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Original Research

Efficacy of trocar site, intraperitoneal, and laparoscopically guided posterior transversus abdominis muscle bupivacaine injection for reducing pain after laparoscopic hysterectomy surgery: A double-blind randomized clinical trial

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ABSTRACT

Background: Few studies have investigated the pain-reducing effects of bupivacaine after laparoscopic hysterectomy. Therefore, this study compared the efficacy of three methods of bupivacaine injection—subcutaneous injection into the trocar site, intraperitoneal injection, and posterior transversus abdominis muscle block under laparoscopic guidance—for reducing pain after laparoscopic hysterectomy; the efficacy of each method was also compared with that of placebo. **Methods**: This double-blind randomized clinical trial study included 95 patients with good general health who underwent elective laparoscopic hysterectomy for benign disease in 2021. The patients were allocated into three intervention groups (subcutaneous injection of 10 cc bupivacaine 0.25%, heavy under trocar sites; 10 cc bupivacaine 0.25%, heavy injection into the transversus abdominis plane block; and 10 cc bupivacaine 0.25%, heavy intraperitoneal injection) and a control group. Abdominal and shoulder pain 2–4, 8, 12, and 24 h after the surgery were compared between groups. **Results**: The four groups were homogenous in age, weight, height, body mass index, surgery duration, surgery type, and family history of cancer ($P > 0.05$). The mean abdominal and shoulder pain score significantly decreased from the first time point (hours 2–4) to 8, 12, and 24 hours after surgery in the trocar site, intraperitoneal, and control groups ($P < 0.001$). However, we did not observe a significant decrease in abdominal and shoulder pain in the transversus abdominis plane block group ($P > 0.05$). **Conclusion**: The present study indicates that bupivacaine administration methods of transversus abdominis plane block and trocar site injection are effective and safe for reducing pain following laparoscopic hysterectomy.

Key words: Laparoscopic hysterectomy surgery, Pain, injection cite, Randomized clinical trial

INTRODUCTION

Laparoscopy is a common surgical method for the diagnosis and treatment of gynecological diseases [1]. During laparoscopy, the surgeon injects carbon dioxide (CO_2) gas into the patient's abdomen (pneumoperitoneum). This inflates the abdomen, allowing the surgeon to see the organs inside the abdominal cavity and perform the surgery. However, the inflation of the abdomen may cause nerve irritation extending from the upper abdomen (diaphragm) to the shoulders and neck. This phenomenon often causes pain, especially in the surgical area and shoulders [2]. Visceral pain or pain at the surgical site is generally caused by stretching in the abdominal cavity and irritation of the peritoneum due to CO_2 gas. In addition, shoulder pain is attributable to the stimulation of the phrenic nerve by injecting CO_2 gas into the abdominal cavity and below the diaphragm. Shoulder pain is also associated with the stimulation of the parietal peritoneum. Patients typically experience severe pain in the first 24 hours after laparoscopic surgery [3]. Evidence suggests that over 80% of women experience pain at the surgical site and shoulder after laparoscopy, which can cause complications, delays in discharge, and rehospitalization [2,4]. These problems increase the financial burden and reduce patient satisfaction [5].

The intraperitoneal injection of several drugs, such as bupivacaine, is a method of reducing pain after laparoscopic surgery [6]. Studies have also investigated other methods to reduce pain after surgery, including local anesthesia [7]. However, pain control after surgery emphasizes non-drug approaches or reduced drug doses [8]; this is because excessive narcotic painkiller use is a clinical challenge that can cause overdose, sedation, increased nausea and vomiting, ileus paralysis, and even death [9,10].

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In addition to the intraperitoneal injection of bupivacaine and other drugs[11], transversus abdominis muscle block injection can also be used to reduce lower abdominal visceral pain after surgery. Posterior transversus abdominis muscle block blocks anterior cutaneous branches T9–T12[12]. In recent years, researchers have directed much attention toward preventive analgesia—specifically, preventing pain transmission before pain stimulation by beginning treatment before pain occurs and continuing treatment afterward[13]. Because of the lack of studies in this field, this study compared the efficacy of three methods of bupivacaine administration—subcutaneous injection, intraperitoneal injection, and posterior transversus abdominis muscle block under laparoscopic guidance—for reducing pain after laparoscopic hysterectomy surgery. The efficacy of each method was also compared with that of placebo.

