Intraperitoneal Sub-Diaphragmatic Instillation of Bupivacaine plus Morphine for Reducing Postoperative Shoulder Pain after Gynecologic Endoscopy

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Background: *Gynecologic endoscopic surgery is a minimally invasive surgical technique for treatment of various gynecologic diseases. When compared to conventional laparotomy, this procedure has advantages in many aspects such as reduced postoperative pain, short hospital stay, and decreased morbidity associated with laparotomy. However, 15 to 30% of the patients experienced moderate or severe postoperative shoulder pain. Methods to minimize postoperative shoulder pain after gynecologic endoscopy are essential to maximize the quality of life of the patients.*
Objective: *To evaluate the benefit of intraperitoneal instillation of bupivacaine plus morphine for reducing postoperative shoulder pain incidence after gynecologic endoscopy.*
Material and Method: *A randomized clinical trial was conducted in 158 patients undergoing laparoscopic procedures. The patients were randomly assigned to receive either 0.5% bupivacaine hydrochloride 20 mL mixed with morphine 3 mg (study group) or normal saline (control group) instillation to subdiaphragmatic area before finishing the procedure. Shoulder pain was evaluated at immediate post-operative time, and at 12 and 24 hours from the termination of surgery. The data of requested analgesic drugs after surgery was also recorded.*
Results: *Baseline characteristics were comparable between the two groups. Diagnosis, laparoscopic procedures, and duration of operation were also comparable. There were comparable proportions of patients reporting shoulder pain at 12 and 24 hours between the study and control group (30.4% and 30.4% at 12 hours, and 11.3% and 21.5% at 24 hours, respectively). Median pain scores at 12 and 24 hours were comparable between the study and control group (3 and 2 at 12 hours, and 4 and 4 at 24 hours, respectively). Requirement of analgesics was slightly greater among control than study group, but without statistical significance (17.7% and 24.1% respectively).*
Conclusion: *Intraperitoneal instillation of bupivacaine plus morphine had no efficiency for reducing postoperative shoulder pain incidence after gynecologic endoscopy.*

Keywords: *Gynecologic endoscopy, Bupivacaine hydrochloride, Morphine*

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Gynecologic endoscopic surgery is a minimally invasive surgical technique for treatment of various gynecologic diseases. When compared to conventional laparotomy, this procedure has advantages in many aspects such as reduced postoperative pain, short hospital stay, and decreased morbidity associated with laparotomy. However, 15 to 30% of the patients experienced various degree of postoperative shoulder pain, which may be moderate or even severe in some cases. Methods to minimize postoperative shoulder pain after gynecologic endoscopy are essential to maximize the quality of life of the patients. Diaphragmatic irritation from CO_2 gas producing pneumoperitonium probably causes the referred pain at scapular area through phrenic nerves[1]. Several interventions have been proposed in order to reduce or eradicate postoperative shoulder pain. Intraperitoneal local anesthetic agent administration has been used to reduce postoperative shoulder pain after different types of endoscopic surgery[2,3].

Previous studies have confirmed that bupivacaine, ropivacaine, tramadol, and lidocaine can be safely used intraperitonium without any complication[4-8,15]. Bupivacaine was the most widely

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used due to the less adverse effects, low price, and easy to prepare[8-11,14-17]. Intraperitoneal administration of opioids in combination with local anesthetic drugs has been evaluated as an alternative approach[13,14,18]. This combination has been suggested to have superior analgesic effects than local anesthetic agents alone due to the addition of opioid activated opioid receptors localized on peripheral sensory nerves.

However, several reports of the effectiveness and clinical value of intraperitoneal local anesthetic drugs and opioid for shoulder pain control after gynecologic endoscopic procedures still show various degrees of controversies[12]. Therefore, the aim of the present study was to evaluate the effectiveness of bupivacaine plus morphine for reduction of shoulder pain in patients undergoing gynecologic laparoscopic procedures.

Material and Method

Patients

The present study was approved by Siriraj Hospital ethic committee for research on humans. Between February and July 2010, 158 patients undergoing elective gynecologic endoscopy and classified as ASA physical status grade I or II were included in this prospective, randomized, double-blinded, and placebo controlled project. All patients, over 18 years old, gave their written informed consent. Patients undergoing emergency gynecologic endoscopic surgery, with contraindications to local anesthetic drugs, opioids and sulfonamides, or with a medical history of asthma, hepato-renal and cardiovascular diseases were excluded. Patients with confirmed side effects of local anesthetic and opioids drugs, unable to perform laparoscopic procedures and converted to exploratory laparotomy, and from whom operative time was in excess of three hours were withdrawn from the study.

