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Intraperitoneal Lavage with Bupivacaine 0.2% and Post-operative Pain in Laparoscopic Colorectal Surgery: A Prospective, Double-Blind, Randomized Controlled Trial

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Abstract

Background: Local anesthetics have been proven as a method to reduce postoperative pain and opioid use. It reduces side effects associated with drug use and may improve patient health and reduce hospital length of stay. The aim of this study was to evaluate the effect of intraperitoneal bupivacaine on post-operative pain in laparoscopic colorectal surgery.

Methods: In this prospective randomized control trial, 63 patients aged 20-70 years candidates for laparoscopic proctectomy or rectopexy surgery, were divided into two groups. In the case group, anastomosis site was washed with 50 mL of bupivacaine 0.2% intraperitoneally. In the control group, equal volume of normal saline was used as placebo. Intravenous autofuser pain control filled with 3 g paracetamol was considered for all patients. Visual analogue scale (VAS) was recorded at 2, 8, 24 hours and narcotic usage was recorded totally for the first 24 hours after the operation.

Results: There was no significant difference between pain scores according to the VAS criteria at 2, 8, and 24 hours after the operation in the case and control groups ($P>0.05$). Total pethidine consumption during the first 24 hours after the operation was lower in the bupivacaine group (49.03 ± 45.77) compared to the control group (77.74 ± 63.50), but the difference was not significant ($P>0.05$). However, the total dose of pethidine used after 24 hours after proctectomy (not rectopexy) was significantly lower in the bupivacaine group than that in the control group ($P<0.05$).

Conclusion: Intraperitoneal lavage with bupivacaine during the operation reduced post-operative total narcotics use in patients who underwent laparoscopic proctectomy, not in rectopexy.

Introduction

Pain is one of the main complications of surgery which affects patients' post-operative period and their satisfaction (1). Post-operative pain control has many influences such as returning to full function, quality of life, and more importantly, early discharge of patients (2). Uncontrolled post-operative pain could stimulate sympathetic pathways, thus, it could increase morbidity and mortality of patients (3,4). Activated sympathetic pathway affects oxygen consumption by myocardium, which leads to high risk of myocardial infarction and ischemia.

Moreover, stimulated sympathetic pathway can delay gastrointestinal movements post-operatively, and results in ileus in the patients. Patients with lower control on their post-operative pain are more prone to pulmonary complications due to few coughs and deep breath as a result of pain. Local analgesics are a standard approach to alleviate the postoperative pain or to reduce drug abuse-related pain (5-7).

Epidural and intrathecal injection of analgesics is a golden standard to manage pain in different abdominal surgeries but this approach can pose prolonged anesthesia, however, concerns about central block still remains as an important issue in geriatrics (8,9). Therefore, due to its prominent role in managing patients, treatment of post-operative pain has become a sort of concern recently.

According to the side effects of different analgesics, post-operative pain controllers such as local anesthesia or opioids are prescribed with lower doses than before, but it may reduce the optimal effects of drugs on pain intensity. Thus, experimental studies claimed that neural block applied before injury could be a choice for lower risks of side effects (10,11).

High doses of oral or intravenous opioid can obviously reduce post-operative pain in patients but increase side effects. Recently, alternative minimal invasive approaches have been used with the lowest side effects to reduce pain. Recently, intra-peritoneal injection of analgesics in laparoscopic cholecystectomy or gynecology-related operations has been introduced (12-17). There are limited studies on the effect of intraperitoneal bupivacaine on pain score of patients after pelvic organs surgeries.

Several systematic studies and meta-analyses have shown short-term benefits for laparoscopic colorectal resection in reducing hospital stay, reducing morbidity, and improving quality of life, compared to classic open approaches (18-24).

Many years ago, liposomal bupivacaine was introduced, however, there are limited studies on its efficacy in laparoscopic colorectal resection. Studies on liposomal bupivacaine in colorectal resection were mostly retrospective studies.

