ANAESTHESIA, PAIN & INTENSIVE CARE
www.apicareonline.com

ORIGINAL ARTICLE

A clinical comparative study of intraperitoneal instillation of ropivacaine alone or ropivacaine with nalbuphine for postoperative analgesia in laparoscopic cholecystectomy

Sanjay Singh[1], M. K. Giri[2], Mayurika Singh[3], Navin Kumar Giri[4]

[1]Assistant Professor;
[4]Postgraduate Resident,
Department of Surgery, Moti Lal Nehru (MLN) Medical College, Allahabad 211002, Uttar Pradesh (India)
[2]Assistant Professor,
Department of Anesthesiology, Moti Lal Nehru (MLN) Medical College, Allahabad 211002, Uttar Pradesh (India)
[3]Assistant Professor,
Department of Radiodiagnosis, Moti Lal Nehru (MLN) Medical College, Allahabad 211002, Uttar Pradesh (India)

Correspondence: Dr Manoj Kumar Giri, PMS Quarters No. 4, SRN Hospital Campus, Allahabad 211002, Uttar Pradesh (India); Phone: +9044479649; E-mail: drmanoj.giri@gmail.com

Received: 21 Feb 2017
Reviewed:
21 Feb, 17 Aug 2017
Corrected:
28 April, 22 Aug 2017
Accepted: 22 Aug 2017

ABSTRACT

Background & objectives: Intraperitoneal instillation of local anesthetic agents with or without opioids has been proposed to reduce postoperative pain after laparoscopic procedures. So, we did a prospective, randomized, double blind, placebo-controlled study to compare the effectiveness of intraperitoneal 0.2% ropivacaine alone or with nalbuphine for postoperative analgesia in laparoscopic cholecystectomy.

Methodology: A total of 90 patients of ASA class I and II for laparoscopic cholecystectomy procedures were enrolled for this study. The drug was instilled intraperitoneally before the removal of trocar at the end of surgery. In Group-1 (n=30): 0.2% ropivacaine + 2 mg nalbuphine in 20 ml, in Group-2 (n=30): 20 ml 0.2% ropivacaine alone and in Group-3 (n=30) normal saline 20 ml were installed intraperitoneally. Postoperative pain was assessed by visual analogue score for 24 hours and when VAS >4, rescue analgesic was administered. The total amount of rescue analgesics given in the postoperative period and side effects were noted in this study.

Results: Intraperitoneal instillation of ropivacaine with nalbuphine significantly reduced immediate postoperative VAS scores (1.0667 ± 0.78, 3.36 ± 1.37 and 5.53 ± 1.85 in Group-1, 2 and 3 respectively). It also reduced VAS at 8 hours after surgery in the Group-1 (0.8 ± 0. 71) compared to the Group-2 VAS (2.73 ± 1.25). The time for the first rescue analgesic requirement was significantly higher in Group-1 (6.15 h) compared to the Group-2 (4.51 h). Total amount of rescue analgesic was required more in Group-2 and Group-3 compared to Group-1.

Conclusion: Addition of nalbuphine to intraperitoneal ropivacaine significantly prolongs the time to first rescue analgesic requirement and reduces the total consumption of rescue analgesics in 24 hours without any significant increase in adverse events in laparoscopic cholecystectomies.

Key words: Ropivacaine; Intraperitoneal Instillation; Nalbuphine; Postoperative analgesia

Citation: Singh S, Giri MK, Singh M, Giri NK. A clinical comparative study of intraperitoneal instillation of ropivacaine alone or ropivacaine with nalbuphine for postoperative analgesia in laparoscopic cholecystectomy. Anaesth Pain & Intensive Care 2017;21(3):335-339

INTRODUCTION

Laparoscopic surgical procedures have almost replaced open surgical procedures because of better and smaller incision, minimal bleeding, less postoperative pain and shorter stays in postoperative period.[1,2,3] Mild to moderate postoperative pain in laaproscopic surgeries is mostly in the upper abdomen, shoulder tip and back

regions. Postoperative pain is more common during the first few hours after surgery and usually reduces over the next 48 to 72 hours.[4] Intra-abdominal cavity stretching, peritoneal and diaphragmatic irritation caused by residual carbon dioxide is most common factors responsible for postoperative pain [5,6]. Local anesthetics agents instillation over intraperitoneum have been used to minimize postoperative pain after laparoscopic surgery[7]. Local anesthetics have been studied for post operative pain relief by instillation over the peritoneal cavity for minimally invasive procedures, such as laparoscopic cholecystectomy and gynecological laparoscopy.[8] Addition of narcotics was thought to be useful in prolongation of the analgesia.

