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Comparison of Preemptive Intraperitoneal Instillation and Nebulisation of 0.5% Ropivacaine in Laparoscopic Cholecystectomy for Post-operative Pain Relief

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Abstract

Objective: The etiology of postoperative pain in patients undergoing laproscopic cholecystectomy is multifactorial consisting of incisional and visceral pain from the operation itself and parietal pain from trauma and irritation to the peritoneum and diaphragm. *Design:* This randamozied single blind study was conducted on 60 patients of either sex undergoing laproscopic cholecystectomy under general anesthesia. Group A [n=30] received 15 ml of 0.5% ropivacaine by instillation and group B [n=30] received 15 ml of 0.5% ropivacane intraperitoneally by piston type of nebulization 10 minutes before surgery and both the groups got 5 ml [0.5%] ropivacaine at the trocar site at the end of surgery. Results: Patients in both the groups were comparable with respect to age, sex and weight [p>0.05]. VAS score for incisional pain was significantly lower in Group A at 1hour and 8 hrs postoperatively [p=0.02 and p=0.04] respectively. At all other intervals the incisional pain, Visceral pain and shoulder tip pain was comparable amongst the two groups [p>0.05]. Time to first analgesia was longer in group A [2.29 hrs] as compared to Group B [1.66 hrs] but was stastically insignifiacant [p>0.5]. Mean total number of analgesic used was 1.4 in both the groups [p=1]. *Conclusion:* Intraoperative subdiaphgramatic and intraperitoneal instillation of ropivacaine 0.5% is beneficial and better modality of pain relief because of ease of technique and better VAS scores as compared to intrperitoneal nebulization of ropivacaine.

Keywords: Intraperitoneal nebulization; Instillation; Ropivacaine; Laproscopic cholecystectomy; Preemptive.

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Introduction

Pain after laparoscopic surgery is the result of surgical manipulations and intraperitoneal insufflation of carbon dioxide causing peritoneal stretching, diaphragmatic irritation, changes in intra-abdominal pH, moreover retention of the insufflated gas in the abdominal cavity after surgery are all attributed for post operative pain.[1] The efficacy of intraperitoneal use of local anaesthetics for postoperative pain relief in laparoscopic

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procedures is still debated. Some studies suggest that local anaesthetic infiltration does attenuate post operative pain after laparoscopic cholecystectomy[2]. Some suggest that it does not improve patient outcome in terms of post operative pain after laparoscopic surgery.[3]

Intraperitoneal aerosolization of local anaesthetics has proven efficient in spreading drugs homogenously throughout the peritoneum[4,5]. This technique combines the effect of gas conditioning and the analgesic benefits of local anaesthetic instillation[4]. Till now there have been only a few trials comparing the analgesic effects achieved with intra-peritoneal nebulisation with intra-peritoneal instillation of local anaesthetic agents in laproscopic cholecystectomy. Optimal management of postoperative pain is important as this procedure is now carried out in an ambulatory setting. Keeping the above factors in mind, the present study was conducted in our institution.

Material and Methods

After approval of Institutional Research and Ethical Committee a prospective randomized single blind [observer was blind to study] was carried out in 60 ASA I and ASA II patients posted for laproscopic cholecystectomy under general anesthesia. Patients were randomly allocated into into two groups of 30 each.

Group A: Subdiaphragmatic and Sub hepatic Instillation of Ropivacaine

Group B: Intraperitoneal Nebulisation of Ropivacaine using piston type air nebulizer

In both the groups, 15ml of 0.5% ropivacaine was given intraperitoneally (by instillation in group A and by nebulisation in group B) immediately after the insertion of trocars and 5ml of 0.5% ropivacaine was infiltrated into the port sites at the end of the surgery.

Exclusion Criteria: Patients with severe chronic obstructive airway disease, Patients with coronary artery disease, History of allergy to Local Anaesthetic agents, Conversion of Laparoscopic Cholecystectomy to Open Cholecystectomy, Intra Operative intra abdominal drain insertion, Age < 20 years and > 60 years.

