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Research Article

**A RANDOMISED CONTROLLED TRIAL IN LIMITED  
RESOURCE SETTING TO EVALUATE THE ROLE OF  
ROPIVACAINE INTRAPERITONEAL INFILTRATION**<sup>1</sup>Saad Bahussein, <sup>2</sup>Dr. Ch. Arslan Ahmad, <sup>3</sup>Dr. Hina Justin<sup>1</sup>Midland Regional Hospital, Portlaoise, Ireland, Saadbahussein@hotmail.com<sup>2</sup>MO, DHQ Hospital Kasur<sup>3</sup>WMO DHQ Hospital Kasur**Abstract:**

**Objective:** In the setting of limited resources, our study aimed at evaluating of (Intra-peritoneal infiltration of Ropivacaine) role in open cholecystectomy for post-operative in analgesia.

**Material and Methods:** Our randomized-controlled trial (RCT) study was carried out at Anaesthesia Dept. of Sir Ganga Ram Hospital, Lahore (June, 2016 to July 2017) on 126 patients. These patients were classified in 2 groups randomly after permission from ethics committee. Study group i.e. 1 was provided (intra-peritoneal ropivacaine) & control group i.e. 2 was given routine (standard analgesia). In all patients after recovery, at 1, 6 & 24 hours' pain was measured on (VAS score 1-10). Those with pain score of four 4 & more were given (nalbuphine 5 mg) IV bolus. All data was analysed by SPSS.

**Results:** Study group has less mean pain score as ( $p < 0.05$ ) than placebo group in a comparison of pain score after 1, 6 & 24 hrs of surgery. Rate of (nausea/vomiting) was found  $p < 0.05$  & it was greater as 62 percent in placebo than as 38 percent in study group. No difference was found as  $p > 0.05$  between groups based on mean age as ( $47.89 \pm 8.56$ ) versus ( $48.75 \pm 9.36$ ), gender as females 70 percent versus 68 percent & time in surgery as  $88.54 \pm 12.34$  minutes versus  $91.70 \pm 13.50$  minutes. Also in (American society of anaesthesiologist) i.e. ASA grades in both (study & placebo) group of patients respectively.

**Conclusion:** In open cholecystectomy, (intra-peritoneal ropivacaine) infiltration assisted in minimizing post-operative pain clearly.

**Keywords:** Postop pain, Open cholecystectomy, Intra-peritoneal ropivacaine.

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**INTRODUCTION:**

Since a century ago (gall bladder) disease has been treated with (open cholecystectomy). Treatment of (cholelithiasis) has been improved with the coming of laparoscopy in year 1990. Now (laparoscopic cholecystectomy) is opted for treating cholelithiasis in every advance set-up [1, 2]. Special equipment & skill is required for (laparoscopic technique). Only surgical option in Pakistan's rural areas is (open cholecystectomy) for (gall bladder disease) [3].

Various dysfunctions of surgery as urinary, circulatory, gastrointestinal, pulmonary dysfunctions can be caused by postoperative pain. It has side effects on the life of a patient. In upper abdomen, surgeries performed as (open cholecystectomy) cause respiratory failure & serious post-operative pain. Delay in recovery, cost of health care & increase of hospital stay may be caused by these dysfunctions. Severe morbidity & mortality in patients can even be produced [4].

All surgical methods have advanced substantially & leading to minimize trauma morbidity & death rate in various (surgical procedures). The hospital stay & cost in health care has also reduced. To minimize post-operative pain, various methods are in practice using many (opioid & non-opioid) analgesics for reducing side effects & reducing pain [5].

For finding effectiveness of (intra-peritoneal local anaesthetics) & opioids for controlling pain, various (clinical trials) have been planned. Usually employed anaesthetics are: morphine, ropivacaine & bupivacaine which are administered when (cholecystectomy surgery) is over. (Intra-peritoneal) use of bupivacaine or (tramadol) is leading to lesser pain scores in various researches [7, 9].

It is found by past researchers that (intra-peritoneal) use of many medicines as lignocaine, fentanyl & tenoxicam may be helping in minimizing (post-operative pain). Few authors favour the use of intra-peritoneal after surgery [6].

