

## GYNECOLOGY

# Intravenous acetaminophen vs saline in perioperative analgesia with laparoscopic hysterectomy



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**BACKGROUND:** Opioids are effective for the treatment of postoperative pain but can cause nausea and are associated with dependency with long-term use. Nonopioid medications such as acetaminophen offer the promise of decreasing these undesirable effects while still providing patient comfort.

**OBJECTIVE:** The purpose of this study was to compare intravenous acetaminophen with placebo and to evaluate postoperative pain control and opioid usage after laparoscopic hysterectomy.

**STUDY DESIGN:** We conducted a prospective double-blind randomized study with 183 patients who were assigned randomly (1:1) to receive acetaminophen or placebo (Canadian Task Force Design Classification I). Patients received either 1000 mg of acetaminophen (n=91) or a placebo of saline solution (n=92) at the time of induction of anesthesia and a repeat dose 6 hours later. Both groups self-reported pain and nausea levels preoperatively and at 2, 4, 6, 12, and 24 hours after extubation with the use of a visual analog scale with a score of 0 for no pain to 10 for highest level of pain. Patients self-reported pain, nausea, and postoperative oral opiates that were taken after discharge. All opiates were converted to milligram equivalents of oral morphine for standardization.

**RESULTS:** There were no significant differences in generalized abdominal pain at any time point postoperatively that included 2 hours (placebo  $3.6\pm 2.5$  vs acetaminophen  $4.4\pm 2.5$ ;  $P=.07$ ) and up to 24 hours (placebo  $3.3\pm 2.4$  vs acetaminophen  $3.6\pm 2.5$ ;  $P=.28$ ). Similar results were observed for nausea scores. There were no differences in opioid consumption at any time point including intraoperatively (placebo  $4.4\pm 3.9$  vs acetaminophen  $3.3\pm 4.0$ ;  $P=.06$ ), post anesthesia care unit (placebo  $10.5\pm 10.3$  vs acetaminophen  $9.7\pm 10.3$ ;  $P=.59$ ), and up to 24 hours after surgery (placebo  $1.4\pm 2.0$  vs acetaminophen  $1.6\pm 2.1$ ;  $P=.61$ ). There were no differences in demographics or surgical data between groups.

**CONCLUSION:** There was no difference between acetaminophen and placebo groups in postoperative pain, satisfaction scores, or opioid requirements. Given the relatively high cost (\$23.20 per dose in our study), lack of benefit, and available oral alternatives, our results do not support routine use during hysterectomy.

**Key words:** intravenous acetaminophen, laparoscopic hysterectomy, postoperative pain

Gynecologic surgery has been revolutionized by the incorporation of minimally invasive techniques.<sup>1</sup> Many gynecologic procedures that once required multiple day hospital admissions are now being performed in same-day surgery centers. Common factors that contribute to delayed discharge are inadequate postoperative pain control and increased nausea and vomiting.<sup>2</sup> A multimodal pain management approach that includes combining different classes of analgesics that act via varying mechanisms is considered optimal for controlling postsurgical pain.<sup>2</sup> By the use of medications that act synergistically, the overall analgesia requirement can often be decreased.<sup>2</sup> Opioids have been found to be highly effective in controlling

postoperative pain; however, they are associated with dose-dependent risks that include nausea, vomiting, constipation, urinary retention, sedation, and respiratory depression.<sup>2</sup> Subsequently, nonopioid options are frequently desired to minimize opioid intake.<sup>3</sup>