We conducted this prospective, randomized, double blind, placebo-controlled study to compare the effectiveness of intraperitoneal 0.2% ropivacaine alone or with nalbuphine for postoperative analgesia in laparoscopic cholecystectomy.

METHODOLOGY

After permission from the institutional ethical committee, a total of ninty adult patients of both sexes between ages 18 to 60 years, ASA I and II, undergoing elective laparoscopic cholecystectomy were divided randomly into three groups of 30 patients each in every group.

Patients were briefed about the visual analogue scale (VAS) on the day previous to the surgery and a detailed explanation of the same was given. The patients were divided into three groups after computer generated randomization and blinding.

Group-1 (n=30): received 20 ml of 0.2% ropivacaine along with 2 mg of nalbuphine

Group-2 (n=30): received 20 ml 0.2% ropivacaine

Group-3 (n=30): received 20 ml of normal saline as placebo

General anesthesia protocol:

All patients were pre-medicated 30 min before with fentanyl 2.0 μg/kg, glycopyrrolate 0.2 mg and ondansetron 0.1 mg/kg with inj midazolam 30 μg /kg intravenously. Preoxygenation was carried out for 3 min with 100% oxygen, and anesthesia was induced with inj propofol (2-2.5 mg/kg) till loss of verbal commands + inj succinylcholine (1.5-2 mg/kg) IV. Intubation by the oral route was done with cuffed PVC endotracheal tube of appropriate size.

Maintenance of anesthesia done with 50:50 $N_2O + O_2$ + isoflurane (0.5-1.0%) + inj vecuronium (0.02-0.04 mg/kg). Mechanical ventilation, with tidal volumes 8 - 10 ml/kg, was adjusted to maintain end-tidal carbon dioxide ($EtCO_2$) between 35 and 40 mmHg. During laparoscopy, intra-abdominal pressure was limited to 10 - 12 mmHg. Non depolarizing muscle blockade was reversed with inj neostigmine 0.05 mg/kg + glycopyrrolate 0.01 mg/kg.

Intra operative monitoring consisted of ECG, NIBP, $EtCO_2$ and pulse oximeter. The study drugs were instilled intraperitoneally before the removal of trocar in equal volumes from all the ports.

In the Post-anesthesia Care Unit (PACU) the visual analogue scale (VAS), Ramsay sedation score and PONV Intensity Scale were used to assess each patient. Postoperative pain assessment was done using VAS score of 0-10 (0 = No pain, 10 = Worst imagined pain). The degree of postoperative pain was assessed using the VAS at 30 min, 1 h, 4 h, 8 h, 12 h, 16 h, and 24 h postoperatively. Those patients who had VAS > 4, were administered a bolus of diclofenac aqueous 75 mg intravenous as rescue analgesia. Breakthrough pain was controlled with inj tramadol 1.0 mg/kg in increments up to a maximum dose of 2 mg/kg. Postoperative complications, e.g. pain, nausea and vomiting, hypotension, bradycardia and itching etc. were be assessed at the above times. Nausea and vomiting, need of any rescue analgesics for pain, any voiding problems, respiratory difficulties were documented by proforma vide infra. Inj ondansetron 0.1 mg/kg was given intravenously for vomiting.

Statistical analysis: Data were presented as mean ± SD or proportion (%). Statistical analysis was performed on SPSS version 12.0 along with an ANOVA test and a $P < 0.05$ was considered significant.

RESULTS

A total of 90 patients participate in this study, and they were subsequently enrolled (n = 30 per group), with no patient dropouts. The groups were similar with respect to age, sex, weight , height and duration of surgery (Table 1).

VAS scores were found lower in the ropivacaine with nalbuphine group (1.0667 ± 0.78) as compared to the ropivacaine alone and saline group, 3.36 ± 1.37 and 5.53 ± 1.85 in Group-2 and 3 respectively) (Table 2).

In saline group, 50 % of the patients demanded the rescue analgesia within the 1st postoperative period. Patients of Group-1 demanded the first dose of rescue analgesic in the 4^{th} postoperative hours.

