

## A randomized controlled study of intraperitoneal vs intraincisional infiltration of local anesthetic levobupivacaine for pain relief in post-laparoscopic hysterectomy cases

Gopal Reddy Narra<sup>1,\*</sup>, Manohar<sup>2</sup>, Aiswarya<sup>3</sup>, Amit Kumar<sup>4</sup>, Monica Krishna<sup>5</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Professor & HOD, <sup>3,4,5</sup>PG Student, Dept. of Anaesthesia, KIMS- NKP

**\*Corresponding Author:**

Email: drgopalreddynarra@yahoo.com

### Abstract

**Introduction and Aim:** Providing postoperative pain relief is a common acceptable practice in modern era. Multimodal combination methods are being used to reduce opioid-related side effects. We conducted a randomized study with 0.125% levobupivacaine in intraincisional infiltration vs intraperitoneal instillation for pain relief after laparoscopic hysterectomies.

**Materials and Method:** In this randomized controlled study 90 patients of laparoscopic hysterectomy were selected. They were grouped as Group-C the control placebo, Group-I received local wound infiltration (intraincisional) of 20 ml solution of 0.125% levobupivacaine while Group-P received 20 ml solution of 0.125% levobupivacaine intraperitoneal space. Recording of post-surgical pain from 0 to 24 hours along with nausea and vomiting was done.

**Results:** Post-operative pain was significantly lower and requirement butorphanol also less in intraincisional infiltration of 0.125% levobupivacaine in group -I (300±470µg) when compared to group-C and P (950±223, 600±502) in 1st 4 hours with significant p-value 0.00041 and in 24 hours group-C {783.33±415.45} group-I {466.67±503.09} and group-P {583.33±457.18} with significant p-value of 0.0013. Regarding opioid requirement in 1st-4 hours in group-C (90%) group-I only (30%) and group-P (60%), in 8-24 hours period in group-C (60%) compared to group-I(40%) and group-P(50%).

**Conclusion:** Incisional infiltration of levobupivacaine is more effective than intraperitoneal instillation in controlling the post-operative pain.

**Keywords:** Laparoscopic hysterectomy, Levobupivacaine, Local anesthetic, Post-operative pain Intraincisional infiltration, Intraperitoneal instillation

**Received:** 18<sup>th</sup> October, 2016

**Accepted:** 3<sup>rd</sup> February, 2017

### Introduction

Pain is a consistent and predominant complaint following surgery. Post-operative pain management minimizes patient suffering and also reduces cardio-respiratory problems and hasten recovery. Regional anaesthetic techniques provide excellent analgesia; with less side-effects.<sup>(1,2)</sup> Opioids side effects restrict their use.<sup>(3)</sup>

After surgical operations incisional infiltration appears to be more helpful,<sup>(4)</sup> to reduce pain along with postoperative nausea and vomiting. Intraperitoneal local anaesthetic has become an important additional tool for postoperative pain relief, in the era of modern surgery which was first described in 1951 by Griffin et al<sup>(5)</sup> and laparoscopic surgical procedures.<sup>(6)</sup>

### Subjects and Method

This present study was conducted in our teaching Institute as a randomized controlled clinical trial in patients who were subjected to laparoscopic hysterectomy from July 2013 to march 2016. After Institutional ethics committee clearance, total of 90 patients, ASA grade I and II and aged between 40 to 55 years were selected, written consent for study taken.

**Exclusion Criteria:** Patients with language barrier, history of hypersensitivity to study drugs, impaired respiratory function, uncontrolled chronic systemic

disease, morbid obesity, liver disorders and history of chronic analgesic, sedatives and steroid intake were excluded.

**Study techniques:** First of all written informed consents were taken from all patients at preanaesthetic checkup time, after proper explanation of the study procedure and about the use of visual analogue scale(VAS) (0=no pain to 10=excruciating pain) in their own language.

**Randomization:** After randomization. Group-C not received any test drug. Group-I received local infiltration (intraincisional) of 20 ml solution of 0.125% levobupivacaine at the end of operation and Group-P received 20 ml solution of 0.125% levobupivacaine intraperitoneal instillation in the raw hysterectomy site after the surgical procedure.