Intravenous acetaminophen was approved by the US Food and Drug Administration in November 2010 for the management of mild-to-moderate pain.<sup>4</sup> The primary advantage of the intravenous route is thought to be increased plasma and effect site concentrations and faster plasma peak concentration.<sup>5</sup> Multiple studies have shown favorable results for both acute and postoperative pain in orthopedic surgery, bariatric surgery, cholecystectomy, cesarean section delivery, and abdominal hysterectomy; however, none have focused specifically on laparoscopic gynecologic procedures.<sup>6–11</sup> The primary study that evaluated intravenous acetaminophen in laparoscopic hysterectomies also included multiple other laparoscopic procedures from a variety

of specialties that included general surgery, urology, and urogynecology.<sup>6</sup> In addition, the intravenous acetaminophen was started on average 19 hours after the conclusion of the case, once the PCA was discontinued. A recent study of women who underwent a hysterectomy and vaginal vault suspension enrolled women to receive 1000 mg of either intravenous acetaminophen or saline solution placebo every 6 hours.<sup>12</sup> The first dose was given within 60 minutes of anesthesia induction, and a total of 4 doses were administered over 24 hours. This study did not demonstrate decreased narcotic use or postoperative pain in the group that received intravenous acetaminophen when compared with the group that received the placebo.

Improved postsurgical pain control that is achieved with intravenous acetaminophen potentially may lead to increased rates of same-day discharge after laparoscopic hysterectomy. Same-day discharge after laparoscopic hysterectomy has been shown to be a safe option with proper patient counseling.<sup>13</sup> In addition, same-day discharge is also

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## AJOG at a Glance

**Why was this study conducted?**

This study was conducted to evaluate the role of administration of intravenous acetaminophen as a preoperative analgesic to reduce postoperative pain, nausea, and opioid use in women who undergo a laparoscopic hysterectomy.

**Key findings**

We demonstrated no difference in self-reported pain, nausea, or opioid use between patients who receive intravenous acetaminophen vs saline solution.

**What does this add to what is known?**

This study does not support findings in other surgical fields for the routine use of intravenous acetaminophen preoperatively.

associated with decreased healthcare expenditures.<sup>14</sup>

The primary outcome of this study was to evaluate the effect of intravenous acetaminophen on general abdominal postoperative pain at 24 hours as reported by patients who underwent laparoscopic hysterectomy on a 0- to 10-cm visual analog scale (VAS). Secondary outcomes included opioid consumption during the subjects' hospitalization and postoperatively, nausea, quality of recovery, and overall satisfaction with surgery at time of discharge.

**Materials and Methods**

This was an institutional review board approved, placebo-controlled, double-blind, randomized controlled trial comparing postoperative pain after laparoscopic hysterectomy with injection of intravenous acetaminophen vs normal saline solution. Institutional Review Board oversight for all hospital sites was provided by the University of Pittsburgh Institutional Review Board (PRO13110403). Surgeries were performed at 1 of 3 hospitals within the University of Pittsburgh Medical Center hospital system; UPMC Magee-Womens Hospital, UPMC Passavant-McCandless and UPMC Passavant-Cranberry. Before enrollment, the study was registered through the US National Institutes of Health clinical trials website ([clinicaltrials.gov](http://clinicaltrials.gov) no. NCT02400580). All hysterectomies were performed between February 2015 and August 2016 by 1 of 4 surgeons who were fellowship-trained in minimally invasive gynecologic surgery. All patients were placed in

low lithotomy position, and each surgeon performed the hysterectomy in a similar fashion, using a similar surgical technique: open entry with a 10-mm Hasson port at the umbilicus and 3 additional ports (5-mm lateral ports in the left lower and right lower quadrants and a 5- or 10-mm suprapubic port), bipolar energy for the vascular pedicles, monopolar for the colpotomy, and vaginal cuff closure with barbed suture.

Subjects were eligible for enrollment if they were 18–75 years old and were scheduled to undergo a laparoscopic hysterectomy. Subjects were required to read and speak English and be able to read and comprehend a VAS. Subjects were excluded if they had an acetaminophen allergy, liver disease, kidney disease, hepatitis C, history of liver failure, consumed >3 alcoholic beverages per day, weighed <50 kilograms, reported daily opiate use, had a positive pregnancy test on day of surgery, or had any contraindication to acetaminophen. In addition, patients with a known malignancy or suspected extensive excision of endometriosis on the bowel or bladder or were undergoing a concomitant pelvic reconstructive procedure were also excluded. Discharge on the day of surgery was not an inclusion or exclusion criteria. Subjects who were deemed eligible for enrollment were approached by their surgeon, who was also an investigator on this study. All participants who agreed to participate signed written informed consent preoperatively. Each subject was assigned randomly with a sequential study number on the day of surgery to either

intravenous acetaminophen or placebo in a 1:1 ratio.

