

# Effect of Intraoperative Intravenous Lidocaine on Postoperative Pain and Return of Bowel Function After Laparoscopic Abdominal Gynecologic Procedures

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Abdominal surgery has a high incidence of postoperative pain and dysfunctional gastrointestinal motility. This study investigated the effect of a continuous intraoperative infusion of lidocaine on patients undergoing laparoscopic gynecologic surgery. In this double-blind, placebo-controlled investigation, 50 subjects were randomly assigned to control and experimental groups. Both groups received an intravenous lidocaine bolus of 1 mg/kg on induction. The experimental group received a continuous lidocaine infusion of 2 mg/kg/h, initiated following induction and discontinued 15 to 30 minutes before skin closure. Controls received a placebo infusion. Patients in the experimental group had lower postoperative day 3 pain scores using a verbal analog scale ( $P = .02$ ).

Morphine equivalent dose at second request for pain treatment in the postoperative anesthesia care unit was lower in the experimental group ( $P = .02$ ). There was a statistically significant difference in time interval from surgical start to return of first flatus between the groups ( $P = .02$ ). Data were analyzed using descriptive and inferential statistics. A  $P$  value less than .05 was considered significant. These study results are consistent with previous research suggesting that intraoperative lidocaine infusion may improve postoperative pain levels and may shorten the time to return of bowel function.

**Keywords:** Intravenous infusion, laparoscopic abdominal gynecologic surgery, lidocaine, morphine consumption, opiate consumption.

**A**cute postoperative pain and postoperative ileus (POI) are common among patients who have undergone abdominal surgical procedures.<sup>1-5</sup> Various analgesic agents have been the primary traditional method in the treatment of postoperative pain. Analgesics are effective in decreasing postoperative pain but can be associated with undesirable side effects, which may include respiratory depression, nausea, vomiting, increased somnolence, and POI.<sup>1-6</sup> Side effects in surgical patients treated for pain can be problematic and can lead to increased patient and institutional costs, longer hospital length of stay, and an overall increase in patient dissatisfaction.<sup>2-4</sup> Anesthetists and surgeons must carefully consider postoperative analgesic regimens and seek methods of pain control that limit undesirable side effects.

One medication that has shown promise in providing analgesia before, during, and after the surgical procedure is lidocaine. Lidocaine is an amide local anesthetic agent that works by blocking sodium channels in the neural

cascade and exhibits inhibitory effects on the neuropeptide chemical mediators, which influence the complex phenomenon of pain.<sup>1-6</sup> Blocking systemic inflammatory responses to surgical stress may result in preservation of bowel motility.<sup>7-13</sup> Recent investigations suggest that intravenous (IV) lidocaine, given as a single dose or as a continuous infusion, may be beneficial in the preservation of gastrointestinal motility and have influence in biochemical pain processes.<sup>2-14</sup> Despite these findings, there are conflicting results with regard to lidocaine efficacy in the provision of analgesia and reduction in POI.

In 3 separate studies, Groudine et al,<sup>1</sup> Rimbäck et al,<sup>3</sup> and Kaba et al<sup>15</sup> observed the effects of intraoperative infusion of lidocaine on bowel activity in patients undergoing radical prostatectomy, cholecystectomy, and laparoscopic colectomy, respectively. Using different measurement techniques, Groudine et al<sup>1</sup> and Kaba et al<sup>15</sup> demonstrated a decreased time interval to return of bowel activity. Rimbäck et al,<sup>3</sup> however, found no statistically significant difference in time to first flatus

or bowel movement but noted that IV lidocaine significantly decreased the duration of postoperative colonic paralysis after major abdominal surgery, as measured by the passage of radiopaque markers. Koppert et al,<sup>2</sup> whose study methods were nearly indistinguishable from those of Groudine and associates,<sup>1</sup> found no statistically significant relationship between the use of lidocaine infusion and the time to first bowel movement following surgery. Koppert et al, however, found that infusion of lidocaine resulted in an overall reduction of analgesic requirements during and following the surgical procedure. Previous efforts to examine the effects of perioperative lidocaine infusion on bowel function used infusion durations of varying length and dissimilar outcome measurement criteria.<sup>3,15</sup> In addition, these studies used inpatient major-surgery populations and did not investigate the efficacy of IV lidocaine infusion in groups of patients undergoing minor laparoscopic surgical procedures who received short-duration perioperative lidocaine infusion. The purpose of this study was to determine the effect of continuous lidocaine infusion initiated before surgical incision and discontinued shortly before skin closure on postoperative pain, analgesic requirements, and incidence of POI in patients undergoing outpatient laparoscopic gynecologic procedures.

