Original Article

DOI: 10.7860/JCDR/2017/26162.10188

Effects of Intraperitoneal Local Anaesthetics Bupivacaine and Ropivacaine versus Placebo on Postoperative Pain after Laparoscopic Cholecystectomy: A Randomised Double Blind Study

NEHA T DAS[1], CHARULATA DESHPANDE[2]

ABSTRACT

Introduction: Laparoscopic Cholecystectomy (LC) is the most frequently performed elective daycare surgery and provision of postoperative pain relief is of importance. After laparoscopic cholecystectomy shoulder and abdominal pain causes considerable distress. Visceral pain during coughing, respiration and mobilization increases morbidity, hospital stay and costs.

Aim: To compare the analgesic efficacy of intraperitoneally instilled equipotent concentrations of bupivacaine and ropivacaine versus placebo in relieving postoperative pain after laparoscopic cholecystectomy when used as a part of multimodal analgesia.

Materials and Methods: In this randomised, prospective, double blind, placebo controlled study, 90 ASA Class I or II patients were randomly divided into three groups of 30 each.

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.

All groups received standard general endotracheal anaesthesia and analgesia with IV paracetamol 15 mg/kg and diclofenac 1.5 mg/kg.

Numerical Rating Scale (NRS) score of analgesia at rest and on cough/movement, duration of analgesia, haemodynamic parameters, need for a rescue analgesic (IV tramadol 1 mg/kg) was recorded and adverse effects of procedure and drugs if any were monitored. Data was analysed with SPSS statistical software version 21.0. One way ANOVA or the Kruskal–Wallis test was used to compare continuous data across all three groups as appropriate. Subsequent analysis of continuous data between two groups was achieved by Tukey's post hoc test. Significance was accepted as $p<0.05$.

Results: The mean NRS was <5 till only four hours in Group S, till eight hours in Group B and till 16 hours in Group R. The duration of analgesia was 13.47±1.38 hours in Group R, 7.93±1.44 hours in Group B and 4.47±0.86 hours in Group S.

Conclusion: Intraperitoneal infiltration of LA significantly reduces pain intensity scores in the early postoperative period after LC surgery and helps in improving the postoperative recovery profile and outcome. This makes LC surgery more amenable to day care surgical setup.

Ropivacaine (0.375%) is more efficacious, longer acting with a higher intensity of postoperative analgesia than bupivacaine (0.25%).

Keywords: Elective daycare surgery, Intraperitoneal instillation, Multimodal analgesia, Postoperative analgesia

INTRODUCTION

Laparoscopic Cholecystectomy (LC) is one of the most frequently performed elective day care procedures. Provision of adequate postoperative pain relief is of considerable importance to enhance recovery. Pain after LC is generally lesser than open cholecystectomy; however postoperative shoulder and abdominal pain still cause considerable distress [1]. Patients often suffer from visceral pain during coughing, respiration and mobilisation. This can lengthen hospital stay, increase morbidity and costs.

The pain after LC may be generated by stretching of the abdominal wall during the pneumoperitoneum and release of inflammatory mediators, local dissection and irritation of the peritoneum produced by blood, bile spillage or CO_2 used for pneumoperitoneum [1].

Instillation of intraperitoneal lignocaine, bupivacaine, levo-bupivacaine and ropivacaine has been used following laparoscopic gynaecological and general surgical procedures to reduce postoperative pain through randomized trials for many years [2-9]. Although a number of these studies have reported a significant reduction in postoperative pain after the use of intraperitoneal LA, others have reported no benefit or reduction in analgesic requirement [10]. This study was conducted to ascertain the analgesic efficacy of intraperitoneally instilled local anaesthetics after LC.

The aim of our study was to evaluate the effects of intraperitoneal local anaesthetics bupivacaine and ropivacaine versus placebo on postoperative pain after LC when used as a part of multi modal analgesia.

