International Surgery Journal
Vasava MA et al. Int Surg J. 2019 May;6(5):1589-1595
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20191875

Original Research Article

Evaluation of superiority of preemptive analgesia with instillation of 0.5% bupivacaine before rather than after surgery for laparoscopic cholecystectomy

Manojo A. Vasava*, Jay M. Makadia

Department of Surgery, Govt. Medical College, Baroda, Gujarat, India

Received: 27 October 2018
Revised: 27 March 2019
Accepted: 28 March 2019

***Correspondence:**
Dr. Manojo A. Vasava,
E-mail: jmmakadia2111@gmail.com

ABSTRACT

Background: The objective of the study was to evaluate the superiority of preemptive analgesia with instillation of 0.5% bupivacaine before rather than after surgery for laparoscopic cholecystectomy.
Methods: A prospective, randomized study of 264 patients in whom laparoscopic Cholecystectomy (LC) was conducted in the department of General Surgery at the SSG and Medical College Baroda during a period of 25 months from October 2010 to October 2012. Randomization was done with prepared close enveloped which randomly allocate the patient in either group A or B. Data collected from each patient were: age, sex, ASA score, hospital stay, duration of surgery, no of trocar used, first request for analgesics, vomiting, duration of surgery, intraperitoneal drain was kept or not , length of hospital stay, any other postoperative complication.
Results: During the period of 24 months total 264 patients were undergone cholecystectomy. On comparison between Group A and B, data shows that the mean VAS is less at all assessment (4, 8 & 24 hrs) for Group A as compared to Group B. Mean parietal pain score VAS is less for Group B as compared to Group A at all assessments.
Conclusions: Use of bupivacaine in optimal dose in GB bed reduced the visceral pain and use in skin, SC tissue, muscular tissue reduced the parietal pain. Use of bupivacaine before GB removal is much more cost effective than after removal of GB.

Keywords: Laparoscopic cholecystectomy, Preemptive analgesia, Visual analouge score

INTRODUCTION

Laparoscopic cholecystectomy (LC) has become the gold standard for treatment of benign gall bladder disease. Laparoscopy provides many benefits over conventional open procedures including faster recovery time, shorter hospital stay, less pain, and in some cases, fewer complications. Despite minimal invasive nature of laparoscopic surgery, pain may be substantial and limit an otherwise expeditious recovery. After open cholecystectomy pain is usually because of large incision of surgery and is of a parietal type. Pain after LC is multifactorial, with pain arising from the incision sites, the pneumoperitoneum and the cholecystectomy. Pain after laparoscopic cholecystectomy can be visceral pain due to cholecystectomy, can be parietal pain due to skin incision for trocar insertion, can be referred pain due to stretching of fibres of diaphragm and due to pneumoperitoneum.

Many factors play an important role in the causation of pain like Humidity and temperature of gas, pressure of pneumoperitoneum during surgery, residual intra-peritoneal gas at the end of surgery, duration of surgery

and length of trocar incision, trauma caused by cholecystectomy itself, type of gas. Postoperative (PO) pain in turn affects postoperative morbidity, hospital stay, increased financial burden on the patient or the state due to increased duration of hospitalisation and inability of the patient to return to his/her job in time.

A number of studies have been done till date to try to assess the effectiveness of different measures to alleviate the PO operative pain after LC. PO pain management has an important role in preventing the postoperative morbidly and its consequences. Pain management has not been standardised at most medical centres in India and abroad and this is reflected in the number of different pain studies after LC available in literature. Analgesia provided before a noxious stimulus, known as pre emptive analgesia, may prevent physiologic changes, resulting in central sensitization and amplification of pain signals. Pre-emptive local anaesthesia, therefore, may be more effective than postoperative anaesthesia administration at preventing postoperative pain. Many experimental and clinical studies have demonstrated the inhibitory effect of pre-emptive analgesia on the development posttraumatic hyperalgesia, resulting in reduced postoperative pain and total analgesic requirements.[1-4]