METHODS

This study was a double-blind randomized clinical trial study involving 95 patients who underwent elective laparoscopic hysterectomy for benign disease at Arash Hospital (affiliated with Tehran University of Medical Sciences). All patients had good general health (classified as American Society of Anesthesiologists (ASA) Grades 1 and 2) and underwent surgery in 2021.

The estimated required sample size was 20 patients per group (three intervention groups and one control group), considering a type 1 error level of 5% and a power of 80% as well as the parameters in Karman *et al.*'s study[14], in which the average pain score after 24 hours in the resting state for the intraperitoneal levobupivacaine and periportal groups were 14.9 ± 7.6 and 9.7 ± 2.2, respectively. The following equation was used to calculate the required sample size in the control group:

Sample size in placebo group = $n \times \sqrt{Number\ of\ treatment\ group} = 20 \times \sqrt{3} = 35$

All patients who were candidates for elective laparoscopic hysterectomy were referred to Arash Hospital and had good general health (ASA grades 1 and 2). Moreover, they were candidates for hysterectomy due to benign disease. Patients with chronic pelvic pain, pregnancy, sensitivity to bupivacaine, emergency surgery, and cancer were excluded from the study.

The Ethical Committee of the Tehran University of Medical Sciences approved the protocol of the present study (ethics committee code: IR.TUMS.MEDICINE.REC.1401.020), and it was registered in the Iranian Registry of Clinical Trials (IRCT registration number: IRCT20110530006640N9, registration date: 2022-09-11).

After providing written informed consent, the patients were allocated into the three intervention groups (subcutaneous injection of 10 cc bupivacaine 0.25%, heavy under trocar sites; 10 cc bupivacaine 0.25%, heavy injection into the transversus abdominis plane block; and 10 cc bupivacaine 0.25%, heavy intraperitoneal injection) and a control group.

The balance block randomization method (considering a block size equal to 19 and five sequences) was used for the randomization process to ensure that the sample size was the same in each group. The study used a double-blind design, so neither the patients nor the pain evaluator were aware of the method of analgesia after laparoscopic hysterectomy surgery. A laparoscopic fellowship doctor performed the anesthesia injection half an hour before the end of anesthesia induction.

Abdominal and shoulder pain were assessed 2–4, 8, 12, and 24 h after the surgery with a visual analog scale (VAS). The nurses of the ward performed scoring after the surgery without knowing the method of anesthesia administration. Complications after surgery, including the amount of narcotic use, the number of diclofenac suppositories and ketorolac ampoules, and nausea and vomiting, were recorded.

The baseline characteristics of the patients in the four groups were compared with the Chi-square test and one-way ANOVA. The mean analgesic dose and mean shoulder and abdominal pain scores at different time points after the intervention were compared with one-way ANOVA. Moreover, differences between the three intervention groups in the changes in the shoulder and abdominal pain scores over time were analyzed by repeated-measures ANOVA. Statistical significance was set as $P \leq 0.05$. All statistical analyses were performed with Stata version 14.

RESULTS

A total of 118 patients were assessed for eligibility; 21 patients did not meet the eligibility criteria, and 2 patients declined to participate in the study. The remaining 95 eligible patients were randomly allocated into the four groups. All patients received the allocated intervention, continued the intervention until the end of the study, and were included in the final analysis (**Figure 1**). **Table 1** displays a comparison of the demographic and clinical characteristics of the patients between study groups. The four groups were