## Materials and Methods

Following approval of the study protocol by the institutional review board, a convenience sample of 50 women was recruited from the preoperative anesthesia clinic for participation in this study. All patients were ASA class I or II, aged 18 years and older, and undergoing elective laparoscopic gynecologic procedures under general anesthesia. Patients were excluded from participation if their medical history revealed previous substance abuse, allergy to amides, or current treatment with antiarrhythmic medications. In addition, patients were excluded if they were pregnant or had a history of chronic pain syndrome or chronic bowel or liver dysfunction. Once inclusion criteria were met, all potential subjects were given a letter of introduction describing the parameters of the study and a copy of the informed consent for review. All potential subjects were instructed to review the informed consent before their presentation to the hospital for their scheduled procedure. All potential subjects were contacted by telephone the night before surgery to discuss patient participation and to answer any questions the patients had regarding the study.

On the morning of surgery, informed consent was obtained following record review and assessment by 1 of the investigators, and all questions were answered. Following informed consent, all subjects were given unique study subject identification (ID) numbers and randomly assigned to either a control or an experimental group. Demographic data (age, height, weight, surgical

procedure, and race) were obtained. A baseline level of abdominal pain was assessed using a 0 to 10 verbal analog scale (VAS), in which a rating of "0" indicated "no pain" and a score of "10" indicated the "worst pain imaginable." All subjects were informed that a 0 to 10 VAS score would be obtained immediately preceding and following any administration or self-administration of any analgesic agent for 72 hours following their procedure.

On the morning of surgery, 1 of the investigators who was not involved in the delivery of anesthesia care prepared a 10-mL and a 60-mL syringe and labeled each syringe with the time and date of preparation and the subject's ID number. Each 10-mL syringe contained 200 mg of 2% lidocaine solution. The 60-mL syringe contained either 1,200 mg of lidocaine (20 mg/mL) or 0.9% normal saline solution. Subjects in the control group were assigned to receive a 60-mL syringe that contained the 0.9% normal saline solution, and those in the experimental group were assigned to receive the 2% lidocaine solution. Each syringe was indistinguishable from the other, and only the investigator who prepared the syringes was aware of their actual composition. The composition of the study syringes was not known to the anesthesia providers or other personnel involved in patient care until the conclusion of the study.

All subjects had an IV infusion of lactated Ringer's solution initiated in the preoperative holding area and could receive midazolam, 0 to 5 mg IV, and/or fentanyl, 0 to 3  $\mu$ g/kg, at the discretion of the anesthetist. All preoperative medications administered were recorded. Once it was determined the subject was ready for surgery, the subject was transported to the operative suite and positioned on the surgical table. Standard monitors, including electrocardiography (ECG), arterial oxygen saturation (SaO<sub>2</sub>), and noninvasive blood pressure devices, were placed, and baseline vital signs were recorded. All subjects were preoxygenated with 100% oxygen via face mask for 3 to 5 minutes before induction of anesthesia. All subjects were then given a bolus dose of 1 mg/kg of lidocaine immediately before induction using the prepared 10-mL syringe. A standard induction IV protocol was used, which included fentanyl, 0 to 5  $\mu$ g/kg; propofol, 2 mg/kg; and succinylcholine, 1 to 1.5 mg/kg, or a nondepolarizing agent of the anesthetist's choice. All medications used for induction were recorded on the data collection sheet and anesthesia record.

Following induction, those subjects assigned to the experimental group received an IV infusion of 2 mg/kg per hour of lidocaine, which was maintained until approximately 15 to 30 minutes before skin closure. This dosing was chosen because it reflected dosing of previous studies, and infusion time was limited to the intraoperative period, as these were outpatient procedures. Control subjects received a 0.9% normal saline placebo at the same rate as that described in the experimental group.

Maintenance of anesthesia was accomplished using isoflurane, 0.5% to 1.5%; sevoflurane, 1.0% to 3.0%; or desflurane, 3.0% to 8.0%, with nitrous oxide, 0% to 50%, and oxygen, 50% to 100%. An additional 0 to 10 µg/kg of fentanyl or another opioid agent of the anesthetist's choice could be administered for perioperative analgesia. All analgesic medications administered during the perioperative period were converted to morphine equivalents before data analysis (Table 1<sup>16-19</sup>). Of note, the published literature regarding the morphine equivalency of 30 mg of IV ketorolac demonstrates variation in observed efficacy, from 7.5 mg to 12 mg of morphine. This study considered 10 mg of IV morphine equivalent to 30 mg of IV ketorolac.

