Research Paper

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A Comparative Study of Intraperitoneal Nebulization Versus Intraperitoneal Instillation of Ropivacaine Hydrochloride and Morphine Sulphate for Postoperative Analgesia in Laparoscopic Surgery

Medical Science

KEYWORDS : Intraperitoneal, ropivacaine, morphine, laparoscopic surgery, pain relief.

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ABSTRACT

Aim: To study the effect of intraperitoneal local anesthetic administration for postoperative pain relief after laparoscopic surgeries.

Method: 60 patients of ASA I & II, aged 18-60years were divided in two groups. At the end of surgery Ropivacaine (0.75%) 2mg/kg & morphine 1% 2mg was nebulized in group N and instilled in group I .Visual analogue score (VAS) for static and dynamic pain, duration of analgesia, total opiate consumption during first twenty four hours, and complications were noted.

Results: VAS(at rest) at 0, 12 and 18 hours was 5.29 ±1.03 vs. 16.30 ±3.61, 15.23±2.25 vs. 32.21±1.53 and 29.46±2.05 vs. 38.60±2.71 respectively(P<0.05).VAS (dynamic) at 0,12 and 18 hours was 12.21±5.05 vs. 23.21±8.65 , 20.40 ±4.87 vs. 41.02±3.45 and 30.81±5.03 vs. 40.30±9.21 respectively(P < 0.05). Incidence of shoulder pain was 33% in I group and 0% in N group. (P< 0.05). Duration of analgesia was 17.57±0.02 hours in group N and 13.48±0.05 hours in group I (P<0.05). Morphine consumption in N group was 2 times lower. (P< 0.05)

Conclusion: Intraperitoneal nebulization with ropivacaine & morphine reduces postoperative pain & referred shoulder pain as well as morphine consumption after laparoscopic surgeries as compared to instillation. Intraperitoneal local administration technique can be used as an alternative to epidural technique as it provides excellent pain relief without any cardio respiratory complications.

INTRODUCTION:

Pain after laparoscopic surgery results from intraperitoneal insufflations of carbondioxide (Co_2) resulting in peritoneal stretching, diaphragmatic irritation, changes in intrabdominal PH and retention of the insufflated gas in the abdominal cavity after surgery.[1] These effects may irritate peritoneal nerves causing visceral and shoulder pain.

Intraperitoneal administration of local anesthetic has been proposed to provide analgesia after laparoscopic surgeries.[2]Intraperibreal ropivacaine nebulization was found to be effective in reducing shoulder pain.[3] Inhaperitoneal nebulization, a new technique of drug administration,is found to provide homogenous spread of drug with significant reduction in post laparoscopic pain.[4,5]Intraperitoneal local anaesthetic instillation can provide pain relief after laparoscopic surgeries but local anaesthetic distribution may not be uniform throughout the peritoneal surface.[3]

Differences between instillation and nebulization techniques are the duration of local anesthetic administration and the potential for systemic absorption. Nebulization technique results in a lower absorption rate of local anesthetic.[6]Intraperitoneal instillation is completed within 1-2 minutes at the end of surgical procedure and after that abdomen is deflated. While intrapertioneal nebulization of local anaesthetic is completed in approximately 15- 20 minutes. During this period, pneumoperitoneum is maintained with intrabdominal pressure of 12-15 mmHg and local anesthetic spreads to the entire peritoneal area. Combinations of intraperitoneal local anesthetic with opioids have been studied in past.[7,8]

This study was designed to assess the efficacy of ropivacaine nebulization using the Omron nebulizer in comparison with intraperitonial ropivacaine instillation for laparoscopic surgery using low dose morphine in both the techniques.

MATERIAL AND METHODS

After getting permission from ethical commitee of institute, written informed consent from each patient,patients aged 18-60 years of either sex belonging to ASA physical status I and II planned for laparoscopic cholecystectomy,nephrectomy,gastrectomy and hemicolectomy were included in this prospective and randomized study. Patients were excluded if they had acute preoperative pain, chronic pain treatment or anti-epileptic therapy, history of alcohol or drug addiction, severe hepatic or renal impairment, allergy to the study drugs and communication problems.