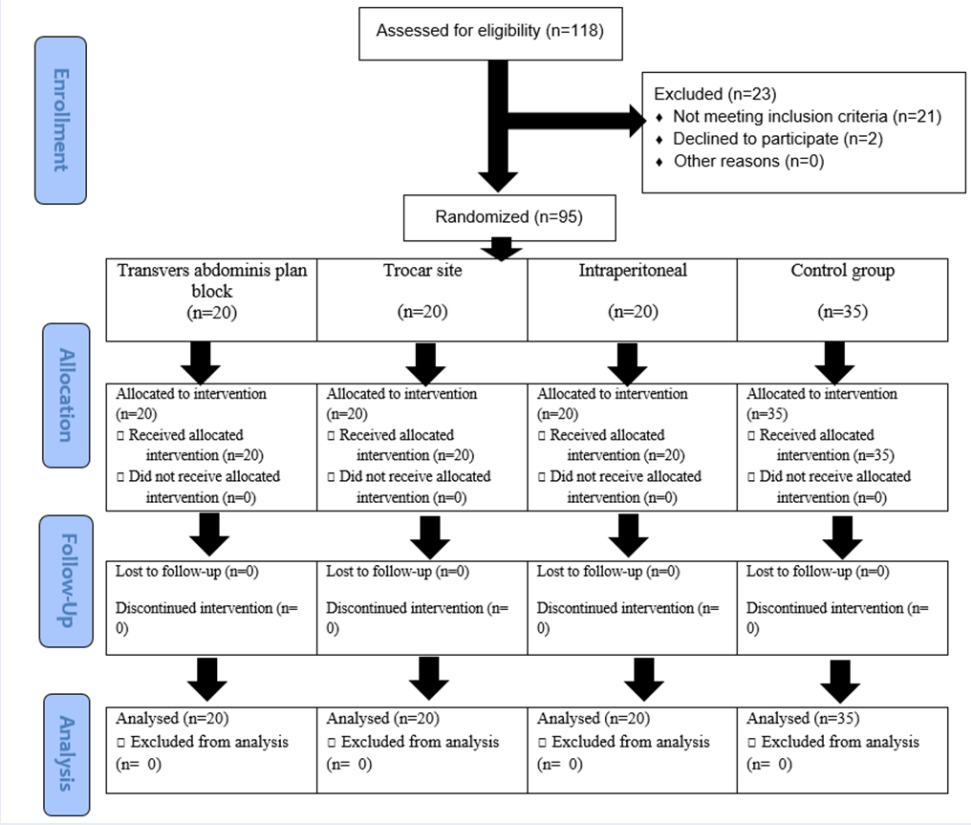

Figure 1: **CONSORT flow-diagram of the allocation of patients to the study groups**.

homogenous in age, weight, height, body mass index (BMI), surgery duration, surgery type, and family history of cancer ($P > 0.05$). The rate of nausea and vomiting was significantly higher in the control group than in the three intervention groups ($P < 0.001$).

Table 2 presents a comparison of the study groups according to the doses of administered analgesics. Patients in the control group received higher doses of narcotics and diclofenac than patients in the transversus abdominis plane block group, who did not receive any narcotics ($P < 0.001$). Patients in the transversus abdominis plane block group received a lower dose of ketorolac (24.54 ± 15.3 mg), and patients in the intraperitoneal group received a higher dose of this drug ($P < 0.001$).

Table 3 and Figure 2 present a comparison of the mean abdominal and shoulder pain scores between the four groups of patients 2–4, 8, 12, and 24 h after the surgery. The mean abdominal and shoulder pain score differed significantly between the groups at the mentioned time points; at most time points, patients in the control group reported higher pain scores, and patients in the transversus abdominis plane block group reported lower pain scores ($P < 0.001$). The mean abdominal and shoulder pain scores were significantly decreased from the first time point (hours 2–4) to hours 8, 12, and 24 after the surgery in the trocar site, intraperitoneal, and control groups ($P < 0.001$). However, we did not observe a significant decrease in abdominal and shoulder pain in the transversus abdominis plane block group ($P > 0.05$).