MATERIALS AND METHODS

This randomized, prospective, double blind study was carried out over a period from January 2012 to December 2014 after obtaining approval from Hospital Ethics Committee and written, informed consent from the participants.

Sample size was calculated using published data of a previous study [11] based on the anticipated difference in the pain score between the bupivacaine and ropivacaine groups. The pain scores with use of 0.25% bupivacaine was (mean±standard deviation) 4.05±1.33. Assuming Type I error of 5% and Type II error of 20% (power of 80%), a decrease in the pain score by 25% (at least one point) was considered clinically significant. This resulted in a sample size of 28 patients for each group calculated by using the formula: $n_1 = n_2 = 16 \times (SD/M1–M2)^2$, where SD is standard deviation, M1–M2 is degree of difference to be detected. We included 30 patients in

each group.

Ninety ASA Grade I and II patients of either sex between the age group of 18-60 years and weighing 45-85 kg, undergoing LC were enrolled in this study. Patients needing bile duct exploration, insertion of a T-drain or patients with acute cholecystitis were excluded. Patients were excluded in case of surgery related complication eg., bile spillage or conversion to open cholecystectomy or if the surgery exceeded 200 minutes. Patients with severe systemic disease, patients on analgesics for any reason and patients with history of allergy to local anaesthetics were excluded.

Each patient was randomly assigned to one of the three groups of 30 patients each using computer generated randomization. Group Saline (S) received 35 ml of 0.9% normal saline, Group Bupivacaine (B) received 35 ml of 0.25% bupivacaine (87.5 mg) and Group ropivacaine (R) received 35 ml of 0.375% ropivacaine (131.25 mg). All the study drugs were prepared and coded by an anaesthetist who was not part of the study and the anaesthetist conducting the study was unaware of the drug being injected. The patient was blind to the drug injected as well.

All patients underwent thorough medical evaluation and investigations. Intraoperative monitoring included cardioscope, NIBP monitor, pulse oximeter, $ETCO_2$ monitor and temperature monitor.

All patients received standard premedication and general endotracheal anaesthesia without use of nitrous oxide. All surgical procedures were performed by an experienced surgeon. Standard 10 mm trocar umbilical port and epigastric ports were used. Intraperitoneal pressure was maintained at 10 mmHg using a flow rate of 3 l/min and the operative table placed in the reverse Trendelenberg with left side down tilting position.

After removal of the gallbladder and haemostasis, residual blood, fluid and CO_2 were thoroughly suctioned. The surgeon instilled 20 ml of test drug in the subdiaphragmatic suprahepatic surface of liver and 5 ml in the gallbladder fossa. The patient was maintained in the right lateral Trendelenberg position for 10-15 minutes. Further, 10 ml was used for port-site infiltration. All patients received 15 mg/kg of IV paracetamol and IV diclofenac 1.5 mg/kg 20 minutes prior to extubation.

Parietal pain (defined as superficial pain located on the abdominal wall, pain felt on touch) and visceral pain (defined as deep, dull, more difficult to localize, inside the abdomen) were assessed with NRS at rest (supine with 10-15 degree head up) and on activity (rising from supine to sitting position and coughing). The incidence of shoulder pain was also recorded.

Pain scores were recorded immediately on arrival in Post Anaesthesia Care Unit (PACU), every 15 minutes for the first hour, half hourly for the second hour and hourly up to the fourth hour and then every four hourly till the 24th hour after surgery. Patients received rescue analgesia in the form of IV tramadol 1 mg/kg along with ondansetron 0.07 mg/kg repeated if necessary to maintain NRS≤5. Haemodynamic parameters and incidence of nausea and vomiting were also recorded in the recovery room.