Anesthesia Technique: Patients were kept nil per orally for at least 6 hrs. In the operation theatre, all patients were connected to monitors and baseline vital data (mean arterial pressure, heart rate, pulse oximetry and respiratory rate) were recorded. Intravenous line was secured and intravenous fluid was started in the contralateral arm. The patient was given Injection glycopyrolate 0.01 mg/kg i.v., injection butorphanol 0.02 mg/kg i.v. as analgesic after preoxygenation with 100% Oxygen for 3 minutes followed by induction with injection thiopentone 5 mg/kg intravenously followed by injection succinyl choline 2 mg/kg intravenously. Airway was secured with appropriate size endotracheal tube and anesthesia was maintained with N_2O (66%), O_2 (33%) and isoflurane (0-1%). Non depolarizing muscle relaxant atracurium (0.5 mg/kg) was used. After insertion of the trocar, in Group A sub diaphragmatic and sub hepatic instillation of 15 ml of 0.5% ropivacaine was done and surgery was started 10 min after the instillation of the drug. In group B, nebulisation with 15 ml of 0.5% ropivacaine was done intraperitoneally. The piston type air nebulizer was kept at a height of 6 ft to minimize contaminated air. Intraperitoneal pressure was maintained between 12-15 mm Hg and gas was vented if pressure increases. At the end of surgery, the port sites were infiltrated with 5 ml of 0.5% ropivacaine in both the groups and isoflurane was stopped, injection ondansetron 0.1 mg/kg was given and muscle relaxation was reversed with injection neostigmine 0.05 mg/kg i.v. and injection glycopyrrolate 0.01 mg/kg i.v. Patient was extubated and 100% O_2 was given via the mask for 5 minutes in operation theatre. Patients were monitored intra-operatively for Heart rate Mean blood pressure Arterial oxygen saturation. These parameters were noted at time of instillation or nebulisation (taken as 0 minutes), then at 3 minutes, 5 minutes, 10 minutes and thereafter every 10 minutes until the end of surgery. Patients were analyzed postoperatively for following parameters:

1. Incisional Pain (At 0, 1, 2, 3, 4, 5, 6, 8, 16 and 24 hrs)
2. Abdominal (Visceral) Pain (At 0, 1, 2, 3, 4, 5, 6, 8, 16 and 24 hrs)
3. Shoulder Pain (At 0, 1, 2, 3, 4, 5, 6, 8, 16 and 24 hrs)
4. Duration between time of extubation and first dose of analgesic (diclofenac)
5. Analgesic requirement for 24 hrs

The Intensity of pain was assessed on Visual Analogue Scale (VAS). Analgesic requirement was assessed in terms of administration of number of injections of diclofenac sodium [75 mg] on demand. Analgesic was given if patient has pain equivalent to VAS of 4 or more.

Results

The data obtained from both the groups was observed and statistically compared using computer software SPSS version 20 and Microsoft excel. Unpaired t- test was used for quantitative data and Mann Whitney U test for non parametric data. A *p*-value of < 0.05 was considered statistically significant.

Both the groups were comparable in demographic variable like age, sex and weight distribution. Mean age (in years) in group A was 41.5 and in group B was 42. The ratio of males: female in group A was 9:21 and group B was 11:19 [$p > 0.05$]. The baseline parameters like heart rate, mean B.P. and SpO_2 were also comparable in both the groups. There was no significant difference found in the heart rate, mean B.P. and SpO_2 at various time intervals during the surgery in group A and B which means that the two techniques had no variation in terms of hemodynamic effects.[$p > 0.05$]

The VAS score was statistically significant While comparing incisional pain at 1 hr (*p*-value 0.02) and 8 hrs (0.042) postoperatively. The pain scores recorded at all other time intervals were found to be comparable with a p-value > 0.05. (Table 1, Figure 1a). The values for visceral pain and shoulder tip pain were found to be statistically comparable at all time intervals [$p > 0.05$] (Table 2 and 3).