The Investigational Drug Service at the Magee Womens Hospital was responsible for the randomization, allocation, storage, and distribution of the study drug for patients who were undergoing surgery at the main hospital. Randomization of participants was allocated with the use of a random sequence generator. The pharmacy was notified by a member of the research team regarding the patients' study identification number, name, date of birth, and date of the consented upcoming surgery. For surgeries performed at the 2 other hospitals, the pharmacist called the Magee Womens Hospital Investigational Pharmacist to obtain each patient's allocation, and the acetaminophen or placebo dose was formulated at that hospital. The patients, surgeons, anesthesiologist, and nursing staff were all blinded to the arm that the patient was allocated to until after the study had been completed.

The intravenous acetaminophen and placebo were placed in identical glass bottles with labels that indicated that they were part of this study and contained either acetaminophen 1000 mg or normal saline solution of an equal volume. Both the study drug and the placebo were administered over a 15-minute period, which is in accordance with the recommendations of the manufacturer of intravenous acetaminophen. The preoperative dose was administered in the operating room, before induction of general anesthesia, by a member of the anesthesia team. The postoperative dose was administered 6 hours after the administration of the first dose, in the postoperative recovery unit.

Anesthesia induction and reversal were standardized. Unless there was a contraindication, all patients received 1–2 mg of midazolam, 4 mg of ondansetron, 2–3 mg/kg of propofol, and 1–1.5 mg/kg of succinylcholine for induction. Anesthesia was maintained with 1.5–2.5% sevoflurane in oxygen, up to 10 µg/kg fentanyl, incremental vecuronium or rocuronium for muscle relaxation, and 4 mg of dexamethasone. Anesthesia was reversed with 0.01 mg/kg

glycopyrrolate and 0.05 mg/kg neostigmine.

Postoperative pain control was standardized for all study participants. The nurses were instructed to refrain from the administration of any acetaminophen products to prevent higher than allowable dosing of acetaminophen in the study drug arm. All study subjects received 30-mg intravenous ketorolac at the conclusion of the case and every 6 hours thereafter for 3 doses, as needed for pain. While in the post anesthesia care unit (PACU), 25- $\mu$ g intravenous fentanyl every 5 minutes up to 100  $\mu$ g was given as needed for pain. No scheduled opiates were ordered. For breakthrough pain, study patients were offered 0.2 mg intravenous hydromorphone every 2 hours. Once tolerating a regular diet, subjects were transitioned to 5 mg oral oxycodone, 1–2 tablets every 4 hours as needed for pain.

Patients were asked to complete a preoperative and postoperative log, rating their nausea and pain in the lower abdomen, upper abdomen, and umbilical area on a 10-cm VAS before surgery and again at 2, 4, 6, 12, and 24 hours after surgery. The patients were instructed how to complete the VAS in the preoperative area, and nurses in the recovery room were given a sheet that had the times to give the form to the patients postoperatively. The VAS is a validated measure for the evaluation of pain, which was administered to all participants.<sup>15</sup> For pain assessment, 0 cm represented no pain and 10 cm represented maximum pain. Patients completed a Quality of Recovery-40 form that asked questions pertaining to general well-being on postoperative day 1 and again at their postoperative visit (generally 4 weeks postoperatively). The QoR-40 was developed to evaluate the quality of recovery from surgery and anesthesia. It measures patient support, comfort pain, physical independence, and emotions after surgery with the use of a Likert scale with scores from 1–5. Patients circle a level of 1 to signify “none of the time” to 5 to signify “all of the time” or any integer between the upper and lower level.<sup>16</sup> To encourage patients to return

