Perioperative Use of Intravenous Lidocaine

Lauren K. Dunn, M.D., Ph.D., Marcel E. Durieux, M.D., Ph.D.

This article has been selected for the Anesthesiology CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

CONCERN about opioid risks in the postoperative period has spurred an increased interest in the use of nonopioid analgesic adjuncts. One drug of potential interest is IV lidocaine, which can be administered in- and/or postoperatively in order to decrease postoperative pain and improve other outcomes. A number of studies and meta-analyses of these studies have been published and show that perioperative lidocaine infusion is indeed effective but that evidence supporting its use varies by surgical procedure. This makes it difficult for anesthesiologists to decide when use of the compound would be clinically indicated.

This article will address this issue. First, a brief overview will be provided of the mechanisms that could explain a prolonged postoperative benefit of perioperative lidocaine infusion. Although these mechanisms are poorly understood, it is important for the clinician to understand how such effects conceivably could happen. The clinical literature on perioperative IV lidocaine will then be reviewed, providing evidence for when this approach may and may not be clinically useful.

This article will focus on the use of perioperative lidocaine infusion for attaining postoperative benefits; intraoperative indications are outside the scope of this article, although several exist. For example, it is effective in blunting cerebral hemodynamic responses to airway manipulation and prevents airway reactivity on emergence in smokers. It also reduces anesthetic requirements by approximately one-third and may reduce neuropathic pain through inhibition of activity in injured afferent nerves.

Pharmacology
The focus of this article will be on lidocaine, as essentially all clinical trials have used this compound. However, there is no a priori reason why the benefits achieved with lidocaine could not be obtained with other local anesthetics, as is indeed suggested by preclinical studies. The reported benefits of perioperative lidocaine infusion include reductions in pain, nausea, ileus duration, opioid requirement, and length of hospital stay (fig. 1). These effects are observed with infusion rates of intravenous lidocaine that mimics plasma lidocaine concentrations obtained during epidural administration (approximately µM). No established mechanistic explanation exists for these effects although a reduction in opioid requirements might be a factor common to several of them. In the majority of trials, the clinical effect of lidocaine exceeded the duration of the infusion by more than 8.5h, which is 5.5 times the half-life of the compound; the temporal extent of this effect is an index used as a measure of preventive analgesia.

The challenge then is to explain how these benefits can occur at the relatively low blood concentrations attained during infusion and how they can persist for many hours or even days after termination of the infusion. It appears that mechanisms are set into motion by lidocaine that persists long after the drug is metabolized to nonbiologically active concentrations. This mechanism is likely not primarily a sodium channel blockade, as (1) typical perioperative blood levels would only block a very small proportion of neuronal sodium channels and (2) at least one target likely to be of importance, the polymorphonuclear granulocyte (PMN), does not express sodium channels. Instead, interference with other molecular targets, in particular those involved in inflammatory signaling, seems likely. However, neuronal effects may play a role as well (e.g., systemic lidocaine blocks excitatory responses in wide dynamic range neurons in the rat spinal cord through a mechanism probably involving strychnine-sensitive glycine receptors). Surgery profoundly affects both pro- and antiinflammatory systems in the body. The antiinflammatory component tends to contribute to infections, whereas the proinflammatory component is involved in some...
postoperative complications (e.g., pain and ileus) and organ failure. Some of these proinflammatory effects are attenuated by perioperative lidocaine infusion. Preclinical studies have shown a multitude of interactions between local anesthetics and the inflammatory system, which have been reviewed in this journal. One potentially important example is the ability of local anesthetics to block priming of PMNs. Priming refers to a process where exposure of cells to certain mediators leads to an exaggerated response (release of cytokines and reactive oxygen species [ROS] such as superoxide anion) when the cells are subsequently activated by a second mediator. This is a pathologic mechanism in several clinical syndromes: adult respiratory distress syndrome is associated with priming, and in patients with sterile inflammation, as occurs in trauma and surgery, PMN production of ROS is much greater than in healthy controls. High ROS, in turn, damages the endothelium and leads to vascular and organ injury. Local anesthetics block PMN priming and do so at very low concentrations (e.g., 0.1 μM lidocaine) as long as the cells are exposed for a prolonged period of time (hours). The underlying mechanism appears to be inhibition of a specific intracellular G-protein signaling molecule (Gq), and this mechanism would explain both the low concentrations at which lidocaine is active and the prolonged duration of effect.

