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A Comparative Study of Intraperitoneal Instillation of Different Volumes and Concentrations of Bupivacaine Versus Transversus Abdominis Plane Block (Tap) for Post-Operative Analgesia in Laparoscopic Cholecystectomy

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ABSTRACT

Background : Laparoscopic [LC] surgeries or minimally invasive surgeries are associated with lesser parietal pain and haemorrhage, compared to the open surgeries. However visceral pain persists. The effect of volume and concentration on intra-peritoneal instillation of local anaesthetics for pain relief has not been studied . In this study we have compared the intra-peritoneal instillation of local anaesthetic with transversus abdominis plane block (TAP). This study is aimed at assessing the superiority of effect of volume of local anaesthetic instilled intra-peritoneally versus TAP block on post-operative pain relief in laparoscopic cholecystectomy.

Methods: Following ethical committee clearance, 60(power of 80%, α error -95%, effect size -200min, SD -200 min) patients between 18-60 years of either sex undergoing laparoscopic cholecystectomy under general anaesthesia were enrolled in this prospective randomized double blind study. General anaesthesia technique was standardized and at the end of surgery, Group A (n=20) received 50 ml of 0.2% bupivacaine intra-peritoneally, whereas group B (n=20) received 100 ml of 0.1% bupivacaine and Group C (n=20) patients received ultrasound guided sub-coastal TAP block bilaterally with 0.2% bupivacaine and normal saline at the start of the surgery. Post operatively, pain was assessed at rest, at respiration and shoulder pain using VAS score by blinded observer. Time to first rescue analgesia and 24 hr rescue analgesic requirement was recorded. Independent sample t test and Mann Whitney U test were applied .

Results: Demographics were comparable. Duration of analgesia was longer in group B [Group A – 480(300-480)minutes, Group B – 960(660-1440) minutes Group C- 360(360-390) minutes] $p < 0.01$. 24 hr analgesic consumption or requirement of rescue analgesia [Paracetamol Group A – 2225±800.2 gm, group B 1052±904gm, Group C 2525±598.6 gm,] $p < 0.01$ and VAS scores (table 1) were lower in group B .

Conclusion: Low concentration high volume of bupivacaine is associated with longer duration of post operative analgesia compared to high concentration low volume and TAP block

Key words: Intraperitoneal, Laproscopic, Cholecystectomy, Bupivacaine, Concentration, Volume, Transversusabdominis plane (TAP)block.

Introduction :

About 10% to 15% of the adult population (females > males) have gallstones. Between 1% to 4% become symptomatic . Cholecystectomy is the mainstay treatment for symptomatic gallstones. Laparoscopic[1] cholecystectomy (removal of gallbladder through a keyhole incision, is now the preferred method of cholecystectomy. While laparoscopic cholecystectomy is generally considered less painful than open surgery- lesser parietal pain and haemorrhage which leads to quicker wound healing and lesser post operative respiratory insult . Despite the mentioned explanation pain is one of the major reasons for delayed hospital discharge after laparoscopic cholecystectomy. Various theories have been put forth to explain this :

- Intra-peritoneal insufflation with carbon di oxide can cause the loss of suction force between the liver and the diaphragm which might cause the referred shoulder pain.
- The carbonic acid that is generated due to the reaction of carbon di oxide intra-peritoneally can cause the peritoneal irritation
- Insufflation causes the parietal stretch which can release the inflammatory markers
- The blood in the peritoneum can cause peritoneal irritation[2]

Multiple strategies has been adopted like – complete removal of the gas , leaving a drain post operatively for effective draining of blood and carbon di oxide but all have been ineffective. Field block has also been tried[3]Multimodal analgesia is therefore necessary for post-operative analgesia.

Intra-peritoneal instillation of local anaesthetic (LA) reduces pain by acting on free nerve endings[4]. Studies assessing the effect of Intra-peritoneal instillation of local anaesthetic on pain has shown mixed results[5,6] . A recent Cochrane review [7] Marginal increase in duration of analgesia after intra-peritoneal instillation of bupivacaine.

Transversus abdominus plane block (TAP) is a peripheral nerve block used to anaesthetize the somatic nerves supplying anterior abdominal wall and drug is deposited between internal oblique and transversus abdominis muscle. [8]

Ultrasound sound guided TAP block enables better deposition of drug into the plane and found to provide better analgesia in laparoscopic cholecystectomy. [9]

There is no published data regarding effect of volume and concentration of LA instilled intra-peritoneally on quality and duration of post op analgesia and comparison of intra-peritoneal instillation of LA versus TAP block for post op analgesia.