Vomiting & nausea are 2 side effects which patients feel while in (open cholecystectomy). Reducing these two is helpful in recovery & less hospital stay.

For minimizing vomiting & nausea, intra-peritoneal administration of bupivacaine, ropivacaine & tramadol showed best outcomes [10].

By using local anaesthetics postoperatively as ropivacaine administered (intra-peritoneal) can speed up recovery, minimize mortality & morbidity. It is done by dampening endocrine, somatic & autonomic

reflexes. In the setting of limited resources, our study aimed at evaluating of (Intra-peritoneal infiltration of Ropivacaine) role in open cholecystectomy for post-operative in analgesia.

**MATERIAL AND METHODS:**

Our randomized-controlled trial (RCT) study was carried out at Anaesthesia Dept. of Sir Ganga Ram Hospital, Lahore (June, 2016 to July 2017) on 126 patients. By non-probability sampling, subjects of age from (20 – 50) years from both genders were selected.

Our patients were classified randomly using (random number tables). By using WHO (sample size calculator), sample size was measured with significance level of 5 percent & 80 percent test power. In addition, (population standard deviation) of eight with (population mean VAS-score) of seven in control & three in study group [11].

Written consent from each patient was taken by briefing them purpose & method of research protocol. Control group was number 2 & managed in routine (standard analgesia) both Ketorolac 30 mg & Nalbuphine ten mg treatment.

Study group was number 1 & given (intra-peritoneal ropivacaine) 0.5 percent ropivacaine in dose of two mg per kilo gram (Diluted in normal saline) for making a volume of fifty ml as an analgesic. It was according to (American society of anaesthesiologists) standards. A clinical check-up of every patient was taken & information of medical illness history was noted. Other investigations like liver functions test, (chest radiograph) with renal profile & blood CP were also conducted.

By the same team of (consultant surgeon), patients have undergone procedure of (open cholecystectomy). We treated every case with propofol (2 – 2.5) mg per kg as a (i.v induction agent) & atracurium with initial dose (0.4 – 0.5) mg per kg for more than 1 minute for relaxation of muscles was given. The subjects were intubated in (deep plane of anaesthesia). Group 2 was given (intravenous analgesia) medicines in which (ketorolac thirty mg & nalbuphine ten mg) are included for post-operative pain administration.

To maintain anaesthesia, (isoflurane in 66 percent nitrous oxide) & oxygen with (atracurium) 0.08 – 0.1 mg per kg for a period of (20 – 45) minutes after 1<sup>st</sup> dose administration. After surgery, (neostigmine & glycopyrrolate) were given to reverse (neuromuscular paralysis). Careful monitoring was done till recovery then patients were shifted to (post- anaesthesia care

unit).

Patients with pain score of 4 or more were given (nalbuphine five mg IV bolus) additionally. A visual analogue score of (0 to 10 (0=no pain, 10 = extreme amount of pain) was used to evaluate pain.

It was described to patients who were consented to be researched in (pre-operative visit). Requirement of post-operative analgesia & all information of (demographic characteristics) was taken with post-operative pain. On a pre-designed form, information about post-operative vomiting & nausea, visual disturbances, respiratory depression, sedation & headache were noted. Data was analysed by SPSS.

Percentages & frequency were measured for qualitative variables and standard deviation & mean were used quantitative variables. To compare mean values of quantitative data, sample t-test and Chi-square test was used to compare proportions of qualitative data among both groups (P-value < 0.05).

### RESULTS:

Total 126 patients were (randomized) in 2 groups in this research & no statistically (significant difference) in average age of patients of both groups as  $48.75 \pm 9.36$  of placebo group &  $47.89 \pm 8.56$  in the study