Objective

The aim of this study was to assess the efficacy of intra-abdominal lavage with bupivacaine and its role on the post-operative pain and the need for narcotics in patients who underwent laparoscopic rectopexy and proctectomy.

Materials and Methods

This is a prospective, randomized, double-blind clinical trial. The study population were candidates for laparoscopic colorectal surgery who referred to Firoozgar Hospital in Tehran in 2018. The sample size was calculated according to the study of Chakravarty et al. (25). The maximum sample size, with 95% confidence level and 90% strength, was estimated to be 31 for each group using STATA software.

In this study, 63 patients with American Society of Anesthesiologists physical status (ASA) 1 and 2 aged 20-70 years candidates for laparoscopic colorectal surgery (proctectomy or rectopexy) were included and simply randomized based on the right digit of their hospital code number. An approval was received by the Ethics Committee of Iranian University of Medical Sciences (Ethical code: IR.iums.rec.1395.135553). The study was registered in Iranian Registry of Clinical Trial site (Registration code: IRCT2017071716151N5). A written informed consent was obtained from each patient.

Exclusion criteria include: administering opioid within 24 hours before the study, obese patients (BMI>30), substance abuse, smoking, any analgesic or illegal drug or alcohol consumption, history of allergy to any of the drugs used in the study, chronic pain syndrome, those with neurological or steroidal disease, those whose pain assessment was unreliable or those operations in which laparoscopic procedure changed to open approach due to any reason. All surgeries were performed by a surgeon subspecialist in colorectal surgery. Patients underwent general anesthesia with approximately the same drugs and similar dosage. They were trained on how to assess post-operative pain by the VAS scoring method. Anesthetic induction protocol was standard for all patients, including intravenous injection of midazolam 25 µg/kg, fentanyl 3 µg/kg, propofol 2 mg/kg, atracurium 0.5 mg/kg, and lidocaine 1.5 mg/kg before intubation. Maintenance included intravenous injection of propofol 50-150 µg/kg/min considering hemodynamic status and anesthetic depth (by BIS), atracurium 0.2 mg/kg every 30 min, with morphine sulfate 0.1 mg/kg in the first 10 min after initiation of anesthesia. Local injection of lidocaine 0.2% was also performed for port site incisions by the surgeon.

Patients were randomly divided into two groups. The amount of opioid and analgesic administered to patients during the operation was almost equal. In the case group, at the end of the operation, 50 ml of bupivacaine 0.2% (20 ml bupivacaine 0.5% added to 30 ml normal saline) was inserted through a laparoscopic port on the anastomosis site and pelvic cavity. In the control group, the same amount of normal saline was used as a placebo. In both groups, the surgeon and the anesthesiology resident who was in charge of pain assessing and recording data, were completely blinded regarding the nature of substances used for lavage. For all patients, 1 g paracetamol was intravenously administered 15 min before the operation end, and a pain control autofuser pump containing 3 g paracetamol was used over a period of 24 hours. The nurse was ordered to administer 0.5 mg/kg pethidine in the case of patient request, or VAS ≥4 and if pain was not relieved within the next half-hour, administration of 0.25 mg/kg pethidine was repeated. The pain score was recorded by the anesthesiology assistant according to the VAS criteria at 2, 8, and 24 hours after the operation. The time of the first drug injection and total amount of opioid use were recorded.

Data analysis

Data were analyzed by SPSS version 22 (IBM SPSS Statistics, USA). Frequency, percentage, mean, and standard deviation were used to describe data. In quantitative variables, Kolmogorov-Smirnov test (KS) was first used to check the normality of the results. Then, for quantitative analysis, independent t-test or Mann-Whitney U test was used. To compare the qualitative variables, Chi-square test or Fisher's exact test was used. Statistical significant level was considered at P=0.05.

Results

In this study, 70 patients were included. Seven patients were excluded due to the exclusion criteria. CONSORT flow diagram of the participants is presented in Figure 1. The two groups were matched regarding their demographic data. There was no significant differences between the two groups regarding age, gender, and weight (P=0.191). Twenty-six patients underwent rectopexy; 16 (61.5%) in the bupivacaine group and 10 (38.5%) in the control group.

