline (S) received 35 ml of 0.9% normal saline, Group Bupivacaine (B) received 35 ml of 0.25% bupivacaine (87.5 mg), Group ropivacaine (R) received 35 ml of 0.375% ropivacaine (131.25 mg). A preoperative visit was conducted one day before the surgery. All patients were advised oral Alprazolam 0.5mg the night before surgery and was fasted as per standard NPO guidelines. On the day of surgery Patients were taken to operation room, standard monitoring, including noninvasive blood pressure, Heart Rate, Oxygen saturation (SpO₂),

End tidal capnography(ET CO₂) and electrocardiography (ECG) was instituted and the baseline hemodynamic parameters (Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, Heart Rate, Oxygen saturation and ET CO₂) was recorded. Intravenous access was secured. Ringer's lactate 10 ml/kg/h was administered until the completion of the study. Local anesthesia test dose was given. After confirming the absence of allergic reaction patients was premedicated with inj. Glycopyrrolate 0.04mg, pre oxygenated with 100% O₂ for 3min with bag and mask. Induction was carried out with inj.fentanyl2mcg/kg, inj.propofol 2mg/kg, inj. succinylcholine 1.5mg/kg and intubated with an appropriate size endo tracheal tube after a loading dose of inj. vecuronium (0.04mg/kg). Anaesthesia was maintained with N₂O:O₂ 2:1, isoflurane 1-2%, inj. Propofol 0.2 mg/kg, inj vecuronium 0.02 mg/kg. No extra dose of analgesia was given intra operatively. All the surgeries were done by trained surgeons. After skin incision 11mm trocar was introduced via umbilical port, abdomen inflated with CO₂ 1 lit/min with intra-abdominal pressure kept around 12-14mmHg, in all patients. After the procedure got over, abdomen was thoroughly washed to remove the blood clots and debris. Inj. Bupivacaine (preservative free) 35 ml of 0.25% (87.5 mg)/ Inj. Ropivacaine (preservative free) 35 ml of 0.375% ropivacaine (131.25 mg) / 35ML of normal saline was instilled intra peritoneally under vision. After the removal of trocar, CO₂ gas was completely evacuated from the abdomen. Patients was kept in Trendelenberg position for 10minutes. If abdominal drain was present was clamped. During the surgery ETCO₂ value was maintained between 25 to 35 mmhg. After the skin closure, adequate spontaneous ventilation and neuromuscular recovery patients was reversed with inj. Neostigmine 40µg/kg and inj.Glycopyrrolate 0.4mg iv and extubated. All the patients were shifted to PACU for observation. outcomes were measured- VAS Score at 0, 1, 2, 3, 4, 5, 6, 10, 12, 24 hours for pain was noted. Inj. Tramadol 1 mg/kg iv was given as the rescue analgesia whenever the VAS score is more than 5 .Total dose of Tramadol required was noted in these periods. Time of the first rescue analgesic requirement and Presence of complications was noted.

RESULTS:

VAS Score in different time interval was compared between Saline, Bupivacaine and Ropivacaine group which showed that there is significant fall in VAS score over time with P Value < 0.0001 which was statistically Highly significant (table no 4). Rescue Analgesia Dose in different time interval between Saline, Bupivacaine and Ropivacaine group showed that there was significant Fall in Rescue Analgesia Dose over time with P Value < 0.05 (table no 4). Systolic Blood Pressure and Diastolic blood pressure in different time interval when compared between Saline, Bupivacaine and Ropivacaine group showed that there was fall in Systolic Blood Pressure and diastolic blood pressure over time with P Value < 0.05 which was statistically significant (table no 4). The Saline Group Mean of Mean Blood Pressure was more than Bupivacaine and Ropivacaine group with P Value > 0.05 which was Non Significant. Mean of Mean Blood Pressure of Bupivacaine group was Slightly More than Ropivacaine group with P Value > 0.05 .Pulse Rate in different time intervals between Saline, Bupivacaine and Ropivacaine group showed that there was significant Fall in Pulse Rate over time with P Value < 0.0001. The Saline Group Mean Pulse Rate was More than Bupivacaine and Ropivacaine group with P Value < 0.0001 which was statistically Highly significant and Mean Pulse Rate of Bupivacaine group was Slightly Less than Ropivacaine group with P Value > 0.05 .There is a significant reduction in nausea and vomiting in the patients who received Bupivacaine or Ropivacaine intraperitoneally when compared with Placebo group.