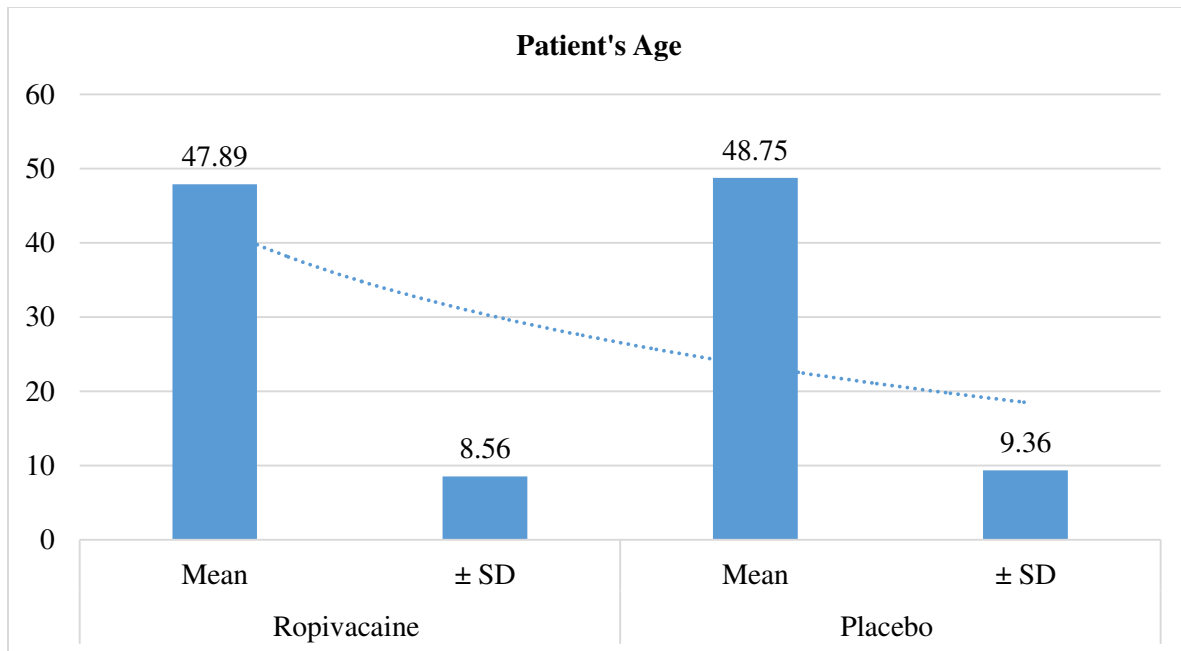
group. Gender distribution of groups was as  $p > 0.05$ . More females were in both groups as 69.84 percent in study & 68.25 percent included in placebo group. Most patients were having (ASA grade II) & no statistical difference as  $p > 0.05$  was in 2 groups. Slightly higher mean operation time in placebo group was  $91.70 \pm 13.50$  & it was more as compare to  $88.54 \pm 12.34$  minutes in (study group) but it was also insignificant as  $p > 0.05$  (Table – I).

After 1, 6 and 24 hours, comparison of mean score of surgery showed that (study Group) i.e. ropivacaine group had clearly ( $p < 0.05$ ) with less score of mean pain than placebo group as  $5.79 \pm 1.21$  versus  $7.00 \pm 1.30$  after one hrs ( $5.27 \pm 1.03$ ) versus ( $4.33 \pm 1.09$ ) after six hrs & ( $2.62 \pm 0.71$  versus  $3.56 \pm 0.86$ ) after 24 hrs of surgery respectively (Table – II). The placebo group had higher rate of (complications) like nausea or vomiting.

Rate of (nausea or vomiting) was found as  $p < 0.05$  higher 39 such as 62 % in placebo group than 24. 38 % of ropivacaine group. No difference as ( $p > 0.05$ ) in hospitalisation of both groups. Mean placebo group hospitalisation was seen ( $5.46 \pm 1.366$ ) days; whereas, study group was ( $5.63 \pm 1.235$ ) days was noted (Table – III).