Clinical Applications
The clinical benefits of perioperative lidocaine infusion have been reviewed in several recent meta-analyses and systematic reviews. Although a majority of these trials are in patients undergoing open and laparoscopic abdominal procedures, data are available for other types of surgery.

Here, the available evidence will be presented from a clinical perspective: the goal is not to provide another systematic review but instead to put the reported findings in a context relevant for the practicing anesthesiologist and to provide evidence for the use of perioperative lidocaine infusion in specific clinical settings. A summary of the available evidence is provided in table 1.

Abdominal Surgery
Perioperative lidocaine infusion, in doses ranging from 1.5 to 3 mg · kg⁻¹ · h⁻¹ (after a bolus of 0 to 1.5 mg/kg), consistently improved postoperative pain scores in patients undergoing open or laparoscopic abdominal surgery. The Visual Analogue Scale (VAS) pain scores were decreased at rest and with activity 24 h after surgery. Pain scores were reduced by an average of 1.1 (95% CI, 0.8 to 1.5) for laparoscopic abdominal procedures and 0.7 (95% CI, 0.5 to 1.0) for open abdominal procedures despite a decrease in early and late opioid consumption: opioid requirements in the postanesthesia care unit (PACU) were reduced by an average of 4.2 mg morphine equivalents (95% CI, 1.9 to 6.4). Cumulative opioid consumption was reduced by 3.3 mg morphine equivalents (95% CI, 1.7 to 4.8 mg) for open abdominal surgery and 7.4 mg morphine equivalents (95% CI, 3.4 to 11.4 mg) for laparoscopic abdominal procedures during the first 24 to 72 h postoperatively. Koppert et al. reported a 35% reduction in morphine consumption between 0 to 72 h after surgery in 40 patients undergoing major abdominal surgery. This reduction in opioid consumption is clinically meaningful when compared to other analgesics such as paracetamol (IV acetaminophen) which, in one meta-analysis, reduced VAS pain scores by 1.6 (95% CI, 1.0 to 2.2) and decreased morphine consumption by 30% in the first 4 h after surgery compared to placebo.

On subgroup analysis, perioperative lidocaine infusion at rates greater than or equal to 2 mg · kg⁻¹ · h⁻¹ was associated with decreased VAS pain scores and opioid consumption in the first 24 h; however, there was no evidence of effect for rates less than 2 mg · kg⁻¹ · h⁻¹. Administration of lidocaine intraoperatively and continuing up to 8 h after surgery was associated with reduced cumulative morphine consumption; however, there was no evidence for effect of perioperative lidocaine with infusion rates beyond 24 h. Total analgesic consumption was reduced up to 35% when lidocaine was continued for 0 to 1 h postoperatively and up to 83% when continued for 24 h in one study.

In patient's undergoing colorectal surgery, perioperative lidocaine infusion was shown to be as effective as epidural administration of local anesthetics with regard to pain scores, opioid consumption, and other outcomes. An older trial found lidocaine infusion to rank between thoracic epidural and opioid-based analgesia after colon surgery.

Figure 1. Effects of intravenous lidocaine. PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting.
### Table 1. A Summary of the Available Evidence

