



Effects of Intraperitoneal Instillation of Local Anesthetic Agents in Laparoscopic Cholecystectomy –A Clinical Comparison Between 0.5% Lignocaine, 0.2% Ropivacaine & 0.125%Bupivacaine

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ABSTRACT

Introduction: Minimal access surgery offers advantages to patients in terms of reduced peri-operative morbidity and shortened recovery times.

Objective: To compare the effects of intraperitoneal instillation of lignocaine, bupivacaine and ropivacaine in patients undergoing laparoscopic cholecystectomy.

Material and Methods: 75 adult patients of ASA physical status I and II in the age group of 20 – 55 yrs were enrolled in the study and divided into 3 groups of 25 each .Group L :20 ml of 0.5% Lignocaine, Group B: 20 ml of 0.125% Bupivacaine , Group R : 20 ml of 0.2% Ropivacaine respectively were instilled intraperitoneally before CO₂ Insufflation .

Results: Age and sex distribution in all the groups were similar. Heart rate, Systolic & Diastolic Blood pressure, Mean arterial blood pressure and mean trend of SpO₂ in all the groups remained similar over the periods. The mean visual analog score in all groups varied considerably within (between time) and between the groups (treatment) especially comparatively higher in Group L at initial hours 15 min to 30 min and at end hours 12-24 hrs as compared to Group B. On an average, the frequency of dosing and mean no. of rescue analgesic doses were higher in Group L, B than R.

Conclusion: We conclude that intraperitoneal instillation of local anaesthetic is an easy, cheap, and reliable method of providing good perioperative analgesia and hemodynamic stability in laparoscopic cholecystectomy .

Keywords: Bupivacaine, Intraperitoneal Local Anaesthetic , Laparoscopic cholecystectomy,. Lignocaine, Ropivacaine.

INTRODUCTION

Minimal invasive surgery is need of the hour in present surgical era, aims at minimizing surgical trauma and hospital stay.¹ First laparoscopic cholecystectomy was successfully performed by

Phillipe Mouret (1987). A multimodal analgesic regimen adds to a stable hemodynamics, peri operatively and reduced postoperative pain, expediting patients recovery and discharge. Local anaesthetic techniques are a part of multimodal

approach¹. Intra-peritoneal instillation of local anesthetic was first described in 1951 by Griffin et al.². The peritoneal cavity is lined by continuous intact sheet of mesothelial cells (peritoneum) covered by a thin film of peritoneal fluid. There is a normal physiological homeostatic steady state with 0 to 3 mmHg of intra-abdominal pressure (IAP).

During Laparoscopy a purposeful pneumoperitoneum (PNP) is created resulting in volume and pressure controlled rise in IAP, producing a dynamic environment. It involves interaction of mechanical stretching of peritoneum, chemical effects of gas(es) used, biologic forces and processes acting on peritoneal structures and neurohumoral factors resulting in respiratory and haemodynamic changes.

Despite these changes, the effects can be mitigated to achieve safe improved clinical outcomes in laparoscopic surgeries. These pathophysiologic hemodynamic changes can be attenuated or prevented by variety of methods viz., optimizing preload before peritoneal insufflation, vasodilating agents, α_2 -adrenergic receptor agonists, opioids, β -blocking agents and intraperitoneal local anesthetic instillation (IPLA). In Laparoscopic cholecystectomy^{3,4,5} IPLA before creating pneumoperitoneum has resulted in a stable perioperative hemodynamics and decreased the incidence of immediate postoperative pain.

The rationale for intraperitoneal local anaesthetic (IPLA) administration is

- (I) Blockade of free afferent nerve endings in the peritoneum.
- (II) Systemic absorption of local anesthetic from the peritoneal cavity may reduce nociception.
- (III) Local anesthetics have anti-inflammatory actions.

- (IV) IPLA attenuates hemodynamic responses to PNP.

MATERIALS AND METHODS

After approval of Institutional Ethics Committee and written informed consent from each patient a double blind prospective randomized study was conducted during June 2011 to December 2012. 75 Adult patients scheduled for elective laparoscopic cholecystectomy under general anaesthesia were included in the study. All patients were assessed pre-operatively to rule out medical disorders and routine preoperative blood investigations were done.

Inclusion criteria: ASA physical status I and II of either sex aged 20 to 55 years, for Elective Laparoscopic Cholecystectomy.

