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Multimodal pain control is associated with reduced hospital stay following open abdominal hysterectomy

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ABSTRACT

Objective: To study the association of a multimodal pain protocol (MMPC) and reduced hospital stay after open abdominal hysterectomy.
Study design: The study design was a comparison of a prospective cohort with a retrospective historical control. We enrolled endometrial cancer patients undergoing open abdominal hysterectomy with lymphadenectomy by the same surgeon. Control patients from 2008 to 2010 who received morphine PCA alone were compared with a similar demographic group of patients from 2011 to 2013 who received MMPC. MMPC consisted of gabapentin (900 mg PO) and acetaminophen (1 g IV) administered 45–60 min preoperatively. The surgical site was injected with bupivacaine with 0.5% epinephrine prior to incision. The postoperative pain control regimen consisted of gabapentin (300 mg PO every 6 h), acetaminophen (1 g IV every 8 h for 24 h postoperatively), ketorolac (15 mg IV every 6 h for 48 h postoperatively), morphine PCA (2 mg IV every 10 min, no basal rate) and oxycodone/acetaminophen (10/325 mg PO every 6 h as needed).
Results: Length of hospital stay (LOH) of the study cohort ($N = 105$ with MMPC) was compared with the historical with postoperative morphine alone ($N = 113$ without MMPC). There were no differences in demographic, uterine cancer stage, or comorbidities between the two arms. The LOH was 1.6 days for patients receiving MMPC and 3.3 days for patients who received morphine alone ($P < 0.001$).
Conclusion: Multimodal pain control is associated with significantly reduced hospital stay after open abdominal hysterectomy.

Introduction

Hysterectomy is the most common major surgery in women in the United States with more than 500,000 cases performed annually [1]. Post-hysterectomy pain management after open abdominal hysterectomy commonly involves patient-controlled analgesia (PCA) pump with a narcotic regimen. Pain after abdominal surgery has two components: somatic and visceral, both initiated by nocireceptor stimulation [2]. Mechanical, chemical, and thermal stimuli all potentiate nocireceptor activation that is transmitted via the spinothalamic tract to the brain stem and somatosensory cortex. Prostaglandins are potent chemical stimulators of nocireceptors, and their inhibition is the basis for the effectiveness of non-steroidal anti-inflammatory drugs NSAIDs. Opiate receptors play an integral role in pain transmission at different levels in the central nervous system as target sites for neurotransmitters and endogenous opiates such as enkalphins and endorphins [3].

We recently published a review article that concluded that a multimodal approach to postoperative pain control is probably more effective than the standard PCA morphine [1]. Multimodal pain control uses different types of pain medication with different mechanisms and toxicities. Thus, the combination of these agents, in addition to standard narcotics, adds to pain control efficacy while reducing side effects. In our review article, we suggested a few nonnarcotic choices for postoperative pain such as anti-inflammatory agents [4–6], nerve blocks [7,8], narcotics [9–11], *N*-methyl-D-aspartate antagonists such as dextromethorphan [12], and other agents with such as magnesium [13,14], gabapentin [15,16], and acetaminophen [17,18].

In contrast to patients undergoing minimally invasive hysterectomies, patients undergoing open abdominal hysterectomies

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have been reported to have longer hospital stay – an average of 3.7 to 4.4 days [19,20] – but usually at a lower cost [21]. Our objective was to study the effectiveness of a multimodal pain control protocol (MMPC) in reducing post-hysterectomy hospital stay in uterine cancer patients undergoing staging by open abdominal hysterectomy.

Materials and methods

Our practice consists of four gynecologic oncologists, but all of the study patients came from one surgeon who maintained a prospective patient database. This surgeon also used open abdominal hysterectomy for all of his patients with uterine cancer during the study period. In contrast, the other three attending physicians had mixed cases of open and minimally invasive hysterectomy and various combination of postoperative pain management. The Hospital Institutional Review Board (BMH IRB 13-49) approved this study. Patients who received MMPC were entered prospectively into the database and data collected from electronic medical records. The historic cohort (without MMPC) data were also collected prospectively for another study but had overlapping similar clinical variables as the study cohort with MMPC. The study design was a prospective cohort with a retrospective historical control. For the cohort without MMPC, inclusion criteria were patients with endometrial cancer whose pain was treated with morphine PCA with PRN intravenous morphine and/or PRN oral oxycodone/acetominophen after open abdominal hysterectomy with pelvic and aortic lymphadenectomy from 2008 to 2010. The morphine PCA settings, as described below, were the same for both cohorts. The same inclusion criteria were used for the patients with similar demographics and cancer from 2011 to 2013 with MMPC. In 2011, MMPC was adopted as this surgeon's standard of care which explained the cut of time between the historical control group and the study group. There was no difference in management of postoperative diet, ambulation and other routine postoperative care during the entire study period. Patients in both historic and study cohorts were operated and managed by the same single attending gynecologic oncologist.