In our study, six patients in both the groups did not require any analgesic during the first 24 hrs after surgery. The mean time in group A was found to be 2.29 hrs (2 hrs 17 min) and that in group B was 1.66 hrs (1 hr 40 min) [$p = 0.35$]. There was no difference in the mean analgesic requirement in both the groups and it was 1.4 doses in 24 hrs. [Table 4]

Table 1: Table showing comparison of incisional pain scores at different time intervals in group A and B

	Group A			Group B			*p*-value
VAS	0	1-3	4 or more	0	1-3	4 or more	
0 hr	20	5	5	12	15	3	0.23 (NS)
1 hr	11	7	6	2	12	12	0.02 (S)
2 hr	6	6	4	1	8	3	0.581 (NS)
3 hr	3	9	0	1	8	0	0.669 (NS)
4 hr	1	10	1	2	7	0	0.405 (NS)
5 hr	1	9	0	2	7	0	0.448 (NS)
6 hr	1	8	1	1	6	2	0.296 (NS)
8 hr	0	7	1	1	6	0	0.042 (S)
16 hr	0	6	0	1	5	0	0.067 (NS)
24 hr	3	3	0	1	5	0	0.241 (NS)

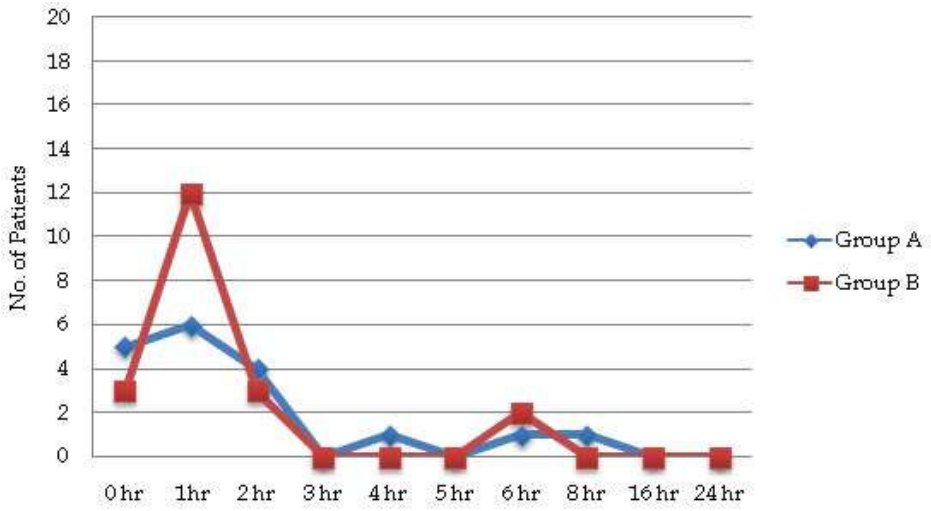

Fig. 1: No. of patients with severe incisional pain (VAS 4 or more)

Table 2: Table showing comparison of visceral pain scores at different time intervals in group A and B

	Group A			Group B			*p*-value
VAS	**0**	**1-3**	**4 or more**	**0**	**1-3**	**4 or more**	
0 hr	20	5	5	14	3	3	0.39 (NS)
1 hr	9	8	7	4	9	13	0.098 (NS)
2 hr	6	6	4	2	7	13	0.755 (NS)
3 hr	2	10	0	1	8	0	0.846 (NS)
4 hr	0	10	2	1	8	0	0.422 (NS)
5 hr	1	9	0	1	8	0	0.243 (NS)
6 hr	1	8	1	0	7	2	0.447 (NS)
8 hr	0	7	1	1	5	1	0.281 (NS)
16 hr	0	6	0	1	5	0	0.093 (NS)
24 hr	3	3	0	1	5	0	0.394 (NS)

Table 3: Table showing comparison of shoulder tip pain scores at different time intervals in group A and B

	Group A			Group B			*p*-value
VAS	0	1-3	4 or more	0	1-3	4 or more	
0 hr	29	1	0	30	0	0	0.317 (NS)
1 hr	23	1	0	25	0	1	0.977 (NS)
2 hr	16	0	0	12	0	0	1 (NS)
3 hr	12	0	0	8	1	0	0.248 (NS)
4 hr	12	0	0	8	1	0	0.248 (NS)
5 hr	10	0	0	8	1	0	0.292 (NS)
6 hr	9	0	0	9	0	0	1 (NS)
8 hr	8	0	0	7	0	0	1 (NS)
16 hr	6	0	0	6	0	0	1 (NS)
24 hr	6	0	0	6	0	0	1 (NS)

