ORIGINAL ARTICLE

Bupivacaine Local Infiltration at Trocar Insertion Sites after Gynecologic Laparoscopic Surgery: A Randomized, Double-blind, Placebo-Controlled Trial

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Objective: To compare local infiltration of bupivacaine with placebo for reducing pain at trocar insertion sites after gynecologic laparoscopic surgery (GLS).

Materials and Methods: A prospective, randomized, double-blind, placebo-controlled trial was conducted on women who underwent GLS at Buddhachinaraj Phitsanulok Hospital, Thailand between September 2021 and March 2022. Eighty subjects were included for this trial. Bupivacaine 0.5% 10-mL was infiltrated at each port site after removing the trocars compared with placebo. Pain intensity was evaluated by visual analog scale (VAS) for four pain points including abdominal parietal pain (APP), abdominal visceral pain (AVP), and right and left shoulder pain at 2, 4, 8, 12, and 24 hours postoperatively.

Results: There were no significant differences in baseline characteristics between the two groups except for parity. APP and AVP had no significant difference in postoperative pain (mean difference –0.23, 95% CI –0.58 to 0.10, p=0.169 and –0.35, 95% CI -0.72 to 0.02, p=0.063, respectively). Only mild pain, with a VAS of 0 to 2, on both sides of shoulder were found in most participants, which had no significant difference between the two groups. Opioid consumption and adverse events were also not a significant difference. Multivariate analysis showed the APP had no significant difference between the two groups after adjusting confounding factors. However, gynecologic cancer and increased age were the significant factors associated with postoperative pain (mean difference 0.60, 95% CI 0.12 to 1.08, p=0.014 and –0.02, 95% CI –0.04 to –0.01, p=0.010, respectively).

Conclusion: Locally infiltrated bupivacaine at trocar insertion sites after GLS did not significantly improve postoperative analgesia.

Keywords: Gynecologic laparoscopic surgery; Postoperative analgesia; Bupivacaine

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Minimally invasive surgery is a contemporary gynecologic surgery that has fewer complications, and shorter hospital stays and recovery time[1-3]. Nonetheless, postoperative pain comprises visceral pain, parietal pain, and referred pain. Meanwhile, post-gynecologic laparoscopy pain composes of deep intra-abdominal pain, incisional pain, and shoulder tip pain due to diaphragmatic irritation[4,5]. These pains are required to be controlled with analgesia. Local wound infiltration at the abdominal port sites is easier administered and has fewer side effects than systemic opioids in immediate postoperative pain control[6-12]. Studies on local anesthesia for pain control after laparoscopic surgery have been reported. Lam et al.[13] found that the combination of local infiltration anesthesia with 1% lignocaine to the port wound pre-incision and pre-closure reduced postoperative pain in pre-closure better than pre-incision with no significant difference in opioid use. Selcuk et al.[14] showed that postoperative pain was reduced by administrating local infiltration of lidocaine both pre-incision and pre-closure to the port wound. However, bupivacaine, a long-acting anesthetic drug, provides satisfactory sensory anesthesia without systemic adverse reactions[6,7] when infiltrated at trocar sites in immediate postoperative gynecologic laparoscopic surgery (GLS) with a means pain score of 25.8 versus 48.6 (p=0.02) was demonstrated by Einarsson et al[15]. In contrast, Tam et al.[16] reported postoperative injection of bupivacaine in trocar port sites did not significantly improve pains score after laparoscopic gynecologic surgery. In addition, Sugihara et al.[17]

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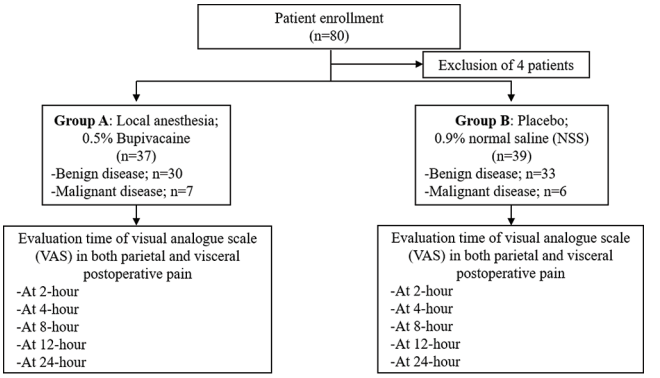

Figure 1. Diagram of patient's flow.

reported that local infiltration anesthesia did not effectively reduce postoperative pain and reduce the dosage of analgesic consumption within 12 hours postoperatively in the whole analysis but was significant in subgroup analysis in the patient who underwent a laparoscopic hysterectomy. To elucidate this controversial issue, the present study was carried out with the aim to evaluate the efficacy of local bupivacaine infiltration at the trocar sites after GLS, and the analgesic consumption.