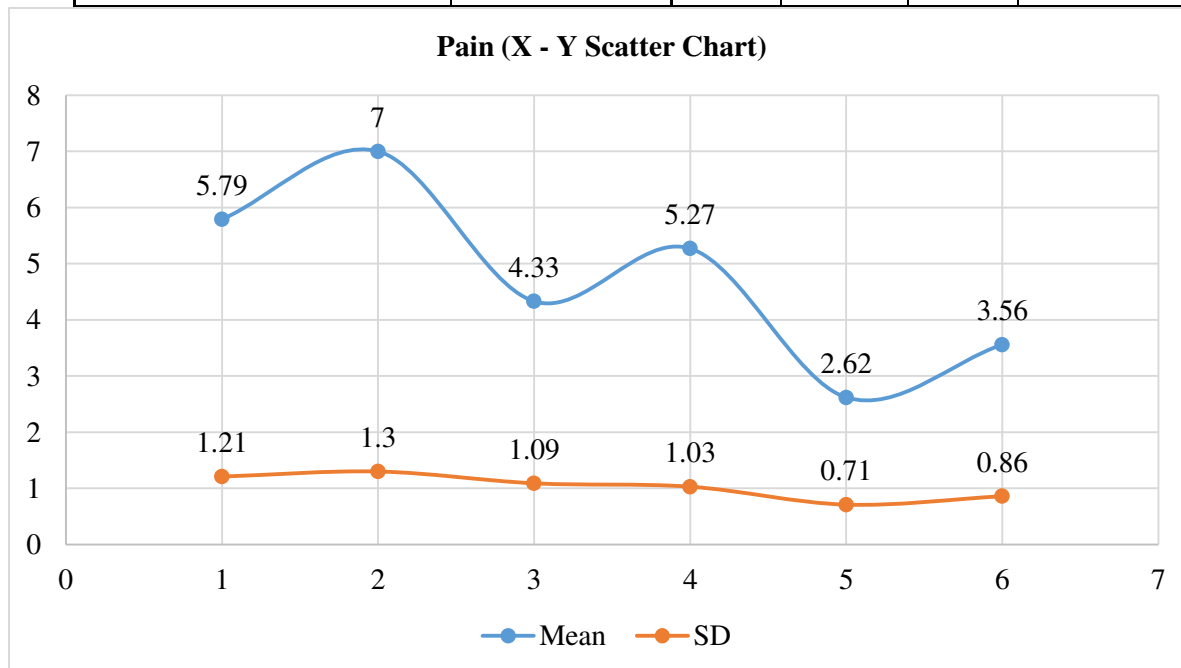
**Table – I:** Comparison of demographic characteristics between both groups

Characteristics		Ropivacaine		Placebo		p-value
		Mean	± SD	Mean	± SD	
Patient's Age		47.89	8.56	48.75	9.36	0.593
Characteristics		Number	Percentage	Number	Percentage	p-value
Gender	Female	44	70	43	68	0.847
	Male	19	30	20	32	
ASA Grade	ASA – I	19	30	15	24	0.176
	ASA – II	39	62	36	57	
	ASA – III	5	8	12	19	



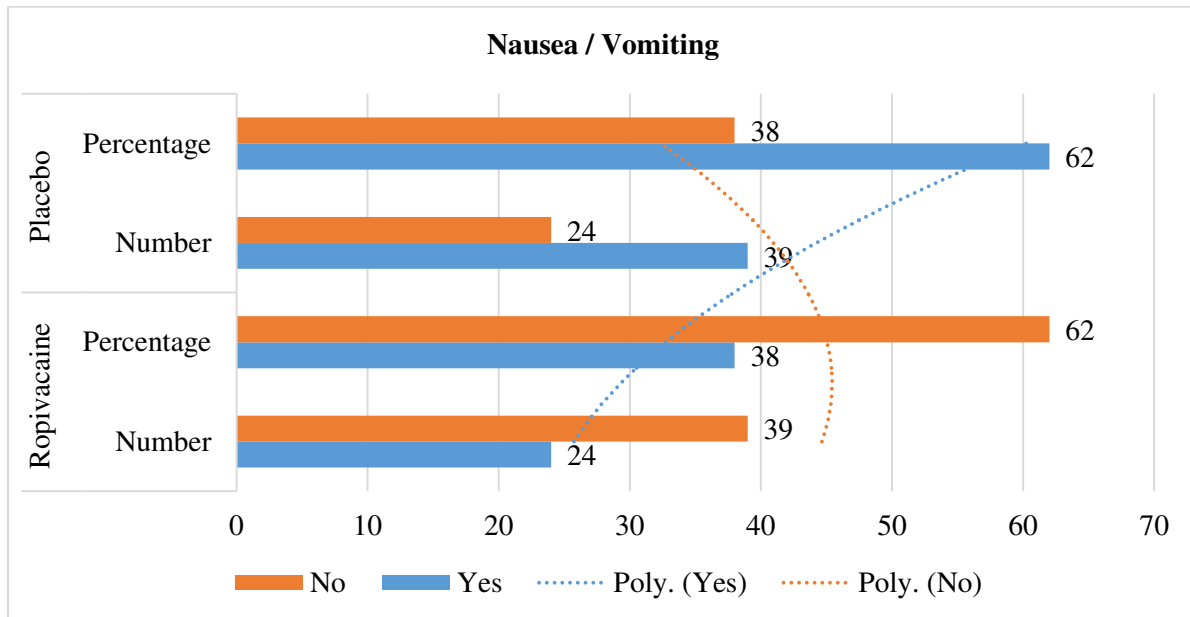
**Table – II:** Comparison of pain score at 1, 6 and 24 hours between both groups