STATISTICAL ANALYSIS

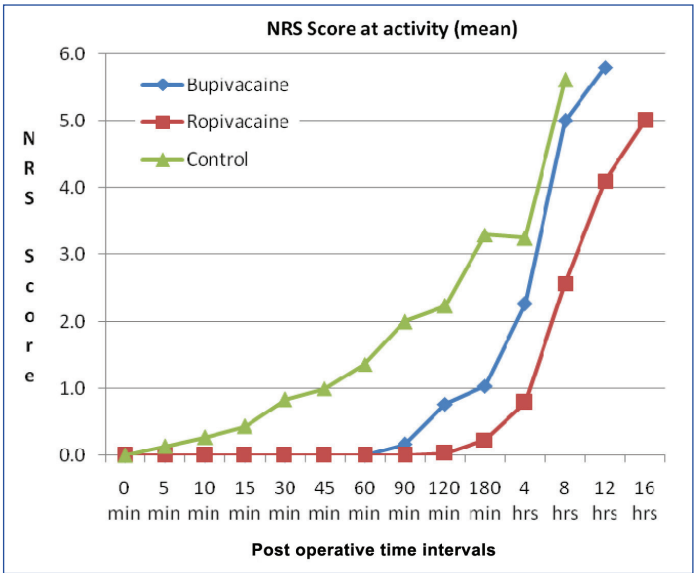
Data was analysed using SPSS statistical software version 21.0. Descriptive statistics were expressed as mean±SD or median (interquartile range, IQR) where appropriate. One way ANOVA or the Kruskal–Wallis test was used to compare continuous data across all three groups as appropriate. Subsequent analysis of continuous data between two groups was achieved by Tukey's post hoc test. Significance was accepted as $p<0.05$

RESULTS

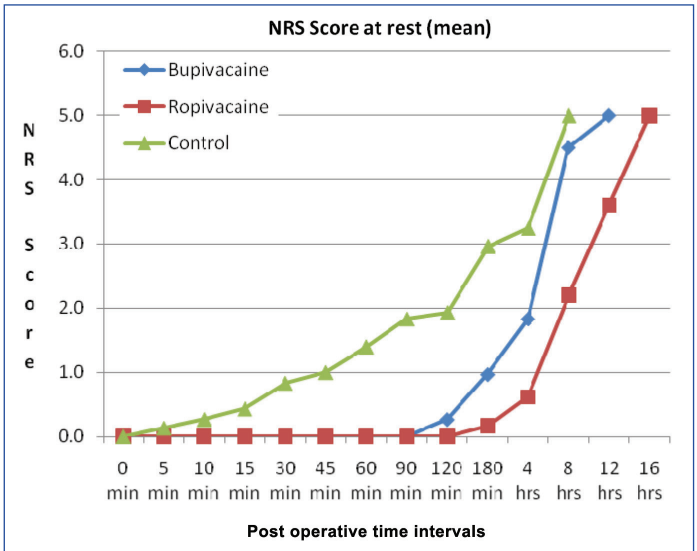
Ninety patients were included in this prospective, randomized, observer blind study with 30 patients in each group. The groups were comparable with regard to age, weight, sex, ASA grade, baseline haemodynamic parameters and duration of surgery [Table/Fig-1].

Variables	Group	Statistics				Kruskal-Wallis test	
		Mean	SD	Median	IQR	Chi-Square	p-value
Age (yrs) ^	B	44.07	9.85	45.50	14.00	3.020	0.22
	R	40.17	11.93	42.50	19.50	NS	
	S	38.70	11.89	39.50	22.50		
Weight (kg) ^	B	64.40	7.06	65.00	8.50	1.797	0.40
	R	62.87	5.46	64.00	10.00	NS	
	S	62.23	5.39	62.00	7.75		
ASA grade ^	B	1.23	0.43	1.00	0.25	1.424	0.49
	R	1.13	0.35	1.00	0.00	NS	
	S	1.13	0.35	1.00	0.00		
Surgery duration	B	1.63	0.58	1.50	0.81	5.003	0.082
	R	1.62	0.54	1.50	0.50	NS	
	S	1.78	0.22	1.75	0.31		
Preop Pulse Rate	B	80.00	9.66	78.00	14.00	1.000	
	R	80.00	9.66	78.00	14.00	NS	
	S	80.00	9.66	78.00	14.00		
Preop SBP	B	119.67	13.77	130.00	20.00	0.197	
	R	119.33	12.58	120.00	20.00	NS	
	S	115.33	6.81	120.00	10.00		
Preop DBP	B	75.87	7.16	72.00	10.50	0.061	
	R	74.73	5.02	71.00	10.00	NS	
	S	72.33	6.79	70.00	10.00		
Sex	B	10 Females		20 Males		0.721	
	R	13 Females		17 Males		Association is not significant	
	S	12 Females		18 Males			