Materials and Methods

Study design and participants

A prospective, randomized, double-blind, placebo-controlled trial was conducted on women that underwent GLS at Buddhachinaraj Phitsanulok Hospital, Thailand between September 2021 and March 2022. The study was approved by the Ethical Committee of the Institutional Review Board (IRB No.055/64). The inclusion criteria were four-port entry gynecologic laparoscopy, Thai language understanding, no allergy to bupivacaine or amide anesthesia, and no history of psychiatry. The patients who were pregnant, had three or five port site entries, or converted to open surgery were excluded. Block of fours randomization was assigned in both groups using 1:1 allocation. Group A was given 10 mL of 0.5% bupivacaine infiltration at the port site after trocars removal and group B was given 10 mL of 0.9% normal saline (NSS) for control (Figure 1). All women gave informed consent before participating in the study.

Eighty patients were enrolled and gave informed consent. Four patients were excluded from the study, with one patient was converted to open surgery, one patient did not understand Thai, and two patients had a 5-port entry operation.

The sample size was estimated using the formula of two dependent means (two-tailed test) that was referenced by Sugihara et al.[17] and used the outcome of visual analog scale (VAS) at two hours after laparoscopic hysterectomy for the Bupivacaine group as 3.2±2.1 and the control group as 5.0±3.0 (p=0.05), with a type I error of 0.05 and a type 2 error of 0.20. The study divided into 33 samples per group from the 66 samples and added 20% to compensate for missing data. Therefore, the calculated sample size was to be 80 participants with 40 participants in each group.

Procedures

The patients were given Cefazolin 1 g intravenously 30 minutes before skin incision, while the obese women received Cefazolin 2 g. Clindamycin 900 mg was used in penicillin-sensitive patients. Induction of anesthesia was established with propofol or thiopental, then an endotracheal tube was placed. Balance anesthesia was maintained with sevoflurane, fentanyl, and muscle relaxant. Only one experienced surgeon performed GLS. Veress's needle was inserted at the umbilical incision to accommodate the pneumoperitoneum with carbon dioxide gas of up to 1.5 to 2 liters. All patients used heated carbon dioxide to insufflate the pneumoperitoneum by KARL STROZ endoflator®. A 12-mm trocar was inserted through the umbilicus followed by a 10-mm 0°-laparoscope. Two 5-mm trocars were placed under direct vision at the level of the lower abdominal quadrants, which was lateral to the rectus abdominis muscles. Another 5-mm cannula was inserted approximately 10 cm above the left lower quadrant trocar parallel to the umbilicus. After the accomplishment of the operation, the envelope was opened to choose the drug between groups A and B. Before skin closure, 10 mL of 0.5% bupivacaine or 0.9% NSS was injected with a 24-Gauge needle at an umbilical port site 4 mL, and other ports 2 mL

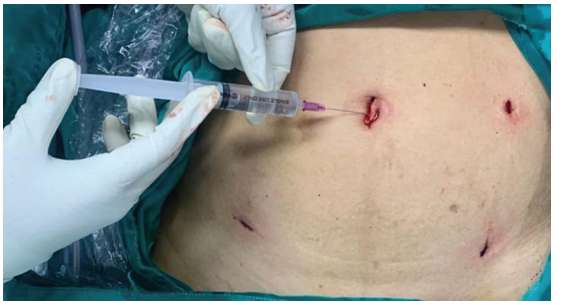

Figure 2. The injection of 10 mL of 0.5% bupivacaine or 0.9% NSS with a 24-Gauge needle at an umbilical port-site for 4 mL and 2 mL were infiltrated into each other port-sites.