Exclusion criteria: Patients with H/O chest pain/palpitations/syncope, Respiratory problems, Hepatic or Renal problems. ECG abnormalities and patients with predicted difficult intubation.

Patients were randomly allocated in to three Groups of 25 in each, GROUP-L, GROUP-B and GROUP-R. General anaesthesia technique included Propofol induction (2-2.5 mg / kg) Fentanyl @ 2 μ g/kg, Vecuronium bromide 0.1mg/kg, Endotracheal intubation and IPPV. Intraperitoneal instillation of respective test drug to each group was instilled percutaneously with spinal needle by lifting up the abdominal wall before peritoneal insufflation. Cases in which air bubbles or fecal matter was aspirated were eliminated from the study. Anesthesia maintained with N₂O: O₂ (50: 50) (Circle system-CO₂ absorber) and 0.5% to 1% Sevoflurane- GE Datex Ohmeda 904 E anesthesia workstation. Monitoring, included ECG, NIBP, SpO₂ and EtCO₂. The parameters recorded during study were Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, SpO₂. During study all parameters were noted at various intervals. Pre-operatively i.e. before premedication (basal line value), at Induction, after

Intubation, after PNP and 5,10, 20,30,40,60 min, End of pneumoperitoneum , Extubation and recorded on a master chart (Microsoft excel sheet). Paracetamol i.v. was used as rescue analgesic in all the groups

At end of surgery residual neuromuscular blockade was reversed with neostigmine 60 µg/ kg and glycopyrrolate 10 µg/kg i.v. After satisfying extubation criteria, trachea extubated and patients were transferred to post-anesthesia care unit (PACU) . All the observations were standardized to 60 minutes post- pneumoperitoneum so as to maintain uniformity in all the cases. Results were expressed as Mean and Standard deviation.

The comparison between the means of three groups was done using one way analysis of variance (ANOVA). The intra-group and inter-group analysis of variance is expressed as Mean Squares (MS) and F test statistic is calculated at $\alpha = 0.05$. A p value < 0.05 is considered statistically significant suggesting that there is significant difference of means in at least two groups. Then, BONFERRONI POST-HOC TEST is used to perform multiple comparisons and identify groups among which there is a significant difference, when F test statistic is significant.

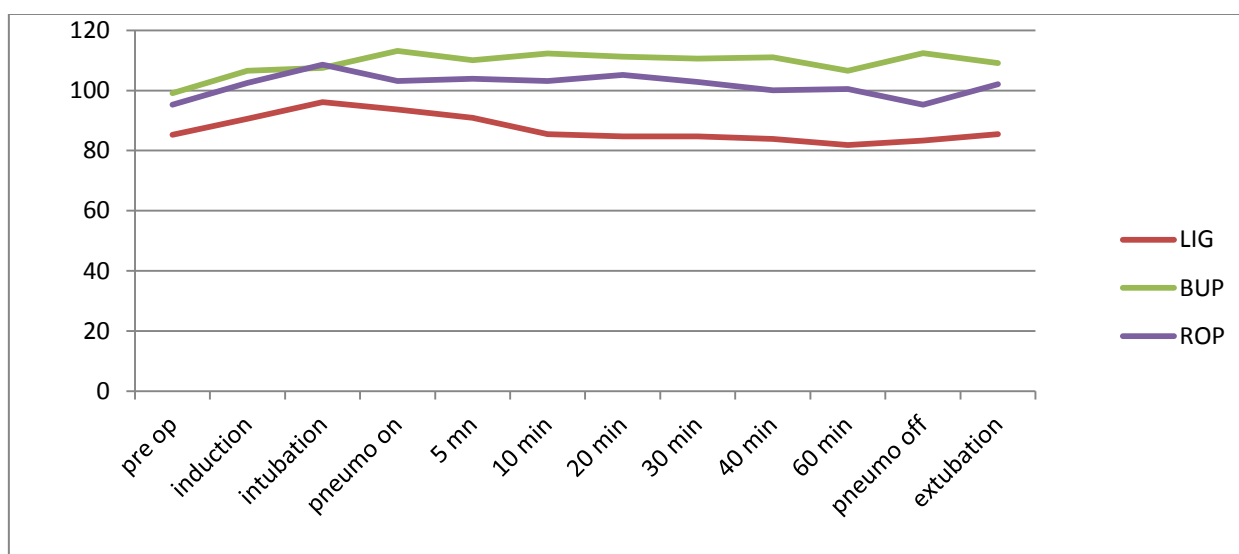
RESULTS

Table 1 . Demographic Profile

Parameters	Group-L (Lignocaine)	Group-B Bupivacaine	Group-R Ropivacaine
Age(Yrs)	40.96	39.60	37.36
Gender Ratio(M:F)	13:12	13:12	11:14