All patients were pre-medicated with glycopyrrolate 0.2 mg, ondansetron 4 mg and ranitidine 150 mg intra-venous half an hour prior to induction of anesthesia. All patients were given standard general anaesthesia with inj.pentothal(5 mg/kg), fentanyl (2 µg/kg) and vecuronium bromide (0.12 mg/kg) to facilitate tracheal intubation. Anesthesia was maintained with 50% N_2O in oxygen with 1-2% sevoflurane. Fentanyl boluses of 1 to 2mcg/kg IV were titrated to maintain mean arterial blood pressure and heart rate ± 20 % of baseline values. Muscle relaxation was achieved with vecuronium bromide. Peroperatively patient was given inj paracetamol 15mg/kg & inj Diclofenac Sodium 75mg. Ventilation (tidal volume 8 - 10 ml/kg) was adjusted to maintain end-tidal carbon dioxide between 35 and 40 mm Hg. During laparoscopy, intra-abdominal pressure was limited to 10 - 12 mmHg. The CO_2 was carefully evacuated at the end of surgery by manual compression of the abdomen with open trocars. At the end of surgery, patients were randomized into two groups.

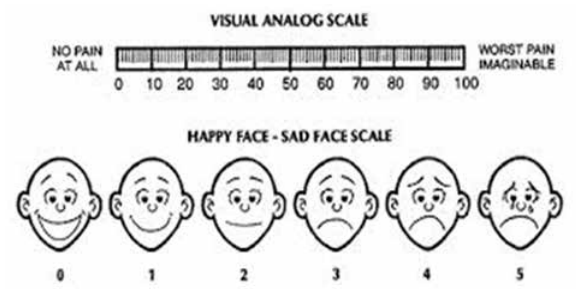
Group N: Patients received 0.75% Ropivacaine 2mg/kg plus Morphine 2mg by nebulization technique (15 ml). (n =30)

Group I: Patients received 0.75% Ropivacaine2 mg/kg plus Morphine 2mg by instillation technique. (15ml).(n =30)

The drug was nebulized and instilled intraperitoneally before the removal of trocar at the end of the surgery. During the operation noninvasive blood pressure, heart rate, $EtCO_2$, and peripheral oxygen saturation were recorded regularly. Surgical wounds were not infiltrated with local anesthetic solution. Before induction of anaesthesia, the patients were instructed how to use a 100 mm visual analogue scale(figure-1) for which 0 mm represented "no pain" and 100 mm represented "worst possible pain". The degree of postoperative pain was assessed using the VAS at 0, 1, 4, 8,

12, and 18 hours post-operatively. Those patients with VAS > 40, were administered a bolus of inj Morphine 1mg IV as rescue analgesia. Ondansetron (4 mg IV) was administered on complaint of nausea and vomiting. Time to first analgesic requirement, total analgesic consumption in the first 24 hours postoperatively and occurrence of adverse events was recorded. Patients were regularly asked about pruritis and shoulder pain. Blood pressure was regularly monitored for episodes of hypotension (MAP<60 mmHg), heart rate was regularly monitored for episodes of bradycardia (heart rate <60). Total duration of surgery was recorded for all cases. All analysis was performed using Graphpad software. P value<0.05 was considered to be statistically significant.

FIGURE-1- VISUAL ANALOGUE SCALE



RESULTS:

Table: 1 Baseline Patient Characteristics

	Group-N (30)	Group-I (30)
Age(Years)	56 ± 4.57	54 ±8.17
Sex (M/F)	16 : 14	17:13
Height (Cms)	156.62 ±7.41	160.34 ±6.43
Weight(Kgs)	60.32 ±5.03	59.13 ±6.53
Duration of Surgery (hrs)	3-8 (4.42)	3-8 (4.24)
Intra op fentanyl(mcg)	200 ± 24	200 ±30

Both the groups were similar for age, sex, physical parameters, duration of surgery & intraoperative analgesic requirement (table 1).