(Figure 2). The skin was closed with polyglactin-910 No.4/0. The postoperative pain was assessed by VAS level between 0 and 10 for the patients. The pain level demonstrates 0 is no pain, 1 to 3 shows mild pain, 4 to 6 displays moderate pain, and 7 to 10 manifests severe pain. The four pain points were abdominal parietal pain (APP), abdominal visceral pain (AVP), and right and left shoulder pain at 2, 4, 8, 12, and 24 hours postoperatively. Parietal pain is caused by irritation of the peritoneal lining that surrounds the abdominal cavity. The pain is well localized and described as sharp or severe. While, visceral pain is experienced when the walls of an organ are stretched and the nerves send signals to the brain, the pain is poorly described as an ache or cramp. The adverse effect of bupivacaine had been observed. Intravenous opioid with tramadol 50 mg, was given to patients who had VAS more than 5, as needed within 24 hours. Oral paracetamol 500 mg was administered after 24 hours.

Statistical analyses

Statistical analyses were performed using intention to treat (ITT) paradigm by the IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA). Baseline characteristics were shown in percentage, mean or median, and standard deviation. Chi-squared test, Wilcoxon rank sum test, Fisher's exact test, Independent sample t-test, and Linear-mixed model assess VAS pain scores between the treatment group and the control group. The p-value less than 0.05 was considered statistically significant.

Results

Eighty patients were enrolled. Four patients were excluded: one patient was converted to open surgery, one patient did not understand Thai, and two patients had a 5-port entry. Of the remaining 76 patients, 37 patients in group A received bupivacaine,

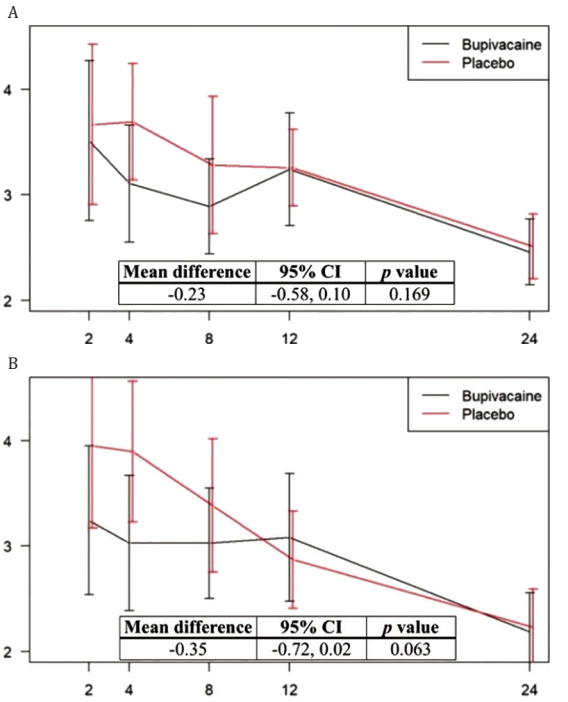

Figure 3. The post-operative abdominal parietal and visceral pain at the time 2, 4, 8, 12, and 24 hours.

A: abdominal parietal pain, B: abdominal visceral pain

and 39 patients in group B received placebo (Figure 1). Mean age, the median of parity, body mass index (BMI), and history of the previous operation were not significantly different between the two groups (Table 1). In addition, the operative type, diagnoses, blood loss, hospital stay, and operative time were not significantly different between the two groups. All participants had no postoperative complications. Level of VAS pain scores showed no significant differences at 2, 4, 8, 12, or 24 hours postoperatively in both groups for parietal and visceral pain (Table 2, Figure 3) (mean difference –0.23, 95% CI –0.58 to 0.10, p=0.169 and –0.35, 95% CI –0.72 to 0.02, p=0.063). Postoperative opioid usage within 24 hours showed no significant difference in the median dose of tramadol (Table 1). The side effects of tramadol included nausea, headache, and dizziness, and had been observed. In addition, all participants had only mild severity of shoulder pain at VAS 0 to 2. Multivariate analysis for significant factors to APP showed bupivacaine group analysis by linear mix model reduced pain score 0.24 better than placebo after adjusting risk but not to a significant difference. Moreover, reducing pain with advanced age and in malignancy diagnosed participants tended to get more pain significantly