Many different methods have been used with conflicting rates of success, to diminish the intensity of PO pain after LC. They include low pressure pneumoperitoneum, gasless technique of LC, use of warm carbon dioxide, peritoneal wash with saline solution, strict surgical technique, perfect haemostasis, trocar site infiltration of anaesthetic drugs, instillation of sub-diaphragmatic region with anaesthetic/analgesic drugs or use of non steroidal anti-inflammatory drugs or dexamethasone. Intensity of pain is also depent on timing of using various type of techniques.[5-7]

Bupivacaine is the most consistently used in studies, typically at a concentration of 0.5%. To gain a major insight into the effectiveness of pre-emptive intra-peritoneal and port site infiltration of Bupivacaine in postoperative pain relief after laparoscopic Cholecystectomy.[8-12]

Bupivacaine is also used in comparison study to test its effectiveness in relieving pain after LC with intravenous analgesics as well saline washing of peritoneum.[13,14]

The present study was carried out in the Department of Surgery Medical College & Sir Sayajirao General Hospital. We hoped to establish conclusive evidence about the efficacy of pre-emptive infiltration of Bupivacaine over infiltration after gall bladder removal and whether one was superior to the other for pain relief. To assess the effectiveness of 0.5% of Bupivacaine for pain control after laparoscopic cholecystectomy (LC) at its optimal dose (2 mg/kg) by intra peritoneal instillation of Bupivacaine with infiltration at each trocar site before dissection of gall bladder. To establish whether either of this procedure is superior to other.

METHODS

A prospective, randomized study of 264 patients of benign Gall bladder disease in whom laparoscopic Cholecystectomy (LC) was conducted in the department of General Surgery at the Sir Sayajirao General Hospital & Medical College Baroda during a period of 25 months from October 2010 to October 2012 In all the cases a detail history, physical examination and investigations were done as per Proforma.

Inclusion criteria

Patients with age >18 years, ASA grade 1 or 2 (American Society of Anaesthesiology) and patients. Posted for elective laparoscopic Cholecystectomy were included in study.

Exclusion criteria

Patients with age <18 years, ASA Grade more than 2 (American Society of Anaesthesiology), pregnancy, acute cholecystitis, choledocholithiasis, conversion of LC to open cholecystectomy, patients allergic to local anesthesia, History of severe systemic disease, After taking informed and written consent, patients were randomized in three groups.

Randomization was done with prepared close enveloped. The day of operation an independent hospital staff randomly opened an envelope with a card in side. Patients were randomized to their respective card group, either ‘A’, or ‘B’.

Group ‘A’ received 2 mg/kg of bupivacaine in 40 ml of saline from which 5 ml infiltration at each trocar site before skin incision, 20 ml of the drug instill under right sub diaphragmatic space, 20 ml of the drug instill over gall bladder through right sub costal trocar incision with 10 cc syringe before dissection of GB

Group ‘B’ received 2 mg/kg of Bupivacaine in 40ml of saline from which, 20 ml of the drug instill in gall bladder fosse through right sub costal trocar incision with 10cc syringe after removal of GB, 20 ml of the drug instill under right sub diaphragmatic space, 5ml at each trocar site after removal of GB

Pre-operative preparation

All patients coming to the Surgical Out-Patient-Department (OPD) with benign Gall Bladder disease were admitted to surgical ward 2 to 3 days before the laparoscopic cholecystectomy. For all patients undergoing laparoscopic Cholecystectomy following preoperative preparation was done. Abdominal ultrasonography, X-ray chest, ECG, complete blood

count, liver function test, random blood sugar, blood urea, serum creatinine.