Routine premedication with midazolam 1mg, glycopyrrolate 0.2mg, ondertone 4g and fentanyl (1.5 µg/ kg) was given. After 8 large breaths 100% pre-oxygenation, induction done with propofol (1.5 to 2 mg/kg) and scoline (2 mg/kg) was given followed by intubation and anaesthesia maintained with intermittent isoflurane (0.3to 0.6%), O<sub>2</sub>/N<sub>2</sub> 0(50%/50%) and vecuronium loading dose followed by intermittent vecuronium injections. Multi para-monitor was used which displays vitals and Etco<sub>2</sub>.

At the end of operation in Group-I intraincisional infiltration of 0.125% levobupivacaine using 5 ml for

each port site for 4 sites a total of 20 ml solution) was given, including the fascia, muscle and pre-peritoneal space. In group -P intra peritoneal sprinkling of the solution was done in the raw post-hysterectomy site at the end of the laparoscopic procedure. Abdominal drains were used where ever necessary but blocked up to half-an-hour in group-P patients. All patients were given analgesic dose of Diclofenac 75 mg IV at the end of the operation.

Reversal of neuromuscular blockade was achieved with intravenous neostigmine and glycopyrrolate as required. Extubation was done after standard criteria for extubation were fulfilled.

Butorphanol (Butrum) was given as rescue analgesic on request first dose 1 mg (1000µg) intravenously and further doses 1 mg intramuscularly in the post-op unit whenever required. The number of patients requiring rescue analgesia was recorded in all groups.

Primary outcomes recorded were severity of postoperative pain and postoperative analgesic requirement and the secondary outcomes were incidence of side effects like postoperative nausea and vomiting (PONV). The pain intensity was assessed by using 10 point visual analogue scale (VAS) 0, no pain; 1-3 mild, 4-6 moderate, 7 -9 severe and 10 worst imaginable pain at rest (static) and during movement and coughing (dynamic). Assessment of pain was done on the arrival of the patient to the recovery area and post-op ward to

till the end of the study, i.e., 24 hours after operation. The severity of postoperative nausea and vomiting (PONV) were graded on four point ordinal scale [0, no nausea or vomiting; 1, mild nausea; 2, moderate nausea; and 3 severe nausea and vomiting. Ondencitran 4mg was given to patients with PONV of grade >2 and VAS > 4 and the times were noted.

**Analysis of data:** After completion of the study, data entered in to Microsoft excel sheet analyzed for means  $\pm$  standard deviation and analgesic treatment in percentages (%). Data was compared between three groups by analysis of variance (ANOVA) and student t-test; p values calculated and p value of less than 0.05 taken as statistically significant.

## Results

The data of 90 patients were assessed for final analysis. There is no statistical significance regarding age, weight and duration of operation (Table 1). There are significant pulse and mean blood pressure differences whenever patient suffered with significant pain (Table 2 & 3). The total consumption Butorphanol 1000µg in the 24-hour postoperative period was reduced by 53.33% in group-I and 42.67% group-P as compared to group-C only 21.33%(Table 4). There was significant difference among the groups in respect to incidence of PONV and shoulder pain (Table 5 and 6).

**Table 1: Patients characteristics**

Characteristics	Group-C (n=30)	Group-I (n=30)	Group-P (n=30)	p-value	* Not statically significant difference in demographic figures and duration of operation.
Age	49.75 $\pm$ 3.75	49.75 $\pm$ 4.07	49.70 $\pm$ 4.05	0.955	
Weight	57.40 $\pm$ 5.69	58.65 $\pm$ 4.73	58.85 $\pm$ 4.09	0.598	
Duration of operation in minutes	113.35 $\pm$ 7.74	115.00 $\pm$ 7.57	114.80 $\pm$ 7.078	0.762	