Table 1. Characteristics of patients

	Bupivacaine group (n=37)	Placebo group (n=39)	p-value
Age (years); mean±SD	44.41±10.78	45.31±12.53	0.738*
Parity; median (Q_1, Q_3)	1 (0, 2)	2 (1, 2)	0.018**
BMI (kg/m^2); median (Q_1, Q_3)	22.77 (20.57, 25.0)	25.33 (22.23, 26.7)	0.076**
Previous surgery; n (%)	24 (64.9)	20 (51.3)	0.334*
Smoking; n (%)	2 (5.4)	2 (5.1)	>0.999***
Preoperative diagnosis; n (%)			0.982*
Benign without clinical pain	22 (59.5)	23 (59.0)	
Benign with clinical pain	7 (18.9)	8(20.5)	
Malignancy	8 (21.6)	8(20.5)	
Postoperative Diagnosis; n (%)			0.922*
Benign without clinical pain	20 (54.1)	22 (56.4)	
Benign with clinical pain	9 (24.3)	10 (25.6)	
Malignancy	8 (21.6)	7 (17.9)	
Operative; n (%)			0.699*
Laparoscopic non-hysterectomy	10 (27.0)	14 (35.9)	
Laparoscopic hysterectomy	21 (56.8)	19 (48.7)	
Laparoscopic complete staging	6 (16.2)	6 (15.4)	
Pathologic result; n (%)			0.917*
Benign	30 (81.1)	33 (84.6)	
Malignancy	7 (18.9)	6 (15.4)	
Estimate blood loss (mL); median (Q_1, Q_3)	30 (20, 100)	30 (15, 75)	0.825**
Length of stay (hours); median (Q_1, Q_3)	71 (68, 72)	70 (68.5, 72.5)	0.992**
Operative time (minutes); median (Q_1, Q_3)	75 (60, 100)	75 (55, 100)	0.743**
Operation time ≥120 minutes; median (Q_1, Q_3)	4 (10.8)	4 (10.3)	>0.999***
Opioid used within 24 hours; n (%)	26 (70.3)	30 (76.9)	0.691*
Opioid used within 24 hours (mg); median (Q_1, Q_3)	50 (0, 100)	50 (50, 100)	0.542**
Adverse effect; n (%)			
Nausea	4 (10.8)	4 (10.3)	>0.999***
Headache	2 (5.4)	1 (2.6)	0.610***
Dizziness	1 (2.7)	2 (5.1)	>0.999***

BMI=body mass index; SD=standard deviation
* Chi-squared test, ** Wilcoxon rank sum test, *** Fisher's exact test

Table 2. Comparison of mean pain scores at each time point in abdominal parietal pain and abdominal visceral pain

Postoperative pain (VAS)	Bupivacaine group (n=37); mean±SD	Placebo group (n=39); mean±SD	Mean difference	95% CI	p-value
Abdominal parietal pain					
2 hours	3.51±2.27	3.67±2.34	0.153	−0.90 to 1.21	0.773
4 hours	3.11±1.66	3.69±1.70	0.584	−0.19 to 1.35	0.135
8 hours	2.89±1.35	3.28±1.99	0.390	−0.39 to 1.17	0.325
12 hours	3.24±1.61	3.26±1.12	0.013	−0.62 to 0.64	0.967
24 hours	2.46±0.93	2.51±0.94	0.053	−0.38 to 0.48	0.805
Abdominal visceral pain					
2 hours	3.24±2.11	3.95±2.39	0.705	−0.33 to 1.74	0.178
4 hours	3.03±1.92	3.90±2.06	0.870	−0.04 to 1.78	0.061
8 hours	3.03±1.57	3.38±1.96	0.358	−0.46 to 1.17	0.384
12 hours	3.08±1.82	2.87±1.42	−0.209	−0.95 to 0.53	0.576
24 hours	2.19±1.10	2.23±1.11	0.042	−0.46 to 0.55	0.870

VAS=visual analogue scale; SD=standard deviation; CI=confidence interval
Independent samples t-test, $p<0.05$

Table 3. Univariate and Multivariate Analysis for significant factor to abdominal parietal pain