Protocols

The patients were randomly allocated to one of the two groups, 0.5% bupivacaine hydrochloride 20 ml plus morphine 3 mg or 20.3 ml normal saline. The standard Gynecologic laparoscopic procedures such as total laparoscopic hysterectomy (TLH), myomectomy, salpingo-oophorectomy, ovarian cystectomy, salpingectomy, or lysis adhesion were performed by four well-trained laparoscopic surgeons. The test solution was drawn into a 20 ml syringe by a nurse and given to the surgeons who did not know the allocation at the end of the surgery before removal of laparoscopic instruments. The test solution was equally injected intraperitonium onto both subdiaphragmatic surfaces by using specific long laparoscopic needle injection instrument (Carl-Storz Germany) under direct vision and the patients still in the deep trendelenburg position. The surgeons tried to manually remove CO_2 gas from the patient's abdomen as much as possible before removing the trocars and closed the surgical wounds.

Two doses of parecoxib 40 mg were administered intravenously, immediately after abdominal wall closure, and 12 hours thereafter. Additional postoperative analgesic drugs could be requested according to patients' requirement: acetaminophen 1,000 mg orally every four hours or pethidine 10 to 25 mg intravenously every four to six hours. Type, amount, and timing of analgesic drugs consumed by the patients were recorded.

Postoperative shoulder pain was assessed using a Numerical rating scale (NRS) from 1 to 10 at 15 minutes, 12, and 24 hours from the termination of surgery. The patients were carefully asked about the abdominal pain and the shoulder pain. The authors used Numerical rating scale, which was one of the most commonly used pain scales in healthcare systems. The numerical rating scale offered the individual in pain to rate their pain score. It was designed to be used by those over the age of nine. The patient had the option to verbally rate their scale from 0 to 10 or to place a mark on a line indicating their level of pain. Zero indicated the absence of pain, while 10 represented the most intense pain possible.

Side effects and postoperative complications were also recorded until 24 hours postoperation.

Data analysis

Data were analyzed by unpaired t-test, Mann-Whitney U test with interquartile range, and Fisher's exact test using SPSS version 13. P-value of less than 0.05 was considered statistical significance different. The authors used Mann-Whitney U test for analyzing the Numerating rating of pain score of the two groups because it was a non-parametric statistical hypothesis test for assessing whether one of two samples of independent observations tends to have larger values than the other and medians are usually recommended in Mann-Whitney U test.

Results

Demographic data (age, weight, and height), ASA physical status, type, and duration of surgery were similar in the two groups (Table 1).

There was no significant difference in the incidence of postoperative shoulder pain in the two groups (Table 2).

Postoperative shoulder pain scores between the two groups also showed no significant difference (Table 3).

Time to first analgesic request, number of patients required additional analgesic drugs, dosage, and type of additional analgesic drugs were not different between the two groups (Table 4, 5).

One patient experienced nausea and vomiting. One patient had minor eczematous rash. No other adverse drug effect was seen.

Discussion

Gynecologic laparoscopic surgery is currently the method of choice for patients and physicians to treat various benign and early stage malignant gynecologic diseases. With its advantages in reduced postoperative pain when compared to exploratory laparotomy, the patients undergoing laparoscopic surgery should have a short hospital stay. However, many patients experienced postoperative shoulder pain, resulting from irritated diaphragm by CO_2 gas[1]. Therefore, adequate pain relief is important. Several methods have been proposed to minimize postoperative shoulder pain after laparoscopic surgery. Intraperitoneal

Table 1. General data of study group and control group

Data	Study group (n = 79)	Control group (n = 79)	p-value
Age (years)	42.2±10.2	39.5±8.6	0.073*
BMI (kg/m^2)	21.5±3.0	22.6±4.2	0.056*
Duration (min)	121.9±49.3	131.0±51.0	0.259*
Diagnosis: n (%)			0.324$^+$
Myoma uteri	38 (48.1)	34 (43.0)	
Endometriosis	27 (34.2)	22 (27.8)	
Ovarian tumor	8 (10.1)	16 (20.3)	
Adenomyosis	6 (7.6)	7 (8.9)	
Operation: n (%)			0.644$^+$
Myomectomy	11 (13.9)	12 (15.2)	
TLH	35 (44.3)	40 (50.6)	
Ovarian cystectomy	14 (17.7)	12 (15.2)	
BSO	10 (12.7)	11 (13.9)	
Lysis adhesion	9 (11.4)	4 (5.1)	