Hence this study was designed to assess the effect of volume and concentration of LA instilled intra-peritoneally and TAP block on post operative analgesia in laparoscopic cholecystectomy.

AIMS AND OBJECTIVES :

- To compare the effect of intra-peritoneal instillation of different volumes and concentrations of bupivacaine versus TAP block on :

I. Duration of post op analgesia.
II. Requirement of rescue analgesia in 24 hours.
III. Side effects ,if any.

METHODOLOGY

This study was conducted in Bangalore Medical College and research institute (BMCRI) and associated hospitals in 2017-2018.

INCLUSION CRITERIA

- Patients aged between 20 – 60 years of either gender posted for elective laparoscopic cholecystectomy
- Patients willing to give informed and written consent
- Patients weighing between 20-60 kg
- Patients belonging to ASA I to ASA II

EXCLUSION CRITERIA

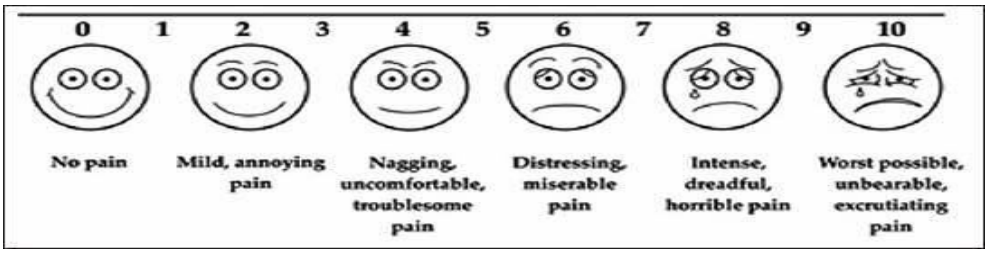
I. Local site infection.
II. Patients with uncontrolled diabetes mellitus.
III. Patients with systemic disorders . (cardiovascular, respiratory and renal systems)
IV. Allergy for local anaesthetics.
V. Chronic pain syndrome.
VI. Neurological disorders ; on psychiatric medications.
VII. Treatment with steroids prior to surgery or regular NSAID use.

METHODS OF COLLECTING DATA :

- This was a prospective randomized observational double blind study. After obtaining institute ethical committee clearance 62 patients were enrolled in the study .Two of them were excluded as they did not meet the inclusion criteria.60 patients were randomized into 3 groups. **Group A** : 50 ml of 0.2% bupivacaine intra-peritoneally **Group B** : 100 ml of 0.1% bupivacaine intra-peritoneally **Group C** : 50 ml of 0.2% bupivacaine via TAP block (25 ml on each side) . Allocation concealment done using sequentially numbered closed envelope method. This was double blind study as the patient were not aware to which group they were allocated to and the anaesthetists who was assessing the post operative pain and vital parameters were also not aware of the group to avoid the observational bias . The patients were assessed in the pre-anaesthetic evaluation well in advance and informed written consent was obtained .

The Sample size was calculated based on pilot study with the hypothesis that high volume low concentration bupivacaine might provide longer duration of analgesia. The power was at 80 % and with an alpha error at 0.05 , keeping the effect size of 200 min (25% difference between two groups with respect to duration of analgesia) and SD 200 minutes a minimum of 16 patients were required in each group .20 patients were included in each group to compensate for drop outs.

- Pre-anaesthetic evaluation was done and patients were educated about VAS (visual analogue scale) along with regular instructions and informed written consent was obtained



- Patients were NPO (nil per oral) for 8 hours prior to surgery.Patients were pre-medicated the night before surgery -Tab Ranitidine 150 mg HS and Tab Alprazolam 0.5 mg HS .IV(intravenous) access was obtained in the pre-operative room and Ringer's lactate was connected after checking the vitals. After shifting the patient to the OR (operating room) monitors were connected (ECG ,SPO_2, NIBP, Entropy ,NMT,$ETCO_2$) Anaesthesia was administered by an anaesthesiologist who was not involved in post-operative monitoring of the patient .Patients were not aware about their group allocation . Patients were premediated with Inj Glycopyrrolate 0.01 mg/kg (iv) ,Inj Midazolam 0.2mg/kg(iv) ,Inj Fentanyl 2µg/kg(iv) . Induction was done using Inj Propofol (1-2.5 mg/kg) (iv)(till entropy was < 60) Inj Vecuronium (0.12mg/kg)(iv) and patient was intubated .Maintenance : 40% oxygen in air ,Intra abdominal pressure was maintained between 12-14mmhg , 0.2%-1% isoflurane (to maintain entropy < 60 and difference between RE and SE <10) ,Ventilation (tidal volume of 6-8ml/kg) to maintain the end tidal C02 between 35-40 mmHg ,intermittent doses of Inj vecuronium bromide(0.01mg/kg)(iv)