Pain	Group	N	Mean	SD	P-Value
Pain score at 1 hour	Ropivacaine	63	5.79	1.21	< 0.001
	Placebo	63	7	1.3	
Pain score at 6 hours	Ropivacaine	63	4.33	1.09	< 0.001
	Placebo	63	5.27	1.03	
Pain score at 24 hours	Ropivacaine	63	2.62	0.71	< 0.001
	Placebo	63	3.56	0.86	

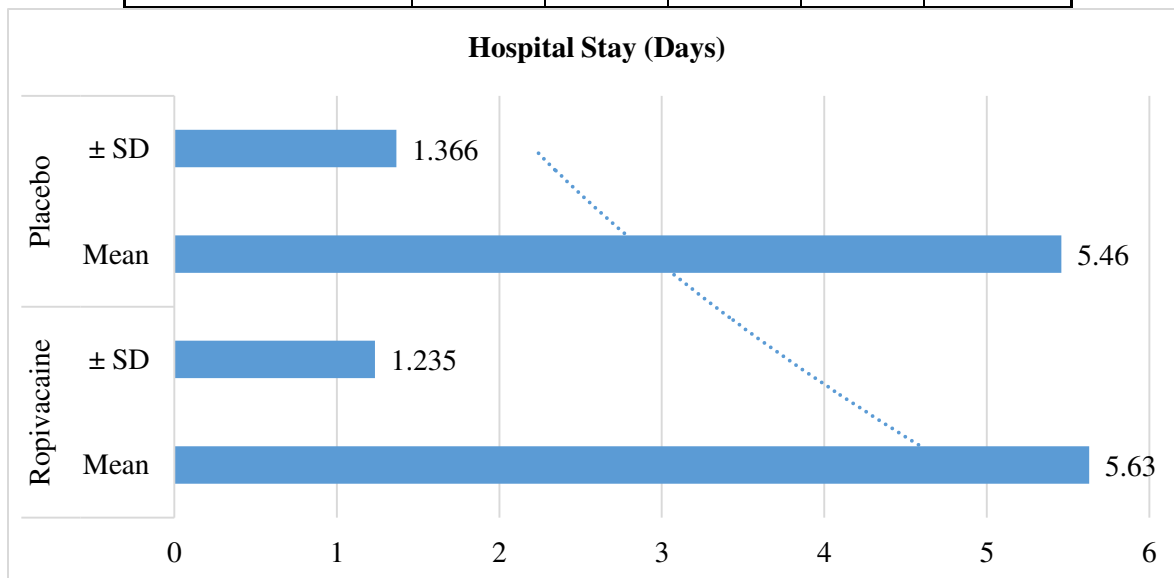


**Table – III:** Comparison of complications and hospital stay between both groups

Nausea/Vomiting	Ropivacaine		Placebo		p-value
	Number	Percentage	Number	Percentage	
Yes	24	38	39	62	0.008
No	39	62	24	38	

**Table – IV:** Hospital Stay

Detail	Ropivacaine		Placebo		P-Value
	Mean	± SD	Mean	± SD	
Hospital Stay (Days)	5.63	1.235	5.46	1.366	0.464



**DISCUSSION:**

The pain score comparison at the interval of one-hour of surgery demonstrated that ropivacaine group had ( $p < 0.05$ ) less (mean pain score) as  $5.79 \pm 1.21$  versus  $7.00 \pm 1.30$  in comparison to (placebo group). Average pain score at six hrs was as  $p < 0.05$  greater in (placebo group) as  $5.27 \pm 1.03$  than ropivacaine group in mean score of pain was observed as  $(4.33 \pm 1.09)$  right after surgery (six hrs interval).