Values are mean ± SD or n (%)
* Unpaired t-test
$^+$ Chi-square test

Table 2. Numbers of patients who have postoperative shoulder pain in first 24 hours divided into pain at 12 hours and 24 hours after operation

Time of shoulder pain	Study group (n = 79) (%)	Control group (n = 79) (%)	p-value*
At 12 hours	24 (30.4)	24 (30.4)	1.000
At 24 hours	9 (11.3)	17 (21.5)	0.086

* Chi-square test

Table 3. Numerical rating scale of pain score at 12 hours and 24 hours after operation

Time of shoulder pain (hrs)	Pain score		p-value*
	Study group (n = 79)	Control group (n = 79)	
At 12 hour	3 (1-10)	2 (1-10)	0.215
At 24 hour	4 (2-8)	4 (2-10)	0.958

Values are medians (interquartile range)
* Mann-Whitney U test

Table 4. Number of patients who require analgesic drug in first 24 hours after surgery

Analgesic	Study group (n = 79) (%)	Control group (n = 79) (%)	p-value*
All patients who receive analgesic drug	14 (17.7)	19 (24.1)	0.33
Paracetamol	7 (8.9)	13 (16.5)	0.15
Pethidine	8 (10.1)	11 (13.9)	0.46

* Chi-square test

Table 5. Dose of paracetamol and pethidine that patients receive for reduce postoperative shoulder pain at first 24 hour

Analgesic	Study group (n = 79) (%)	Control group (n = 79) (%)	p-value*
Paracetamol (mg)	1,000 (500-3,000)	1,000 (1,000-2,000)	0.76
Pethidine (mg)	25 (20-55)	50 (25-75)	0.31

Values are medians (interquartile range)
* Mann-Whitney U test

instillation of local anesthetic drugs and opioids under direct vision in sub-diaphragmatic area has been shown to decrease this pain[8,12]. However, only a few reports that focused on postoperative shoulder pain have been recorded in gynecologic patients. Therefore, the authors studied the efficacy of 0.5% bupivacaine hydrochloride 20 ml plus 3 mg morphine instillation in sub-diaphragmatic area at the end of various gynecologic procedures to reduce postoperative shoulder pain. However, the present results failed to demonstrate its superior analgesic efficacy when compared to placebo. Kieta et al also reported that the prophylactic intraperitoneal injection of bupivacaine and morphine did not produce significant analgesia after gynecologic endoscopic surgery compared to a multimodal analgesia regimen[12]. However, their report had small sample size and focused on overall postoperative pain.

The present study was a randomized double-blinded placebo controlled trial with a sample size of 158 patients. The authors used computerized random allocation and we found no difference between baseline characteristics such as age, weight, and type of operation between treatment and control groups.

The authors also tried as much as possible to minimize any bias that may interfere with the present results. The control group received an equal amount of normal saline fluid as the amount of analgesics in the treatment group. Parecoxib was given immediately at the end of operation as routine analgesia for all patients. The authors used Numerical Rating Scale (NRS) to access pain in all patients who had preoperative preparation to understand this technique.

In the present study, the incidence of postoperative shoulder pain, pain score and additional analgesic requirement were not statistically different between two groups.

These results showed that bupivacaine hydrochloride plus morphine intraperitoneal instillation after gynecologic laparoscopy did not reduce postoperative shoulder pain in any aspect. The possible explanation might be from the low pain score in these minimally invasive surgeries, so we could not detect significant analgesic effects from the patients. Postoperative analgesic drugs, such as parecoxib, acetaminophen, and pethidine, also reduced postoperative pain score. The amount and dosage of analgesic drugs delivered to subdiaphragmatic area may be insufficient and diluted by intraperitoneal fluid and blood. However, the amount and dosage that the authors used were studied with regard to safety of the patients, so we decided not to increase them due to our patients' safety. In addition, having no inflammatory process at subdiaphragmatic area to stimulate peripheral opioid receptor might reduce the analgesic effect of morphine.

