Effect of Intraperitoneal Aerosolization of Bupivacaine for postoperative pain management in Laparoscopic Surgeries

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Abstract

Aim: To evaluate the effectiveness of intraperitoneal aerosolization with 3ml bupivacaine on acute postoperative visceral pain.

Materials and methods: 64 patients aged 18-60 years of ASA grades I and II undergoing laparoscopic surgery were randomly allocated to two equal comparable groups of 32 each. Group C: (Control Group) received 3ml of intraperitoneal saline aerosolization and Group L (Local anaesthetic group) received intraperitoneal aerosolization with 3ml of 0.5% Bupivacaine. Anaesthetic techniques were standardized. The degree of pain at rest and on movement by Verbal Numerical Rating Scale (VNRS) was collected in the postoperative ward at 6, 12, 24 and 48h after surgery. The total dose of rescue analgesics consumed, incidence of postoperative shoulder pain, nausea and vomiting were recorded.

Results: Out of 64 patients included in the trial, two patients from each group were excluded from analysis due to conversion to open surgery. A significant reduction in VNRS was found on movement at 6h (4.3±1.4) after surgery in group L. There was no significant difference in VNRS at rest at any time and dynamic VNRS at 12, 24 and 48hours. 56.7% of patients in the group L complained of shoulder pain. The total doses of postoperative rescue analgesics consumed were significantly lesser in group L. The patient satisfaction scores were significantly better in the local anaesthetic group at 24h (6.1±0.7) and were comparable at 48h.

Conclusion: Bupivacaine aerosolization reduces dynamic visceral pain at 6h after surgery and reduces postoperative rescue analgesic consumption. The patient satisfaction scores were better in the local anaesthetic group at 24h. There was no difference in incidence of shoulder pain, nausea and vomiting.

Key words: intraperitoneal aerosolization, bupivacaine, laparoscopic surgery, acute postoperative visceral pain

Introduction

For some patients, pain following laparoscopy might be considerable or even severe, necessitating opiate medication. Surgical manipulations, intraperitoneal insufflation of carbon dioxide (CO_2), causing peritoneal stretching, diaphragmatic irritation, and variations in intra-abdominal pH, which result in peritoneal nerve irritation, have all been linked to visceral and shoulder pain during laparoscopic procedures. After laparoscopic surgery, an intraperitoneal local anaesthetic instillation may give pain relief, however the distribution may not always be homogeneous over the peritoneal surface[1-5]. Intraperitoneal local anaesthetic aerosolization ensures that local anaesthetic drug is evenly distributed throughout the peritoneal cavity[6-8].

Many trials of intraperitoneal aerosolization with a lower dosage of ropivacaine have been conducted. To the best of our knowledge, there has been no research on intraperitoneal aerosolization using 3ml of bupivacaine. The purpose of this study was to evaluate the effect of intraperitoneal aerosolization using 3ml bupivacaine on acute post-operative visceral pain alleviation after laparoscopic surgery, as

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measured by VNRS ratings at rest and on movement total dose of rescue analgesics consumed at 24 and 48h, incidence of post-operative shoulder pain, nausea and vomiting.

Materials and Methodology:

After receiving Institutional Ethical Committee clearance, this prospective, double-blind, randomized clinical trial was conducted from July 2021 to February 2022 and registered in the Clinical Trial Registry of India with registration number CTRI/2021/07/035174 [Registered on the 27th of July, 2021]. The clinical trial was carried out in compliance with the Helsinki Declaration 2013 for medical research involving human beings. The CONSORT standards (https://www.consort-statement.org) were used to design the study. The study involved 64 patients of either gender, between the age of 18 and 60 years who underwent elective laparoscopic surgery under general anesthesia (GA). Written informed consent was obtained from each patient. During the pre-anaesthetic evaluation, the eligible patients were taught VNRS scoring. Patients with poorly managed HTN/DM, kidney or liver disorders, asthma, obesity, IHD, pregnant or breastfeeding mothers, known bupivacaine allergy or hypersensitivity, use of opioids prior to surgery, progressive neurodegenerative disorders, seizures or chronic therapy with antiepileptic drugs, alcohol or drug substance abuse, any kind of communication problem, neurologic or psychiatric disease, and conversion of laparoscopic surgery to open were all excluded from the study.

Using a computer-generated randomization table, patients were assigned to one of two groups: Group C (Control Group) received 3ml of saline aerosolization and Group L (Local anaesthetic group) received intraperitoneal aerosolization with 3ml of bupivacaine 0.5% using (Aeroneb Pro) nebulizer equipment. An anaesthesiologist who was not involved in data collection performed allocation concealment using serial numbers, coded, sealed envelopes, which were decoded at the end of the trial.