**TABLE 1**

**Comparison of demographics and concomitant procedures**

Variable	All patients (N=183)	Placebo (n=91)	Acetaminophen (n=89)
Age, y	42.4	42.1±8.2	41.8±8.3
Right salpingo-oophorectomy, n (%)	3 (1.6)	2 (2.2)	1 (1.1)
Left salpingo-oophorectomy, n (%)	10 (5.5)	4 (4.3)	6 (6.6)
Bilateral salpingo-oophorectomy, n (%)	28 (15.3)	13 (14.1)	15 (16.5)
Ureterolysis, n (%)	13 (7.1)	8 (8.7)	5 (5.5)
Excision of endometriosis, n (%)	22 (12.0)	12 (13.0)	10 (11.0)

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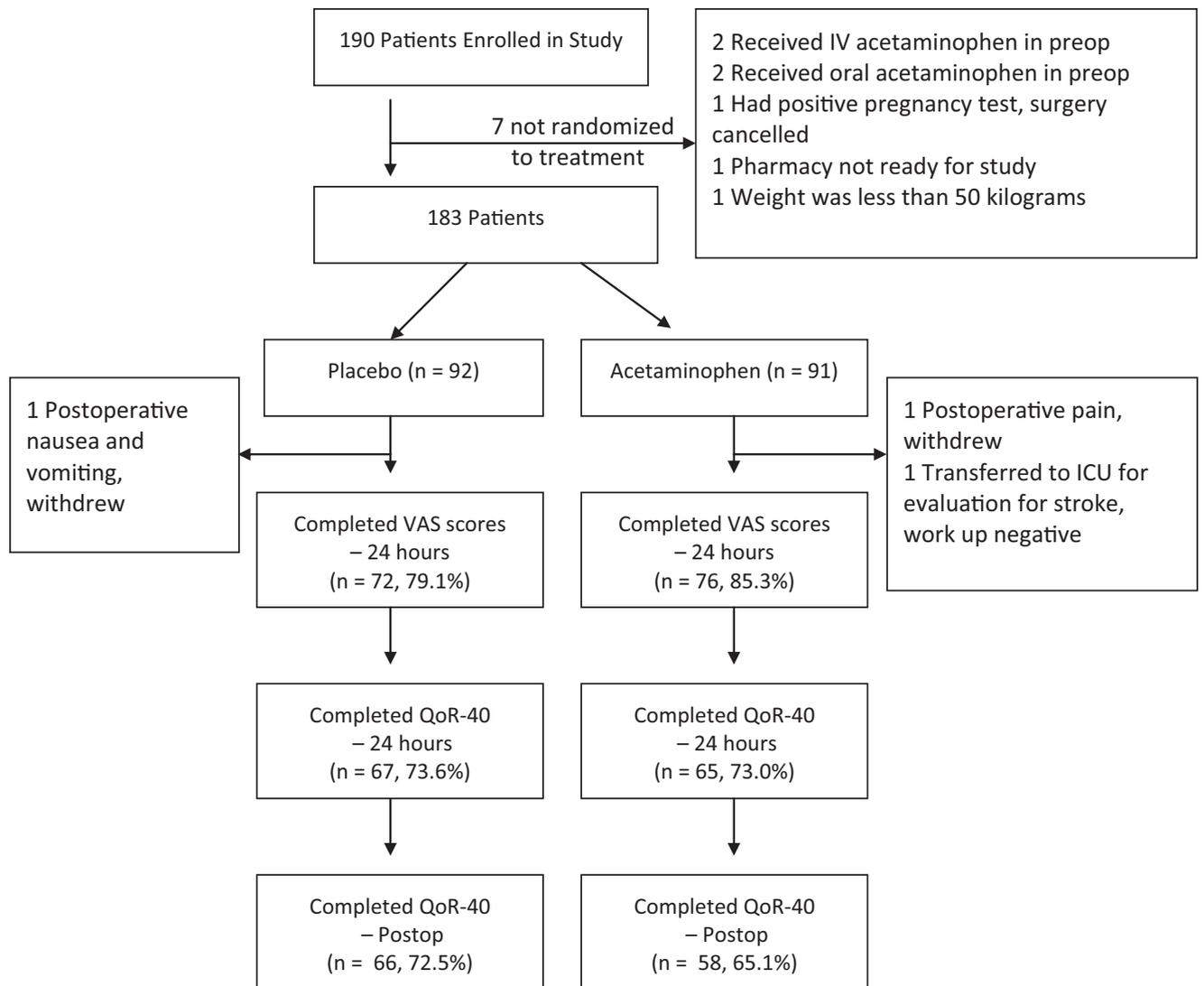
the forms, participants were offered a \$15 gift card to [Amazon.com](https://www.amazon.com) if they completed all portions of the study.