FIGURE-2-STATIC VAS

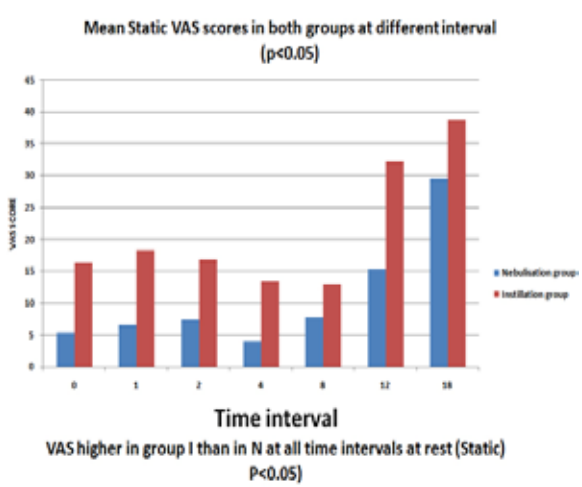


FIGURE-3 DYNAMIC VAS

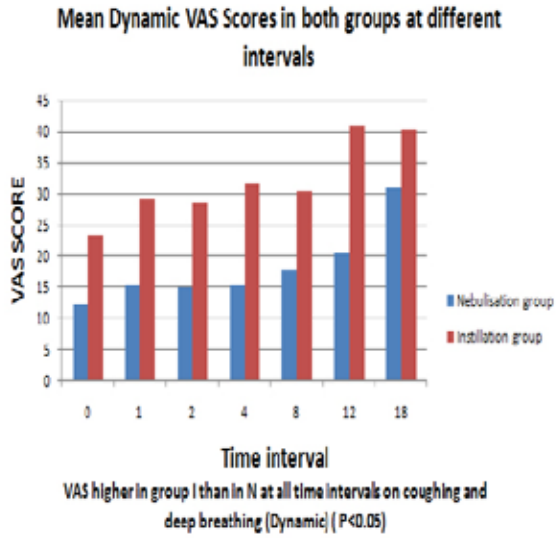


Table: 2-Postoperative total analgesic dose consumption during first 24 hours and mean time to first rescue analgesic requirement.

	Nebulization	Instillation
Total dosage of rescue analgesia required	10	30
Time to 1st Analgesic requirement (hrs.)	17.57± 0.02 hrs	13.48± 0.05 hrs

Time to requirement of first dose recue analgesic was longer in group N than in group I indicating better & longer pain relief in N group as compared to group I.($p < 0.05$).

Total analgesic consumption was more in group I as compared to group N. (P<0.05) (Table 2).Second dose of morphine was repeated when needed.

Table: 3-Complications

	Nebulization	Instillation
Nausea	0	4
Vomiting	2	4
Hypotension (<20% of border line)	2	4
Bradycardia (<20% of borderline)	2	2
Shoulder pain	0	10
Respiratory depression	-	-
Sedation	--	-
Pruritus	-	-
Subcutaneous emphysema	-	-

Shoulder pain was not found in any patients in group N while five patients had shoulder pain in group I. It was statistically significant. (P < 0.05) In I group four patients had nausea & vomiting while in N group, no patient had nausea, and only two patient had vomiting. No patient had pruritus, respiratory depression, sedation, and subcutaneous emphysema.(Table-3)

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Table: 4 Postoperative Heart Rate and Blood Pressure

Time	Heart Rate		Systolic BP		Diastolic BP		Mean	
	N	I	N	I	N	I	N	I
0 hr	85.92±8.36	82.06±5.69	118.84±5.42	124.12±10.18	78.04±6.76	79.24±11.56	87.68±8.60	91.88±8.08
1 hr	78.24±8.32	80.35± 6.36	119.86±5.64	118.92±9,83	80.58±4.67	76.08±11.28	89.88±7.87	87.20±9.84
4 hrs	84.32±8.69	81.43±5.35	122.80±7.19	121.24±9.36	82.24±5.89	80.08±10.53	93.20±9,50	90.28±11.57
8 hrs	85.80±3.69	84.34±6.92	122.80±4.25	121.36±8.72	81.04±5.98	78.04±9.62	93.84±9.37	90.00±10.12
12 hrs	84.60±5.32	89.62±5.34	122.60±5.29	123.24±9.2	82.68±4.68	79.84±9.21	94.48±9.32	92.36±10.01
18 hrs	83.88±7.92	88.69±6.98	122.84±5.65	124.08±8.52	82.76±5.94	80.90±8.6	94.06±9.18	92.44±10.45
24 hrs	84.32±8.69	81.43±5.35	122.80±7.19	121.24±9.36	82.24±5.89	80.08±10.53	93.20±9,50	90.28±11.57

There was no significant difference in hemodynamic changes in intraoperative as well as postoperative periods in both N & I groups.(Table-4) Hypotension occurred in two patients in N group and four patients in I group. Whereas in both the groups two patients had bradycardia. No patient presented signs of local anesthetic toxicity in the perioperative period.