Technique of laparoscopic cholecystectomy

A fully informed written consent was taken informing about the laparoscopic procedure, its complications and the need, if necessary for conversion to open cholecystectomy. In all patients undergoing laparoscopic cholecystectomy of inj. Cefotaxime (1 gm) was given preoperatively. General anaesthesia was given to all the patient with routine pre medication. Patient was placed in supine position with 150 head tilt which improves diaphragmatic function and respiratory status. Catheterization was done if the bladder was found to be full. Pneumoperitoneum was created either open or closed method according to surgeon preference and gall bladder was dissected out from its bed by blunt and sharp dissection and was removed either from subcostal or umbillical port according to surgeon's preference. Assessment of the nature of pain was done (visceral, parietal or shoulder pain) & its intensity was recorded on VAS (visual Analogue scale) after 4 hrs, 8 hrs & 24 hrs of surgery.

The VAS was a 10 mm horizontal scale representing varying intensities of pain, with end points labelled as ''no pain'' and ''worst possible pain." VAS scale was explained to the patient preoperatively.

Following data was also recorded:

- First request for analgesics
- Vomiting
- Duration of surgery
- Intraperitoneal drain was kept or not
- Length of hospital stay
- Any other postoperative complication.

Statistical analysis

Continuous data between the two groups were recorded as mean±standard deviation and compared by the nonparametric Mann whiteny U test. A $p<0.05$ was considered statistically significant. All statistical analyses were performed by using SPSS 17.0 software for Windows.

RESULTS

A prospective, randomized study of 264 patients of benign gall bladder disease in whom laparoscopic cholecystectomy (LC) was conducted in the department of General Surgery at the Sir Sayajirao General Hospital & Medical College Baroda during a period of 25 months from October 2010 to October 2012. A total of 264 patients were included in this study. The total patient population included 195 females and 69 males.

Demographic and operative details of analysed data

Out of the 264 patients 74% of the patients were females and 26% were males. There were 69 males and 195 females for data analysis. The mean age of the 88 patients analysed was 45.96 years±11.48 SD. There was no significant difference between the groups with regard to age. There was no significant difference between the three groups as regards to body weight of the patients operated. Distribution of the patients as per the ASA was similar across both the groups.

Intra-peritoneal drain

In Group A only 15 patients out of 132 required intra-peritoneal drain placement, in Group B it was 24 out of 132.

Comparison of analgesic requirement in both groups

Intra-peritoneal drain was removed on 2nd PO day in all 117 patients. In Group A 30 patients required PO analgesics, out of those 30 patients 15 had Intra-peritoneal drain.

In Group A all patients with post-op Intra-peritoneal drain required analgesics & only 15 patients without drain required PO analgesics.

Table 1: Demographic and operative details of analysed data.

Group	Patients	Sex (M/F)	Age (years) Mean±SD	Surgery duration Mean±SD	ASA I/II	Weight (kg) Mean±SD	Hospital stay (days) Mean±SD	Trocars
A	132	39/93	46.93±10.52	85.11±18.52	126/6	55.95±7	3±1	4
B	132	30/102	43.72±11	84.77±18.44	120/12	55.81±6.40	3±2	4

Table 2: Total number of patients who required post operative analgesic.

	No. of patients who need analgesics	1st dose req.	2nd dose req.	Intra-peritoneal drain kept
Group A	30/132	10 hrs	24 hrs	15/132
Group B	60/132	08 hrs	24 hrs	24/132

102 patients without drain never asked for PO analgesic. In Group B 60 patient's required PO analgesics out of 132 patients Out of those 60 patients 24 patients had intraperitoneal drain. 66 patients never asked for analgesics in this group.

On comparing study Group A with Group B for post-operative analgesics requirement, PO analgesic requirement was less in group A & 'p' value was highly significant ($p<0.05$) at 4hr, 8hr in visceral, parietal, and also at 24 hr in shoulder pain After 24hr in visceral, parietal pain difference is not significant in group A and group B.

Table 3: Comparisons between two groups for post-op analgesics (injection tramadol) requirement at 4hrs.