- Intra operatively -HR , SBP , DBP ,MAP, SPO2 IAP was recorded at 5 min .Supplemental dose of fentanyl (1µg/kg)(iv)was given if there was > 20% increase in the HR and BP. At the end of the surgery after complete evacuation of CO_2 ,drug solution was prepared by an anaesthesiologist not involved in the study according to the numbers in the envelope**Group A** : given *50 ml* of *0.2%* bupivacaine **Group B** : given*100 ml* of *0.1%* bupivacaine .Through the retraction port onto the gall bladder bed and sub diaphramatic region and Trendelenberg position was given for 10 min . GROUP C patients received TAP Block USG guided block was administered sub-coastally bilaterally –25 ml of 0.2% on each side . Patients were extubated and shifted to the recovery room .In the recovery room : HR, SBP, DBP, MAP .VAS for pain – pain at rest (VAS static) and Pain on deep inspiration (VAS dynamic)was recorded at immediate post-operative(0),1^{st} ,2^{nd} ,3^{rd} ,4^{th} ,5^{th} ,6^{th} ,8^{th} ,12^{th} ,16^{th} & 24^{th} post-

operative hours. Duration of analgesia : time interval from drug instillation to the demand for first rescue analgesic.Patient was given Inj paracetamol 15mg/kg as an rescue analgesia when the VAS reached a value of 3 or more (maximum of 3 doses in 24 hours)Even after 20 min of Inj Paracetamol infusion if pain persists Inj Tramadol 2mg/kg was given intravenously .Side effects like peri-oral numbness ,headache, blurring of vision , tachycardia was all monitored .

STATISTICAL ANALYSIS

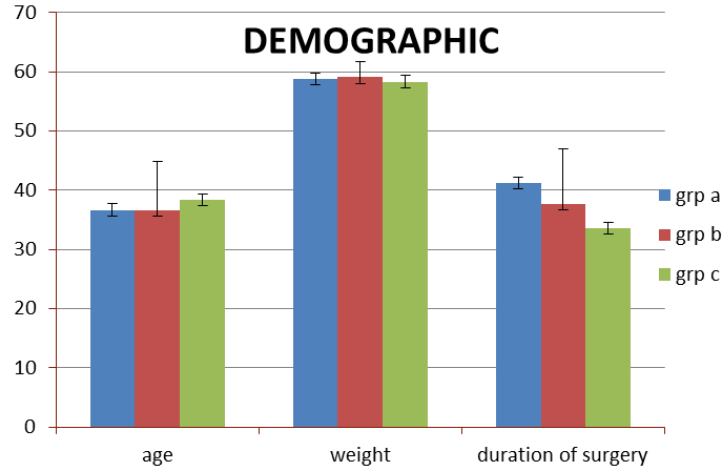
- Data was tabulated in microsoft excel sheet after collection .Quantitative variables were expressed as mean ± SD/median(IQR) and categorical variables as frequencies & percentages.*Shapiro-Wilk Test* was applied for normality of data (quantitative data).Chi-Square/Fisher exact test was applied for categorical data.One way ANOVA/ Kruskal Wallis test for was used for quantitative data.Mann-Whitney U test was inter group comparison.P value < 0.05 was considered statistically significant.Medcalc, OpenEpi.com softwares were used for the analysis .

RESULTS

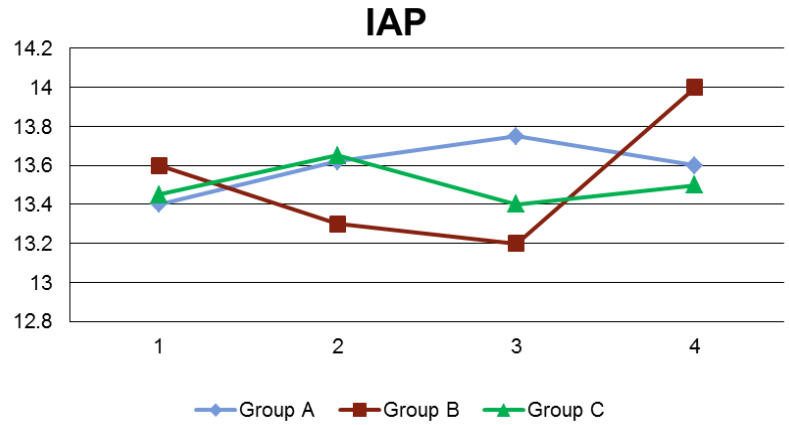
The study empanelled 62 patients, they were accessed for eligibility to be included in the study. Two out of the 62 patients did not meet the eligibility criteria and were excluded from the study .This was a prospective randomized observational double blind study .Allocation concealment done using sequentially numbered closed envelope method.60 patients were randomized into 3 groups**.Group A** : *50 ml of 0.2%* bupivacaine intra-peritoneally .**Group B** : *100 ml of 0.1%* bupivacaine intra-peritoneally. In Group A and Group B at the end of the surgery after complete evacuation of CO_2 ,drug solution was prepared by an anaesthesiologist not involved in the study according to the numbers in the envelope.Through the retraction port onto the gall bladder bed and sub diaphramatic region and Trendelenberg position was given for 10 min .**Group C** : *50 ml* of 0.2% bupivacaine via TAP block (25 ml on each side)- USG guided block was administered sub-coastally bilaterally –25 ml of 0.2% on each side