While the present results showed the lower incidence of postoperative shoulder pain at 12 and 24 hours in the treatment group (9 patients) compared to the control group (17 patients), it is of statistical insignificance. However, the power of this data was 0.42, which is inadequate to conclude this difference. Therefore, additional study with a greater population should be performed.

A potential limitation of the present study is that we cannot control anesthetic premedication and anesthetic drugs during operation due to the variation

of anesthesiologists. However, we standardized our postoperative analgesic drugs protocol.

Conclusion

In this prospective, randomized-controlled study showed that intraperitoneal instillation of bupivacaine plus morphine had no efficiency for reducing postoperative shoulder pain incidence after gynecologic endoscopy.

Potential conflicts of interest

None.

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การให้ยา bupivacaine ร่วมกับ morphine ในช่องท้องผู้ป่วยเพื่อลดอุบัติการณ์ความเจ็บปวดบริเวณไหล่ภายหลังการผ่าตัดผ่านกล้องทางนรีเวชวิทยา

ปวิตร สุจริตพงศ์, พักตร์ประภา ไชยภักดี, กรกฎ ศิริมัย, อัมพัน เฉลิมโชคเจริญกิจ, ประสงค์ ตันมหาสมุทร

ภูมิหลัง: *การผ่าตัดทางนรีเวชด้วยวิธีการผ่านกล้อง ได้แก่ การผ่าตัดถุงน้ำรังไข่, การผ่าตัดท่อนำไข่ และการผ่าตัดมดลูก มีข้อดี คือ ทำได้ง่าย, มีความเจ็บปวดน้อย และมีผลข้างเคียงน้อยกว่าเมื่อเทียบกับการผ่าตัดด้วยวิธีการเปิดช่องท้อง แต่ผู้ป่วยประมาณร้อยละ 15-30 มีความเจ็บปวดบริเวณไหล่หลังผ่าตัด บางรายมีความเจ็บปวดมากจนไม่สามารถทนได้ ดังนั้นการหาวิธีลดอาการปวดไหล่จึงเป็นสิ่งจำเป็น*

วัตถุประสงค์: *เพื่อศึกษาประโยชน์ของการใส่ยา bupivacaine ร่วมกับ morphine ลงในช่องท้องก่อนเสร็จการผ่าตัดผ่านกล้องทางนรีเวช ในการช่วยลดอุบัติการณ์อาการปวดไหล่ภายหลังทำการผ่าตัด*

วัสดุและวิธีการ: *คณะผู้นิพนธ์ทำการศึกษาเชิงทดลองแบบมีกลุ่มควบคุม เพื่อทดสอบถึงประโยชน์ของการใส่ยา bupivacaine ร่วมกับ morphine ลงในช่องท้องก่อนเสร็จการผ่าตัดผ่านกล้องทางนรีเวชเพื่อช่วยลดอุบัติการณ์อาการปวดไหล่ภายหลังทำการผ่าตัด ในผู้ป่วย 158 ราย ระหว่างวันที่ 1 เดือนกุมภาพันธ์ พ.ศ. 2553 ถึงวันที่ 31 เดือนกรกฎาคม พ.ศ. 2553*

ผลการศึกษา: *ผู้ป่วยที่มีอาการปวดไหล่หลังผ่าตัดในช่วง 12 ชั่วโมงแรกในกลุ่มศึกษาและในกลุ่มควบคุมมีจำนวนเท่ากันคือ 24 ราย (ร้อยละ 30.4) ($p = 1.000$) และผู้ป่วยที่มีอาการปวดไหล่หลังผ่าตัดในช่วง 24 ชั่วโมงแรกในกลุ่มศึกษาคือ 9 ราย (ร้อยละ 11.3) และในกลุ่มควบคุมคือ 17 ราย (ร้อยละ 21.5) ($p = 0.086$) โดยไม่พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ จำนวนผู้ป่วยที่ขอยาแก้ปวดในกลุ่มศึกษาคือ 14 ราย (ร้อยละ 17.7) และในกลุ่มควบคุมคือ 19 ราย (ร้อยละ 24.1) ซึ่งไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p = 0.33$)*

สรุป: *การให้ยา bupivacaine hydrochloride ร่วมกับ morphine ในช่องท้องระหว่างทำการผ่าตัดผ่านกล้องทางนรีเวชไม่สามารถลดอาการปวดไหล่หลังการผ่าตัดได้ และไม่มีผลต่อการขอรับยาแก้ปวดหลังผ่าตัด*