	Group A & B at V4 hrs	Group A & B at P 4 Hrs	Group A & B at S 4 Hrs
Mann-whitney U value	621.500	626.500	706.500
P value	0.003	0.003	0.019
Significance (p<0.05)	Significant	Significant	Significant

Table 4: Comparisons between two groups for post-op analgesics (injection tramadol) requirement at 8 hrs.

	Group A & B at V 8 hrs	Group A & B at P 8 hrs	Group A & B at S 8 hrs
Mann-whitney U value	651.500	639.000	670.000
P value	0.003	0.004	0.009
Significance (p<0.05)	Significant	Significant	Significant

Table 5: Comparisons between two groups for post-op analgesics (injection tramadol) requirement at 24 hrs.

	Group A & B at V 24 hrs	Group A & B at P 24 hrs	Group A & B at S 24 hrs
Mann-whitney U value	913.500	927.000	701.500
P value	0.607	0.693	0.015
Significance (p<0.05)	Not significant	Not significant	Significant

Table 6 shows comparison between two Groups by Mann Whiteny U Test.

On comparison between Group A and B, data shows that the mean visceral pain score VAS is less at all assessment (4hrs, 8 hrs & 24 hrs) for Group A (36.63<52.38, 37.31<51.69, 45.74<43.26) as compared to Group B.

Table 6: Statistical analysis of vas by Mann-Whiteny U test.

	Group	Total patient	Pain score
Visceral pain 4 hrs	A	132	36.63
	B	132	52.38
	Total	264	
Parietal pain 4 hrs	A	132	36.74
	B	132	52.26
	Total	264	
Shoulder pain 4 hrs	A	132	38.56
	B	132	50.44
	Total	264	
Visceral pain 8 hrs	A	132	37.31
	B	132	51.69
	Total	264	
Parietal pain 8 hrs	A	132	37.02
	B	132	51.69
	Total	264	
Shoulder pain 8 hrs	A	132	37.13
	B	132	51.27
	Total	264	
Visceral pain 24 hrs	A	132	45.74
	B	132	43.26
	Total	264	
Parietal pain 24 hrs	A	132	43.57
	B	132	45.43
	Total	264	
Shoulder pain 24 hrs	A	132	38.44
	B	132	50.56
	Total	264	

Mean parietal pain score VAS is less for Group B as compared to Group A (36.31<51.69, 37.02<51.98, 43.57<45.43) at all assessments (4, 8 and 24 hrs).

The mean duration of surgery for all the patients analyzed was 78.08 minutes±18.77 SD. There was no significant difference between these two groups in relation to the duration of surgery. There was no significant difference in the postoperative hospital stay of the patients in both the groups. There was no major post-operative complication noted in any of Group. None of patients developed trocar site infection.

DISCUSSION

Pre-emptive analgesia is analgesia provided before a noxious stimulus and is type of treatment that reduces central and peripheral sensitizations which effectively reduce postoperative pain means preoperative administration of drugs that modulate the development of

the nociception process in the intra and postoperative period, which results in a reduced postoperative requirement of painkillers. Postoperative pain after LC remains a major problem for the laparoscopic surgeon and anaesthesiologists. Now days many hospitals LC is performed as a day care procedure emphasizes the need for early and appropriate PO pain relief so that the patient has a painless discharge PO Bupivacaine a local anaesthetic agent use in this study for infiltration and intraperitoneal instillation both before and after removal of gall bladder because it is most commonly used in most of previous study.

A vial of 20 ml of 0.5% Bupivacaine is available at a cost of Rs.40. This cost is economically more demanding as compared to injection Tramadol which costs Rs 20 per dose. The peak serum level of intraperitoneal Bupivacaine is reached 20 to 30 min after application and lasts for 2 to 24 hours after surgery.