Demographic comparison.

Table



There was no statistically significant difference amongst the groups with respect to - age , gender.



The intra abdominal pressure(IAP) was maintained under 14 mmHg when checked at every 15 minutes interval after the insulffation of the abdomen with carbon di oxide.

Post operative analgesia :

Duration of post-operative analgesia was assessed post-operatively by the post –operative staff who were not aware of which group the patient belonged to avoid the bias.

Various parameters were used to assess and analyse the pain –

- In the recovery room :
  - Heart rate (HR),Systolic blood pressure(SBP),diastolic blood pressure(DBP),mean arterial pressure(MAP)
  - VAS (visual analogue scale) for pain –
    - pain at rest (VAS static),
    - Pain on deep inspiration (VAS dynamic)

Recorded at immediate post-operative zero(immediately after shifting) ,1st ,2nd ,3rd ,4th ,5th ,6th ,8th ,12th ,16th & 24th post-operative hours.

- Duration of analgesia(Duration of analgesia : time interval from drug instillation to the demand for first rescue analgesic.) was longest in Group B (high volume low concentration bupivacaine ie *100 ml* of *0.1%* bupivacaine) being 960 minutes compared to Group A(low volume high concentration bupivacaine *50 ml* of *0.2%* bupivacaine) and Group C (USG guided block was administered sub-coastally bilaterally –25 ml of 0.2% on each side) which is statistically significant with a p value of <0.01

- Requirement of rescue analgesia (Patient was given Inj paracetamol 15mg/kg as an rescue analgesia when the VAS reached a value of 3 or more -maximum of 3 doses in 24 hours.Even after 20 min of Inj Paracetamol infusion if pain persists Inj Tramadol 2mg/kg was given intravenously) was significantly low in Group B being 1050±904 g in comparison to Group A (2225±800.2 g) and Group C (2525±598.6 g) was statistically significant with a p value <0.01.