DISCUSSION

Hysterectomy surgery is a common major surgical procedure in women [15]. Patients experience less postoperative pain and lower morbidity with laparoscopic hysterectomy than with open surgery, and they recover more quickly and stay in the hospital for a shorter time [16]. After laparoscopic surgery, uncontrolled pain negatively impacts patients' well-being by disrupting their sleep and potentially causing myocardial infarction, cardiac arrhythmia, ileus, and poor wound healing [17]. In recent years, alternative methods of pain relief, such as intraperitoneal local anesthesia, have become increasingly popular because

Table 1: Demographic and clinical characteristics of the participants

Variables		Treatment groups Treatment groups				P-value
		Group 1 (N = 20)	Group 2 (N = 20)	Group 3 (N = 20)	Group 4 (N = 35)	
Continuous variables		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age (year)		43.77 ± 9.14	38.20 ± 13.65	40.50 ± 11.48	39.64 ± 10.56	0.41
Weight (Kg)		73.1 ± 10.83	70.35 ± 10.41	70.10 ± 13.01	69.45 ± 10.23	0.68
Height (cm)		161.94 ± 5.55	164.7 ± 4.52	162.1 ± 4.77	162.51 ± 4.77	0.26
BMI (Kg/m^2)		27.46 ± 4.16	26.1 ± 4.81	26.69 ± 5	26.37 ± 4.21	0.79
surgery duration (Hour)		2.11 ± 0.23	2.13 ± 0.24	2.22 ± 0.15	2.15 ± 0.31	0.51
Categorical variables		N (%)	N (%)	N (%)	N (%)	< 0.001
Nausea	Yes	0	0	6 (30)	29 (82.9)	
	No	20 (100)	17 (100)	14 (70)	6 (17.1)	
Vomiting	Yes	0	0	2 (10)	11 (31.4)	< 0.001
	No	20 (100)	17 (100)	18 (90)	24 (68.6)	
Family	No	19 (95)	19 (95)	20 (100)	35 (100)	0.41
	Yes	1 (5)	1 (5)	0	0	
Surgery type	TLH ± BSO	12 (60)	13 (76.5)	16 (84.2)	20 (57.1)	0.47
	TLH	6 (30)	4 (23.5)	3 (15.8)	12 (34.3)	
	TLH ± LSO	2 (10)	0	0	1 (2.9)	
	TLH ± RSO	0	0	0	2 (5.7)	

Group 1: Transvers abdominis plan block, **Group 2**: Trocar site, **Group 3**: Intraperitoneal, **Group 4**: Control group

they have fewer side effects and require less invasive approaches [18].

Non-opioid pain therapy has been evaluated in patients undergoing laparoscopic and vaginal hysterectomies. It is challenging to draw convincing conclusions from the literature on this subject because the data are heterogeneous and contradictory [19]. Therefore, it is essential to conduct high-quality research on each medication type and approach for post-hysterectomy pain management. Bupivacaine is a well-known local anesthetic that reduces sodium permeability, increases the threshold of action, and prevents nerve conduction [20].

This study compared the efficacy of three methods of bupivacaine administration for reducing pain after laparoscopic hysterectomy. The patients in transversus abdominis plane block and trocar site groups did not report any nausea or vomiting. Patients in the transversus abdominis plane block group did not receive any narcotics and received lower doses of ketorolac and diclofenac than patients in the other groups. Moreover, patients in this group had the lowest abdominal and shoulder pain scores. Previous meta-analyses have found that bupivacaine has no major side effects in patients undergoing laparoscopic gynecologic surgery who received intraperitoneal local analgesia, and bupivacaine was effective in reducing postoperative pain [21,22].

