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Preemptive Intramuscular Diclofenac for Pain Relief after Total Abdominal Hysterectomy

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ABSTRACT

Objectives: To evaluate the effectiveness of preoperative intramuscular diclofenac for pain relief after total abdominal hysterectomy.

Methods: A prospective double-blind, randomized study was conducted in 37 patients who underwent total abdominal hysterectomy at our institution between September 2012 and January 2013. The patients were randomly allocated into two groups to receive either single intramuscular 75 mg diclofenac (treatment group; n = 18) or normal saline (control group; n = 19) 20 min before surgery. Total consumption of meperidine over a 24-h period were recorded. The degrees of postoperative pain were assessed at 4, 8, 12, and 24 h postoperatively by using a numeric rating scale and the adverse events relevant to diclofenac were observe.

Results: The mean 24-h postoperative meperidine consumption in the treatment group was insignificantly lower compared to that in the control group (46.11+24.77 mg and 68.42+44.63 mg, respectively, p=0.069). Mean pain scores at 4, 8, 12, and 24 h postoperatively in the treatment group were lower than those in the control group (2.83 vs 4.53, p=0.052; 2.83 vs 4.89, p=0.031; 2.78 vs 4.68, p=0.044; 1.28 vs 1.89, p=0.296, respectively). No serious adverse events were observed in both groups.

Conclusion: Preoperative intramuscular diclofenac significantly reduced pain scores at 8 and 12 h (while insignificantly decreased 24-h meperidine consumption) after total abdominal hysterectomy.

Keywords: preemptive, diclofenac, total abdominal hysterectomy

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Introduction

Postoperative pain after total abdominal hysterectomy (TAH), especially within the first 24 hours, is the major suffering that requires pain control. Although opioids are commonly used for pain relief, there are many adverse effects such as respiratory depression, itching, nausea and vomiting[1]. From the knowledge about pain pathway, tissue trauma induces the expression of cyclooxygenase-2 (COX-2) leading to the release of prostaglandins (PGs), which stimulate both central and peripheral sensitization[2,3]. For this reason, non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac that have an inhibitory effect on PGs production may be an promising alternative[3,4].

Nowadays, preoperative analgesia has been use in combination with the conventional postoperative analgesia for improving pain control. Diclofenac is widely used as analgesic drug because of its effectiveness, low price, easy to use and safety. After intramuscular injection of 75 mg diclofenac, it offers better analgesic effect than rectal route[5], rapid onset within 20 minutes[6] and long lasting effect for 12 hours[6,7]. With these properties, preoperative intramuscular diclofenac may play an important role for postoperative pain relief in fasting patients undergoing intraabdominal surgery. Since there are no available information regarding the role of preoperative diclofenac on postoperative outcome in this kind of surgery, we conducted this study to assess the effect of preoperative intramuscular diclofenac on pain relief after total abdominal hysterectomy.

Materials and methods

The prospective double-blind randomized controlled study was conducted after approval of the Institutional Review Board Faculty of Medicine Vajira Hospital Certificate of Approval.

The patients undergoing elective TAH with/without salpingo-oophorectomy (SO) under standard general anesthesia at the department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital between September 1, 2012 and January 31, 2013 were recruited into this study. The enrolled subjects were aged 20-60 years, who had a diagnosis of benign gynecologic diseases. Exclusion criteria were the patients who had any underlying diseases contraindicated for NSAIDs including peptic ulcer, asthma, bleeding disorders and impaired renal or hepatic function, sensitivity to NSAIDs, obesity (BMI >30 kg/m^2), and inability to use a patient-controlled analgesia system (PCA) for postoperative pain control. Informed consents were obtained from all patients prior to the procedure.

All participants were randomly allocated into one of the two groups by table of randomization. The treatment group received single intramuscular (IM) 75 mg diclofenac 20 minutes before surgery while the control group received single IM 3 ml of normal saline.

The sequential random number code was enclosed in a sealed envelope for ensuring allocation concealment. All patients underwent TAH with/without SO and received a standard general anesthesia. The patients and the assessors were blinded to the allocation.

Before the operation, all patients were instructed how to use the PCA devices and how to assess pain by using a numeric rating scale (NRS) ranging from 0 (no pain) to 10 (worst possible pain) at 4-h, 8-h, 12-h and 24-h postoperation. All patients received oral midazolam 7.5 mg as premedication. General anesthesia was induced with thiopental 5 mg kg-1 and vecuronium 0.1 mg kg-1 before endotrachial intubation. The anesthesia was maintained with 2% sevoflurane, 67% nitrous oxide in oxygen and fentanyl 2 mcg kg-1. When the operation was finished, patients received intravenous atropine 1.2 mg and neostigmine 2.5 mg for reversal of muscle relaxant.

During the first 24 h post surgery, all patients received intravenous (IV) meperidine for pain control by using PCA (10 mg bolus and 10 min lockout). Pain scores were assessed by the attending nurse who had been well trained by the researchers and was unaware of the treatment allocation. The patients' characteristics, operative details, pain scores, consumption of meperidine during the first 24 h and side effects were recorded.