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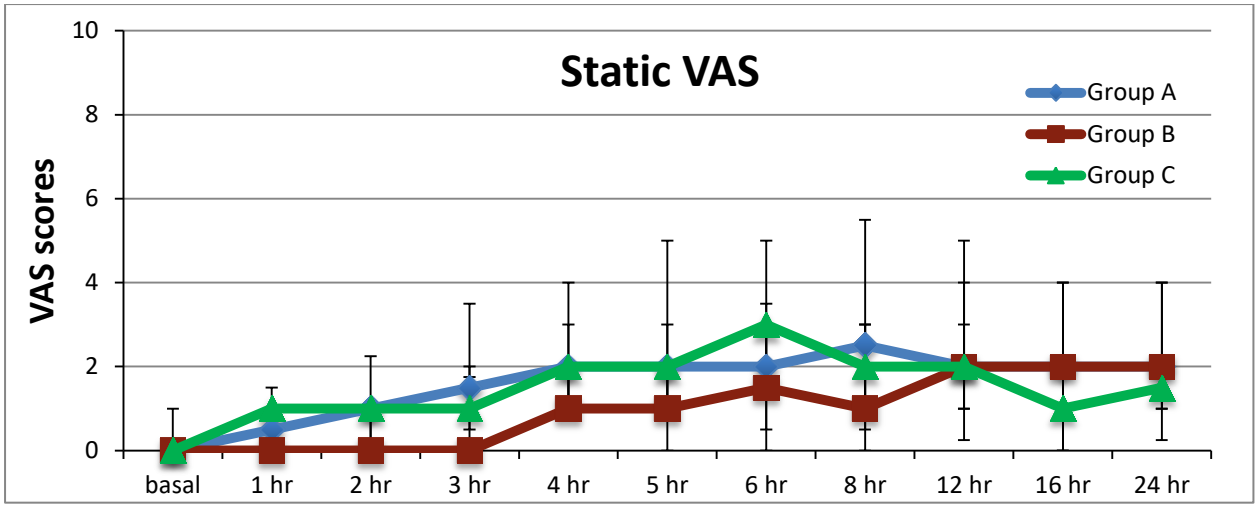
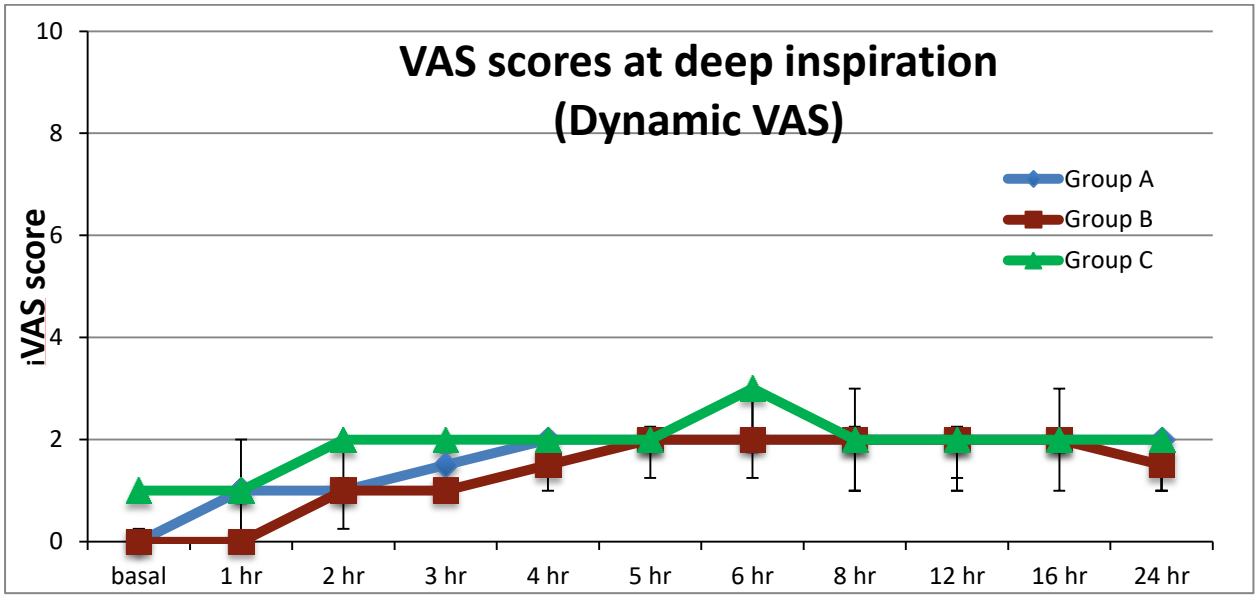


Average static VAS (pain at rest) was less in Group B(1.04±0.4) in compared to Group A(1.55±0.2) and Group C(1.4±0.3) with p value <0.01



Average Dynamic VAS (pain on deep inspiration) was less in Group B(1.45±0.4) in compared to Group A (1.85±0.3) and Group C(1.81±0.2) with p value <0.01 Vitals intra-operatively was comparable across the groups-

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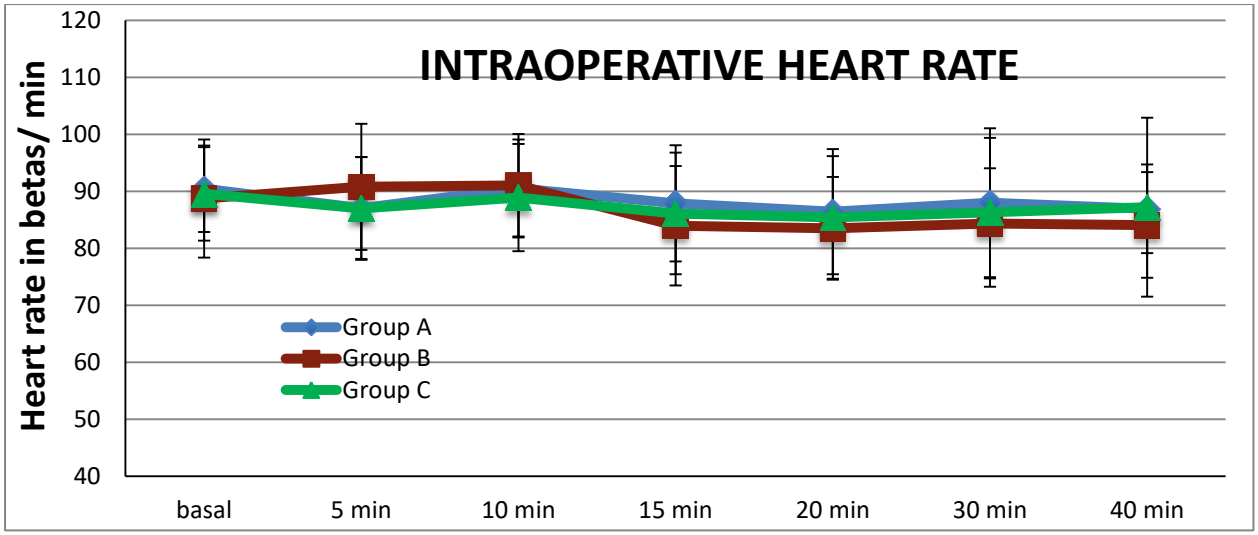