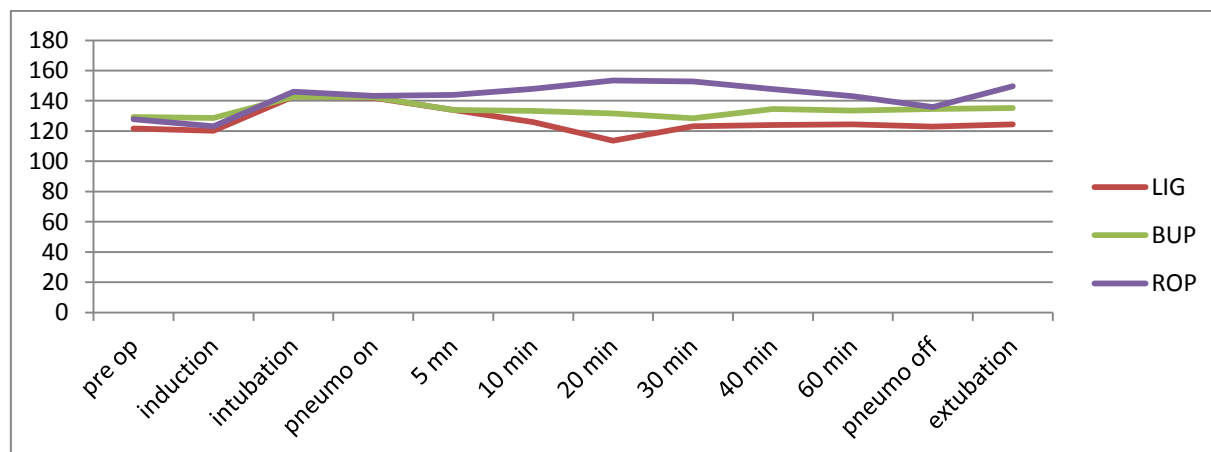
Demographically there is no significant difference were found with respect to age and sex factors.

Figure -2 . Changes in mean pulse rate between three groups.



There is significant difference in the heart rate throughout the surgery between LIGNOCAINE group and the other two groups

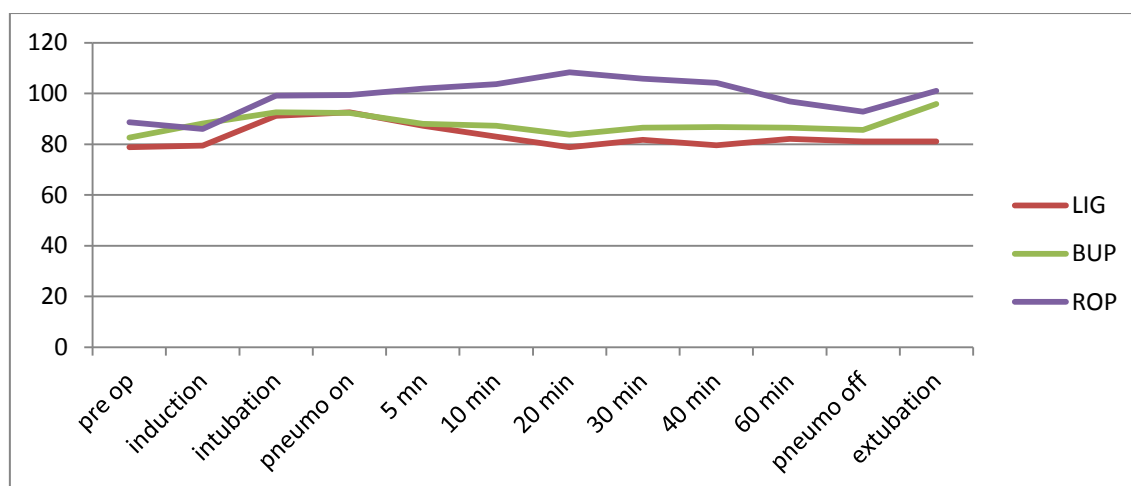
Figure-2: Changes in mean systolic blood pressure between three groups



The systolic blood pressures are not significant between the lignocaine and bupivacaine groups till the first 10 min from start of pneumoperitoneum, then after lignocaine group systolic pressures are on the lower side than bupivacaine group.