Normal saline group required more frequent dosing. Total doses of rescue analgesia were lowest in

Table 1: Baseline characteristics

Variable	Group1	Group-2	Group-3	p value
Age (Yrs)	37.6 ± 12.28	36.89 ± 12.59	40.60 ± 11.09	0.454
Sex (M:F)	07:23	09:21	12:18	0.628
Weight (Kg)	50.23 ± 4.62	50.33 ± 4.45	50.9 ± 4.93	0.837
Height (cm)	149.83 ± 5.92	149.76 ± 5.91	150.16 ± 6.04	0 .961
Duration of surgery (minutes)	82.2 ± 8.25	89.2 ± 8.69	81.6 ± 8.73	0.36

Table 2: Mean visual analogue scale pain score. Data given as Mean ± SD

Group	Immediately After Surgery	1 h	4 h	8 h	12 h	16 h	24 h
Group-1	1.0667 ± 0.78	0.4 ± 0.49	0.56 ± 0.50	0.8 ± 0.71	2.3 ± 1.02	3.56 ± 0.89	4.53 ± 1.45
Group-2	3.36 ± 1.37	1.73 ± 1.87	2.8 ± 1.62	2.73 ± 1.25	3.96 ± 1.49	4.46 ± 1.04	5 ± 0.83
Group-3	5.53 ± 1.85	5.06 ± 1.31	1.6 ± 0.49	2.26 ± 0.78	2.86 ± 0.86	5.46 ± 1.88	7.16 ± 0.69
p value	< .0001	< .0001	< .0001	< .0001	< .0001	< .0001	< .0001

Table 3: Number of patients require rescue analgesics. Data given as N (%)

Time Interval	Group-1	Group-2	Group-3
Immediate postoperatively	0 (0)	7 (0.23)	16 (0.53)
1st postoperative hour	0 (0)	7 (0.23)	12 (0.4)
4th postoperative hour	1 (0.033)	9 (0.3)	10 (0.33)
8th postoperative hour	7 (0.23)	7 (0.23)	14 (0.46)
12th postoperative hour	8 (0.26)	15 (0.5)	17 (0.56)
16th postoperative hour	11 (0.36)	16 (0.53)	25 (0.83)
24th postoperative hour	17 (0.56)	20 (0.66)	30 (100)
Total dose of rescue analgesia required in the group over 24 h period	44	81	124

Table 4: Incidence of pruritus, emesis, hypotension, bradycardia and shoulder pain n three groups [N (%)]

Adverse effects	Group-1	Group-2	Group-3	p value
Pruritus	6 (20)	2 (6)	1 (3)	0.084
Emetic symptoms	4 (10)	3 (10)	9 (30)	0.069
Hypotension	3 (10)	0 (0)	1 (3)	0.166
Bradycardia	9 (30)	1 (3)	1 (3)	0.002
Shoulder pain	0 (0)	0 (0)	6 (20)	< 0.001

Table 5: Postoperative Ramsay Sedation Scale (RSS) [Mean ± SD]

Time period	Group1	Group-2	Group-3	p value
Immediate postoperatively	4.56 ± 0.50	2.40 ± 0.50	2.26 ± 0.44	< .001
1st postoperative hour	3.96 ± 0.49	1.93 ± 0.25	1.90 ± 0.30	< .001
4th postoperative hour	2.43 ± 0.50	1.83 ± 0.37	1.66 ± 0.47	< .001
8th postoperative hour	2.26 ± 0.44	1.73 ± 0.44	1.43 ± 0.50	< .001
12th postoperative hour	1.50 ± 0.50	1.26 ± 0.44	1.06 ± 0.25	< .065
16th postoperative hour	1.33 ± 0.47	1.20 ± 0.40	1.00 ± 0.00	< .0253
24th postoperative hour	1.10 ± 0.35	1.13 ± 0.34	1.03 ± 0.18	0.392

nalbuphine with ropivacaine group and highest in normal saline group (Table 3).

Time to request for the first dose rescue analgesia was longer in the ropivacaine with nalbuphine group than ropivacaine group or saline group . Total analgesic consumption was maximum in saline group and minimum in ropivacaine with nalbuphine group (Table 3).

The incidence of pruritis was more with ropivacaine with nalbuphine group than other groups, but this difference was found to be statistically non-significant ($p = 0.084$). Postoperative emesis was more in normal saline group. Incidence of hypotension and bradycardia was more in Group-1 than other groups but this difference was found to be non-signigicant. Shoulder pain was not observed in any of the three groups in the first 8 h postoperatively; however, after 8 h, its incidence was statistically significant in saline group patients. No shoulder pain was observed in patients receiving ropivacaine alone or with nalbuphine even after 8 h postoperatively (Table 4).

Sedation level of the patients was assessed based on the Ramsey sedation scale. Sedation scores were statistically higher in the ropivacaine with nalbuphine group as compared with ropivacaine alone or saline group in immediate postoperative period (Table 5).

