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Effect of Bupivacaine Local Infiltration Compared with Parecoxib Intravenous Administered in Post Surgical Pain Management Following Total Abdominal Hysterectomy

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ABSTRACT

Objectives: To compare effect of bupivacaine local infiltration with parecoxib intravenous administered for post surgical pain relief in woman undergoing abdominal hysterectomy.

Materials and Methods: From August 2014 to January 2015, 42 patients scheduled for abdominal hysterectomy under general anesthesia were randomly allocated to 2 groups. Group P (n=21) were received 40 mg intravenous parecoxib and group B (n=21) were received 0.5% bupivacaine 20 mL intraoperative injection to incisional surgical site before the subcutaneous fat and skin were closed. All patients were received morphine patient-controlled analgesia (PCA) at ward.

Main outcome measures: Pain scores, morphine consumption, sedation score and nausea or vomiting were assessed at 2, 6, 10, 14 and 26 hours after surgery. Antiemetic requirement, pruritus and satisfaction scores were evaluated at 26 hours after surgery.

Results: No significant differences between 2 groups in age, BMI, surgical time and intraoperative dose of fentanyl were found. Pain scores at rest were significantly lower (p=0.045) in the P group at 2, 14 hours after surgery. There were no significant differences in pain scores during movement, morphine consumption, sedation score, nausea or vomiting, antiemetic requirement, pruritus and satisfaction scores between 2 groups.

Conclusion: The use of parecoxib with PCA morphine in post operative analgesia reduced pain significantly when compared with bupivacaine at 2 and 14 hours after surgery.

Keywords: parecoxib, bupivacaine, abdominal hysterectomy, pain score, post operative pain

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การศึกษาเปรียบเทียบผลของการฉีด bupivacaine บริเวณแผลผ่าตัดกับการให้ parecoxib ทางเส้นเลือดดำเพื่อบรรเทาอาการปวดในผู้ป่วยที่รับการผ่าตัดมดลูกทางหน้าท้อง

เพ็ญพักตร์ เจนสารศาสตร์, ณัฐพงศ์ อิศรางกูร ณ อยุธยา, วัลภา อานันทศุภกุล, อมรรัตน์ ตั้งจิตบำเพ็ญบุญ

วัตถุประสงค์: *เพื่อเปรียบเทียบผลของการฉีด bupivacaine บริเวณแผลผ่าตัดกับการให้ parecoxib ทางเส้นเลือดดำเพื่อบรรเทาอาการปวดในผู้ป่วยที่รับการผ่าตัดมดลูกทางหน้าท้อง*

วัสดุและวิธีการ: *ผู้ป่วย 42 ราย ที่ได้รับการผ่าตัดมดลูกทางหน้าท้อง ภายใต้การระงับความรู้สึกแบบทั่วไป ถูกสุ่มออกเป็นสองกลุ่ม กลุ่ม P จำนวน 21ราย ได้รับยา parecoxib ขนาด 40 มิลลิกรัม ทางหลอดเลือดดำ และกลุ่ม B จำนวน 21 ราย ได้รับการฉีดยา 0.5% bupivacaine ปริมาณ 20 มิลลิลิตร เข้าผิวหนังบริเวณแผลผ่าตัดก่อนทำการเย็บปิดชั้นไขมันและผิวหนัง จากนั้นผู้ป่วยจะได้รับ morphine ผ่านทางเครื่องระงับปวดด้วยตัวเองที่หอผู้ป่วย เก็บข้อมูลการประเมินคะแนนความปวด ปริมาณ morphine ที่ใช้ คะแนนความง่วงซึม อาการคลื่นไส้อาเจียน ที่ 2, 6, 10, 14 และ 26 ชั่วโมงหลังการผ่าตัด และข้อมูลการได้รับยาแก้คลื่นไส้อาเจียน อาการคัน และคะแนนความพึงพอใจที่ 26 ชั่วโมงหลังการผ่าตัด*

ผลการศึกษา: *ไม่พบความแตกต่างระหว่างผู้ป่วยทั้งสองกลุ่มในเรื่องของอายุ, BMI, ระยะเวลาการผ่าตัด และปริมาณยา fentanyl ที่ใช้ระหว่างการผ่าตัด คะแนนความปวดขณะนอนนิ่งต่ำกว่าอย่างมีนัยสำคัญทางสถิติ (p=0.045) ในกลุ่ม P ที่เวลา 2 และ 14 ชั่วโมงหลังการผ่าตัด ส่วนคะแนนความปวดขณะขยับตัว ปริมาณ morphine ที่ใช้ คะแนนความง่วงซึม อาการคลื่นไส้อาเจียน การได้รับยาแก้อาเจียน อาการคัน และคะแนนความพึงพอใจระหว่างสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ (p>0.05)*

สรุป: *การให้ parecoxib ร่วมกับ morphine ทางเส้นเลือดดำผ่านทางเครื่องระงับปวดด้วยตัวเอง ช่วยลดอาการปวดหลังผ่าตัดได้มากกว่าอย่างมีนัยสำคัญทางสถิติ เมื่อเทียบกับการให้ bupivacaine ฉีดเข้าผิวหนังบริเวณแผลผ่าตัด*

Introduction

Inappropriate management of post operative pain can lead to adverse physiological, psychological, economic and social effects[1]. Good pain control can prevent those negative outcomes[2].