Additional data points that were collected included time to the first rescue dose of opiates and total amount consumed. All opiates were converted to milligram equivalents of oral morphine for standardization (described in a later section). In addition, study drug infusion times, date of surgery, date and time of PACU and hospital discharges, and concomitant surgical procedures performed. Nausea was reported with the VAS, and vomiting was recorded by asking if the patient had vomited since completion of the previous questionnaire.

In a previous study that compared intraoperative instillation of bupivacaine vs saline solution for the reduction of postoperative pain after laparoscopic hysterectomy, the median 1-hour VAS score was 4.3 cm in the placebo group.<sup>17</sup> The power calculation determined that a sample size of 70 in each group was found to have 80% power to detect at least a 0.6 cm difference between the placebo group and the intravenous acetaminophen group based on the Mann-Whitney *U* test evaluated with 0.05 two-sided significance level. To account for a 10% attrition rate, enrollment of 154 participants was required, which would provide 70 participants in each arm. A sample size of 70 per group

was found to have 80% power to detect at least a 40% difference in opioid use between the 2 groups, assuming a median opioid use of 33 milligram equivalents of oral morphine in the placebo group.<sup>17</sup> This study was powered to have >90% power to detect 20% difference in quality of life measures. Because of the implementation of discharge on the day of surgery during the course of the study, there was a higher than expected rate of patients lost to follow up, an attrition rate of 21%. The total enrollment was increased from 154 participants to 190 participants to accommodate for the higher attrition rate.

The analysis for this study was generated with SAS software (version 9.3; SAS System for Windows; SAS Institute Inc, Cary, NC). Continuous data were summarized with the use of means and standard deviations and compared with the use of *t*-tests. Categorical data were summarized with the use of frequencies and percentages and compared with the use of Chi squared or Fisher's exact tests, as appropriate. Patient VAS pain scores were compared between the intravenous acetaminophen and placebo groups. If normally distributed, the data were described with means and standard deviations and compared with the use of a *t*-test. If not normally distributed, the data were described with the use of medians and

**FIGURE**  
**Flow of study participants**

ICU, intensive care unit; IV, intravenous; Preop, preoperative; QoR, Quality of Recovery; VAS, visual analog scale.

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interquartile ranges and compared with the use of the Rank Sum test. Significance level was defined as 5% ( $P < .05$ ).

## Results

This study enrolled 190 women with a mean age of 42.4 years (Table 1). A total of 10 women did not complete the study (Figure). Average age was 42.4 years; average surgical duration, skin incision to skin closure, was 160 minutes. One hundred eighty patients received either intravenous acetaminophen preoperatively (n=89) or placebo (n=91). All

subjects underwent a laparoscopic hysterectomy. Concomitant procedures are described in Table 1.

Pain scores were recorded at 2, 4, 6, 12, and 24 hours postoperatively; the pain score at 24 hours was the primary outcome of the study. VAS scores are reported as mean±standard deviation; comparisons between treatment groups are performed with *t*-tests (Table 2). At 2 hours postoperatively, there were no differences in VAS scores between the intravenous acetaminophen or placebo groups in any abdominal location.