MMPC consisted of preoperative gabapentin (900 mg PO) and acetaminophen (1 g IV) administered 45–60 min before skin incision. The skin overlying the operative site was injected with 0.5% bupivacaine with epinephrine prior to skin incision. Postopererative analgesia consisted of gabapentin (300 mg PO every 6 h), acetaminophen (1 g IV every 6 h for 24 h posteroperatively), ketorolac (15 mg IV every 6 h for 24 h postoperatively), morphine PCA (2 mg IV every 10 min, no basal rate, for the first night postoperatively) and oxycodone/acetaminophen (10/325 mg PO every 6 h as needed). Patients were excluded if they had abnormal liver function test or creatinine $\geq$ 1.5 mg/dl. The exclusion was done prior to enrollment into the study. Metoclopromide and ondansetron were given postoperatively for nausea for both cohorts. A more complete description of MMPC is noted in Table 2.

The length of hospital stay (LOH) of the study cohort (with MMPC) was compared with the historical cohort undergoing similar procedures with postoperative morphine (without MMPC) by the same surgeon. LOH was defined as the number of days a patient stayed in the hospital from the date of admission to the date of discharge. Criteria for discharging patients required that patients have a pain level below 4 (scale 1–10), tolerate regular diet, can self-ambulate, and have no nausea. The postoperative management and the criteria of discharging patients were the same throughout the study period from 2008 to 2010 for the historical cohort as well as for the cohort who received MMPC. All patients were advanced to regular diet as tolerated on the same day of surgery. Morphine PCA, IV fluid and the Foley catheter were discontinued on postoperative day 1. Nurses actively assisted with ambulation on postoperative day 1 in both cohorts.

All hysterectomy incisions were midline supra-umbilical abdominal incisions and were performed by one gynecologic oncologist assisted by resident physicians. The technique for uterine cancer surgical staging followed the Gynecology Oncology Group surgical protocol [22]. After abdominal hysterectomy and bilateral salpingo-oophorectomy, pelvic lymphadenectomy was performed by removing all the lymph tissues from four locations on each side of the pelvis: (1) common iliac, (2) external iliac, (3) internal iliac, and (4) obturator fossa. The borders of the pelvic lymphadenectomy were the circumflex iliac vein distally, the midcommon iliac proximally, the ureter medially, and the genitofemoral nerve laterally. The paraaortic nodes were removed from the midcommon iliac to the level of the inferior mesenteric artery bilaterally. In our institution, lymphadenectomy is performed in all patients with uterine cancer and undergoing hysterectomy. Data on race, age, body mass index (BMI), staging, estimated blood loss (EBL), American Society of Anesthesiologists (ASA) Physical Status classification system, and LOH were retrieved from the database.

A minimum of 86 patients from the cohort with MMPC and 86 without MMPC protocol were necessary to detect a 1-day difference in hospital days between the two groups to be statistically significant (alpha = 0.05, two-tailed) with 90% power, assuming the standard deviation of hospital days was 2. Before the study, we set a goal of having at least 100 patients for each group in case of incomplete data collection. Our concern for incomplete data was unfounded for the electronic medical record system was more helpful than we initially thought.

Results were summarized in mean and standard deviation for continuous variables and frequency and percentage for categorical variables, unless otherwise specified. Two-sample *t*-test was used to compare the two groups for continuous variables, chi-square or Fisher's exact test for nominal variables, and Mantel test for ordinal variables. Significance level was set at 5%. All analyses were done using SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

Prospective data was collected on 218 total patients: 105 patients received MMPC and 113 historical controls received morphine PCA alone. The age, demographic and morbidity of both arms were statistically similar except for ASA status (Table 1). One very young patient (age 17 years old) was diagnosed with Cowden's syndrome and uterine cancer. The oldest age of our patient was 94 years old. However, the hospital stay was significantly shorter for patients receiving MMPC (Table 1).

Only three patients had stage IV uterine cancer (two patients with MMPC and one patient without MMPC). Thus, we combined stage III and IV into one group. Likewise, there were only five patients with Anesthesia Society of America Physical Status Classification Score ASA Score IV (three patients with MMPC and two patients without MMPC). Thus, we combined patients with ASA Scores III and IV into one class. Five patients met the inclusion criteria but were excluded from the study because of having a diagnosis of kidney or liver failure before surgery and before enrollment into the study.

Patients did not receive pain medications other than MMPC or morphine PCA with the PRN medications above. No patients in the study received spinal, epidural or neuroaxial analgesia. Ten patients (9.5%) who received MMPC were readmitted within 30 days of their original surgery. They were readmitted with the diagnosis of wound infection (three patients), nausea and postoperative ileus (two patients), urinary tract infection (one patient), pulmonary embolism (one patient), fever of unknown