The primary outcome was postoperative meperidine consumption within 24 h, and the secondary outcomes were pain scores during the first 24 h and side effects.

The sample size was calculated from the data of the primary outcome in a preceding pilot study. The mean meperidine consumption from PCA in 5 patients who underwent TAH under GA without preemptive medicine was 66 mg. The expected dose of mean meperidine consumption was 46.2 mg if 30% decrease was assumed. With a power of 90% at a significant level of 0.05, 18 patients were needed in each group. After adding 10% for possible missing data in each group, 40 patients were required.

Statistical analysis was performed using the SPSS software package version 11.5 (SPSS Inc, Chicago, IL, USA). Continuous variables were presented as mean and standard deviation (SD), and categorical variables were presented as number (%). Differences between outcomes of the two groups were evaluated by using chi-square test or unpaired t-test as appropriate. All outcomes were considered significant only if the P-value was less than 0.05.

Results

Forty patients were recruited but three of them were excluded because of the criteria (one was diagnosed gynecologic cancer, the other one underwent oophorectomy and the rest received spinal block). From all 37 enrolled participants, there were 18 of them in the treatment group and 19 in the control group. Both groups had similar age, BMI, indication for surgery, type of skin incision, operation time and blood loss (Table 1).

Within 24 h postoperation, the mean meperidine consumption in the treatment group was 32.61% lower than that in the control group (46.11±24.77 mg vs 68.42±44.63 mg, respectively) (p=0.069).

Table 1. Patients' characteristics and surgical data

Characteristic	Treatment (N = 18)	Control (N = 19)	p
Age (yr) mean ± SD	44.06±5.93	42.89±4.19	0.499[a]
Body mass index, No.(%)			0.402[b]
≤ 25 (kg/m^2)	11 (61.1)	9 (47.4)	
> 25 (kg/m^2)	7 (38.9)	10 (52.6)	
Previous surgery, No.(%)			0.413[b]
No	8 (44.4)	11 (57.9)	
Yes	10 (55.6)	8 (42.1)	
Indication for surgery, No.(%)			0.909[b]
Uterine pathology	11 (61.1)	12 (63.1)	
Ovarian pathology	4 (22.2)	1 (5.3)	
Uterine and ovarian pathologies	3 (16.7)	6 (31.6)	
Type of skin incision, No.(%)			
Pfannenstiel	12 (66.7)	13 (68.4)	
Low midline	6 (33.3)	6 (31.6)	
Operative time (min), Mean±SD	210.56±46.17	190.26±43.86	0.180[a]
Blood loss (ml), Mean±SD	513.89±301.37	447.37±272.58	0.487[a]

[a]unpaired t-test; [b]Chi-Square

All the mean pain scores at 4-h, 8-h, 12-h, and 24-h in the treatment group were lower than those in the control group, but there was statistical significance of the mean pain scores only at 8-h and 12-h postoperation (Table 2).

The comparable adverse effects (nausea and vomiting) in the treatment and the control groups were reported (55.6% and 31.6%, respectively) (p=0.141). Moreover, anti-emetic drugs (intravenous metoclopramide 10 mg) were similarly needed in the treatment group (27.8%) and in the control group (21.1%) (p=0.634). No patients in both groups complained about pain at injection site, and no sign of infection or hematoma was noted.

Table 2. Postoperative meperidine consumption and pain scores.

	Treatment (N = 18)	Control (N = 19)	p
Meperidine consumption (mg), Mean ± SD	46.11 ± 24.77	68.42 ± 44.63	0.069
ostoperative pain score at (h), Mean ± SD			
4	2.83 ± 2.28	4.53 ± 2.82	0.052
8	2.83 ± 2.81	4.89 ± 2.75	0.031**
12	2.78 ± 2.60	4.68 ± 2.95	0.044**
24	1.28 ± 1.74	1.89 ± 1.79	0.296

**significant at level p<0.05

Disscussion

The present study demonstrated insignificant 32.61% decrease in the meperidine consumption in preoperative diclofenac administration. In addition, there was significant decrease in the mean pain scores at 8-h and 12-h post surgery in the treatment group, although there was a trend toward significant decrease in pain score at 4-h and no difference in pain score at 24-h was observed. There were comparable adverse effects in both groups.

With the rapid onset of diclofenac, it may be suitable for preoperative use. However, with its action lasting for 12-h6, 7, pain occurred beyond that period might not be relieved properly. These might explain the results of no difference pain score at 24-h and an insignificant decrease in overall meperidine consumption.

The insignificant decrease in pain score at 4-h postoperation might be explained by unclear patients' consciousness enough for accurate pain assessment after waking up from the general anesthesia. However, it was nearly statistically significant with P-value of 0.052. The pain score at each point of time after the surgery in the treatment group was lower than that in the control group. The reason of this result might be explained by the synergistic effect of diclofenac and meperidine that could delay the flare up of postoperative pain.

From the previous studies, Bourlert A, et al, reported that the patients undergoing caesarean section who received a single dose of intramuscular 75 mg diclofenac postoperation had significant lower postoperative morphine requirement than that who received intramuscular sterile water, but the levels of pain in both groups were not significant difference[3].