Although the intravenous acetaminophen group reported slightly higher generalized abdominal pain (4.39) as compared with the placebo group (3.61), this was not statistically significant ( $P=.07$ ). This continued through 24 hours, with no significant differences in generalized abdominal pain at 4 hours (placebo  $3.5 \pm 2.2$  vs acetaminophen  $3.9 \pm 2.5$ ;  $P=.31$ ), 6 hours (placebo  $3.6 \pm 2.3$  vs acetaminophen  $3.8 \pm 2.4$ ;  $P=.15$ ), 12 hours (placebo  $3.3 \pm 2.1$  vs acetaminophen  $3.7 \pm 2.6$ ;  $P=.27$ ), or at 24 hours (placebo  $3.3 \pm 2.4$  vs

TABLE 2

**Visual analog score for pain score recorded before and after hysterectomy between intravenous acetaminophen and placebo plus overall satisfaction**

Variable <sup>a</sup>	All patients	Placebo	Intravenous acetaminophen	P value
<b>Before surgery</b>				
Generalized abdominal pain	1.14±1.81	0.92±1.42	1.34±2.11	.159
Upper abdomen	0.48±1.07	0.33±0.48	0.63±1.40	.081
Lower abdomen	1.29±2.03	0.96±1.59	1.61±2.35	.054
Umbilical	0.32±0.55	0.32±0.53	0.33±0.57	.951
Nausea	0.63±1.44	0.54±1.19	0.72±1.65	.455
<b>2 Hours</b>				
Generalized abdominal pain	4.02±2.57	3.61±2.52	4.39±2.57	.070
Upper abdomen	1.88±2.29	1.39±1.82	2.29±2.56	.020
Lower abdomen	4.57±2.84	4.17±2.88	4.91±2.77	.123
Umbilical	2.54±2.58	2.22±2.44	2.81±2.67	.176
Nausea	0.83±1.51	0.79±1.53	0.86±1.51	.784
Vomiting, n (%)	4 (2.2)	3 (3.3)	1 (1.1)	Not available
<b>4 Hours</b>				
Generalized abdominal pain	3.74±2.22	3.54±2.23	3.92±2.22	.314
Upper Abdomen	1.80±2.05	1.76±1.91	1.83±2.18	.828
Lower Abdomen	4.38±2.38	4.15±2.46	4.59±2.31	.276
Umbilical	2.21±2.41	2.20±2.42	2.22±2.42	.957
Nausea	1.27±2.11	1.26±2.10	1.27±2.14	.982
Vomiting, n (%)	3 (1.6)	1 (1.1)	2 (2.2)	.620
<b>6 Hours</b>				
Generalized abdominal pain	3.56±2.29	3.28±2.18	3.82±2.38	.155
Upper abdomen	1.97±2.25	1.65±1.90	2.27±2.51	.103
Lower abdomen	4.11±2.49	3.83±2.44	4.38±2.53	.189
Umbilical	2.52±2.51	2.48±2.53	2.55±2.52	.859
Nausea	1.39±2.26	1.45±2.26	1.32±2.27	.729
Vomiting, n (%)	8 (4.4)	2 (2.2)	6 (6.6)	.144
Pain medications, n (%)	88 (48.1)	46 (50.0)	42 (46.2)	.400
<b>12 Hours</b>				
Generalized abdominal pain	3.49±2.40	3.25±2.09	3.71±2.65	.266
Upper abdomen	2.15±2.28	2.03±1.97	2.27±2.54	.537
Lower abdomen	3.96±2.62	3.79±2.37	4.12±2.83	.458
Umbilical	2.62±2.42	2.57±2.34	2.66±2.50	.830
Nausea	1.17±2.02	1.30±2.18	1.06±1.87	.484
Vomiting, n (%)	7 (3.8)	3 (3.3)	4 (4.4)	.774
Pain medications, n (%)	110 (60.1)	54 (58.7)	56 (61.5)	.755

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(continued)

TABLE 2

**Visual analog score for pain score recorded before and after hysterectomy between intravenous acetaminophen and placebo plus overall satisfaction** (continued)