Also, 37 patients underwent proctectomy; 16 (43.2%) in the bupivacaine group and 21 (56.8%) in the control group. Demographic characteristics of the participants are presented in Table 1.

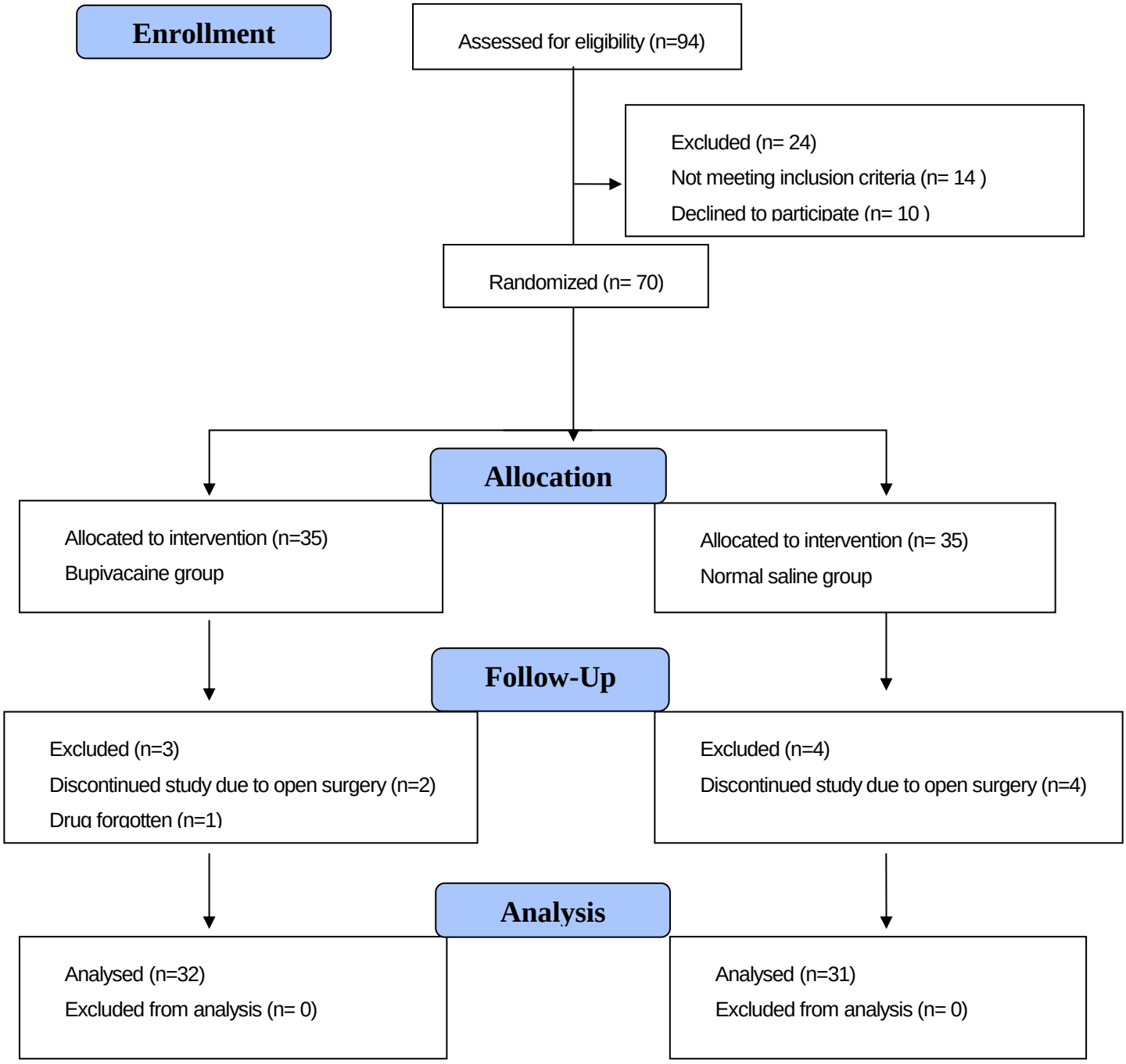

Figure 1. CONSORT diagram

Table 1. Demographic characteristics of participants

Characteristic	Group		P-value
	Bupivacaine (n=32)	Control (n=31)	
Age (Year) Mean ±SD	46.13 ± 15.43	50.11 ± 29.25	0.191
Gender			
Male	16 (50%)	11 (35.5%)	0.311
Female	16 (50%)	20 (64.5%)	
Rectopexy	16 (61.5%)	10 (38.5%)	0.115
Proctectomy	16 (43.2%)	21 (56.8%)	0.203

The time between the first administration of pethidine and the end of operation was longer in the bupivacaine group than the control group, but the difference was not significant (P>0.05). However, total amount of pethidine used after 24 hours of the operation was lower in the bupivacaine group than the control group, but the difference was not significant (P>0.05). Despite the fact that total amount of pethidine used after 24 hours of proctectomy was significantly lower in the bupivacaine group than the control group (P<0.05). However, this difference was not significant for those who underwent rectopexy (P=0.177) (Table 2).

Table 2. Analgesic prescription data

Analgesic Report	Bupivacaine Group	Control Group	P-value
The first analgesic request after surgery (min) (n=63)	89.39 ± 63.21	40.49 ± 29.30	0.313
Rectopexy (n=26)	53.67 ± 41.42	41.30 ± 26.42	0.902