DISCUSSION

Postoperative pain from laparoscopic surgeries is mainly due to stretching of visceral and parietal peritoneum and referred shoulder pain. All of these differ from each other in the form of intensity, latency and duration.[9] We found that pain intensity was lower in patients who received intraperitoneal nalbuphine with ropivacaine compared with those who received intraperitoneal saline during the first 8 h after recovery. The total dose of rescue analgesics used was markedly reduced in patients with intraperitoneal ropivacaine and nalbuphine group.

Kang H et al[10], studied intraperitoneal instillation of ropivacaine for postoperative pain relief in laparoscopic appendectomy and found lower fentanyl consumption as rescue analgesic in the ropivacaine group as compared to placebo, this also supports our study in which reduced requirement of rescue analgesic diclofenac in ropivacaine alone and ropivacaine with nalbuphine as compare to placebo saline group. Previous studies[11,12,13] in different types of laparoscopic surgeries with intraperitonial ropivacaine also support our result for better postoperative pain relief. Opioids intraperitoneally like morphine[14,15], fentanyl [16], or tramadol[17,18,19] have shown good results in postoperative analgesia and also support our results, but we did not find any previous study in which intraperitoneal nalbuphine was administered for postoperative pain relief.

Contrary to our findings, Ali et al.[20] did not find appreciable analgesia in patients undergoing abdominal hysterectomy for intraperitoneal administration of a local anesthetic into the pelvic cavity. Schulte-Steinberg et al.[21] also did not find significant analgesia after intraperitoneal morphine in laparoscopic cholecystectomy.

The incidence of shoulder pain was lower in intraperitoneal nalbuphine or ropivacaine group compared with the control saline group. Narchi et al.[12] showed that there was less postoperative shoulder pain with intraperitoneal saline plus lidocaine. However, previous studies[17,18] with intraperitoneal opioids found a non-significant difference for shoulder pain as compared to placebo. This was not in agreement with our results, because none of these studies used intraperitoneal nalbuphine.

PONV was greater in patients with intraperitoneal nalbuphine or saline than in patients given intraperitoneal ropivacaine alone. However, previous studies[21,22] did not show any statistical difference between patients given either intraperitoneal local anesthetics or opioids for the incidence of PONV.

CONCLUSION

The combination of intraperitoneal ropivacaine and nalbuphine is superior to plain ropivacaine for reducing postoperative pain in patients undergoing laparoscopic surgery, without any significant increase in adverse events. Ropivacaine with or without nalbuphine reduces not only the intensity of pain, but also the total dose of rescue analgesic consumption. Ropivacaine alone or with nalbuphine also reduces the incidence of shoulder pain, but bradycardia was significantly higher in these patients. Therefore, we conclude that intraperitoneal instillation of ropivacaine with nalbuphine reduces not only the intensity of visceral, parietal and shoulder pain but also the total rescue analgesic dose consumption.

Source of Support: Nil

Conflict of Interest: None declared

Authors Contribution:

SS: conduct of study and literature search
MKG: Design of study and manuscript editing
MS: Study analysis and literature research
NKG: conduction of study work and statistical analysis