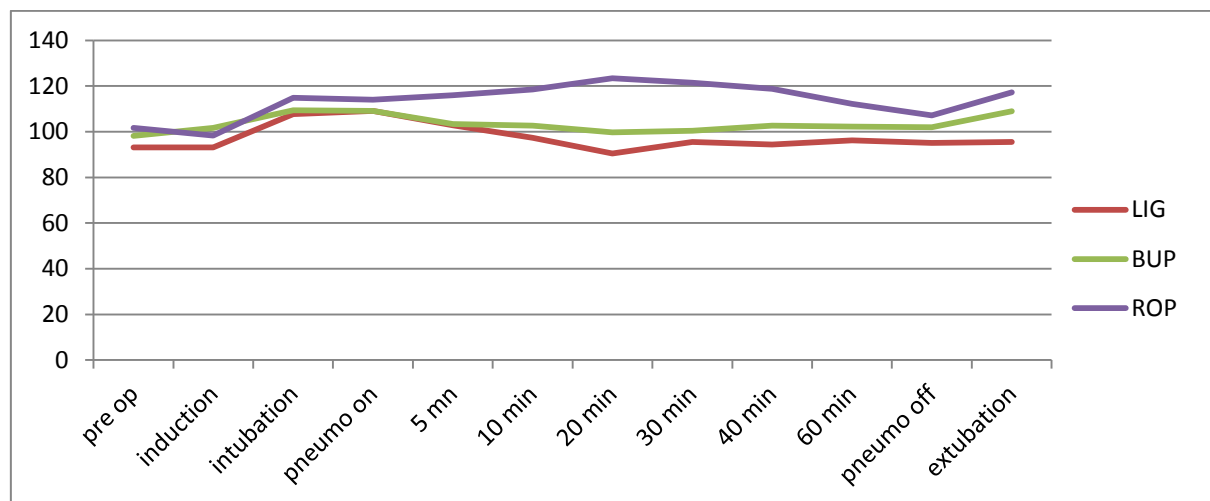
Lignocaine group > Bupivacaine group > Ropivacaine group is the order of effectiveness in attenuating the systolic blood pressure.

Figure-3: Changes in mean diastolic blood pressures between three groups



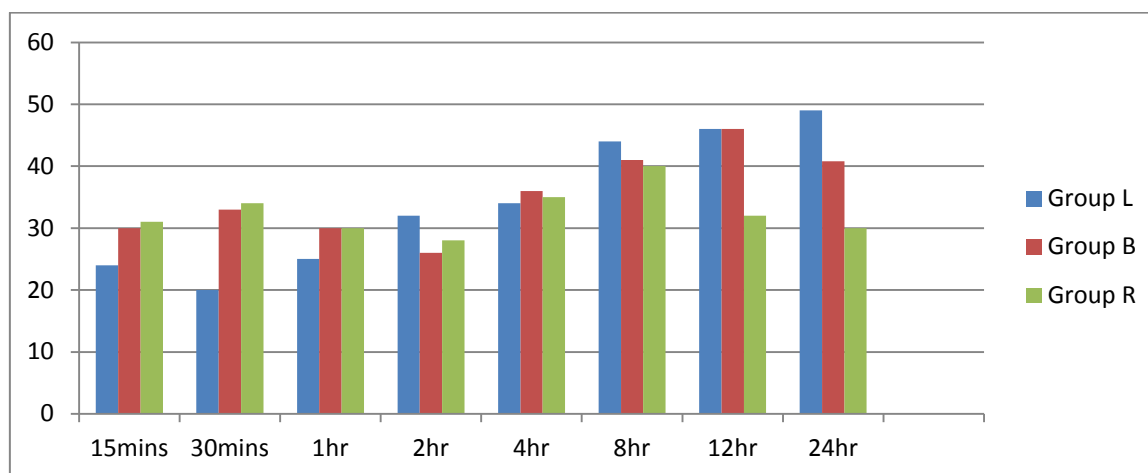
There is not much significance between the lignocaine and bupivacaine groups. Both lignocaine and bupivacaine groups maintained lower levels of diastolic blood pressures than ropivacaine group.