Table 4: Time of first analgesic dose and total analgesic requirement in the post-operative period

No. of doses	**0**	**1**	**2**	**3**	**Mean doses in 24 hrs**	**Mean time (hrs) to 1st analgesic**
Group A	6	9	12	3	1.4	2.29*
Group B	6	8	14	2	1.4	1.66*

*p=0.35

Discussion

Laparoscopic surgeries have become increasingly popular mainly due to the lower perioperative morbidity, less postoperative pain, reduced postoperative infections, less scar deformations and shorter length of stay in the hospital as compared to open surgery. Although local anaesthetic instillation intraperitoneally and at the site of incisions has been shown to reduce postoperative pain and analgesic requirement, but it is not enough to eliminate visceral and shoulder pain. One possible reason could be the non-uniform distribution of the local anaesthetic in the peritoneal cavity. This led to the use of nebulisation as a new modality to deliver drugs intraperitoneally. It has been reported to provide a homogenous spread of drug allowing a better distribution throughout the peritoneum.[6]

In our study, the duration of analgesic effect of 100 mg ropivacaine when instilled into the peritoneal cavity was found to be 2 hr 17 min as compared to Labaille T *et al.*[7], who found the duration of analgesia to be 1 hr 10 min while using 100 mg of ropivacaine. This could be attributed to the fact that the incision sites were not infiltrated with local anaesthetic and moreover, the rescue analgesic was administered to the patients at a VAS score of ≥ 3 by them we prescribed rescue analgesia at a VAS score of ≥ 4. Another reason for a shorter pain free period in their study could be a longer duration of surgery, mean duration being 125 min but in our study 20-50 min in most of the cases. They also used 300 mg of ropivacaine in one of the groups and found that a higher dose did not improve clinical effectiveness but lead to excessively large plasma concentrations of the drug.

In our study, the analgesic effect of ropivacaine, either instilled or nebulized into the peritoneal cavity, were almost comparable. However, at 1 hr and 8 hrs postoperatively instillation proved to be better than nebulization in terms of a lower VAS score. This is in accordance with the results of the study conducted by Buccerio M[6] *et al.* who also concluded that abdominal pain was comparable in instillation and nebulization group. But they found a significant difference in analgesic efficacy of the two techniques in terms of shoulder pain with nebulization being more effective than instillation. 25 patients of nebulization group as compared to no patient in the instillation group had shoulder pain. The possible reason for this reason could be the use of Aeroneb Pro system, which is a microvibration based nebulization device, by Buccerio M[6] *et al.* for nebulization. This device generates aerosol particles with mass median diameter < 5 microns, thus ensuring an efficient drug delivery. On the other hand, in our study, we used a custom made nebulization device using a piston nebulizer which generates comparatively larger size aerosol particles. Thus the complete delivery of drug into the peritoneal cavity could not be assured. Another difference was the use of 60 mg ropivacaine in their nebulization group in comparison to 100 mg used in our study. This could be a probable reason for a higher incidence of postoperative nausea and vomiting seen in the nebulization group of their study (22%) as compared to ours (3%). This study was in accordance with ours as they too did not use a control group. This was because previous studies have shown controversial benefits of intraperitoneal instillation.

In a study conducted by Bissgard T[8] *et al.*, both intraabdominal and shoulder pain after laparoscopic cholecystectomy decreased significantly in the ropivacaine instillation group for 2 hrs postoperatively. From 3 hr onwards, both shoulder pain and intraabdominal pain began to increase. However, this was not the case in our study. The difference could possibly be attributed to the lower concentration of ropivacaine used which was 0.2% in their study as compared to 0.5% ropivacaine used in our study. Moreover, in our cases, the drug was preferentially sprayed on the right hemidiaphragm but they instilled the drug on both sides of the diaphragm. Although they used a higher total dose of ropivacaine, i.e. 286 mg, most of it was given at the incision sites (210 mg) and a comparatively less dose was given intraabdominally. This well explains why incisional pain was well controlled even beyond 3 hrs whereas intraabdominal and shoulder pain increased at 3 hrs postoperatively.