At Ramathibodi Hospital, the patients undergoing abdominal hysterectomy were not allowed to have any food or drink in the first day after the operation. Oral analgesic drugs were not permitted for pain relief. The intravenous parecoxib was administered to reduce post operative pain. In patients who have contraindications for this drug use such as allergy to NSAIDs or selective COX-2 inhibitors, history of gastrointestinal hemorrhage, stroke, myocardial infarction, uncontrolled hypertension, congestive heart failure, severe impaired renal and hepatic function, the pain was controlled by morphine intravenous bolus dose or via PCA. The patients may have more side effects from morphine (nausea or vomiting, pruritus and sedation). Analgesic drugs local intrasurgical wound infiltration was reported to have benefit in post operative pain control[3].

The authors were interested in comparing the effectiveness of post operative pain control after abdominal hysterectomy between intravenous parecoxib and bupivacaine local infiltration.

Materials and Methods

The prospective, double-blinded, randomized clinical trial was conducted at the gynecologic ward and the operative room, Department of Obstetrics and Gynaecology, Ramathibodi Hospital. After approval by the Ethical Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University on June 30, 2014. The patients were enrolled. The inclusion criteria were women age between 18 and 60 years, BMI ≤ 30 kg/m^2, scheduled for elective abdominal hysterectomy for benign gynecologic diseases under general anesthesia, ASA status I-II[4], no history of medical diseases; myocardial infarction, uncontrolled hypertension, congestive heart failure, severe impaired renal function (serum creatinine > 1.5 mg/d), impaired hepatic function (Child-Pugh: class C), stroke, gastrointestinal bleeding, no mental or physical inability to handle a PCA device and to answer pain assessment questions, no allergy to opioids, NSAIDs, parecoxib, sulfonamides and bupivacaine. After obtaining informed consent, 42 women were enrolled in the study from August 2014 to January 2015.

The patients were randomly allocated by computer generated random numbers into 2 groups; group P (n=21) and group B (n=21). The day before surgery, the patients were trained to the use of PCA device. Anesthesia was performed using fentanyl 1-2 ug/kg, thiopental 3-5 mg/kg, atracurium 0.5 mg/kg. Orotracheal intubation was facilitated, and anesthesia was maintained with seroflurane, N_2O, O_2, atracurium and fentanyl in appropriate doses. Abdominal hysterectomy was done with standard technique. Before the subcutaneous fat and skin were closed, group P was received intravenous parecoxib 40 mg by the anesthesiologist whereas group B was administered 0.5% bupivacaine 20 mL intraincisionally. The drug was infiltrated into the dermal layer around the skin incisional wound by the surgeon. The patients and the evaluators were blinded of the interventions.

After the operation, the patients were transferred to and observed at post anesthesia care unit (PACU) for 2 hours, analgesia with intravenous morphine 2-3 mg per dose was provided as the patients needed. Thereafter, patients were transferred to the gynecologic ward and PCA with intravenous morphine were given to the patients. The PCA device was programmed to deliver as a 1-mL bolus dose of morphine (1 mg/mL) on demand with a lockout interval of 5 minutes. No medication with analgesic effect was administered within 26 hours after the operation.

Abdominal pain intensity at rest and during movement (during sitting up) was assessed at 2, 6, 10, 14 and 26 hours after the operation using visual analogue pain score ranging from 0 (no pain) to 10 (worst pain imaginable). At the same time, nausea or vomiting was assessed by rating score; 0 = no nausea or vomiting, 1 = nausea and 2 = nausea with vomiting. When nausea or vomiting occurred, ondansetron 4 mg was given as needed. Sedation was assessed by using

"Pesero Opioid-Induced Sedation Scale (POSS)[5]; S = sleep, easy to arouse, 1 = awake and alert, 2 = slightly drowsy, easily aroused, 3 = frequently drowsy, arousable, drifts off to sleep during conversation and 4 = somnolent, minimal or no response to verbal or physical stimulation. Morphine consumption was also recorded.

Pruritus and patient satisfaction were assessed using the score ranging from 1 = dissatisfaction to 5 = highest satisfaction and total antiemetic requirement during PCA use were recorded.