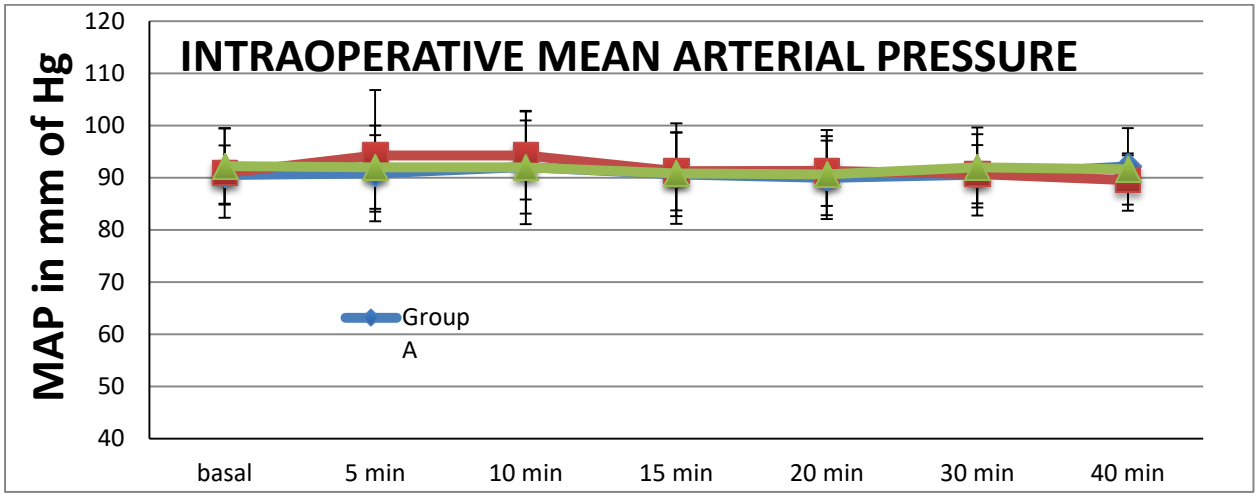

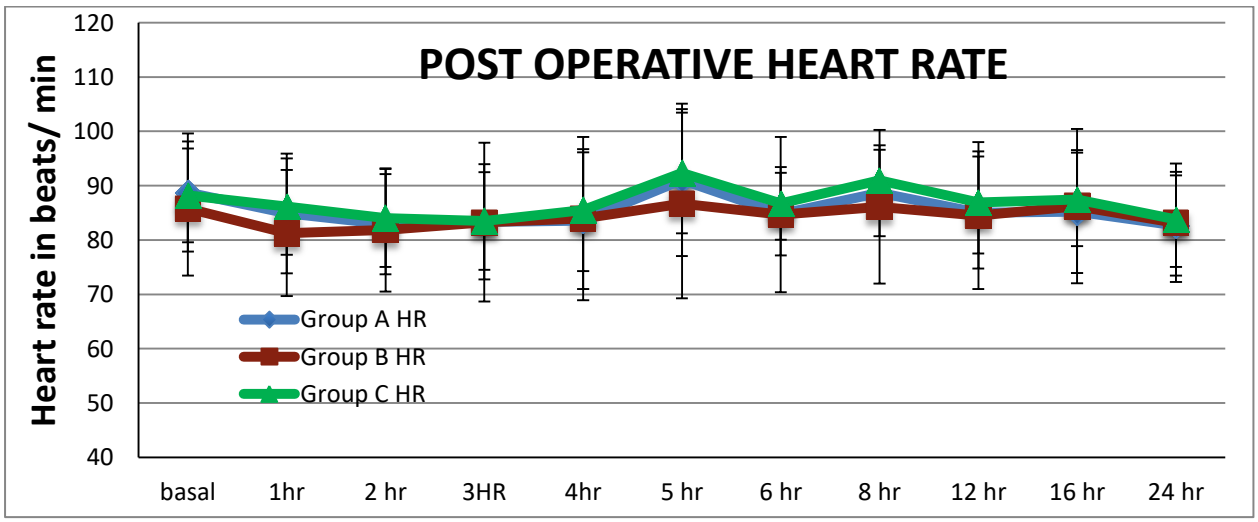

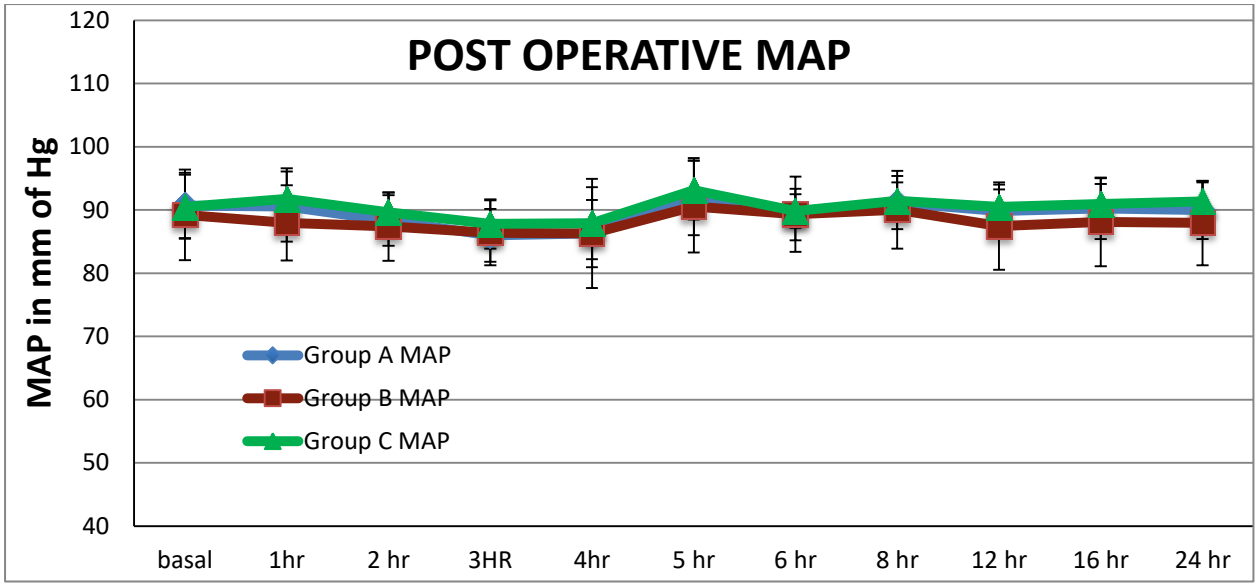

- Supplemental dose of fentanyl : 25µg used in one patient in Group A
- Inj Tramadol as rescue analgesia was not given to any of the patients
- One patient in Group B complained of pain abdomen on 3rd post-operative day (??Adhesion)

DISCUSSION :

Laparoscopic cholecystectomy[1] (Laparoscopic [LC] surgeries or minimally invasive surgeries are associated with lesser parietal pain and haemorrhage, compared to the open surgeries is now the preferred method of cholecystectomy. While laparoscopic cholecystectomy is generally considered less painful than open surgery, pain is one the major reasons for delayed hospital discharge after laparoscopic cholecystectomy. The pain after laparoscopic cholecystectomy could be incisional pain, shoulder pain, or abdominal pain . The aetiology of abdominal pain and shoulder pain after laparoscopic cholecystectomy is unclear. Peritoneal irritation, caused by carbonic acid and creation of space between diaphragm and liver, leading to loss of suction support of the heavy liver have been suggested as possible mechanisms of pain.

However, use of an overnight drain to let out the gas on the presumption that carbon dioxide in the sub-diaphragmatic space is the reason for the pain has not been effective in the reduction of pain.

Newer theories of visceral pain has been postulated -

- peritoneal stretching (insufflation)
- release of inflammatory mediators
- Irritation due to collected blood.[3]

Multimodal analgesia is therefore necessary for post-operative analgesia[4,5]Local anaesthetics inhibit voltage-gated sodium channels. This results in decreased excitability of nerves

transmitting pain The intra-peritoneal instillation of the local anaesthetic could be by washing the gallbladder bed of the liver with the local anaesthetic instillation under the diaphragm , or as an aerolized spray in the general peritoneum could dilute the inflammatory substances .
Transversus abdominus plane block (TAP) is a peripheral nerve block used to anaesthetize the somatic nerves supplying anterior abdominal wall and drug is deposited between internal oblique and transversus abdominis muscle which can block the incisional or port site block. Ultra sound guided TAP block enables better deposition of drug into the plane and found to provide better analgesia in laparoscopic cholecystectomy.
There has been No published data regarding:

- Effect of volume and concentration of LA instilled intra-peritoneally on quality and duration of post op analgesia.
- Comparison of intra-peritoneal instillation of LA versus TAP block for post op analgesia.