**Table 2: Heart rate-post-operative period. Time in hours**

Time	Group-C	Group-I	Group-P	p-value	*There was statistically significant difference in heart rate, during the post-operative periods. Whenever the patient felt pain the pulse rate and blood pressure increased.
0 h	83.58 $\pm$ 8.24	78.12 $\pm$ 8.59	77.92 $\pm$ 9.04	0.0089	
1 h	83.19 $\pm$ 8.22	81.58 $\pm$ 8.67	79..08 $\pm$ 7.82	0.115	
4 h	84.36 $\pm$ 7.82	79.14 $\pm$ 8.45	79.58 $\pm$ 9.58	0.018	
8 h	86.92 $\pm$ 4.74	84.36 $\pm$ 4.27	84.17 $\pm$ 3.67	0.011	
16 h	86.86 $\pm$ 3.60	85.08 $\pm$ 5.10	95.05 $\pm$ 2.77	0.088	
24h	87.11 $\pm$ 3.05	84.56 $\pm$ 8.67	84.14 $\pm$ 4.25	0.046	

**Table 3: Mean blood pressure -post-operative period**

Time	Group-C	Group-I	Group-P	p-value	*There was statistically significant difference in mean blood pressure during the post-operative periods in different groups.
0	94.19 $\pm$ 8.34	88.19 $\pm$ 8.59	87.92 $\pm$ 9.04	0.009	
1	92.58 $\pm$ 8.24	89.08 $\pm$ 7.82	91..58 $\pm$ 8.67	0.110	
4	94.58 $\pm$ 8.24	89.14 $\pm$ 8.45	89..39 $\pm$ 9.58	0.059	
8	97.36 $\pm$ 3.43	95.14 $\pm$ 3.86	95.56 $\pm$ 5.11	0.045	
16	97.06 $\pm$ 5.73	95.03 $\pm$ 5.04	94.86 $\pm$ 3.84	0.033	
24	97.31 $\pm$ 3.26	93.31 $\pm$ 5.01	95.31 $\pm$ 3.09	0.004	

**Table 4: Post-operative pain, using visual analogue scale in all groups having more than 4 and given Butorphanol dose**

Time	Group-C	Group-I	Group-P	*Post-operative pain was significantly lower in group -I (intracincisional infiltration of levobupivacaine 0.25%) than control group and group-P (intraperitoneal infiltration of levobupivacaine 0.25%).  Shoulder pain is less in Group-P
0 -4 hours	27 (90)	9 (30)	18 (60)	
4 -8 hours	24 (80)	12 (70)	22 (73.3)	
16-24 hours	18 (60)	12 (40)	15 (50)	
2.Shoulder pain	18 (60%)	15 (50 %)	3 (10 %)	

**Table 5: Butorphanol dose in 1000µg**

Time	Group-C	Group-I	Group-P	p-value	* This difference also reported from 0-4 hours and 0- 24 hours post-operatively. Although pain scores were less in group-I when compared with the control group-C and group-P, yet it is statistically significant in 1 <sup>st</sup> 0-4 hours and in 0- 24 hours.
0 -4 h	950±223	300±470	600±502	0.00004	
4 -12 h	800±410	700±470	750±444	0.7753	
12-24 h	600±502	400±502	400±502	0.3547	
0-24 h	783.33±415.45	466.67±503.09	583.33±457.18	0.0013*	

**Table 6: Showing post-operative side effects**

Side Effects	Group-C	Group-I	Group-P	*Nausea vomiting more in group-C, less in group-I and more less in group-P.
Nausea	9 (30%)	5 (16.6%)	2 (6.6%)	
Vomiting	6 (20%)	1 (3.3%)	1(3.3%)	
Shoulder pain	18(60%)	15(50%)	2(6.6%)	
Minor allergic reactions	nil	nil	Nil	
Major allergic reactions	nil	nil	Nil	

## Discussion

Origin of pain after laparoscopic surgery is due to multiple factors, from the incision sites (somatic pain), from the bed of operation (visceral pain) and pneumoperitoneum irritation (shoulder pain).<sup>(7)</sup> Intraperitoneal local anesthesia's (IPLA) is likely to block free afferent nerve endings in the peritoneum. Systemic absorption of local anesthetic from the peritoneal cavity may also play a part in reducing nociception. Some researchers suggested that local anaesthetic block reduce incisional pain. The local anesthetic drugs prevent or reversibly reduce the rate of depolarization<sup>(8)</sup> and sufficient to control pain in early period.<sup>(9)</sup> Unlike most previous studies we compared intra-incisional vs intraperitoneal infiltration of local anesthetic by using 0.125%, levobupivacaine not with lignocaine and bupivacaine. Our results are comparable with that of Lepner et al,<sup>(10)</sup> we also compared both into incisional and intraperitoneal infiltration of local anesthetic. Our results shows (Table 4) that there is significant requirement of opioid to control pain in group-C {27 (90 %)} group-I {9 (30 %)} group-P {18 (60 %)} when compared. Our results also show overall opioid requirement group-C(76.67%) compared to group-I(46.67%) and group-P(60%) and in 24 hours period and requirement of opioid in group-C{783.33±415.45} group-I{466.67±503.09} and group-P 583.33±457.18 with a significant p-value of 0.0013\*.