Variable <sup>a</sup>	All patients	Placebo	Intravenous acetaminophen	P value
24 Hours				
Generalized abdominal pain	3.34±2.36	3.11±2.22	3.55±2.47	.275
Upper abdomen	2.25±2.33	1.79±1.96	2.67±2.58	.025
Lower abdomen	3.76±2.57	3.48±2.50	4.02±2.61	.208
Umbilical	2.73±2.49	2.44±2.34	3.01±2.60	.181
Nausea	0.77±1.41	0.85±1.58	0.69±1.25	.508
Vomiting, n (%)	3 (1.6)	2 (2.2)	1 (1.1)	.517
Pain medications, n (%)	124 (67.8)	61 (66.3)	63 (69.2)	.653
Satisfaction with surgery at time of discharge	7.95±2.26	8.15±2.18	7.76±2.32	.319

<sup>a</sup> Data are given as mean±standard deviation, unless otherwise indicated.

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acetaminophen 3.6±2.5;  $P=.28$ ). Similar results were observed for questions regarding pain in the upper abdomen, lower abdomen, and umbilical area. Although the acetaminophen group had slightly higher pain scores at all time points, they required fewer pain medications (Table 3), which reinforced the

finding that these differences were not clinically significant.

Opioid consumption was evaluated with the use of milligram equivalents of oral morphine (MEQ) for standardization. These conversions were based on the American Pain Society guidelines and supporting review papers regarding

equianalgesic dosing.<sup>18–20</sup> We analyzed opioid consumption intraoperatively, in the PACU, and at incremental time points up to 24 hours postoperatively. Intraoperatively, the placebo group required 4.4±3.9 mg of MEQ; the acetaminophen group required 3.3±4.0 mg of MEQ ( $P=.06$ ). Although this

TABLE 3

**Comparison of treatment groups**

Variable	Acetaminophen (n=89), mean±standard (interquartile range)	Placebo (n=91), mean±standard (interquartile range)	P value
Total operative time, min	156.1±41.9 (92.0–283.0) <sup>a</sup>	164.6±47.8 (89.0–314.0) <sup>b</sup>	.21
Time to fall asleep, min	32.7±7.3 (15.0–49.0) <sup>a</sup>	32.4±7.3 (18.0–58.0) (n=88) <sup>a</sup>	.78
Time to wake up, min	15.1±5.9 (6.0–45.0) <sup>a</sup>	16.2±8.1 (3.0–68.0) <sup>a</sup>	.27
Ondansetron			
Induction, mg	5.0±1.9 (0.0–12.0)	4.8±1.6 (4.0–8.0)	.57
Post anesthesia care unit, mg	1.3±2.2 (0.0–8.0)	1.2±2.3 (0.0–12.0)	.88
Total (induction+post anesthesia care unit)	6.2±2.9 (0.0–16.0)	6.0±2.9 (4.0–20.0)	.64
Operating room morphine equivalents	3.3±4.0 (0.0–19.6)	4.4±3.9 (0.0–18.4)	.06
Post anesthesia care unit morphine equivalents	9.7±10.3 (0.0–52.8)	10.5±10.3 (0.0–55.0)	.59
6-Hour postoperative morphine equivalents	0.6±1.2 (0.0–6.0)	0.8±1.4 (0.0–6.0)	.34
12-Hour postoperative morphine equivalents	1.2±1.4 (0.0–6.0)	1.3±1.7 (0.0–8.0)	.65
24-Hour postoperative morphine equivalents	1.6±2.1 (0.0–12.0)	1.4±2.0 (0.0–10.0)	.61
Total morphine equivalents (operating room +post anesthesia care unit+6hr+12hr+24 hr)	16.4±11.5 (0.0–62.8)	18.4±11.8 (2.0–66.6)	.24

<sup>a</sup> N=88; <sup>b</sup> N=89.