In another study conducted by Goldstein A[2] et al., who used 150 mg of ropivacaine instillation, the mean number of rescue analgesic doses (morphine in this case) was 0.35, whereas in our study the mean number of rescue analgesic doses (diclofenac) was 1.4. This difference could be because of a higher dose of ropivacaine used in their study as compared to 100 mg in ours. However, the rescue analgesia usage was comparable to ours i.e. mean doses amounting to 1.5 in their study as compared to 1.4 in ours.

The incidence of postoperative nausea and vomiting in the study conducted by Goldstein A[2] *et al.* in the ropivacaine group was (15%) slightly higher than our study (10%). Because of study conducted in gynecological procedures with a more extensive surgical manipulation and a longer duration of surgery as compared to laparoscopic cholecystectomy. Moreover, tubal manipulation, which was required in a good number of cases, is known to cause more nausea and vomiting. In accordance with our study, this study also reported no hemodynamic adverse effects of ropivacaine in the patients.

In the study conducted by Callesen T[9] *et al.*, who used instillation of a total dose of 285 mg ropivacaine intraperitoneally, the incidence of postoperative nausea and vomiting was 13% which is comparable to that in our study i.e. 10% in the instillation group. The mean duration of analgesia in this study was around 4 hrs, whereas it was 2 hrs 17 minutes in the instillation group in our study. The difference could be because of the use of a significantly higher dose of ropivacaine i.e. 285 mg as compared to 100 mg in our study.

Conclusion

Our study concluded that intraperitoneal administration of ropivacaine is beneficial in controlling postoperative pain in patients undergoing laparoscopic cholecystectomy, with instillation being a better mode of administration of the drug as compared to nebulisation. In our study, the local anesthetic has been administered before the surgical dissection thus, its role is in "pre-emptive analgesia" which refers that previously administered medications modulate the arousal of nociceptive action in the postoperative period. Moreover, ropivacaine does not seem to have any adverse effects on the hemodynamics of the patient and as it provides analgesia for 2-3 hrs only as far as visceral pain is concerned thus, its combination with other drugs should be tried to prolong the duration of analgesia.

Limitation of the study

1. The number of patient taken was small as only 60 patients were enrolled in the study.
2. Piston type of air nebulization was used instead of aeroneb pro technology as it was not available in our institution.

Conflict of interest: This study did not receive any grant or help from any pharmaceutical company at any level.

References

1. Mouton WG, Bessell JR, Otten KT, *et al.* Pain after laparoscopy. Surg Endosc. 1999;13: 445–8.
2. Goldstein A, Grimault P, Henique A, *et al.* Preventing postoperative pain by local anaesthetic instillation after laparoscopic gynecologic surgery: A placebo-controlled comparison of bupivacaine and ropivacaine. Anesth Analg. 2000;91:403–7.
3. Kaufman Y, Hirsch I, Ostrovsky L, *et al.* Pain relief by continuous intraperitoneal nebulization of ropivacaine during gynecologic laparoscopic surgery- a randomized controlled study and review of literature. J Minim Invasive Gynecol. 2008;15(5):554–8.
4. Ingelmo PM, Somaini M, Bucciero M, *et al.* Nebulisation of local anaesthetics in laparoscopic surgery: A new tool for postoperative analgesia. European Journal of Pain Supplements 2010;4:235–8.
5. Greib N, Schlotterbeck H, Dow WA, *et al.* An evaluation of gas humidifying devices as a means of intraperitoneal local anaesthetic administration for laparoscopic surgery. Anesth Analg. 2008;107:549–51.
6. Buccerio M, Ingelmo PM, Fumagalli R, *et al.* Intraperitoneal ropivacaine nebulization for pain management after laparoscopic cholecystectomy: a comparison with intraperitoneal instillation. Anesth Analg. 2011;113:1266–71.
7. Labaille T, Mazoit JX, Paqueron X, *et al.* the clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. Anesth Analg. 2002;94:100–5.
8. Bisgaard T, Klarskov B, Kristiansen VB, *et al.* Multi-regional local anaesthetic 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. Callesen T, Hjort D, Mogensen T, *et al.* Combined field block and i.p. instillation of ropivacaine for pain management after laparoscopic sterilization. Br J Anaesth. 1999;82:586–90.