When group-I and P are compared there is a significant reduction of opioid in first 4 hours 9 (30%),

18 (60%) and also in 8-24 hours 12(40%), 15(50%) respectively when compared to control. Elhakim et al.<sup>(11)</sup> have shown that intraperitoneal Lidocaine reduces effectively both shoulder pain and abdominal postoperative pain. Shoulder pain is very less in group-P 3(6.6%) (Table 4) in compared to group-C 18 (60%) and group-I 15 (50%). Post-op nausea, vomiting and shoulder pain more in control group-C and Intra incisional group-I when compared intraperitoneal instillation group-P(Table 4 & 6).

Decreased pain scores were observed in our study and showing a clear trend towards reduced opioid consumption. This data is consistent with data from other trials in evaluating the effectiveness of local anesthesia use after laparoscopic surgery.<sup>(12)</sup>

## Conclusions

We conclude that infiltration of local anesthetic is useful adjunct as part of a multimodal analgesic regimen to further relieve the postoperative pain and opioid requirement. It is also significant that the shoulder pain is less with intraperitoneal instillation. Both combined Intra incisional and intraperitoneal routes are more useful. Levobupivacaine readily available, and has limited side effects when compared to bupivacaine. This technique must be adopted laparoscopic surgeries.

## References

1. Abigail Whiteman, MA MB BChir FRCA, Novel techniques of local anaesthetic infiltration; Contin Educ

- Anaesth Crit Care Pain (2011)doi: 10.1093/bjaceaccp/mkr026First published online: July 12, 2011.
2. Kucuk C, Kadiogullari N, Canoler O, Savli S. A Placebo-controlled comparison of bupivacaine and ropivacaine instillation for preventing postoperative pain after laparoscopic cholecystectomy. *Surg Today* 2007;37:396-400.
  3. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. *Eur J Surg* 2001;167:84-96.
  4. Moinicke S, Mikkelsen S, Wetterslev J, Dahl JB. A qualitative systematic review of incisional local anaesthesia for post-operative pain relief after abdominal operations. *Br J Anaesth* 1998;81:377-83.
  5. Griffin EM, Prystowsky H, Hingson RA. The use of topical anaesthesia of the peritoneum in poor risk surgery and in augmenting inadequate vertebral conduction anaesthesia. *N Z Med J.* 1951;50:31-3.
  6. Kahokehr A, Sammour T, Srinivasa S, Hill AG. Systematic review and meta-analysis of intraperitoneal local anaesthetic for pain reduction after laparoscopic gastric procedures. *Br J Surg.* 2011;98:29-36.
  7. 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;79:130-6.
  8. Bisgaard T, Klarskov B, Kristiansen VB, Callesen T, Schulze S, Kehlet H, et al. Multi-Regional local anesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: A randomized, double-blinded, placebo-controlled study. *Anesth Analg* 1999;89:1017-24.
  9. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy. *Anesthesiology* 2006;104:835-46.
  10. Lepner U, Goroshina J, Samaritel J. Postoperative pain relief after laparoscopic cholecystectomy: A randomised prospective double-blind clinical trial. *Scand J Surg* 2003;92:121-4.
  11. Elhakim M, Elkott M, Ali NM, Tahoun HM. Intraperitoneal lidocaine for postoperative pain after laparoscopy. *Acta Anaesthesiol Scand* 2000;44:280-4.
  12. Mraovic B, Jurisic T, Kogler-Majeric V, Sustic A. Intraperitoneal bupivacaine for analgesia after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand.* 1997;41:193-196.