DISCUSSION

Postoperative pain is multifactorial in origin, and therefore, multimodal therapy may be needed to optimize pain relief. Local anesthetic techniques are part of the multimodal approach to postoperative pain management.[2, 4] We compared the effects of intraperitoneal ropivacaine nebulization with intraperitoneal instillation of ropivacaine after laparoscopic surgeries. The main finding of this study is that in comparison with ropivacaine instillation, ropivacaine nebulization significantly reduced the VAS scores and incidence of shoulder pain.

Pain after laparoscopic surgeries, particularly shoulder pain and diffuse abdominal pain, remains a problem.The exact origin of pain during laparoscopy is unclear, shoulder pain and diffuse abdominal pain may be due to peritoneal stretching and diaphragmatic irritation associated with CO2 pneumoperitoneum[1]. Incisional pain is less intense than visceral pain, owing to the small abdominal incisions made in the abdominal wall for the trocars and limited damage to abdominal wall. Our results showed that incisional pain is less intense than visceral pain and worsen only by coughing and deep breathing. This can be explained by that deep breathing and coughing cause intense abdominal muscle contraction.

In comparison with instillation group, nebulization group provides better pain relief, as there were significant difference between pain scores in both the techniques.VAS(at rest) immediately postoperatively was 5.29 ±1.03 vs 16.30 ±3.61 and at 12 and 18 hours was 15.23±2.25 vs 32.21±1.53 and 29.46±2.05 vs. 38.60±2.71 respectively(P<0.05).VAS (on deep breathing and coughing)in immediate postoperative period was 12.21±5.05 vs. 23.21±8.65 and at 12 and 18 hours was 20.40 ±4.87 vs. 41.02±3.45 and 30.81±5.03 vs. 40.30±9.21 respectively(P < 0.05). In a study done by P M Ingelmo et al., Ropivacaine (1% , 3 ml) was nebulized intraperitoneally for pain control after laparoscopic cholecystectomy. They found that fewer patients in ropivacaine nebulization showed a dynamic vas score ≥30 mm at 6 hours and 12 hours after surgery in comparison with those receiving saline nebulization. They also noted reduction in morphine consumption 42% in preoperative nebulization group and 29% in postoperative nebulization group in comparison with placebo group on the first postoperative day. The reduced shoulder pain observed in our study was also reported by them using bupivacaine nebulized in the peritoneal cavity at the end of surgery. The authors reported that this delivery method generated a "foggy" environment, which may suggest that the peritoneal cavity was completely covered.[5]

Duration of analgesia is prolonged in nebulization technique when compared to instillation. The cause may be slower absorption of drug .[6] Dolphine Betton et al in their study observed that the pharmacokinetic profile of Ropivacaine nebulization is similar to direct intraperitoneal instillation but with a lower absorption rate. In our study, opioid requirement is two times higher in instillation group as compared to nebulization group.

Addition of opioids to local anesthetic significantly decrease total analgesic requirement, prolonged the time to first rescue analgesia without any significant adverse events [7, 8]

The nebulization system (Omron) used in this study consists of a commercially available high-frequency vibrating membrane nebulizer, which is reusable and easy to assemble. Because the particle size generated by the device is small (Mass Median Diameter <10μm), the local anesthetic would spread uniformly throughout the peritoneal cavity as well as to the most remote parts of the peritoneum and thus may be beneficial to improve pain relief after laparoscopic procedures. This may explain the lower incidence of shoulder pain in the nebulization group. This is similar to study done by Buccero et al .They found that intraperitoneal ropivacaine nebulization decreased shoulder pain. One of the factors that might contribute to failure of the instillation technique mainly related to inadequate distribution of local anesthetic throughout peritoneal cavity.[3]

Different nebulizers have markedly different performance characteristics, which could result in different efficacy and safety of the medication being administered via these devices.[11, 12, 13]

There are studies using morphine as IV bolus at the end of surgery and for intravenous patient controlled analgesia in major surgeries[9, 10]

One of the limitations of the nebulization technique is that the small droplets size creates a "foggy" environment, which may interfere with the surgeon's vision. Thus, local anesthetic nebulization may not be feasible throughout the surgical procedure. Therefore, we performed the nebulization after the surgery was completed just prior to exsufflation of the pneumoperitoneum.