The surgery was done using the three-access approach, and the pneumoperitoneum was achieved using non-heated, non-humidified CO2. Between the insufflator and the insufflation tube, the nebulization unit was connected. Aerosolization was done with a nebulizer through the main trocar until the available dose was exhausted. To avoid any residual air, the pneumoperitoneum was released and re-insufflated with CO2 after the exsufflation was complete.

All patients were given oral Alprazolam 0.5 mg the night prior to the surgery and were kept nil per oral for at least 6 hours. After 5 minutes of settling in the operative room, routine standard monitors such as continuous ECG, NIBP, and pulse oximeter were set up, and the patients' baseline heart rate, blood pressure, and oxygen saturation (SpO2) were recorded. For drug and fluid delivery, a 20G intravenous (IV) cannula was secured.

All patients were given intravenous (IV) Glycopyrrolate (0.005 mg/kg), IV Midazolam (0.03 mg/kg), and IV Fentanyl (2 mcg/kg) for analgesia. Following preoxygenation, patients were administered 2 mg/kg IV Propofol till loss of verbal response. Tracheal intubation was aided by IV Vecuronium 0.1 mg/kg after check ventilation. Patients were maintained with a 40:60 mixture of Oxygen and Nitrous oxide, as well as Isoflurane and Vecuronium.

The drugs were prepared in a clear 5ml syringe by an anaesthesiologist who was not engaged in the data collection. Group C received 3ml of NS and group L received 3ml of 0.5% Bupivacaine. The anaesthesiologist was authorised to disclose the contents of the syringe to the case anaesthesiologist in the event of an emergency involving the study or study drugs. The signs of local anaesthetic toxicity (e.g., unexplained hypotension, intraoperative arrhythmias, and unexplained delayed awakening) were monitored and recorded.

Intravenous Ondansetron 0.15mg/kg and a bolus of 15 mg/kg Paracetamol (up to 1 g) were given 30 minutes before the surgery ended. The wound was infiltrated with 5 mL of 0.5% Bupivacaine at the port site. With Neostigmine (0.05 mg/kg) and IV Glycopyrrolate (0.01 mg/kg), the residual neuromuscular blockade was reversed. After witnessing adequate functional recovery and respiratory efforts, patients were extubated. Patients with an Aldrette score of >9, were transferred from the post-anesthesia care unit. Inj Diclofenac BD was given to all of the patients, and Inj Tramadol was used as a rescue analgesic, given on request and VNRS >4.

With a power of 80% and a confidence interval of 95%, a minimum sample size of 29 subjects in each group was required. However, considering 10% dropout rate and/or a protocol violation, we included 32 individuals in each group. The data was entered into an excel sheet and analysed with SPSS Version 20 (Statistical Package for Social Sciences). The mean, standard deviation, and proportions (percentages) were calculated as descriptive statistics. Independent sample t test and Chi Square test were employed to evaluate the hypothesis. Statistical significance was defined as a p value of less than 0.05.

Conversion to an open procedure was seen as a protocol violation, and these individuals were

eliminated from further investigation. For the patients' safety, the excluded patients were given the same anaesthetic and analgesia regimen and evaluations until they were discharged from the hospital.

At the following time points in the Post-operative ward, an investigator blinded to group allocation assessed and collected data (6, 12, 24 and 48 hours after the end of surgery). A verbal numerical rating scale (VNRS: 0 = no pain, 10 = extremely severe pain) was used to assess pain severity. At 6, 12, 24, and 48 hours, all patients were asked to rate their non-wound pain at rest (VNRSR) and on movement (dynamic VNRS=VNRSD on deep breathing and/or hip flexion). A patient satisfaction score (0 = highly displeased, 10 = entirely satisfied) was used to assess the patient's satisfaction with the pain management at 24 and 48 hours. The total number of rescue analgesic doses consumed at 24 and 48 hours was documented, as well as the incidence of shoulder pain, nausea, vomiting, and symptoms of local anaesthetic toxicity.

Results

Figure 1 shows a CONSORT flow diagram for this study where 64 patients were enrolled after meeting the required eligibility, two patients in each of the groups were excluded because of conversion to open surgery, 60 patients were analysed with 30 in each group. The two groups were comparable in patient characteristics with respect to age, mean weight, gender, ASA physical status, and type of surgery (P>0.05) [Table 1].