Factor	n	Univariate analysis			Multivariate analysis		
		Crude MD	95% CI	p-value	Adjust MD	95% CI	p-value
Bupivacaine group	37	–0.24	–0.58 to 0.10	0.169	–0.35	–0.72 to 0.02	0.064
Age (years)	76	–0.01	–0.03 to 0.00	0.093	–0.02	–0.04 to –0.01	0.010*
BMI (kg/m^2)	76	0.01	–0.03 to 0.05	0.576	0.00	–0.04 to 0.04	0.959
Parity	76	0.01	–0.15 to 0.17	0.890	–0.01	–0.23 to 0.20	0.913
Previous surgery	44	0.15	–0.20 to 0.49	0.406	0.33	–0.04 to 0.70	0.080
Hysterectomy	52	0.17	–0.20 to 0.53	0.365	0.24	–0.19 to 0.68	0.274
Histopathology of malignancy	13	0.49	0.04 to 0.94	0.034	0.60	0.12 to 1.08	0.014*
Operative time >120 minutes	8	–0.02	–0.57 to 0.54	0.950	–0.27	–0.88 to 0.34	0.386
EBL ≥100 mL	20	–0.14	–0.53 to 0.24	0.467	–0.05	–0.46 to 0.35	0.794

BMI=body mass index; EBL=estimate blood loss; MD=mean difference; CI=confidence interval

* $p<0.05$ is considered statistically significant, Linear mixed model

(mean difference 0.60, 95% CI 0.12 to 1.08, p=0.014 and –0.02, 95% CI –0.04 to –0.01, p=0.010) (Table 3).

Discussion

Pain is a personalized experience in each patient, which is influenced by the biological response, social context, and psychological status[1-5]. In the present study, the local anesthesia, bupivacaine, injection at trocar sites made no significant improvement of VAS in both parietal pain and visceral pain after GLS when compared with the placebo, which is in line with the previous reports[10-15]. This finding can be explained as the postoperative pain after GLS was mild to moderate pain at 2 to 4 points, so the patients can tolerate such pain well without requiring more potent analgesia[7,8]. Moreover, the action of anesthesia at the time of surgery may be prolonged to the immediate postoperative period, thus, could facilitate less postoperative pain[15,17-19]. However, Sugihara et al.[17] found a longer surgery and more extensive operation such as hysterectomy or laparoscopic oncological surgery significantly consumed more analgesia and shorter time to use analgesia compared with a placebo.

Contradictorily, Alessandri et al.[20] demonstrated that preemptive infiltration of levobupivacaine at trocar sites of GLS could significantly reduce postoperative pain at 6 and 12 hours with pain score of 4.5±1.2 versus 6.2±1.8 (p=0.008) and 3.4±0.9 versus 5.9±1.4 (p=0.004), respectively, but with no significant result at 24 hours after the operation due to the pain intensity that had markedly reduced. A similar finding by Einarsson et al.[15] showed that infiltration of bupivacaine at trocar sites of GLS had a significant decrease in pain scores at 1 hour with a means pain score of 25.8 versus 48.6 (p=0.02) but was not statistically different at 4 and 24 hours after surgery. Therefore, local infiltration of bupivacaine can reduce the immediate postoperative pain. In the current study[13-15,17-21], the postoperative pain had differences in the early period at 2, 4, and 8 hours, but did not reach statistical significance. To minimize GLS pain, studies used intraperitoneal aerolization of anesthetic, heating, and humidifying of carbon dioxide insufflation as an alternative method[22]. The finding of the present study implied that postoperative pain after GLS was less intense and local bupivacaine might not benefit enough to use at the postoperative period. According to the multivariate analysis of the present study, the authors found that the patients experienced less severity of pain by increasing age, which does not correspond with the other studies. However, the confirmed malignancy cases suffered more severity of pain, which corresponds to the result of Sugihara et al[17]. This may be due to the longer operative time, more operations, as well as more dosages of opioids that were needed.

The strength of the present study was randomization double-blind to evaluate pain outcomes and GLS was performed by one experienced surgeon to avoid the disparity among surgeons. Nevertheless, this can simultaneously be considered as a limitation of the study because it did not allow for generalization as there were fewer surgeons involved. Further study should be carried out by more gynecologic surgeons to add a generalizability of the procedure.

Conclusion

GLS minimizes postoperative pain to mild to moderate degrees. Thus, locally infiltrated bupivacaine at the trocar insertion site after GLS did not significantly improve postoperative pain.

What is already known on this topic?

The local anesthesia is not statistically significant for pain management in GLS. Is it really necessary for this type of operation?

What does this study add?

Only oral forms of analgesics are needed in GLS. However, in other than gynecological malignancies, extra painkillers may be essential.

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Conflicts of interest

The authors declare no conflict of interest.

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