REFERENCES

1. Buanes T, Mjåland O. Complications in laparoscopic and open cholecystectomy: a prospective comparative trial. Surg Laparoscopy Endosc. 1996;6:266–72. [PubMed]
2. Mendoza-Sagaon M, Hanly E, Talamini M, Kutka M, Gitzelmann C, Herreman-Suquet K, et al. Comparison of the stress response after laparoscopic and open cholecystectomy. Surg Endosc. 2000;14:1136–41. [Free full text]
3. Jatzko GR, Lisborg PH, Pertl AM, Stettner HM. Multivariate comparison of complications after laparoscopic cholecystectomy and open cholecystectomy. Ann Surg. 1995;221:381 [PubMed] [Free full text]
4. Gupta R, Bogra J, Kothari N, Kohli M. Postoperative analgesia with intraperitoneal fentanyl and bupivacaine: A randomized control trial. Can J Med. 2010;1(Suppl 1):1–9.
5. Diemunsch P, Fourgeaud L. SchoefflerP.Outpatient Laparoscopy. Cah Anesthesiol 1993; 41:385–391. [PubMed]
6. Jakson SA, Laurence AS, Hill JC. Does post-laparoscopy pain relate to residual carbon dioxide? Anaesthesia 1996; 8:441–445. [PubMed] [Free full text]
7. Zmora O, Stolik-Dollberg O, Bar-Zakai B, Rosin D, Kuriansky J, Shabtai M. Intraperitoneal bupivacaine does not attenuate pain following laparoscopic cholecystectomy. JSLS. 2000 Oct-Dec;4(4):301-4. . [PubMed] [Free full text]
8. Helvacioglu A1, Weis R. Operative laparoscopy and postoperative pain relief. Fertility and Sterility, Fertil Steril. 1992 Mar;57(3):548-52.[PubMed]
9. Choi JB, Kang K, Song MK, Seok S, Kim YH, Kim JE. .Pain Characteristics after Total Laparoscopic Hysterectomy. Int J Med Sci. 2016 Jul 5;13(8):562-8. doi: 10.7150/ijms.15875. eCollection 2016.[PubMed] [Free full text]
10. Kang H, Kim BG .Intraperitoneal ropivacaine for effective pain relief after laparoscopic appendectomy: a prospective, randomized, double-blind, placebo-controlled study,J Int Med Res. 2010 May-Jun;38(3):821-32. [PubMed]
11. Park YH, Kang H, Woo YC, Park SG, Baek CW, Jung YH, et al. The effect of intraperitoneal ropivacaine on pain after laparoscopic colectomy: a prospective randomized controlled trial. J Surg Res. 2011 Nov;171(1):94-100. doi: 10.1016/j.jss.2010.03.024. [PubMed]
12. Cha SM, Kang H, Baek CW, Jung YH, Koo GH, Kim BG, et al.Peritrocal and intraperitoneal ropivacaine for laparoscopic cholecystectomy: a prospective, randomized, double-blind controlled trial. J Surg Res. 2012 Jun 15;175(2):251-8. doi: 10.1016/j.jss.2011.04.033.[PubMed]
13. Somaini M, Brambillasca P, Ingelmo PM, Lovisari F, Catenacci SS, Rossini V, Bucciero M, et al. Effects of peritoneal ropivacaine nebulization for pain control after laparoscopic gynecologic surgery.J Minim Invasive Gynecol. 2014 Sep-Oct;21(5):863-9 [PubMed]
14. BP Butala, VR Shah, K Nived . Randomized double blind trial of intraperitoneal instillation of bupivacaine and morphine for pain relief after laparoscopic gynecological surgeries. Saudi J Anaesth. 2013 Jan-Mar; 7(1): 18–23. doi: 10.4103/1658-354X.109800. [PubMed] [Free full text]
15. Hernández-Palazón J, Tortosa JA, Nuño de la Rosa V, Giménez-Viudes J, Ramírez G, Robles R. Intraperitoneal application of bupivacaine plus morphine for pain relief after laparoscopic cholecystectomy. Eur J Anaesthesiol 2003; 20:891–896. [PubMed]
16. Singh A, Mathur SK, Shukla VK. Postoperative analgesia with intraperitoneal ropivacainewith and without fentanyl after laparoscopic cholecystectomy: a randomized double-blind controlled trial.OA Anaesthetics 2013 May 01;1(1):9. [Free full text]
17. Akinci SB, Ayhan B, Aycan IO, Tirnaksiz B, Basgul E, Abbasoglu O, et al. The postoperative analgesic efficacy of intraperitoneal tramadol comparedto normal saline or intravenous tramadol in laparoscopic cholecystectomy. Eur J Anaesthesiol. 2008 May;25(5):375-81. doi: 10.1017/S0265021508003694. [PubMed]
18. Memis D, Turan A, Karamanlioglu B. Intraperitoneal tramadol and buvacaine in total abdominal hysterectomy. Eur J Anaesthesiol 2005; 22:804–805.
19. B Karsli, N Kayacan, G Zorlu, G Arici, M Erman. The effects of intraperitoneal tramadol, tenoxicam and bupivacaine on pain relief after laparoscopic gynaecological procedures. Pain Clin 2003; 15:281–287. [Free full text]
20. Ali PB, Cotton BR, Williamson KM, Smith G. Intraperitoneal bupivacaine or lidocaine does not provide analgesia after total abdominal hysterectomy. Br J Anaesth 1998; 80:245–247. [PubMed]
21. Schulte-Steinberg H, Weninger E, Jokisch D, Hofstetter B, MiseraA, Lange V, et al. Intraperitoneal versus interpleural morphine or bupivacaine for pain after laparoscopic cholecystectomy. Anesthesiology 1995; 82:634–640. [PubMed] [Free full text]
22. G. Pappas-Gogos, K. E. Tsimogiannis, N. Zikos, K. Ni-kas, A. Manataki and E. C. Tsimoyiannis, Preincisional and Intraperitoneal Ropivacaine plus Normal Saline Infusion for Postoperative Pain Relief after Laparoscopic Cholecystectomy: A Randomized Double-Blind Controlled Trial. Surg Endosc. 2008 Sep;22(9):2036-45. doi: 10.1007/s00464-008-9762-x. [PubMed]

★★★★★