Antinausea medications were administered at the anesthetist's discretion, and neuromuscular blockade could be antagonized using IV neostigmine, 0.05 mg/kg, and glycopyrrolate, 0.01 mg/kg.

• **Postoperative Measures.** After endotracheal extubation, subjects were transported to the postanesthesia care unit (PACU). Total surgical time (measured in minutes from surgical incision to skin closure), anesthesia time (measured as arrival time in the operating room to arrival in the PACU, in minutes), medications given, and start-stop time of the study drug infusion were documented. It also was noted whether an oral or nasogastric tube was placed perioperatively and maintained following the surgical procedure.

On admission to the PACU, an Aldrete score and baseline postoperative VAS for pain were assessed as soon as the subject was alert and able to answer questions. Subjects verbalizing pain were administered morphine, 1 to 4 mg IV, every 5 minutes up to a total dose of 0.15 mg/kg, or another analgesic of choice. Subjects could also receive a selection of antiemetics for nausea and vomiting. The PACU personnel noted the time, type, dose, and route of administration for any PACU analgesic or antiemetic medication. For those subjects requesting analgesia in the PACU, a VAS score for pain was noted immediately before administration of an analgesic and every 15 minutes thereafter for 30 minutes. Each subsequent analgesic administration required a new VAS regimen. Once PACU discharge criteria were met, Aldrete and VAS scores were obtained and subjects were discharged to the ambulatory surgery department (ASD) unit. Additionally, it was noted whether flatus had occurred while the patient was in the PACU.

Following admission to the ASD, arrival time was noted, and all subjects were assessed via auscultation for the presence or absence of bowel sounds. All subjects were instructed to inform ASD personnel if they experienced flatus while in the ASD, and the time of flatus return was recorded on a data collection sheet. Complaints of pain were treated using the regimen ordered by the attending surgeon, and the dose, time,

Medication	Equivalent to morphine (10 mg IV)
Fentanyl	100 µg IV <sup>a</sup>
Meperidine	75 µg IV <sup>a</sup>
Oxycodone	20 mg PO <sup>a</sup>
Oxycodone-acetaminophen (Percocet, 5/325 mg)	6 tablets <sup>a</sup>
Hydrocodone	30 mg PO <sup>a</sup>
Hydrocodone-acetaminophen (Vicodin, 5/500 mg)	6 tablets <sup>a</sup>
Hydromorphone	1.4 mg IV <sup>b</sup>
Ketorolac (30 mg)	10 mg IV <sup>c</sup>

**Table 1. Morphine Equivalents**

Abbreviations: IV indicates intravenously; PO, orally.

<sup>a</sup> McKay et al.<sup>16</sup>

<sup>b</sup> Jacox et al.<sup>17</sup>

<sup>c</sup> Brown et al.<sup>18,19</sup>

and route of any analgesic administered in the ASD were noted. If the subject required an analgesic in the ASD, a 0 to 10 VAS pain score was obtained and recorded immediately before analgesic administration and 15 minutes following administration for each analgesic administered. Nausea or vomiting was treated with the outpatient antiemetic medication prescribed by the surgical team, and the number of episodes of nausea and vomiting and antiemetic medications administered was recorded.

All subjects were evaluated for signs and symptoms of lidocaine toxicity while in the hospital. These signs may include circumoral numbness, tinnitus, anxiety, headache, nausea and vomiting, seizure activity, and ECG irregularities.

On discharge from the ASD, the time of discharge was noted and a final 0 to 10 VAS pain score was measured and recorded. All subjects were given discharge instructions and a home data collection sheet on which they were instructed to note the following: time and date of return of bowel function (described as “the time to first flatus or bowel movement”), incidence of any nausea or vomiting, and their analgesic requirements for the first 72 hours following discharge to home. All subjects were also asked to rate their level of pain using the 0 to 10 VAS scale immediately before any analgesic self-administration. All subjects were contacted 1, 2, and 3 days after surgery by the research team to ascertain pain scores, daily medication requirements, return of bowel function, and incidence of nausea or vomiting. Again, all analgesics administered were converted to morphine equivalents before analysis. At each phone interview all subjects were asked to rate their overall level of satisfaction with their postoperative recovery experience using a 1 to 5 scale. A score of 1 indicated very dissatisfied; 2, somewhat dissatisfied; 3, neither satisfied nor dissatis-