There are many scientific studies done in this field but the results are difficult to compare because of the varied clinical settings, different drugs and their dosages, application sites, comparators and pain outcomes reported. Demographic data across similar studies done Total patients evaluated in different studies ranged from 40 to 120. Female patients were more predominance in all the studies including the present study which is natural because of the high incidence of gall stone disease in female patients. Determining the sex incidence in any pain study is important because women report more pain than men. In this present study the mean age was 45 years. Most of the other patient details across all the comparable studies were similar. The mean operative time in our set up was on the higher side. Patients in our set up are from the poor socioeconomic background and also come from far flung villages, hence most of the patients have an extended hospital stay for social reasons and it was same in all the group of patients.

PO pain after LC is considered mainly from three sources. Incision sites on the abdominal wall causing parietal pain. Pneumoperitoneum associated with local (peritoneal and diaphragmatic stretching, ischaemia, acidosis) and systemic (hypercarbia causing sympathetic excitability resulting in amplification of local tissue inflammatory response) changes resulting in shoulder pain. Post cholecystectomy wound in the liver bed causing visceral pain.

Large group of patients' constituent of abdominal pain after LC arises from the incision sites (50-70%), pneumoperitoneum (20-30%), cholecystectomy (10-20%).[1,2]

Some studies have diametrically gives an opposite view suggesting that visceral pain is predominant in the early PO phase after LC.[10] Parietal pain is less intense after LC due to small abdominal incisions and limited trauma to the abdominal wall. Shoulder tip pain which is insignificant in the early PO period increases to become the main complaint on the second day after lessening of the.[10] Shoulder tip pain is due to distension of peritoneal cavity by insufflated CO_2 causing diaphragmatic stretching temporary phrenic nerve neuropraxia, Loss of visceral surface tension due to creation of pneumoperitoneum leading to increase tension on the phrenohepatic ligaments, peritoneal trauma caused by chemical irritation, ischaemia and compression. We were meticulous in PO deflation after LC. This may partly explain the low incidence. The other possible theory could be the illiteracy level in our patients and a lack of understanding about shoulder pain.

Techniques of post cholecystectomy analgesia

There are many approaches has been tried with varying rates of success to diminish the intensity of post-operative pain after LC. These include low-pressure pneumoperitoneum, gasless technique for laparoscopy, local anaesthetic (LA) infiltration at trocar site, Saline washout of peritoneal cavity, instillation of the sub-diaphragmatic region with a local anaesthetic, usually using bupivacaine, combined method of instillation of local anaesthetic drug in peritoneum and trocar site infiltration.[1-6,8-14]

Instillation of intra-pleural bupivacaine after LC.[9-15] Use of conventional opioid and non-opioid analgesics in the postoperative period.

Visceral and parietal pain accounted for most of the pain in early postoperative period (4 hrs & 8 hrs) in this study. Visceral pain score (36.63 & 52.38) & parietal pain score (37.51 & 52.26) and shoulder pain score (38.56 & 50.38) were the highest at 4hrs and 8 hrs. Though Joris et al and Verma have concluded from their study that visceral pain is predominant we were unable to concur with them as both the scores were similar. The process of instillation of intra-peritoneal local anaesthetic (LA) drugs impact on the PO pain. They include timing of the intra-peritoneal administration of bupivacaine –"pre-emptive analgesia" before the dissection rather than at the end has been found to be more effective in some studies.[1,3,5] Pre emptive analgesia is preoperative administration of drugs that modulate the development of nociception process in the intra and postoperative periods resulting in reduced PO requirement of analgesics. Proper method of solution application by placing patient in Trendelenburg position to allow for dissemination of fluid beneath the diaphragm and gall bladder bed resulting in better analgesia.[1,2]

In this present study, we used Bupivacaine at the optimal dose 2 mg/kg to increase the contact time of Bupivacaine at the Gall Bladder bed and sub hepatic space before removal of gall bladder so as to increase absorption and get maximum post-operative pain relief which was compare with after removal of gall bladder.