[Table/Fig-1]: Comparison of ASA grade, demograpic and baseline parameters.
Preop-Preoperative
NS-Not significant
p-value>0.001-Not significant



[Table/Fig-2]: NRS score at activity.



[Table/Fig-3]: NRS score at rest.

NRS: The pain during the postoperative period was assessed by NRS score. Zero minute was taken as the first reading in the PACU. NRS score was recorded at rest as well as on activity (movement from supine to sitting and coughing) [Table/Fig-2,3].

At zero to 15 minutes: Group R (ropivacaine), Group B (bupivacaine) and Group S (control) had statistically and clinically equivalent NRS scores (p-value > 0.05) at rest as well as on movement.

From 15 minutes to 120 minutes: The NRS scores at rest as well as on movement in Group R and Group B were significantly lower compared to Group S (p-value<0.05).

In Group R, the mean NRS score on activity as well as at rest was '0' for 120 minutes.

In Group B, the mean of NRS score on movement was '0' for a period of 60 minutes and NRS score on rest was '0' for 90 minutes however both the scores were less than '1' for 120 minutes.

The difference in the mean NRS scores on movement and rest between Group B and Group R was not statistically significant (p>0.05) during the first 120 minutes and thus, the analgesia was comparable.

From 120 minutes to eight hours: The mean NRS score on movement and at rest was significantly lower in the B and R groups as compared to S group.

The mean NRS score on movement in Group R was '0' at 120 minutes and 2.6 at eight hours which was lower than the mean of NRS score on movement in Group B (0.8 at 120 min and 5 at eight hours) and S (2.2 at 120 min and 5.6 at eight hours). This difference was statistically (p-value<0.05) as well as clinically significant throughout this period. Patients from Group S required rescue analgesia at eight hours and observation period ended in this group.

In Group R, the NRS score at rest was '0' at 120 minutes and 2.2 at the end of eight hours. In Group B, the mean of NRS score at rest was 0.3 at 120 minutes and 4.5 at the end of eight hours. This difference in NRS scores at rest between Group R and B was statistically significant (p<0.01).

This shows that both ropivacaine and bupivacaine provided effective analgesia for eight hours postoperatively and ropivacaine provided more profound analgesia.

From eight hours to 16 hours: Only patients from Group R continued to have effective analgesia with readings of NRS on activity as well as NRS at rest <5 till 16 hours into the postoperative period. During this period both NRS scores were statistically lower than in Group B (p<0.001).

In Group B, the mean of NRS score on movement reached >5 by 12 hours and received rescue analgesia.

Thus, intraperitoneal local anaesthetic infiltration in the gallbladder fossa and suprahepatic surface provided more effective and prolonged analgesia as compared to intraperitoneal saline instillation. Use of ropivacaine significantly prolonged and improved the analgesia as assessed by NRS score.

Duration of analgesia: The duration of postoperative analgesia was counted from the first reading in PACU to the time of administration of rescue analgesia. Rescue analgesia was administered when the NRS score was >5 in the form of IV tramadol (1 mg/kg).

The mean of duration of analgesia in Group S was 4.47±0.86 hours, in Group B 7.93±1.44 hours and in Group R 13.47±1.38 hours during the postoperative period. Thus, the mean duration of analgesia in Group R was almost double the duration of analgesia observed in Group B and three times the duration of analgesia observed in Group S. This difference was statistically as well as clinically significant.