Measure	Control (n = 21)	Experimental (n = 24)
Age (y; mean ± SD)	31 ± 5	31 ± 6
Height (cm; mean ± SD)	165 ± 7	165 ± 6
Weight (kg; mean ± SD)	72 ± 13	78 ± 15
Surgical time (min; mean ± SD)	46 ± 28	40 ± 17
Infusion time (min; mean ± SD)	60 ± 31	54 ± 20
PACU time (min; mean ± SD)	64 ± 43	59 ± 36
ASD time (min; mean ± SD)	138 ± 69	141 ± 54
Total hospital time (min; mean ± SD)	319 ± 124	303 ± 81
Surgical procedure (No.)		
Bilateral tubal ligation	7	15
Diagnostic laparoscopy	11	8
Laparoscopic salpingectomy-oophorectomy	1	1
Laparoscopic laser treatment of adhesions	1	0
Laparoscopic ovarian cystectomy	1	0
Volatile agent (No.)		
Isoflurane	1	2
Sevoflurane	3	4
Desflurane	17	18
50% N <sub>2</sub> O (supplemental)	5	5
Orogastric/nasogastric tube (No.)		
Yes	19	22
No	2	2

**Table 2. Comparison of Groups**

No significant differences were noted between groups.

Abbreviations: PACU, postoperative anesthesia care unit; ASD, ambulatory surgery department; and N<sub>2</sub>O, nitrous oxide.

fied; 4, somewhat satisfied; and 5, completely satisfied.

- **Statistical Analysis.** Before initiation of the study, a power analysis was performed. Previous studies<sup>1,2</sup> indicated that the mean postoperative analgesic requirements would be 159 ± 73 mg in the placebo group compared with 103 ± 72 mg in the experimental group. Using this expected magnitude difference between the control and experimental groups, and using an  $\alpha$  of .05 and a  $\beta$  of .20, it was determined that 22 subjects in each group would achieve a power of .82. Factoring in a 10% attrition rate increased our sample size to 50 subjects (25 subjects in each group).

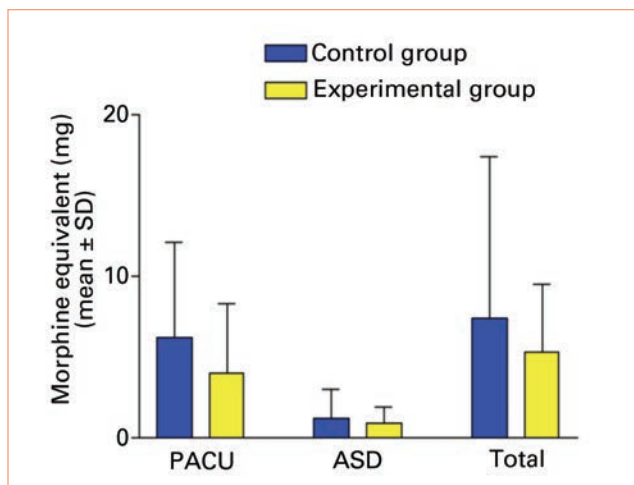
Statistical analysis was performed using SPSS software version 17.0 (SPSS, Chicago, Illinois). Data analysis was accomplished using descriptive and inferential statistics. Demographic data and frequency data were analyzed using a  $\chi^2$  test and Pearson correlation. The VAS scores, time data, and analgesic requirements were analyzed using a Student *t* test. A *P* value less than .05 was considered significant.

## Results

A total of 50 subjects were enrolled, and 5 subjects were withdrawn from the study, leaving 45 subjects (control group, 21; experimental group, 24) for final analysis. Of

the 5 subjects who were withdrawn, 2 subjects were excluded because of protocol violations (both in the control group), 2 subjects did not complete follow-up (1 in each group), and 1 subject required readmission to the hospital for protracted nausea and vomiting (control group).