Surakarn J, et al, found that the patients undergoing caesarean delivery who received two doses of intramuscular 75 mg diclofenac (within 2 hours postoperation and then at 12 hours) did not required rescue tramadol for pain control compared to 20% of patients in control group, and pain scores at 6-h, 12-h, 24-h were also significantly less in the diclofenac group. There was no side effect of diclofenac reported[7].

In addition, Hodman NB, et al, reported that the patients undergoing abdominal surgery who received two doses of intramuscular 75 mg diclofenac (immediate postoperation and then at 12 hours) required significantly

lower dose of morphine for pain relief compared to the placebo group, and pain score at 4-h postoperation was also significantly lower in the diclofenac group[8].

The different outcomes among the present and previous studies might be explained by the varieties of studied population, sample sizes, surgical procedures, dosage of diclofenac, and different guidelines for postoperative pain relief.

The comparable adverse effects such as nausea and vomiting in both groups might be from meperidine consumption in both groups were not highly enough to present the major side effects in this study. There was also no complaint of pain, hematoma or infection at injection site in all patients. Actually, nausea and vomiting could be induced by using anesthesia or the surgical procedure itself, therefore it was possible that side effects reported in these patients were multifactorial rather than the results of diclofenac alone.

This is the first randomized study that determines the effectiveness of preoperative diclofenac for pain relief after TAH with/without SO with the most accurate dosage of analgesia required in each patient by using PCA. Additionally, the results could be applied clinically for avoidant of opioid use and its side effects. However, the limitation of this study was small sample size. Therefore, further studies with larger sample size are needed to assure.

In conclusion, preoperative IM diclofenac reduced meperidine consumption and pain scores at 4-h and 24-h postoperation insignificantly while pain scores at 8-h and 12-h were significantly declined. The comparable adverse effects were found in both groups.

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การได้รับยา diclofenac ฉีดทางกล้ามเนื้อก่อนการผ่าตัดเพื่อลดอาการปวดภายหลังการผ่าตัดมดลูกทั้งหมดผ่านทางหน้าท้อง

ศิริพร ประยูรหงส์, สาวินี รัชชานนท์, เถาวลัย ถาวรามร, สุจารีย์ ภู่พิพัฒน์ภาพ

วัตถุประสงค์ *: เพื่อศึกษาประสิทธิภาพของยา diclofenac ฉีดเข้ากล้ามเนื้อก่อนการผ่าตัดเพื่อลดอาการปวดหลังการผ่าตัดมดลูกทั้งหมดผ่านทางหน้าท้อง*

วัสดุและวิธีการ *: การศึกษาวิจัยเป็นแบบการทดลองแบบสุ่มในผู้ป่วย 37 คน ที่ได้รับการผ่าตัดมดลูกทั้งหมดผ่านทางหน้าท้องในโรคที่ไม่ใช่โรคมะเร็งที่ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์วชิรพยาบาล ในช่วง 1 กันยายน 2555 ถึง 31 มกราคม 2556 โดยแบ่งเป็น 2 กลุ่ม คือ ผู้ป่วย 18 คนได้รับยา diclofenac 75 มิลลิกรัม ฉีดเข้ากล้ามเนื้อ กับผู้ป่วย 19 คนได้รับน้ำเกลือ 3 มิลลิลิตร ฉีดเข้ากล้ามเนื้อ ก่อนการผ่าตัดนาน 20 นาที ประเมินปริมาณการใช้ยา meperidine ใน 24 ชั่วโมง และความรุนแรงของอาการปวดหลังการผ่าตัดชั่วโมงที่ 4, 8, 12 และ 24 โดยใช้คะแนนความปวดเป็น NRS (numeric rating scale) และผลข้างเคียงที่เกิดขึ้น*

ผลการวิจัย *: ค่าเฉลี่ยของปริมาณการใช้ยา meperidine หลังการผ่าตัด 24 ชั่วโมง ในกลุ่มทดลองต่ำกว่ากลุ่มควบคุมอย่างไม่มีนัยสำคัญ (46.11+24.77 mg และ 68.42+44.63 mg, ตามลำดับ, p=0.069) คะแนนความปวดที่ชั่วโมงที่ 4, 8, 12 และ 24 ในกลุ่มทดลองต่ำกว่าในกลุ่มควบคุม (2.83 vs 4.53, p = 0.052; 2.83 vs 4.89, p = 0.031; 2.78 vs 4.68, p=0.044; 1.28 vs 1.89, p=0.296, ตามลำดับ) ไม่พบผลข้างเคียงอย่างรุนแรงทั้งสองกลุ่มการทดลอง*

สรุป *: การได้รับยา diclofenac ก่อนการผ่าตัดสามารถลดอาการปวดหลังการผ่าตัดได้อย่างมีนัยสำคัญที่ ชั่วโมงที่ 8 และ 12 ในขณะที่ปริมาณการใช้ยา meperidine ใน 24 ชั่วโมง หลังการผ่าตัดลดลงอย่างไม่มีนัยสำคัญ*