This shows that the duration of analgesia was longer in the local anaesthesia groups where intraperitoneal local anaesthetic infiltration in the gallbladder fossa and suprahepatic surface was provided. Use of ropivacaine significantly prolonged and improved the analgesia as assessed by NRS score. No patient from our study complained of shoulder pain.

Intraperitoneal infiltration in gallbladder fossa and suprahepatic surface with bupivacaine and ropivacaine also helped in maintaining better haemodynamic profile in the postoperative period. Ropivacaine had a more profound and longer duration of analgesia as compared to bupivacaine.

We observed for various complications like nausea, vomiting, bradycardia, respiratory depression, hypotension and sweating in all patients. No patient from the entire study population had any incident of any of these complications. This shows that intraperitoneal instillation of ropivacaine and bupivacaine in the volume and dose used in our study is not associated with any adverse effects.

DISCUSSION

LC is a minimally invasive surgery and widely performed as a day care procedure. Postoperative pain control is of essence directed at early mobilization, recovery and discharge. The origin of pain after LC is multifactorial and complex in nature. It has parietal (abdominal wall), visceral (intra-abdominal) and referral (shoulder tip) components and effective analgesic treatment should be multimodal [1,12].

Lower abdominal pressures and shorter duration of surgery are associated with lower incidence and severity of shoulder pain after LC and therefore surgical method influences postoperative referral

pain. Port site infiltration alleviates parietal pain and intraperitoneal local anaesthetics help alleviate visceral pain. Several studies [1,2,9,13] have investigated and demonstrated good analgesia after wound infiltration using local anaesthetics in laparoscopic cholecystectomy.

Many clinical trials have been carried out to assess analgesic effects local anaesthetics instilled intraperitoneally into the gallbladder bed and right subdiaphragmatic space [9]. The rationale for this route is that the peritoneum is exposed to block the visceral nociceptive conduction from the area of tissue damage and the peritoneum, thereby providing an additional mechanism of analgesia. However, absorption from the large peritoneal surface may be a further mechanism of analgesia. Intraperitoneal administration of local anaesthetic has also been shown to reduce nausea and vomiting [14].

The intraperitoneal route for administration of local anaesthetic is best suited in ambulatory anaesthesia set up as it is simple to perform and does not involve additional invasive techniques such as central neural axial block. The only limiting factor to its use as a routine analgesic technique is the dose and duration of action of local anaesthetic. Thus, local anaesthetics that have a longer duration of action and safe pharmacological profile are needed.

Bupivacaine is the most commonly used local anaesthetic for intraperitoneal infiltration since 1991 [6-8]. Ropivacaine, is an attractive alternative to bupivacaine. The analgesic effects and duration of ropivacaine are similar to those of racemic bupivacaine but with a reduced risk of cardiac and systemic toxicity, thus allowing administration of a larger and more potent dose [3].

There is plenty of evidence in literature [9] regarding analgesic efficacy of intraperitoneal infiltration of bupivacaine in the dose ranging 50–200 mg in volumes ranging from 10–100 ml. Intraperitoneal instillation of plain bupivacaine in the dose of 100–150 mg produces plasma concentration in the range of 0.92–1.14 µg/ml which is well below the toxic concentration of 3 µg/ml. This study used a total of 87.5 mg of bupivacaine in 35 cc.

Ropivacaine has lower risk of systemic and cardiac toxicity and thus a larger and more potent dose can be safely administered.
Ropivacaine in the dose of 150 mg instilled intraperitoneally produces morphine sparing effect for the duration of 24 hour which is statistically significant when compared with placebo during gynaecological laparoscopy [5]. Studies have evaluated doses of ropivacaine [3] as large as 300-375 mg for inguinal hernia infiltration or intraperitoneal injection and have not observed any clinical evidence of toxicity. This study used a total of 131.25 mg of ropivacaine.