Both groups were equivalent in relation to demographic variables, surgical time, anesthesia time, nasogastric or orogastric tube insertion, length of infusion, type of surgical procedure, volatile agent used and supplemental use of nitrous oxide, and PACU or ASD times (Table 2). Decreased overall analgesic requirements were noted in the experimental group compared with the control group but failed to achieve statistical significance at any time interval (Figure 1). Pain scores were similar between the groups except on postoperative day 3 measurements, when the overall VAS score was 3.5 ± 3.1 in the control group compared with 1.6 ± 2.4 in the experimental group (*P* = .02; Figure 2). When time to first flatus was analyzed, a significant difference between the groups was noted, with the control group requiring 1,319 ± 809 minutes compared with 768 ± 464 minutes in the experimental group (*P* = .02). No differences were noted between groups in time to first bowel movement (*P* = .59; Figure 3). No subjects experienced signs or symptoms of lidocaine toxicity. All subjects were



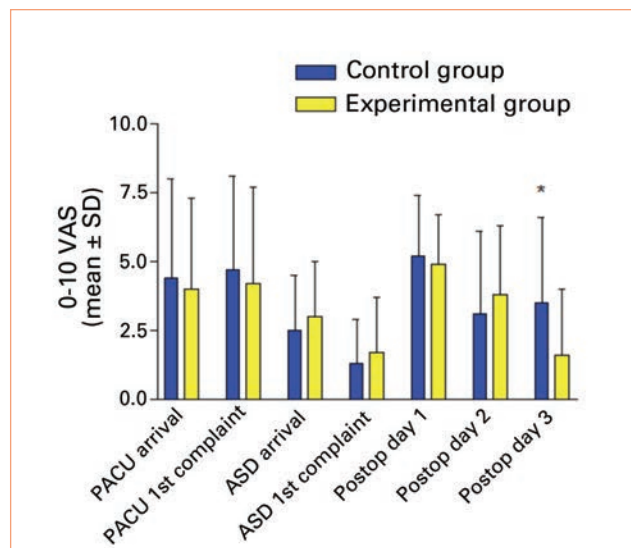
**Figure 1.** Total Analgesic Requirements (in morphine equivalents)  
Abbreviations: PACU, postoperative anesthesia care unit; ASD, ambulatory surgery department.

administered a prophylactic antiemetic agent (ondansetron) intraoperatively, and no differences were noted in antiemetic requirements between groups in the PACU or ASD. No differences between groups were noted regarding the need for neuromuscular reversal with neostigmine between groups. Complete satisfaction with their anesthesia and postoperative recovery experience was noted to be higher in the experimental group (92%) compared with the control group (71%) but did not achieve statistical significance ( $P = .08$ ).

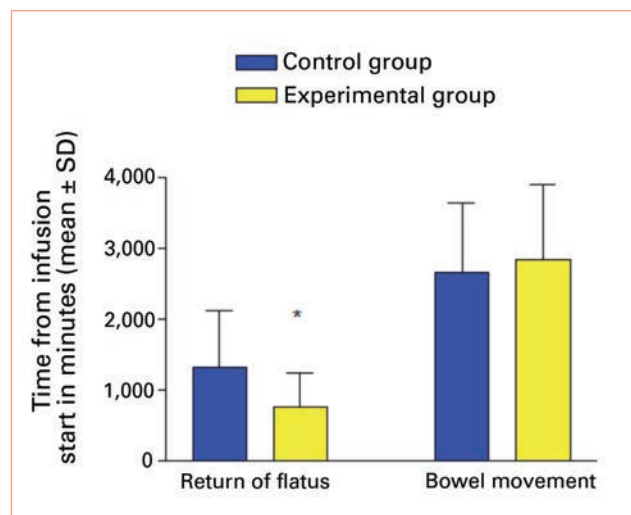
## Discussion

Laparoscopic gynecologic procedures were once limited to diagnostic studies. Economic viability and increased surgical skill have greatly increased the popularity of these procedures, and they are now a commonly employed technique for gynecologic surgery.<sup>20</sup> This study suggests that administration of perioperative lidocaine infusion in patients undergoing same-day gynecologic laparoscopic surgery may improve postoperative analgesia, reduce postoperative opioid requirements, and accelerate the return of first flatus. Specifically, this investigation found results similar to those of previous investigations conducted with longer infusion times across a variety of surgical populations.<sup>1,2,5,15</sup> The relative safety, economy, and ease with which IV lidocaine can be administered lends itself to inclusion in a multimodal anesthetic and warrants further study. Perioperative lidocaine infusion has been investigated in open abdominal, urologic, and orthopedic surgery populations. However, few investigations have focused on laparoscopic procedures, and the authors are aware of no published study of lidocaine infusion used in patients undergoing gynecologic outpatient surgery.