Proctectomy (n=37)	115.43 ± 85.02	41.43 ± 30.56	0.222
Total pethidine consumption in the first 24 h (mg) (n=63)	49.03 ± 45.77	77.74 ± 63.50	0.083
Rectopexy (n=26)	29.01 ± 26.33	54.33 ± 47.99	0.177
Proctectomy (n=37)	58.57 ± 50.35	99.68 ± 69.67	0.044

There was no report of any respiratory depression after pethidine injection.

The VAS scores of patients in 2, 8, and 24 hours after the operation were recorded. There was no significant differences in the VAS scores between the two groups (P>0.05) (Table 3)

Table 3. VAS after surgery

Visual Analog Scale	Bupivacaine Group	Control Group	P-value
2 hours after surgery (n=63)	5.37 ± 2.81	5.68 ± 2.71	0.489
Rectopexy (n=26)	4.93 ± 2.71	5.30 ± 2.62	0.741
Proctectomy (n=37)	5.81 ± 2.92	6.15 ± 2.77	0.694
8 hours after surgery (n=63)	5.02 ± 2.51	5.34 ± 2.59	0.665
Rectopexy (n=26)	4.68 ± 2.38	4.50 ± 2.06	0.737
Proctectomy (n=37)	5.31 ± 2.67	5.78 ± 2.78	0.731
24 hours after surgery (n=63)	4.19 ± 2.08	4.37 ± 2.44	0.869
Rectopexy (n=26)	4.64 ± 2.06	5.02 ± 1.88	0.520
Proctectomy (n=37)	3.93 ± 2.14	4.05 ± 2.67	0.891

Discussion

In this randomized double-blind clinical trial, the effect of the use of bupivacaine to alleviate post-operative pain following laparoscopic colorectal surgeries, was evaluated. As patients were pain free during general anesthesia, bupivacaine was used for intraperitoneal lavage to induce analgesia during emergence of anesthesia and after that.