Figure-4: Changes in mean arterial pressure between three groups



Lignocaine group maintained lower levels of MAP throughout the procedure. Whereas in bupivacaine group the MAP levels were maintained lower levels during the late half of the procedure. The order of effectiveness in attenuating the MAP is lignocaine group > bupivacaine group > ropivacaine group.

Figure-5: Post-Operative Pain Levels (VAS SCORES)



In the post operative period, mean VAS in all the study groups varied considerably within (between time) and between groups (treatment) especially comparatively higher in Group L at initial hours 15 min to 30 min and at end hours 12-24 hrs as compared to Group B and Group R. Rescue analgesic was administered for a VAS score of > 40.

Table-2: Requirement of rescue analgesic doses postoperatively.

Rescue Analgesia At Time (min)	Group L (n = 25)	Group B (n=25)	Group R (n=25)
1 st DOSE	26.50 ± 11.40	242.50±118.56	248.50±114.56
2 nd DOSE	246.42±114.42	427.20 ± 125.28	427.20 ± 125.28
3 rd DOSE	360.82±156.72	677.40 ± 134.33	698.54 ± 142.68
4 th DOSE	432.54±221.48	NIL	NIL
5 th DOSE	524.43±264.51	NIL	NIL

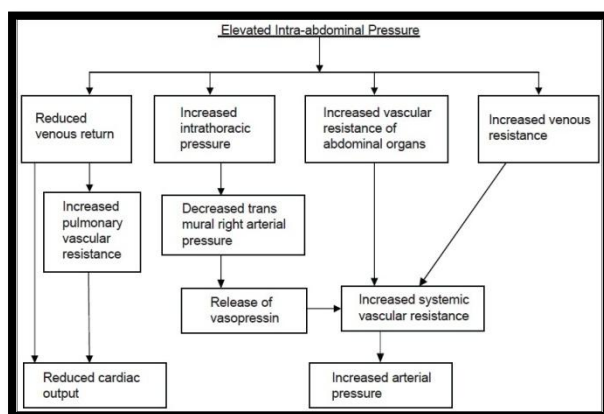
On an average the frequent dosing of rescue analgesia were highest in Group L after initial 4hrs of post operative period followed by Group B & Group R. Further, the requirement in subjects was also highest in Group L (Table-4). The mean no. of rescue analgesia doses of Group L (3.84 ± 0.75) was comparatively higher than both Group B & Group R (2.12 ± 0.33). Comparing mean no. of rescue analgesia doses between the groups, unpaired t-test revealed significantly different no. of rescue analgesia doses among the groups ($p < 0.001$).

In all the groups, the treatment related adverse events were mostly emetic symptoms and shoulder pain with highest being in Group L. However, Hypotension, Bradycardia and Sedation were not seen. The frequency of Emetic symptoms ($\chi^2 = 12.32, p = 0.002$) and shoulder pain ($\chi^2 = 29.55, p < 0.001$) were significantly higher in Group L in immediate postoperative period

DISCUSSION

Peritoneal insufflation during laparoscopic cholecystectomy results in physiological effects via two different mechanisms.⁴

1. Mechanical effects relating to increased intraperitoneal pressure.



2. Chemical effect of CO₂ include – Dessication , Hypoxia and Acidosis.

Cardiac Arrhythmias during laparoscopy are due to - Hypercarbia, Acidosis, Sympathetic stimulation from decreased venous return and Vagal

stimulation(Bradyarrhythmias) by stretching of peritoneum.

Moderate to severe hypercarbia – PVCs, VT and even VF.

Prevention - minimizing IAP (≤ 12 mm of Hg) and proper preoperative hydration and monitoring the end-tidal CO₂ (et-CO₂).

Postoperative pain in Laparoscopic Cholecystectomy is multifactorial in origin, and IPLA is one of technique in multimodal therapy to optimize pain relief. Previous studies agree that pain from laparoscopy consists of three components, visceral, parietal, and referred shoulder pain.⁶ caused by stretching of the intra-abdominal cavity 2 (Joris et al 1995), peritoneal inflammation and phrenic nerve irritation due residual carbon dioxide.