It was observed after 1 day of surgery that (ropivacaine) had significantly  $p < 0.05$  less mean (pain score) as  $2.62 \pm 0.71$  in comparison with as  $3.56 \pm 0.86$  in (placebo group). Due to undesired (surgical complication) or signs of (local anaesthetic toxicity) as hypotension, bradycardia or uncontrolled pain, no patient was excluded.

Out of various analgesics as ketorolac, nalbuphine, or fentanyl used commonly intravenously for control of (post-operative pain), (intra-peritoneal ropivacaine) has given good outcomes in contrast of these (i.v analgesics). Using (intra-peritoneal ropivacaine) has good efficacy having not any increase in side effects in reducing post-operative pain after (cholecystectomy surgery) [12].

After (open cholecystectomy), major reason of post-operative pain due to stimulation of (sensory nerves) in the area of skin incision & (injured soft tissues). Because of release of (inflammatory mediators) with (systemic effect), tissues respond as inflammation as a result of (tissue damages) [13].

To control post-operative pain is much crucial as it may arise various complications in which inflammatory responses, metabolic & (pulmonary dysfunction) are included. Their link is with physiological & (hemodynamic changes) which are due to (spinal reflex spasms), (diaphragmatic dysfunction) & endocrine. To manage pain in main (surgical procedures) as (open cholecystectomy) is mandatory as it may cause effects on respiratory system badly.

An area is used for incision in (open cholecystectomy) which hinders (respiratory movements). It causes (poor cough reflex) & results in pneumonia & atelectasis [14]. Many methods are employed for controlling post-operative pain in which epidural anaesthesia, (wound infiltration of local anaesthetics), (intra-peritoneal infiltration of local anaesthetics) & (patient controlled analgesia) i.e. PCA [15, 18].

Our outcomes are comparable to a research done in India in which (bupivacaine) is compared to

(pethidine). That study has pain scores among (30 – 360) minutes based on VAS score & were same as our results [19]. Instead of bupivacaine, (ropivacaine) is used in our study. It has similar efficacy compared with bupivacaine but because of lesser (lipophilicity), it is less neurotoxic & (cardio toxic) [20].

Same outcomes were noted in following researches: Singh et al24, Ahmed et al22, Shukla et al21 & Singh et al13. The rate of (nausea or vomiting) was found as  $p < 0.05$  as greater 39 at 62 percent in (placebo group) compared to 24 at 38 percent in (ropivacaine group). The results of this study were good as compare to past studies although side effects were normally linked to (placebo group) [23]. Hospital stay results were almost same in both groups & no significant  $p > 0.05$  difference. Average hospital stay in placebo group was  $(5.46 \pm 1.366)$  days & in study group  $(5.63 \pm 1.235)$  days which are comparable to past researches [24].

Results of this study in (open cholecystectomy) support the use of (intra-peritoneal ropivacaine). It is good to control post-operative pain & minimizing complications as (shoulder tip pain) & (nausea or vomiting) after (open cholecystectomy).

**CONCLUSION:**

Study group has less mean pain score as ( $p < 0.05$ ) than placebo group in a comparison of pain score after 1, 6 & 24 hrs of surgery. Rate of (nausea/vomiting) was found  $p < 0.05$  & it was greater as 62 percent in placebo than as 38 percent in study group. No difference was found as  $p > 0.05$  between groups based on mean age as  $(47.89 \pm 8.56)$  versus  $(48.75 \pm 9.36)$ , gender as females 70 percent versus 68 percent & time in surgery as  $88.54 \pm 12.34$  minutes versus  $91.70 \pm 13.50$  minutes. Also in (American society of anaesthesiologist) i.e. ASA grades in both (study & placebo) group of patients respectively.

In those patients experiencing (open cholecystectomy), (intra-peritoneal infiltration of ropivacaine) can be employed as much effective (post-operative analgesia).

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