Recent evidence suggests that instillation of local anaesthetics both into the peritoneum and into the incision may be required after LC. Instillation of ropivacaine 286 mg in 66 ml in this way during laparoscopic cholecystectomy produced lower pain scores and reduced morphine requirements compared with placebo [12]. Thus, we used intraperitoneal instillation along with peritrocar infiltration for postoperative pain relief after LC.

The multimodal approach to postoperative pain management [15] involves the use of opioids, Non-Steroidal Anti Inflammatory Drugs (NSAIDs), paracetamol and local anaesthetics. The standard analgesia regimen used at our hospital, includes the administration of IV paracetamol 15 mg/kg and IV diclofenac sodium 1.5 mg.

Potency wise the equipotent concentration of 0.25% bupivacaine is 0.375% ropivacaine (potency ratio 1:1.5) since the MLAC values for ropivacaine are 50% higher than that of bupivacaine [16]. A 35 ml of both the drugs was used in our study and the total dose of the local anaesthetic (87.5 mg of bupivacaine and 131.25 mg of ropivacaine) was safely below the toxic levels (2 mg/kg of bupivacaine and 4 mg/kg of ropivacaine).

Ahmed BH et al., in their study concluded that normal saline instillation also provides analgesia [17]. Donatsky AM et al., conducted a systematic review to study the role of intraperitoneal saline in prevention of postoperative pain in LC [18]. Their findings also support the analgesic action of normal saline in the form of intraperitoneal instillation. Thus, we compared the effect of intraperitoneal local anaesthetic drugs with normal saline.

Narchi P et al., compared 0.5% lignocaine and 0.125% bupivacaine intraperitoneal infiltration with normal saline and control in day-case laparoscopic surgeries [19]. Local anaesthetics were found to be more effective in reducing postoperative shoulder pain and analgesic requirements were lesser in the local anaesthetic groups. Our study also found that intraperitoneal local anaesthetics provide better analgesia as compared to that of saline.

Roberts KJ et al., compared 0.25% bupivacaine and normal saline given subcutaneously in trocar sites, subdiaphragmatically and intraperitonealy as a topical wash [20]. VAS scores were lowest for the longest period in the subdiaphragmatic group rather than the intraperitoneal wash technique. In our study also, NRS scores were lowest for the longest period in the ropivacaine group followed by bupivacaine group as compared to saline.

Pappas-Gogos G et al., compared preincisional trocar site infiltration and intraperitoneal instillation with ropivacaine plus normal saline infusion after LC for postoperative pain relief [2]. They concluded that infiltration around the trocar site with intraperitoneal infiltration using ropivacaine results in low VAS scores and prolonged analgesia. Our study found that both peritrocar and intraperitoneal instillation of ropivacaine achieved lowest NRS scores for longer duration.

Kim TH et al., instilled ropivacaine (2 mg/kg) intraperitonealy at the beginning of laparoscopy. VAS scores were significantly lower in the ropivacaine group as compared to the normal saline group [21].

Goldstein A et al., compared intraperitoneal instillation of 20 ml of bupivacaine 0.5%, ropivacaine 0.75% or saline at the end of surgery [5]. All patients received analgesia with acetaminophen and ketoprofen IV infusions. The morphine consumption at wake-up and over the first 24 hour was significantly lower in Group B and in Group R than in saline group. The morphine sparing effect of ropivacaine was significantly greater than that of bupivacaine. They concluded that local anaesthetic instillation (ropivacaine rather than bupivacaine) at the end of laparoscopy prevents postoperative pain and dramatically decreases the need for morphine.

Our finding of a more efficacious pain relief by local anaesthetic instillation and peritrocar infiltration (ropivacaine over that of bupivacaine) over that of normal saline (control) is in keeping with the findings of above studies.

Since visceral pain is affected and increased by movement, we assessed pain scores at rest and on movement from supine position to sitting. In our study, we noticed that the NRS score on movement was only marginally higher than NRS score at rest in all the three groups and this difference was not clinically or statistically significant. Thus, mobilization did not significantly increase pain.