Role of intraperitoneal drain

Use of intra-peritoneal drain PO after LC leads to drainage of bupivacaine through the drain and increases post-operative analgesic requirement. In Group A 30 patients' required PO analgesics, of which 5 had post-operative intra-peritoneal drain. In Group B total 60 patients required PO analgesia out of which 24 patients had intraperitoneal drain. In both the group analgesic requirement was 100% in patients with drain. Use of intra- peritoneal drain may be ineffective in the control of visceral pain in such patients and lead to increase in postoperative analgesic requirement.

Role of bupivacaine infiltration at trocar sites

In the present study Bupivacaine 5 ml at each trocar site before skin incision infiltrated which significantly reduced the parietal pain at 4hr (36.74<52.26) and at 8hr (37.02<51.98) as compared to Group B in early post-operative period ($p<0.05$). Parietal pain comes near to the baseline within 24. These findings support the findings of two previous studies where local infiltration of Bupivacaine at its optimal dosage at trocar sites reduced parietal pain.[1,4,5]

Analgesic requirement

Bupivacaine in pre-emptive form of administration with its optimal dose reduces the PO analgesic requirement as compared to postoperative group. About 60 patients (45%) from group B required analgesics within 8 hrs, as compared to 30 patients (22%) for Group A. There was a clinically significant decrease in the mean analgesic requirement in Group A as compared to the Group B.

Complication of drug

No local or intra-peritoneal complications were observed in our patients, which could be attributed to the study. The use of local anaesthetic drug (Bupivacaine), either intraperitoneal or trocar site infiltration in muscular fasciae at its optimal dose (2mg/kg), was found to be safe for use in our patients.

Limitations of the study

Instillation of Bupivacaine before creation of pneumoperitoneum is more difficult so there is not a absolute pre-emptive study. Although all surgeries followed a strict protocol, the patients were operated by a number of surgeons with varying experiences; hence minor variations in surgical technique may have been there. Though the patients were properly educated about VAS, some illiterate patients may not have adequately understood the instruction and accordingly in certain instances they may not have revealed their pain appropriately.

Table 7: Comparison of different study and present study for different data.

Study	Sample size	Laparoscopiy	Comparison	Local anae. used	Patients blinding	Clinician blinding	Dos (in min)
Barczynski et al 2006[1]	120	LC	Pre incisional vs placebo & pre intra vs placebo	2 mg/kg B	Yes	Yes	56.1±12.7
Maestroni et al. 2002[2]	60	LC	Pre intra vs placebo	5 mg/kg	-		67.3±21
Joris et al. 1995[10]	40	LC	post intra vs placebo	80 ml intra peritoneal 0.125% B	Yes	Yes	
Lee et al[5]	157	LC	Pre vs post incisional vs placebo pre intra vs post intra vs placebo	20 ml 0.25%B at incision or 40 ml intra peritoneal 0.25% B	Yes	No	70.6±29
Chundrigar et al 1993[9]	60	LC	Post intra vs placebo	20 ml 0.25% B	Probably Yes	No	48.5
Pasqualucci et al[3]	120	LC	Pre intra vs post intra & pre intra vs placebo	20 ml 0.5% B with epinephrine	Yes	Yes	125±36
Szem et al[14]	55	LC	Pre intr vs placebo	100 ml 0.1% B	Yes	Probably yes	
Present study	264	LC	Pre intra and local vs post intra and local	60 ml 0.5% B	Yes	-	78.08±18.77