Despite of significant reduction in pain scores, shoulder pain

and opioid consumption in nebulization group, there are no significant difference in hemodynamic changes and any other complications like nausea, vomiting, pruritus, respiratory depression, and sedation.

We used ropivacaine in the dose of 0.75% ,15ml (112.5mg) in our study and did not find any side effect related to local anesthetic (hypotension, delayed awakening and arrhythmia). Labile et al[14] used intraperitoneal ropivacaine during laparoscopic cholecystectomy in the dose of 100mg and 300mg and found reduction in postoperative pain. However, they did not find any statistically significant difference in visceral pain scores, time to first rescue morphine in PACU, total consumption of morphine and incidence of nausea and vomiting. Smaller dosage provided similar analgesia with significantly smaller plasma concentrations than the larger dosage.

To conclude intraperitoneal nebulization of ropivacaine and morphine was associated with better pain relief, decrease incidence of shoulder pain and less morphine consumption in postoperative period after laparoscopic surgeries in comparison with instillation technique.

REFERENCE

1 J. I. Alexander. Pain after laparoscopy. British journal of anaesthesia.1997; 79:369–378. | | 2 Dinesh Singh, Jaishri Bogra, Sulekha Saxena et al. The Effect of Intraperitoneal Ropivacaine for Post-Operative Pain Management in Patients Undergoing Laparoscopic Cholecystectomy. Open journal of anaesthesiology.2013; 3:193-98. | | 3 Mario Bucciero, Pablo M. Ingelmo et al. Intraperitoneal Ropivacaine Nebulization for Pain Management after Laparoscopic Cholecystectomy: A Comparison with Intraperitoneal Instillation. Anesthesia & Analgesia.2011; 113:1266-71. | | 4 Alkhamesi NA, Peck DH, Lomax D, Darzi AW. Intraperitoneal aerolization of bupivacaine reduces postoperative pain in laparoscopic surgery. Surg Endosc 2007; 21: 602–6. | | 5 P. M. Ingelmo M. Bucciero M. Somaini, Intraperitoneal nebulization of ropivacaine for pain control after laparoscopic cholecystectomy. British journal of anaesthesia.2013; 1-7. | | 6 Delphine Betton, PharmD, Nicolas Greib, Herve Schlotterbeck, The Pharmacokinetics of Ropivacaine After Intraperitoneal Administration: Instillation Versus Nebulization www.anesthesia-analgesia.org 2010; 111:1140-45. | | 7 A Singh, SK Mathur, VK Shukla. Postoperative analgesia with intraperitoneal ropivacaine with | in addition, without fentanyl after laparoscopic cholecystectomy: OA Anaesthetics.2013; 1:1-9. | | 8 Butala, Bina P.; Shah, Veena R.; Nived, K.Randomized double blind trial of intraperitoneal instillation of bupivacaine and morphine for pain relief after laparoscopic gynecological surgeries. Saudi Journal of Anaesthesia; 2013; 7: 18-23. | | 9 Zhao LY, Ye TH, Zhang YZ, Zhao H. Combination of morphine with low-dose naloxone for intravenous patient-controlled analgesia].Zhongguo Yi Xue Ke Xue Yuan Xue Bao.2005: 27; 228-31. | | 10 Adriaenssens G, Vermeyen KM, Hoffmann VL, Mertens E, Adriaensen HF. Postoperative analgesia with IV patient-controlled morphine: effect of adding ketamine. British journal of Anaesthesia, 1999:83; 393-6. | | 11 Bauer A, McGlynn P, Bovet LL, Mims PL, Curry LA, Hanrahan JP. Output and aerosol properties of five nebulizer/compressor systems with arformoterol inhalation solution. Respi Care 2009; 54:1342-7. | | 12 Okapo SO1, Gupta J, Martinez E, Mark R. In vitro deposition properties of nebulized formoterol fumarate: effect of nebulization time, airflow, volume of fill and nebulizer type. Curr Med Res Opin 2009; 25:807-16. | | 13 Reisner C, Katial RK, Bartelson BB, Buchmeir A, Rosenwasser LJ, Nelson HS. Characterization of aerosol output from various nebulizer/compressor combinations. Ann Allergy Asthma Immunol. 2001; 86:566-74. | 14 Labaille T1, Mazoit JX, Paqueron X, Franco D, Benhamou D. The clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. Anesthesia & Analgesia. 2002; 94:100-5, | |