Joris J et al., conducted a study on the effects of intraperitoneal bupivacaine on characteristics of pain after LC [22]. They found that mobilization did not significantly increase VAS. Our finding is similar in that NRS score did not significantly increase with activity.

In another meta-analysis, intraperitoneal LA did not significantly alleviate abdominal pain on activity but was effective on visceral pain in a resting state [23].

We did not observe any incidence of shoulder pain; this could have been due to meticulous absorption of gas at the end of surgery as well as suprahepatic surface instillation and maintenance of Trendelenberg position for atleast 10 minutes.

A meta-analysis in 2015 by Choi GJ et al., also showed that intraperitoneal instillation of local anaesthetics significantly reduced incidence and severity of shoulder pain [23]. In our study too,

intraperitoneal local anaesthetics led to no incidence of shoulder pain.

The ropivacaine and bupivacaine groups had stable haemodynamics and this can be attributed to the better analgesia provided by the local anaesthetics over that of normal saline.

Adverse effects associated with the use of local anaesthesia, such as allergic reactions and local tissue, cardiovascular, central nervous system and systemic toxicity were not observed in our study with the use of local anaesthesia. No patient from the entire study population had any complications. This shows that intraperitoneal instillation of ropivacaine and bupivacaine in the volume and dose used in our study is not associated with any adverse effects.

LIMITATION

The limitation of our study is that the power of study is less and therefore the sample size is small. A larger sample size will establish further conclusive evidence.

CONCLUSION

Trocar site infiltration and intraperitoneal instillation in the gallbladder fossa and subdiaphragmatic hepatic surface using ropivacaine (35 ml of 0.375%) and bupivacaine (35 ml of 0.25%) at the end of surgery as a part of multimodal analgesia provide safe and effective somato-visceral analgesia in patients undergoing LC. Ropivacaine provides a more profound and prolonged analgesia as compared to bupivacaine.

This technique of providing postoperative analgesia is simple, effective and will help in improving the postoperative recovery profile of the patient and help in making it a truly out-patient based surgery.

REFERENCES

[1] Bhardwaj N, Sharma V, Chari P. Intraperitoneal bupivacaine instillation for postoperative pain relief after laparoscopic cholecystectomy. Indian J Anaesth. 2002;46(1):49-52.

[2] Pappas-Gogos G, Tsimogiannis KE, Zikos N, Nikas K, Manataki A, Tsimoyiannis EC. Preincisional and intraperitoneal ropivacaine plus normal saline infusion for postoperative pain relief after laparoscopic cholecystectomy: a randomized double-blind controlled trial. Surg Endosc. 2008;22(9):2036-45.

[3] Labaille T, Mazoit JX, Paqueron X, Franco D, Benhamou D. The clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. Anaesth Analg. 2002;94:100-05.

[4] Betton D, Greib N, Herve S, Joshi GP. The pharmacokinetics of ropivacaine after intraperitoneal administration instillation versus nebulisation. Anaesth Analg. 2010;111:1140-45.

[5] Goldstein A, Grimault P, Henique A, Keller M, Fortin A, Darai E. Preventive postoperative pain by local anaesthetic instillation after laparoscopic gynaecologic surgery: a placebo-controlled comparison of bupivacaine and ropivacaine. Anaesth Analg. 2000;91(2):403-07.

[6] Ng A, Swami A, Smith G, Davidson AC, Emembolu J. The analgesic effects of intraperitoneal and incisional bupivacaine with epinephrine following total abdominal hysterectomy. Anaesth Analg. 2002;95:158–62.

[7] Raetzell M, Maier C, Schroder D, Wulf H. Intraperitoneal application of bupivacaine during laparoscopic cholecystectomy—risk or benefit? Anaesth Analg. 1995;81(5):967-72.