Statistical analysis

A sample size of 19 patients per group was calculated to receive the p-value of 0.05, a power of 0.80 to detect the difference in pain score between groups of 2. Ten percent data loss was added, therefore 21 patients per group were recruited.

Statistical analysis was performed with STATA software using Chi-square or Fisher's exact test and student's t-test. Values for quantitative variables were reported as mean (95% confidence interval, CI) and mean ± SD (standard deviation) and for qualitative variables as count and percent. A value of $p<0.05$ was considered statistically significant.

Results

Forty two women completed the study; there were 21 women in each group. There were no significant differences between 2 groups in age, BMI, surgical time, fentanyl consumption during course of operation, skin incision and type of surgery as shown in Table 1.

Women in group P expressed significantly less pain only at rest at 2 and 14 hours after the operation. There were no significant differences in pain during movement and morphine consumption between 2 groups that were shown in Table 2.

The frequency of nausea or vomiting and sedation were low and not different among 2 groups as shown in Table 3. The mean (95% CI) of antiemetic consumption (mg) was 1.90 (0.42-3.39) in group P and 2.67 (0.73-4.61) in group B and p value was 0.519. The patients experienced pruritus only 4 and 3 in group P and group B respectively, with p-value 1.000. The patient satisfaction in pain control was mostly as highest satisfaction level and no one revealed dissatisfaction that were shown in Table 4.

Table 1. Demographic data of patients.

	Parecoxib (n=21)	**Bupivacaine (n=21)**	**P**
Age (yr)*	45.71 (42.92-48.52)	47.42 (44.92-49.93)	0.347
BMI (kg/m^2)*	22.69 (21.31-24.08)	22.83 (21.72-23.95)	0.870
Surgical time (min)*	114.5 (101.2-127.9)	126.4 (109.7-143.1)	0.253
Fentanyl consumption (ug)*	111.9 (89.5-134.3)	117.1 (94.9-139.4)	0.730
Type of operation**			
- TAH	9 (42.86%)	9 (42.86%)	1.000
- TAH + BSO	8 (38.10%)	9 (42.86%)	
- TAH + others	4 (19.05%)	3 (14.29%)	
Skin incision**			
- Low midline	14 (66.67%)	18 (85.71%)	0.277
- Pfannenstiel	7 (33.33%)	3 (14.29%)	

* Data were expressed as mean (95% CI)

** Data were expressed as count (percent)

Table 2. Post operative pain and morphine consumption at 2, 6, 10, 14 and 26 hours after operation between parecoxib and bupivacaine.

	Parecoxib (n=21)	Bupivacaine (n=21)	P
Pain score at rest			
2	3.76 ± 2.90	5.00 ± 3.03	0.045
6	3.14 ± 2.35	3.24 ± 1.81	0.877
10	2.57 ± 2.04	2.71 ± 1.65	0.817
14	0.67 ± 1.49	1.90 ± 1.73	0.045
26	0.57 ± 1.12	1.71 ± 1.49	0.064
Pain score during movement			
2	6.00 ± 3.13	6.38 ± 2.78	0.561
6	5.05 ± 2.25	5.48 ± 1.83	0.513
10	4.19 ± 1.69	4.67 ± 2.31	0.467
14	2.95 ± 1.56	3.38 ± 2.01	0.513
26	2.52 ± 1.78	3.38 ± 1.88	0.191
Morphine consumption (mg)			
2	3.86 ± 1.77	2.48 ± 2.18	0.139
6	3.48 ± 4.04	4.71 ± 4.77	0.184
10	2.00 ± 2.98	3.05 ± 3.15	0.261
14	1.62 ± 2.29	1.62 ± 1.53	1.000
26	1.48 ± 2.50	2.95 ± 4.02	0.113
Total	12.43 ± 7.67	14.33 ± 10.38	0.732

Data were expressed as mean ± SD

Table 3. Nausea/vomiting score and sedation score in each group.

Time (hr)	Nausea/ vomiting score	Group P (n=21)	Group B (n=21)	P	Sedation score	Group P (n=21)	Group B (n=21)	P
2	0	17	17	1.000	S	3	6	0.277
	1	4	3		1	18	14	
	2	0	1		2	0	1	
6	0	17	17	0.417	S	11	9	0.758
	1	2	4		1	10	12	
	2	2	0		2	0	0	
10	0	17	17	1.000	S	15	15	1.000
	1	4	3		1	6	6	
	2	0	1		2	0	0	
14	0	17	16	1.000	S	16	14	0.484
	1	2	3		1	4	7	
	2	2	2		2	1	0	

Table 3. Nausea/vomiting score and sedation score in each group. (Cont.)