Some studies have been performed on the effect of bupivacaine in appendectomy and hysterectomy (10,15,16). Some meta-analysis and randomized trials have confirmed the positive effect of intraperitoneal bupivacaine in reducing post-operative pain in adult elective surgery (26,27). Di Pace et al. (2009) performed a study on different aspects of intraperitoneal analgesics including urology operations, appendectomy, cholecystectomy, varicocele and ovarian surgeries, and showed benefits of the use of intraperitoneal analgesics (28). El Basha et al. (2015) reported beneficial outcomes of the use of intraperitoneal local anesthetic (IPLA) in laparoscopic cholecystectomy and undescended testis (29). Also, Galante et al. (2014) showed strong effects of the use of IPLA in pediatrics (30). Hamill JK et al. showed discordant outcomes in acute inflammatory condition of appendectomy. They introduced no benefit of the use of IPLA in appendectomy, which is somewhat consistent with the results of this study (31).

In a meta-analysis by Raman et al. (2018), the use of lipoprotein bupivacaine as a topical anesthetic, was associated with a reduction in opioid use at 48 and 72 hours after colorectal surgery (32), which is consistent with the results of the present study. In a study by Stuhldreher et al. (2012), the amount of opioid use one day after laparoscopic colorectal surgery in patients without local anesthesia did not differ with those receiving topical bupivacaine (33).

Jain et al. (2018) reported that the administration of intraperitoneal bupivacaine reduced the need for post-operative narcotic drugs after laparoscopic cholecystectomy (34).

Toleska et al. (2018) also reported that pain level according to the VAS criteria, at 1, 4, 8, 12, and 24 hours after the operation was lower in the intraperitoneal bupivacaine group than in the non-bupivacaine group,

which is consistent with the results of the present study (35).

Yari et al. (2014) found that there was no difference between the amount of drug use and the time of the first request for post-operative analgesics in laparoscopic cholecystectomy between the group receiving intraperitoneal bupivacaine and the control group, which is not consistent with the results of the present study. At most post-operative times, there was no difference between the pain level according to the VAS criteria between the intraperitoneal bupivacaine and control groups (36).

Ghorbani et al. (2017) demonstrated that the pain score according to the VAS at 1, 6, and 24 hours after laparoscopic cholecystectomy was lower in patients who received bupivacaine. Also, the use of opioid was lower in the group who received intraperitoneal bupivacaine (37), which is consistent with the results of this study.

Total amount of pethidine use 24 hours after the operation was lower in the bupivacaine group than the control group, but the difference was not significant. It was revealed that there was no significant difference in the VAS scores between the two groups. However, it seems that those who underwent proctectomy benefit from intra-abdominal bupivacaine lavage much more than those who underwent ventral rectopexy. In rectopexy, only the anterior part of rectum is dissected and a mesh is inserted and fixed to sacrum promontory, and finally, peritoneum is closed. But in proctectomy, rectum and sigmoid are dissected from the parietal peritoneum, a coloanal anastomosis is performed, and a temporary diverting ileostomy is placed. Therefore, due to more tissue damages and dissection in proctectomy and also longer duration of the operation, patients need analgesics more than those who underwent rectopexy. According to the previous studies on appendectomy or cholecystectomy, there is no apparent effect of intra-abdominal lavage with bupivacaine like rectopexy here, which might be due to less tissue destruction as mentioned above (27,28,31,36).

The VAS score remained equal in 2 groups by use of more analgesics in proctectomy compared to rectopexy. However, in rectal cancer, patients received radiotherapy 8 weeks before the operation, which affected pain perception apparently more than rectopexy. Also, ileostomy in proctectomy could increase pain perception in patients.

The present study had also some limitations. One of the limitations is subjective assessment of pain in patients. The use of objective stress assessment methods by some biomarkers or other pain assessment methods or even adding patients sedation score to routine evaluation may yield better results. Also, there are limited data about the use of bupivacaine in pelvic organ surgeries. It is suggested to perform further studies on patients who undergo such operations in a larger sample size to obtain better and more detailed outcomes.

Conclusion

Intraperitoneal lavage with bupivacaine during the operation reduced post-operative total narcotics usage in patients who underwent laparoscopic proctectomy, not in those who underwent rectopexy.

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Conflict of Interests

The authors declare that they have no conflict of interests.

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