Hence this study was designed to assess effect of volume and concentration of LA instilled intra-peritoneally and TAP block on post operative analgesia in laparoscopic cholecystectomy.

In this study we enrolled 62 patients out of which 2 did not fit into the inclusion criteria and in total 60 patients were enrolled who then grouped into three groups (Group A Group B and Group C) This was a prospective randomized observational double blinded study .**Group A** : *50 ml of 0.2%* bupivacaine intra-peritoneal **Group B** : *100 ml of 0.1%* bupivacaine intra-peritoneally. In Group A and Group B at the end of the surgery after complete evacuation of CO_2 ,drug solution was prepared by an anaesthesiologist not involved in the study according to the numbers in the envelope.Through the retraction port onto the gall bladder bed and sub diaphramatic region and Trendelenberg position was given for 10 min .**Group C** : *50 ml* of 0.2 bupivacaine via TAP block (25 ml on each side)- USG guided block was administered sub-coastally bilaterally –25 ml of 0.2% on each side Patients receiving high volume low concentration bupivacaine (Group B) hadLonger duration of post operative analgesia,Lesser requirement of rescue analgesia and Fewer side effects

When compared to patients receiving low volume high concentration bupivacaine(Group A) and TAP block(Group C)
The study done by Jiranantarat V et al[9] (Jr of medical asso. Thailand) 0.25% 20 ml bupivacaine was instilled intraperitoneally among the subjects but there was no post operative analgesia.In yet another study by Ahmad et al [10] (British journal of surgery) the same concentration as Jiranantarat V et al [9]was used with higher volume 0.25% 40 ml bupivacaine there was no significant pain relief.

Abdel Raouf et al[7] (Eygptian journal of anaesthesia) conducted with 50 ml bupivacaine with 0.25% concentration which did not show any pain relief.Rajesh Kumar Meena et al[3] (International journal of anaesthesiology,pain,icu) conducted the study with similar concentration and volume as Abdel Raouf et al (Eygptian journal of anaesthesia) 0.25% 50 ml bupivacaine and noticed post-operative analgesia .

There were varying outcomes with the various volumes of drug used in studies ,in our study we therefore used 50 ml and 100 ml keeping the mass of the drug constant.

Cochrane review[6] showed lesser vas when drug was instilled at the end of the surgery.
In our study drug was instilled at the end of the surgery after desufflation.

In a study conducted by Scheinin et al [11](ACTA Anaestisiol Scand.1995 Feb;39(2): 195-8 with 60 subjectsWith 20 patients receiving 0.15% in 100 ml of bupivacaine was instilled in 20 patients - there was no significant difference in time to first demand of rescue analgesia , severity of post operative pain and amount of rescue analgesia.In our study 20 patients received 0.1% 100 ml bupivacaine - had post operative analgesia for an average duration of 960 minutes and the amount of rescue analgesia required was significantly low.

El-Dawlalty et al[8] (BrJ Anaesth 2009 Jun 102(6):736-7- A comparative study with 42 patients, Group A who recieved 0.5% 20 ml bupivicaine and Group B received tap block.Group A had lesser requirement of opioid in the post-operative period. We observed similar results with lesser requirement rescue analgesia.

Yet another study by Rao V Kadam et al[12] 2011 (Journal Of Anesthesiology , Clinical pharmacology)-Intraperitoneal instillation of la provided better anlagesia than tap block which can possibly be attributed to lack of effect of tap block on visceral pain.
The limitations of the study were :

- The blood levels of the drug was not measured.
- The patients were not followed up beyond 24 hours hence effect on duration of hospital stay and recovery could not be assessed.

CONCLUSION :

Group B - Duration of analgesia(Duration of analgesia : time interval from drug instillation to the demand for first rescue analgesic.) was longest in Group B (high volume low concentration bupivacaine ie *100 ml* of *0.1%* bupivacaine) being 960 minutes compared to Group A(low volume high concentration bupivacaine *50 ml* of *0.2%* bupivacaine) and Group C (USG guided block was administered sub-coastally bilaterally –25 ml of 0.2% on each side) With requirement of lesser rescue analgesia and lower VAS score .

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