Time (hr)	Nausea/ vomiting score	Group P (n=21)	Group B (n=21)	P	Sedation score	Group P (n=21)	Group B (n=21)	P
26	0	17	17	1.000	S	12	12	1.000
	1	4	3		1	9	9	
	2	0	1		2	0	0	

Data were expressed as count

Table 4. Patient satisfaction score.

Patient satisfaction score	Parecoxib (n=21)	Bupivacaine (n=21)	P
3 (satisfaction)	2	2	0.844
4 (very satisfaction)	1	3	
5 (highest satisfaction)	18	16	

Data were expressed as count

Discussion

Abdominal hysterectomy is one of the most common procedures. It is associated to pain in the gynecologic operation. Noxious perception begins in periphery, extends up the neuraxis, and terminates at supraspinal regions responsible for interpretation and reaction. Pain perception is dependent on the degree of noxious stimulation, local descending inhibition from CNS centers, and response of second order transmission cells[6].

Pain signal from the uterine corpus transmits to the brain via spinal cord at the T11-12 levels, where as spinal cord levels of S2-4 receive signals from the cervix, vagina and perineum.

PCA is an effective and efficient method for controlling post operative pain with low risk of oversedation. Risk factors for oversedation and respiratory depression include opioid-naive status, obesity, age, mental status, and multiple comorbid conditions such as intrinsic lung disease, obstructive sleep apnea (OSA), and renal and hepatic impairment. This study selected appropriate patients to receive PCA by using developing criteria from previous work of Craft J.[7] STOP questionnaire was used as a tool to screen patients for OSA[8]. From previous study, morphine was used as the opioid of choice with a dose of 1 mg at patient's request, with a lockout period (5 minutes) to prevent overdosing[6].

Nonsteroidal anti-inflammatory drugs and selective cyclooxygenase-2 (COX-2) inhibitors use was reported reduction of postoperative opioid consumption[9, 10]. Parecoxib, a COX-2 selective inhibitor, is effectively used in post operative pain management. Initial dose is 40 mg and maximum daily dose is 80 mg. Onset of action is 10-23 minutes and peak effect is within 2 hours. The duration of action is 6 to more than 12 hours. The advantage of this drug is sparing COX-1 dependent physiologic processes in tissues[11]. The study of Ng A et al. suggested using intravenous parecoxib 40 mg on induction of anesthesia resulted in lower 24 hours morphine consumption by PCA than the placebo (54 vs 72 mg)[9]. Another study revealed the use of intravenous parecoxib 40 mg followed by 40 mg every 12 hour for 48 hours after the gynecologic tumor operation had a morphine-sparing effect and significantly lower visual analogue scale (VAS) both at rest and during moving comparing with placebo[10].

Local anesthetic injection at the surgical site has been demonstrated to be beneficial in multimodal analgesia[3]. Bupivacaine blocks both the initiation and conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions. Onset of action is 1-17 minutes, duration 2-9 hours depending on route and dose. The maximum dose is 175 mg for local infiltration[11]. The study of Lowenstein L et al., evaluated the impact local lidocaine infiltration for abdominal hysterectomy, showed a significant reduction in post operative pain in the first 8 hours[12]. But the study of Jabalameli M et al., reported pain scores were significantly lower only in pethidine and tramadol postoperative subcutaneous infiltration group compared with bupivacaine and placebo group in patients undergoing cesarean section[13].

This current study was the first study to compare the effect of intravenous parecoxib with bupivacaine local infiltration for post surgical pain relief in woman undergoing abdominal hysterectomy. There were no significant differences between 2 groups in demographic data, so the results of this study in each group could be comparable. The overall pain scores were lower in P group and significantly lower in pain scores at rest at 2 and 14 hours after surgery. These could be explained because intravenous parecoxib reduced both somatic and visceral pain whereas bupivacaine acted only at incisional site, duration of action of parecoxib is longer than bupivacaine and inflammatory substances production were initially inhibited by parecoxib. Both drugs had no remain action after 12 hours, at 14 and 26 hours there were no differences in pain scores. The pain scores at 6, 10 and 26 hours at rest of two groups were not significant different, this may be due to inadequate sample size. Morphine consumption in both groups were low when compared with previous studies[9, 10] and no significant difference between groups, which resulted in comparable morphine side effects. The limitation of this study may be inadequate sample size to show the significant difference of pain scores in some period. Further study with larger sample size is needed to find the difference in pain scores of other periods and morphine consumption. Although both drugs have limited duration of action, we evaluated the 26 hour post operative period to find whether there was difference in morphine consumption and pain score. Most patients prefer PCA because they needed lower dose of opioids to relieve pian.

Conclusion

From the results of this current study, the author concluded that the use of parecoxib with PCA morphine reduced pain at rest at 2, 14 hours post operation significantly when compared to bupivacaine with PCA morphine and there was no difference in side effects and morphine consumption by PCA in both groups.

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