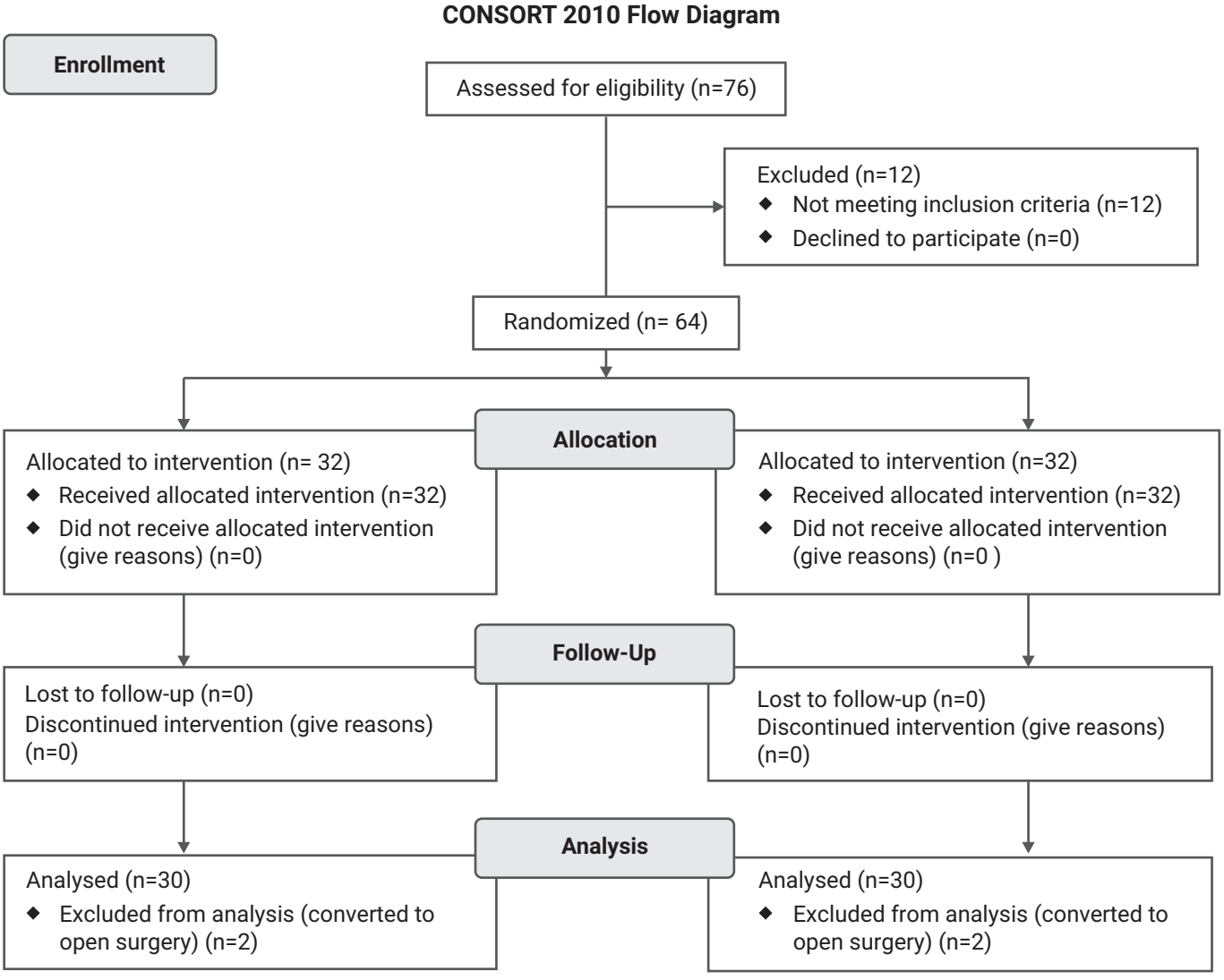

Figure 1: CONSORT flow diagram of patients included in the trial

Table 1: Comparison of Demographic data

Parameters		Group C (n=30)	Group L (n=30)	P value
Age in years		42.87±10.0	41.5±11.0	0.618(NS)
Weight in Kilograms		68.07±7.1	67.2±7.9	0.658(NS)
Gender	Male	20.0%	21.7%	0.793(NS)
	Female	30.0%	28.3%	
ASA	ASA 1	26.7%	25.0%	0.796(NS)
	ASA 2	30.0%	25.0%	
Type of surgery	Lap Appendectomy	21.7%	25.0%	0.827(NS)
	Lap Cholecystectomy	30.0%	21.7%	
	Lap Hernia repair	5.0%	3.3%	

Data in mean and standard deviation, percentage total, S= statistically significant, NS= not significant

Table 2: Comparison of VNRS at rest (VNRSR) and on movement (dynamic=VNRSD) between the groups