Intravenous lidocaine has long been a proven agent



**Figure 2.** Verbal Analog Scores for Pain  
Abbreviations: VAS, verbal analog score; PACU, postoperative anesthesia care unit; ASD, ambulatory surgery department; postop, postoperative. Asterisk indicates statistically significant at  $P < .05$ .



**Figure 3.** Time to Return of Flatus and Bowel Movement  
Asterisk indicates statistically significant at  $P < .05$ .

in the reduction of perioperative pain. Since 1951, when Keats et al<sup>21</sup> first documented a positive analgesic effect on postoperative pain, investigation and interest in perioperative IV local anesthetic infusion has continued. A 2010 systematic review of multiple studies documented a reduction in perioperative pain when IV lidocaine infusions supplement general anesthetics.<sup>22</sup> Previous studies were limited to inpatient procedures with lidocaine infusions ranging between 6 hours and greater than 24 hours.<sup>1,15</sup> This investigation studied outpatient procedures with an average lidocaine infusion duration of 57 minutes.

The shortened infusion times employed in this study resulted in similar outcomes related to bowel function

and postoperative pain when compared with previous studies using much longer infusion times. Other perioperative lidocaine studies used methods that initiated infusions before skin incision and continued for some time postoperatively. This protocol dictated that the anesthetic provider control initiation and discontinuation of the lidocaine infusion before patient discharge from the operating room. Although postoperative VAS pain scores were not different between groups through day 2, postoperative day 3 VAS scores were significantly lower in the experimental group ( $P = .02$ ). Intravenous lidocaine administered in the intraoperative period would clearly have been metabolized by postoperative day 3. Even with continuous administration, the half-life of lidocaine is approximately 1.5 to 2 hours.<sup>23</sup> Although the exact mechanism and analgesic-sparing effect of parenterally administered lidocaine is unclear, some authors<sup>2</sup> speculate that it acts more as an antihyperalgesic than as a direct analgesic. Central sensitization is known to be induced by the mechanosensitive nociceptor class of receptors. These nociceptors are known to be sensitive to small-dose lidocaine.<sup>2</sup> Additionally, lidocaine inhibits *N*-methyl-D-aspartate receptors.<sup>15</sup> When systemic lidocaine is administered during the operative period, it likely prevents the induction of central hyperalgesia, leading to the observed morphine-sparing effects.

The return of bowel function is an important aspect in surgical recovery, even though the incidence of ileus after gynecologic endoscopy is less than 1%.<sup>24</sup> Alteration of bowel function following surgery may result from individual patient stress, bowel preparations, surgical intrusion into the peritoneum, and physical manipulation of the bowel. Intravenous lidocaine reduces postoperative bowel dysfunction through a number of mechanisms. First, the antihyperalgesic properties of lidocaine reduce postoperative pain, providing an opioid-sparing effect and lessen the impairment of the colonic transport associated with opioids.<sup>1,2,22</sup> Second, lidocaine has a direct excitatory action on gastrointestinal smooth muscle.<sup>3,25</sup> Third, lidocaine can block the inhibitory reflexes within the intestinal wall that decrease gastrointestinal motility.<sup>3</sup> Fourth, IV lidocaine administration has anti-inflammatory properties that may counteract the inflammatory actions of histamine, prostaglandins, and kinins, which reduce gastrointestinal motility.<sup>3,25-28</sup> This investigation found a statistically significant decrease in time to first flatus, suggesting that lidocaine infusion during outpatient surgical procedures may speed return to normal bowel function. These findings were consistent with a previous study by Kaba et al<sup>15</sup> and other reviews.<sup>22,29</sup>

Limitations of our study included reliance on the accuracy of patient self-reported data; reliance on a convenience sample recruited from 1 center, which may limit the generalizability of the results; and the lack of accounting for over-the-counter medications. Whereas ketorolac

was converted to morphine equivalents, its frequency of use was not specifically analyzed in each group. This is important to note because of the drug's anti-inflammatory properties, which could potentiate those of lidocaine; however, it could be reasonably inferred that each group had an equal probability of receiving the drug, suggesting that ketorolac use likely did not account for the observed differences between the groups.

This study attempted to examine the effects of perioperative lidocaine infusion on pain, as measured by VAS scores, and on bowel function, as subjectively reported by patients undergoing laparoscopic gynecologic outpatient surgery. Results of this study are consistent with previous research suggesting that intraoperative lidocaine infusion may improve postoperative pain levels and may shorten the time interval to return of bowel function.

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