[8] Scheinin B, Kellokumpu I, Lindgren L, Haglund C, Rosenberg PH. Effect of intraperitoneal bupivacaine on pain after laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 1995;39:195–98.

[9] Moiniche S, Jorgensen H, Wetterslev J, Berg J. Local anaesthetic infiltration for postoperative pain relief after laparoscopy: a qualitative and quantitative systematic review of intraperitoneal, port-site infiltration and mesosalpinx block. Anaesth Analg. 2000;90:899–912.

[10] Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anaesthesia in laparoscopic cholecystectomy: a systematic review and meta-analysis. Anaesth Analg. 2006;103:682–88.

[11] Chakravarty N, Singhai S, Shidhaye RV. Evaluation of intraperitoneal bupivacaine for postoperative analgesia in patients undergoing laparoscopic cholecystectomy: a prospective randomized trial. Anaesth Pain Intens Care. 2014;18(4):361-66.

[12] Trikoupi A, Papavramidis T, Kyurdzhieva E, Kesisoglou I, Vasilakos D. Intraperitoneal administration of ropivacaine during laparoscopic cholecystectomy 14AP125. Eur J Anaesth. 2010;27(47):222.

[13] Bisgaard T, Klarskov B, Kristiansen VB, Callesen T, Schulze S, Kehlet H, et al. Multi-regional local anaesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: A randomized, double-blinded, placebo-controlled study. Anaesth Analg. 1999;89:1017–24.

[14] Loizides S, Gurusamy KS, Nagendran M, Rossi M, Guerrini GP, Davidson BR. Wound infiltration with local anaesthetic agents for laparoscopic cholecystectomy. Cochrane Database Syst Rev. 2014;12(3):CD007049.

[15] Michaloliakou C, Chung F, Sharma S. Preoperative multimodal analgesia facilitates recovery after ambulatory laparoscopic cholecystectomy. Anaesth Analg. 1996;82:44–51.

[16] Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anaesthetics, ropivacaine and levobupivacaine. Acta Biomed. 2008;79:92-105.

[17] Ahmed BH, Ahmed A, Tan D, Awad ZT, Al-Aali AY, Kilkenny J, et al. Post-laparoscopic cholecystectomy pain: effects of intraperitoneal local anaesthetics on pain control--a randomized prospective double-blinded placebo-controlled trial. Am Surg. 2008;74(3):201-09.

[18] Donatsky AM, Bjerrum F, Gögenur I. Intraperitoneal instillation of saline and local anaesthesia for prevention of shoulder pain after laparoscopic cholecystectomy: a systematic review. Surg Endosc. 2013;27(7):2283-92.

[19] Narchi P, Benhamou D, Fernandez H. Intraperitoneal local anaesthetic for shoulder pain after day-case laparoscopy. Lancet. 1991;338:1569–70.

[20] Roberts KJ, Gilmour J, Pande R, Nightingale P, Tan LC, Khan S. Efficacy of intraperitoneal local anaesthetic techniques during laparoscopic cholecystectomy. Surg Endosc. 2011;25(11):3698-705.

[21] 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;79:130-36.

[22] Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. Anaesth Analg. 1995;81:379–84.

[23] Choi GJ, Kang H, Baek CW, Jung YH, Kim DR. Effect of intraperitoneal local anaesthetic on pain characteristics after laparoscopic cholecystectomy. World J Gastroenterol. 2015;21(47):13386–95.

PARTICULARS OF CONTRIBUTORS:

1. Associate Consultant, Department of Anaesthesia, Jupiter Hospital, Mumbai, Maharashtra, India.
2. Professor, Department of Anaesthesia, TNMC and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Charulata Deshpande,
2/24, Haji Ali Govt Colony, K. Khadye Marg, Mumbai-400034, Maharashtra, India.
E-mail: desh56@hotmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jan 01, 2017**
Date of Peer Review: **Jan 28, 2017**
Date of Acceptance: **Apr 06, 2017**
Date of Publishing: **Jul 01, 2017**