Table 3: Mean And SD Of The Various Parameters

S. NO	PARAMETERS	GROUP	MEAN	STANDARD DEVIATION
1	VAS SCORE	SALINE (S)	4.51	1.20428
		BUPIVAICAINE(B)	3.093333	1.2582047
		ROPIVAICAINE (R)	2.080807	1.256597
2	RESCUE ANALGESIA DOSE	SALINE (S)	0.35667	0.3465
		BUPIVAICAINE(B)	0.1074073	0.2634712
		ROPIVAICAINE (R)	0.104667	0.144598
3	SYSTOLIC BLOOD PRESSURE	SALINE (S)	128.39	30.2045
		BUPIVAICAINE(B)	119.98519	8.5487008
		ROPIVAICAINE (R)	121.3333	10.04183
4	DIASTOLIC BLOOD PRESSURE	SALINE (S)	81.7167	10.7385
		BUPIVAICAINE(B)	79.285186	7.2868978
		ROPIVAICAINE (R)	78.82	7.939183

5	MEAN BLOOD PRESSURE	SALINE (S)	96.2067	10.8422
		BUPIVAICAINE(B)	92.807779	6.926545
		ROPIVAICAINE (R)	92.79667	7.868998

Table 4: P Value And Inference

parameter	S AND B	S AND R	B AND R
VAS SCORE	P < 0.0001	P < 0.0001	P < 0.0001
	Highly significant	Highly significant	Highly significant
RESCUE ANALGESIA DOSE	P < 0.0001	P < 0.0001	P > 0.05
	Highly significant	Highly significant	Non significant
SYSTOLIC BLOOD PRESSURE	P > 0.05	P > 0.05	P > 0.05
	Non significant	Non significant	Non significant
DIASTOLIC BLOOD PRESSURE	P < 0.05	P > 0.05	P > 0.05
	Non significant	Non significant	Non significant
MEAN BLOOD PRESSURE	P < 0.05	P > 0.05	P > 0.05
	Non significant	Non significant	Non significant

(S-saline group, B-bupivacaine group, R-ropivacaine group)

DISCUSSION:

In the recent years Laparoscopic techniques have gained popularity, mainly due to the fact that it involves small incision, short hospital stay and early ambulation. Although Laparoscopic techniques has got various advantages on its own, it cause excessive pain postoperatively due to the peritoneal stretching because of insufflation of gases . Instillation of local anaesthetic solution intraperitoneally, as a mode of providing postoperative analgesia, has been studied extensively. It has the added advantage of early ambulation, reduced incidence of postoperative nausea vomiting and reduces the use of parental opioids and NSAIDs. All the groups were comparable with respect to the demographic datas including Age, Sex, Height, Weight, BMI and duration of surgery. Pain is better controlled in Bupivacaine and Ropivacaine group than Saline group and Ropivacaine group had better Pain control than Bupivacaine group as a study conducted by Neha T Das et al⁽⁵⁾ which was a randomised, prospective, double blind study, in which Group S received intraperitoneal infiltration with 35 ml of 0.9% normal saline, Group B with 35 ml of 0.25% bupivacaine and Group R with 35 ml of 0.375% ropivacaine. They used the Numerical Rating Scale (NRS) score of analgesia and studied analgesia score at rest and on cough/movement, duration of analgesia, need for a rescue analgesic (IV tramadol 1 mg/kg) concluding that Ropivacaine (0.375%) was more efficacious, longer acting with a higher intensity of postoperative analgesia than bupivacaine (0.25%). another study conducted by Radhey Sharan et al⁽⁶⁾ where Group A patients received 20 mL of 0.5% bupivacaine and Group B patients received 20 mL of 0.5% ropivacaine intraperitoneally after cholecystectomy. They concluded that visual analog scale (VAS) score was significantly lower in Group B, Verbal rating scale score was significantly lower in Group B, with longer duration of analgesia in this group and low Rescue analgesic requirement in Group B. Rescue Analgesia Dose in different time intervals between Saline, Bupivacaine and Ropivacaine group showed that there was significant Fall in Rescue Analgesia Dose over time and Mean Rescue Analgesia Dose of Bupivacaine group was Slightly More than Ropivacaine group with a pvalue of >0.05 inferring Rescue Analgesia Dose required in Saline group was more as compared to Bupivacaine and Ropivacaine group but no significant Difference in Requirement in Rescue Analgesia Dose in between Bupivacaine and Ropivacaine group. This difference in the Inj Tramadol requirement closely correlates with the study done by H. kang, B.Gkim et al⁽⁷⁾ where the Total amount of Fentanyl consumed in the study in control group was 420µg compared with Ropivacaine group which was about 300µg. Frequency of pushing the button in PCA was lower in Ropivacaine group compared to control group. Palmes et al⁽⁸⁾ also supports our study in which they used 0.5% lignocaine before the pneumo peritoneum vs 0.5% lignocaine after the surgery. Analgesic piritramide consumption in both groups were 11.1 vs 18.5 with p=0.002 when compared to the control group. 24 hour Mean Systolic, Diastolic and Mean Blood Pressure when compared between Saline, Bupivacaine and Ropivacaine group showed that there was no significant variation same as a study conducted by Canan Kucuk et al⁽⁹⁾ who compared Placebo with Bupivacaine, Ropivacaine in two different doses in the prevention of post-operative pain after laparoscopic cholecystectomy. Totally 80 patients were taken, and they randomly divided into 4 groups -group S, group R1, group R2,

group M who received saline, Ropivacaine 100mg with Adrenaline 1:200,000, Ropivacaine 150 mg-with Adrenaline 1:200,000, Bupivacaine 100 mg respectively inside the peritoneum after the end of the surgery. They compared the VAS score, 24 hour morphine requirement, sedation, hemodynamics, respiratory rate in the postoperative period over 24 hours inferring there was no significant difference in MAP, Heart rate, respiratory rate, sedation scale, complications in between all the 4 groups. Our study inferred that Bupivacaine and Ropivacaine group Pulse rate was better controlled than Saline group and The Mean Pulse Rate of Bupivacaine group was slightly less than Ropivacaine group with P Value > 0.05 supported by a prospective, randomized, double-blind study done by Radhey sharan et al⁽⁶⁾. They concluded that Pulse rate, systolic blood pressure, and diastolic blood pressure were comparatively lower in Group B than in Group A. There is a significant reduction in nausea and vomiting in the patients who received Bupivacaine or Ropivacaine intraperitoneally when compared with Placebo group. Among the 90 patients, 7 patients from the Placebo group had postoperative Nausea and vomiting, when compared to Bupivacaine and Ropivacaine group, where the incidence of Postoperative Nausea and vomiting is less (2 patient in each group) may be the reason for this high incidence of PONV(Post Operative Nausea Vomiting) in the Placebo group, is due to the higher requirement of rescue analgesia in the form of opioids(Tramadol), which is one among the risk factors for PONV. In our study no significant complications were noted like seizure and allergic reaction, Sai Sandhya et al⁽¹⁰⁾ and Andrei Goldstein and Patrik Grimault et al⁽¹¹⁾ also demonstrated that their study was without any complications.

CONCLUSION:

We conclude that IntraPeritoneal Instillation of Local Anaesthetic Drug is useful for Post operative Pain relief and better control of postoperative Nausea and Vomiting for Patients undergoing Laproscopic Cholecystectomy and 0.375% Ropivacaine is Better Analgesic when compared to intraperitoneal 0.25% Bupivacaine with well maintained Hemodynamics Postoperatively.

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