CONCLUSION

Use of bupivacaine intraperitoneally at its optimal dosage (2 mg/kg) instilled in the gall bladder bed and sub diaphragmatic space before dissection of gall bladder in LC significantly reduces visceral as well as shoulder pain when compared with another group which use after removal of gall bladder. Use of bupivacaine (0.5%) infiltration at its optimal dosage (2 mg/kg) in the skin, subcutaneous tissue, muscular fasciae of trocar site before skin incision significantly reduces parietal pain in post-operative period compared to after removal of trocar in LC. When used at its optimal dose 2 mg/Kg, bupivacaine was found safe and easy to use without any adverse effects. Visceral pain, parietal pain, shoulder pain was predominant in early postoperative period after LC caused by surgical trauma at gall bladder bed and abdominal incision. Although instillation of bupivacaine before removal of gall bladder rather than after reduces the post-operative pain and analgesic and it is cost effective in patients from poor socioeconomic background in India.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Barczynski M, Konturek A, Herman RM, Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of pneumoperitoneum for laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study. Surg Endosc. 2005;20:1088-93.
2. Maestroni U, Sortini, Devito C, Pour Morad Kohan Brunaldi F, Anania G, et al. A new method of preemptive analgesia in laparoscopic Cholecystectomy: a randomized, double-blind, placebo-controlled study. Surg Endosc. 2002;16:1336-40.
3. Pascqualucci A, De Angelis V, Contardo R, Colo F, Terrosu G, Donini A, et al. Preemptive analgesia: A randomized, double-blind, placebo-controlled study. Anesthesiol. 1996;85:11-20.
4. Coughlin SM, Karanicolas PJ, Heather MA, Bilge Kanbur, Savas K, Colquhoun PHD. Better late than never? Impact of local analgesia timing on postoperative pain in laparoscopic surgery: a systemic review and metaanalysis: Surg Endosc. 2010;24:3167-76.
5. Lee IO, Kim SH, Kong MH. Pain after laparoscopic cholecystectomy: the effect and timing of incisional and intraperitoneal bupivacaine. Can J Anaesth. 2001;48:545-50.
6. Mixter CG, Hackett TR. Pre-emptive analgesia i the laparoscopic patient. Surg Endosc. 1997;11:351-3.
7. Moiniche S, Jorgensen H, Wetterslev J, and Dahl JB. Local Anesthetic Infiltration for Postoperative Pain Relief After Laparoscopy. Anesth Analg. 2000;90:899-912.
8. Kaholkar A, Sammour T, Soop M, Hill AG. Intraperitoneal use of local anaesthetic laparoscopic Cholecystectomy: systematic review and metaanalysis of randomized contolled trials. J Hepatobiliary Pancreat Sci. 2010;17:637-56.
9. Chundrigar T, Hedges AR, Morris R. Intraperitoneal bupivacaine for effective pain relief after laparoscopic cholecystectomy. Ann R Coll Surg Engl. 1993;75:437-9.
10. Joris J, Thiry E, Paris P. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. Anesth Analg. 1995;81:379-84.
11. Lepner U, Goroshina J, Samaru¨tel J Postoperative pain relief after laparoscopic cholecystectomy: a randomised prospective double-blind clinical trial. Scand J Surg. 2003;92:121-4.
12. Gerardo Castillo-Garza, MD, Jose´ A. Díaz-Elizondo, MD, Carlos A. Cuello-García, MD,Oscar Villegas-Cabello, MD Irrigation with Bupivacaine at the Surgical Bed for Postoperative Pain Relief After Laparoscopic Cholecystectomy. JSLS. 2012;16:105-11.
13. Jabbour-Khoury SI, Dabbous AS, Gerges FJ, Azar MS, Ayoub CM, Khoury GS. Intraperitoneal and Intravenous Routes for Pain Relief in Laparoscopic Cholecystectomy JSLS. 2005;9:316-21.
14. Szem JW, Hydo L, Barie. A double – blinded evaluation of intraperitoneal bupivaciane vs saline for the reduction of postoperative pain and nausea after laparoscopic Cholecystectomy. Surg Endosc. 1996;10:44-8.
15. Raetzell M, Maier C, Schrijder D, Wulf H. Intraperitoneal Application of Bupivacaine During Laparoscopic Cholecystectomy-Risk or Benefit? Anesth Analg. 1995;81:967-72.

Cite this article as: Vasava MA, Makadia JM. Evaluation of superiority of preemptive analgesia with instillation of 0.5% bupivacaine before rather than after surgery for laparoscopic cholecystectomy. Int Surg J 2019;6:1589-95.