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difference trends toward statistical significance, it is difficult to predict whether a reduction of 1.1 MEQ (equivalent to 1.1 mg of morphine or 0.25 mg of hydromorphone) would be clinically significant. Anesthesia induction times and wake-up times were similar between the groups (Table 3). While in the PACU, the groups had similar opioid requirements with subjects in the placebo group requiring  $10.5 \pm 10.3$  mg of MEQ, and the acetaminophen subjects requiring  $9.7 \pm 10.3$  mg of MEQ ( $P=.59$ ). Opioid consumption was then evaluated at 6, 12, and 24 hours postoperatively with patients who reported the amount of medication that they used since the previous time point. All time points showed similar requirements between the 2 arms (Table 3). Total opioid requirements, defined as total MEQs from induction of anesthesia through 24 hours postoperatively, were similar between groups, with the placebo group requiring  $18.4 \pm 11.8$  mg of MEQ and the acetaminophen group requiring  $16.4 \pm 11.5$  mg of MEQ ( $P=.24$ ).

Satisfaction with pain control, as measured with the VAS, was recorded at 24 hours and 1 month postoperatively, with no difference found between the placebo and intravenous acetaminophen groups. Nausea was reported with the VAS, and vomiting was recorded by asking whether the patient had vomited since completion of the previous section. Nausea and vomiting scores at 24 hours postoperatively were similar between the placebo group (1.55) and intravenous acetaminophen group (1.56), with no significant difference ( $P=.883$ ).

## Comment

This blinded, randomized controlled trial that compared intravenous acetaminophen with placebo at the time of laparoscopic hysterectomy did not show a difference between pain VAS scores or opioid consumption at any time point postoperatively. Satisfaction with pain control at 24 hours and 4 weeks postoperatively were also not different between the groups.

Enhancing postoperative pain control through a multimodal pain regimen is essential for optimizing recovery and

encouraging same-day discharge after hysterectomy. Pain regimens that focus on the use of opiates have significant limitations as the result of associated side-effects that include nausea, vomiting, and constipation.<sup>21</sup> Intravenous acetaminophen has shown encouraging results with decreased opioid use and shorter lengths of stay in alternate studies. Our study did not reveal this trend for laparoscopic hysterectomies, because no difference was found in pain VAS scores, opioid consumption, satisfaction, or nausea scores between the 2 groups. The lack of benefit to intravenous acetaminophen also has been confirmed after vaginal hysterectomy with intraperitoneal vault suspension.<sup>12</sup>

A possible explanation that our results may not have revealed a benefit to the use of intravenous acetaminophen is that pain scores are already low after a laparoscopic hysterectomy. This is shown with the 2-hour postoperative VAS score of 4.39 for the intravenous acetaminophen group and 3.61 for the placebo group. With low pain scores at baseline, a significant difference is difficult to identify. Another consideration is that, although acetaminophen may provide a synergistic enhancement of other medications used in the Enhanced Recovery After Surgery protocol, the effect may be too small to detect in a study of this size.

Strengths of this study include the randomized, double blind study design. The preoperative and postoperative pain regimens were standardized to maximize detection of changes that were specific to the addition of intravenous acetaminophen. The surgical technique was also standardized with uniform port placement and surgical steps that were executed by all 4 surgeons who were fellowship-trained in minimally invasive gynecologic surgery. In addition, multiple locations of upper and lower pelvic pain were evaluated at strict pre- and postoperative time requirements. Extended followed up was executed with incorporation of satisfaction scores at 24 hours and 1 month postoperatively to assess long-term impacts of this pain regimen. Limitations included generalizability because only laparoscopic hysterectomy procedures were

included in this study. More extensive procedures, which may be associated with greater postoperative pain, potentially could show a benefit from intravenous acetaminophen.

No differences were demonstrated between the intravenous acetaminophen and placebo groups in measures of postoperative pain, opioid consumption, nausea, or satisfaction after laparoscopic hysterectomy. Given the relatively high cost (\$23.20 per dose in our study), lack of benefit, and available oral alternatives, our results do not support routine use during hysterectomy. ■

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