VNRS scores	Group C (n=30)	Group L (n=30)	P Value
VNRSR 6 h	5.4±0.9	5.00±1.0	0.105(NS)
VNRSR 12 h	4.4±0.7	4.10±0.7	0.168(NS)
VNRSR 24 h	3.6±1.2	3.10±1.0	0.079(NS)
VNRSR 48 h	2.9±0.8	2.47±0.7	0.024(NS)
VNRSD 6 h	5.17±0.8	4.3±1.4	0.005(S)
VNRSD 12 h	4.13±0.8	4.2±0.8	0.134 (NS)
VNRSD 24 h	3.23±1.0	3.0±0.7	0.083 (NS)
VNRSD 48 h	2.33±0.8	2.5±0.5	0.157 (NS)

Data in mean and standard deviation, S= statistically significant, NS= not significant

There was no significant difference in VNRS at rest, but significant difference in dynamic VNRS at 6h after surgery (Table 2).

The incidence of nausea and vomiting were comparable between the groups, patients who received bupivacaine aerosolization required lesser rescue analgesics compared to the control group at 24 and 48h after surgery. Patients who received bupivacaine aerosolization also had better patient satisfaction scores at 24h but there was no significant difference amongst the two groups at 48h (Table 3).

Table 3: Comparison of postoperative parameters

Postoperative parameters		Group C	Group L	P Value
Nausea	Yes	6.7%	8.3%	0.718 (NS)
	No	43.3%	41.7%	
Vomiting	Yes	3.3%	3.3%	1.000 (NS)
	No	46.7%	46.7%	
No of doses of Rescue analgesia in 24h	0	0%	21.7%	0.000 (S)
	1	48.3%	26.7%	
	2	1.7%	1.7%	
No of doses of rescue analgesia in 48h	0	15.0%	33.3%	0.014 (S)
	1	33.3%	16.7%	
	2	1.7%	0%	
Patient satisfaction at 24h		4.77±0.7	6.1±0.7	0.000 (S)
Patient satisfaction at 48h		5.20±0.8	5.3±1.0	0.779 (NS)

Data in mean and standard deviation, percentage total, S= statistically significant, NS= not significant

Also, 20 out of 30 patients in the control group complained of shoulder pain and 17 out of 30 patients complained of pain in the local anaesthetic group. There was no significant difference in shoulder pain amongst the groups. None of the patients exhibited signs of local anaesthetic toxicity.

Discussion:

Morbidity, pain and hospital stay are lower with laparoscopic operations with early ambulation. Discomfort, notably shoulder pain and widespread abdominal pain, persists following laparoscopic surgeries[9,10].

Because of the non-uniform distribution of local anaesthetics in the peritoneal cavity with intraperitoneal local anaesthetic instillation, they may not completely relieve visceral and shoulder pain. The technique of intraperitoneal aerosolization provides for consistent drug distribution in the peritoneal cavity[11,12].

Ingelmo et al showed that using 30mg ropivacaine aerosolization resulted in fewer patients with dynamic VAS ratings >3 at 6 and 24 hours, but we discovered that VNRS were decreased only at 6 hours after surgery, possibly because to the lower dose of bupivacaine (15mg) employed. Ingelmo et al[12] and Bhatia et al[13] found that postoperative rescue analgesic intake was lower in the local anaesthetic group.

We found no significant difference between the two groups, unlike Buccerio et al[14] and Kumar et al[15], who found a lower incidence of shoulder pain. This is likely due to lower dose of bupivacaine used.

In contrast to our study, Kaufman et al[16] utilised 10ml of ropivacaine and found a greater rate of nausea and vomiting, which they attributed to the higher dose of local anaesthetic medication. One of the aerosolization technique's drawbacks is that the microscopic droplets create a "foggy" atmosphere, which can impair the surgeon's vision[14-17]. We chose a lower volume of bupivacaine to reduce the aerosolization time as a result, the less 'fog' duration in the surgical area. There were no signs of local anaesthetic toxicity in any of the patients.

Conclusion:

In comparison to the control group, intraperitoneal aerosolization with 3ml of bupivacaine reduces dynamic VNRS at 6 hours after surgery and postoperative rescue analgesic consumption till 48h. Patients with bupivacaine aerosolization had better patient satisfaction scores at 24 hours but at 48h after surgery the patient satisfaction rates were comparable. Intraperitoneal aerosolization with 3ml of bupivacaine did not reduce the incidence of shoulder pain. There was no difference in incidence of nausea and vomiting between the two groups.

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Conflict of interest: Nil
Source of funding: Nil

Date received: 2nd Jan, 2022
Date accepted: 18th April, 2022