Our results are consistent with those previous reports that have examined intraperitoneal local anesthesia for postoperative pain control [23,24]. However, other results contradict those of the present study. Another double-blind, randomized controlled trial reported that intraperitoneal bupivacaine instillation at the end of laparoscopic hysterectomy did not reduce postoperative pain, and overall patient satisfaction and complication rates were unchanged, as were opioid analgesic use, hospital stay length, and opioid analgesic use. However, laparoscopic gynecologic

Table 2: Doses of administered analgesics according the study groups

		Group 1 N (%)	Group 2 N (%)	Group 3 N (%)	Group 4 N (%)	p value
Narcotic	Mean ± SD	0	0.20 ± 0.41	1.25 ± 0.63	1.45 ± 0.51	< 0.001
	0 mg	20 (100)	16 (80)	2 (10)	0	< 0.001
	25 mg	0	4 (20)	11 (55)	19 (54.3)	
	50 mg	0	0	7 (35)	16 (45.7)	
Diclofenac	Mean ± SD	186.36 ± 56.02	220 ± 110.5	335 ± 81.27	402.85 ± 51.36	< 0.001
	0 mg	1 (5)	3 (15)	0	0	< 0.001
	100 mg	1 (5)	0	0	0	
	200 mg	17 (75)	8 (40)	1 (5)	0	
	300 mg	1 (5)	8 (40)	13 (65)	4 (11.4)	
	400 mg	0	1 (5)	5 (25)	26 (74.3)	
	500 mg	0	0	0	5 (14.3)	
	600 mg	0	0	1 (5)	0	
Ketorolac	Mean ± SD	24.54 ± 15.3	36.81 ± 20.56	68 ± 24.62	42.86 ± 15.06	< 0.001
	0 mg	5 (25)	3 (15)	0	0	< 0.001
	30 mg	14 (70)	10 (50)	4 (20)	20 (57.1)	
	60 mg	1 (5)	7 (35)	16 (80)	15 (42.9)	

Group 1: Transvers abdominis plan block, **Group 2**: Trocar site, **Group 3**: Intraperitoneal, **Group 4**: Control group

surgery resulted in low levels of self-reported postoperative pain in both groups[25]. Moreover, the results of El Hachem *et al.*'s study found no statistically significant difference in pain reduction between injection in the transversus abdominis plane block site versus injection in the trocar area[26]. Contrary to the results of the present study, Tam *et al.* demonstrated that bupivacaine injection at the trocar site did not significantly improve pain scores after laparoscopic surgery[27]. This difference could be partially explained by the difference in sample size and thus the difference in power.

In line with the results of the present study, a study conducted by Elkabarity *et al.* in 2020 showed that patients who received subcutaneous bupivacaine injection as transversus abdominis plane block had significantly lower pain scores in the first 24 hours after surgery compared with those who received intraperitoneal injections, and they received significantly fewer narcotics. They concluded that this form of injection allows superior pain control and reduces the need for opioids after the operation[28].

One limitation of the present study is that the surgeries were performed by two surgeons, and the patient-reported pain scores were collected by two people; therefore, inter-rater variability may have affected the results. Second, we conducted this study only on patients undergoing laparoscopic hysterectomy surgery, and therefore, more evidence is necessary to generalize the findings of this study to patients receiving other types of surgery.

CONCLUSIONS

This study showed that bupivacaine administration methods of transversus abdominis plane block and trocar site injection were effective and safe for reducing pain after laparoscopic hysterectomy.

ABBREVIATIONS

ASA: American Society of Anesthesiologists; **BMI**: Body mass index; **SD**: Standard deviation; **VAS**: Visual analog scale

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Table 3: Mean comparison of abdominal and shoulder pain after the intervention at different time points