Several studies have shown that visceral pain is the major component of pain during laparoscopy. Intra-peritoneal injections of local anaesthetic (IPLA) have been used as "visceral blocks" since as early as 1950 and proposed to minimize postoperative pain 5 (Zmora et al 2000) and attenuate hemodynamic responses to PNP⁶. Local anaesthetics are also known to have anti-inflammatory actions⁴ and mechanisms may be prostaglandin antagonism, inhibition of leukocyte migration and lysosomal enzyme release. A proinflammatory cytokine cascade in the peritoneal cavity, with direct action on the visceral afferents and vagus as a major vehicle, is a feasible contributor to postoperative visceral pain perception and the "sickness response." By using IPLA it may be possible to modulate peritoneal and visceral signaling to the brain, thereby attenuating the metabolic impact of visceral surgery. Kahokehr et al. investigated the effects of intraoperative peritoneal instillation of ropivacaine after colectomy improves early surgical recovery.⁷

Recently peripheral use of local anesthetics for postoperative pain relief has become a popular practice in laparoscopy surgeries.⁶ Labaille et al.

have shown intraperitoneal local anaesthetic instillation to be safe, with a pharmacokinetic profile similar to that of extravascular administration and no toxic local anesthetic plasma concentrations. Intraperitoneal instillation of 20 ml of 0.5% bupivacaine provides effective analgesia with plasma concentration below toxic levels (0.92-1.14 µg/ml). Several reports^{9,10} have shown that the range of mean plasma concentration after intraperitoneal administration of plain bupivacaine 100-150 mg. is well below toxic concentration of 3µg/ml. Narchi et al. showed that intraperitoneal instillation of 100 mg bupivacaine did not cause toxicity. This technique is safe with good pain relief in initial few hours post operatively.⁸

Patric Narchi et al. have reported that intraperitoneal instillation of both bupivacaine and lignocaine are effective in reducing perioperative pain for 24 hours.⁸

Studies conducted by Chundrigar et al. and Stein et al. showed similar results with mean duration of analgesia lasting for 2-8 hours only, which is in concordance with pharmacological profile of the drug also.^{11,12} Malhotra et al. found that 100 mg of intraperitoneal bupivacaine provides pain relief for a longer duration (8 hours) compared to 50 mg of drug (4-6 hours). Analgesic requirement was also less in the 100 mg group after laparoscopy surgery.¹³

There are studies indicating the usefulness of IPLA for postoperative analgesia. Most of these studies have been on Bupivacaine and its usefulness in postoperative analgesia in view of its longer duration of action and stable hemodynamics in the postoperative period due to good comfort levels of the patient. There are no significant studies on the usefulness of instillation of local anaesthetics into the peritoneal cavity in attenuating haemodynamic responses in laparoscopic surgeries. This idea of utilizing, local anaesthetic agents like lignocaine, bupivacaine and ropivacaine in our study and is based on the fact that these drugs not only have the potential for

postoperative analgesia but also peri-operative analgesia.

When the abdominal cavity is anaesthetized by local anaesthetic agents due to the topical action and subsequent systemic benefits, instillation of CO₂ in high pressure in laparoscopy doesn't lead to much stimulation of mechanoreceptors and stretch receptors and the subsequent increases in pulse rate and blood pressure.

Our study is simply an extension of the benefits of local anesthetic agents used in postoperative analgesia to perioperative analgesia. Based on the fact, that a good depth of anaesthesia and analgesic comfort leads to minimal or negligible hemodynamic disturbances due to laparoscopy. All the three drugs lignocaine, bupivacaine and ropivacaine have topical as well as systemic analgesic properties, and this is what we have preferably utilized in our study. When a drug can be effective in the postoperative period for analgesia it has to be effective also in the perioperative period.

Many methods are described in preventing hypertension tachycardia due to pneumoperitoneum and local anesthetics are a part of it. Local anesthetics are being used by other methods (viz., local infiltration) but none have been utilized or described by intraperitoneal route. Statistical analysis of our study reveals that lignocaine 0.5% was better and consistent in maintaining stable haemodynamics intra-operatively than the bupivacaine 0.125% and ropivacaine 0.2%

CONCLUSION

Intraperitoneal local anesthetic (IPLA) instillation before creating pneumoperitoneum is an easy, effective and very useful technique to alleviate perioperative hemodynamic perturbations and provide effective analgesia.

In our study it was concluded that intraperitoneal instillation of 0.5% lignocaine was superior to 0.125% bupivacaine and 0.2% ropivacaine in the initial periods of PNP. BUPIVACAINE and ROPIVACAINE show their benefits towards the

later half of operative procedure and post operative period. Ropivacaine in view of better cardiovascular safety profile can be an alternative for Bupivacaine .

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