Pain		Treatment groups				P-value
		Group 1 (Mean ± SD)	Group 2 (Mean ± SD)	Group 3 (Mean ± SD)	Group 4 (Mean ± SD)	
Abdominal pain	2-4 hours after surgery	1.04 ± 0.21	2.3 ± 0.73	2.4 ± 0.6	3.31 ± 0.53	< 0.001
	8 hours after surgery	1.18 ± 0.50	2 ± 0.92	2.74 ± 0.56	3	< 0.001
	12 hours after surgery	1.59 ± 0.50	1.75 ± 0.72	2.63 ± 0.49	2.17 ± 0.43	< 0.001
	24 hours after surgery	1.27 ± 0.46	1.4 ± 0.68	2.1 ± 0.45	2	< 0.001
	48 hours after surgery	1.09 ± 0.29	1.05 ± 0.69	1.8 ± 0.52	1.8 ± 0.41	< 0.001
Shoulder pain	2-4 hours after surgery	1.04 ± 0.21	2.25 ± 0.71	2.20 ± 0.61	3.11 ± 0.41	< 0.001
	8 hours after surgery	1.85 ± 0.87	2.47 ± 0.69	2.94 ± 0.69	2.94 ± 0.23	< 0.001
	12 hours after surgery	1.54 ± 0.51	1.50 ± 0.76	2.50 ± 0.61	2.28 ± 0.45	< 0.001
	24 hours after surgery	1.18 ± 0.39	1.50 ± 0.68	2.10 ± 0.55	2 ± 0.001	< 0.001
	48 hours after surgery	1.09 ± 0.29	1.05 ± 0.68	1.70 ± 0.47	1.77 ± 0.42	< 0.001

Group 1: Transvers abdominis plan block, **Group 2**: Trocar site, **Group 3**: Intraperitoneal, **Group 4**: Control group

AUTHOR'S CONTRIBUTIONS

All authors had the same contribution in different parts of the data collection and manuscript writing. MNM developed the study idea. NM analyzed the data. All authors read and approved the final manuscript.

FUNDING

Tehran University of Medical Sciences Funded the present study.

AVAILABILITY OF DATA AND MATERIALS

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Ethical Committee of the Tehran University of Medical Sciences approved the protocol of the present study (ethics committee code: IR.TUMS.MEDICINE.REC.1401.020), and it was registered in the Iranian Registry of Clinical Trials (IRCT registration number: IRCT20110530006640N9, registration date: 2022-09-11).

CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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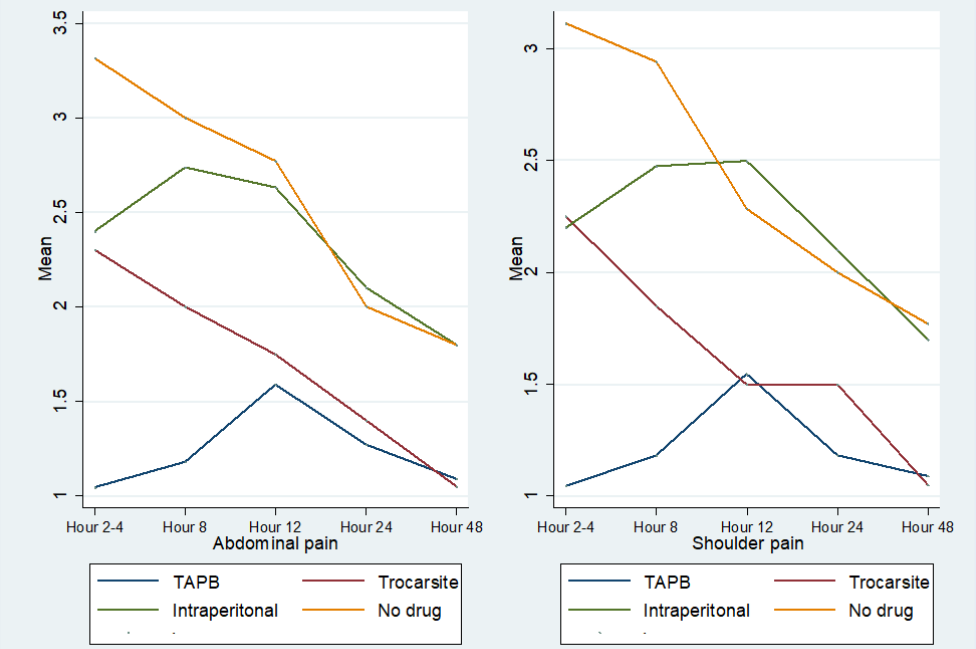

Figure 2: **The changes in the abdominal and shoulder pain between the four groups of patients at 2-4, 8, 12, and 24 h after the surgery**.

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