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>References</th>
<th>Bolus</th>
<th>Infusion</th>
<th>Duration</th>
<th>Results</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Open abdominal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>Kuo et al. 2006&lt;sup&gt;23&lt;/sup&gt;</td>
<td>2 mg/kg</td>
<td>3 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>30 min before to end surgery</td>
<td>Decreased pain scores and opioid consumption; decreased nausea, duration of ileus, and length of hospitalization</td>
<td>Strong: benefit shown in multiple studies or meta-analyses</td>
</tr>
<tr>
<td></td>
<td>Heroeoder et al. 2007&lt;sup&gt;24&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg/min</td>
<td>Before induction to 4h PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Swenson et al. 2010&lt;sup&gt;21&lt;/sup&gt;</td>
<td>No bolus</td>
<td>1–3 mg/min</td>
<td>Before induction to return of bowel function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal</td>
<td>Koppert et al. 2004&lt;sup&gt;25&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>5 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>30 min before incision to 1h PO</td>
<td>Decreased pain scores and opioid consumption; duration of ileus</td>
<td>Strong: benefit shown in multiple studies or meta-analyses</td>
</tr>
<tr>
<td></td>
<td>Baral et al. 2010&lt;sup&gt;26&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>1.5 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>30 min before incision to 1h PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Laparoscopic abdominal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colectomy</td>
<td>Kaba et al. 2007&lt;sup&gt;27&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt; during surgery, 1.33 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt; PO</td>
<td>Induction to 24h PO</td>
<td>Decreased pain scores and opioid consumption; duration of ileus</td>
<td>Strong: benefit shown in multiple studies or meta-analyses</td>
</tr>
<tr>
<td></td>
<td>Wongyingsinn et al. 2011&lt;sup&gt;27&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt; during surgery, 1 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt; PO</td>
<td>Before induction to 48h PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tikul's et al. 2014&lt;sup&gt;28&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt; during surgery, 1 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt; PO</td>
<td>Before induction to 24h PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>Lauwick et al. 2008&lt;sup&gt;29&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Induction to end of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saadawy et al. 2010&lt;sup&gt;30&lt;/sup&gt;</td>
<td>2 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Before induction to end surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>Kim et al. 2013&lt;sup&gt;31&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Preoperatively to end surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>De Oliveira et al. 2014&lt;sup&gt;32&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Before induction to end surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendectomy</td>
<td>Kim et al. 2011&lt;sup&gt;33&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>2 min before induction to end surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td>Lauwick et al. 2009&lt;sup&gt;34&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Induction to end surgery</td>
<td></td>
<td>Moderate: small benefit, limited number of studies</td>
</tr>
<tr>
<td></td>
<td>Groudine et al. 1998&lt;sup&gt;35&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>1.5 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Before induction to 60 min after skin closure</td>
<td>Decreased pain, opioid consumption, ileus duration and length of hospital stay</td>
<td>Moderate: small benefit, limited number of studies</td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td>Terkawi et al. 2014&lt;sup&gt;36&lt;/sup&gt; and 2015&lt;sup&gt;37&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Induction to 2h after surgery</td>
<td>Decreased incidence of chronic pain at 3 and 6 months</td>
<td>Moderate: small benefit, limited number of studies</td>
</tr>
<tr>
<td></td>
<td>Choi et al. 2012&lt;sup&gt;38&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>1.5 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>30 min before incision to skin closure</td>
<td>No effect on pain scores, opioid consumption, or PONV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grigoras et al. 2012&lt;sup&gt;39&lt;/sup&gt;</td>
<td>1.5 mg/kg</td>
<td>1.5 mg · kg&lt;sup&gt;-1&lt;/sup&gt; · h&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Before induction to 60 min after skin closure</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thoracic</strong></td>
<td>Cui et al. 2010&lt;sup&gt;40&lt;/sup&gt;</td>
<td>No bolus</td>
<td>33 μg · kg&lt;sup&gt;-1&lt;/sup&gt; · min&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>Induction to skin closure</td>
<td>Decreased pain and opioid consumption</td>
<td>Moderate: small benefit in one study</td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>References</th>
<th>Bolus</th>
<th>Infusion</th>
<th>Duration</th>
<th>Results</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory</td>
<td>McKay et al. 2009</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg⁻¹ · h⁻¹</td>
<td>Before induction to end surgery</td>
<td>Decreased pain PACU, faster discharge</td>
<td>Moderate: small benefit, limited number of studies</td>
</tr>
<tr>
<td></td>
<td>De Oliveira et al. 2012</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg⁻¹ · h⁻¹</td>
<td>Before induction to end surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multilevel spine</td>
<td>Farag et al. 2013</td>
<td>No bolus</td>
<td>2 mg · kg⁻¹ · h⁻¹</td>
<td>Induction to PACU discharge (maximum 8 h)</td>
<td>Decreased pain score, improved quality of life 1 and 3 months PO</td>
<td>Moderate: small benefit in one study</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Insler et al. 1995</td>
<td>1.5 mg/kg</td>
<td>30 μg · kg⁻¹ · min⁻¹</td>
<td>After induction to 48 h in ICU</td>
<td>No effect on pain scores or opioid consumption</td>
<td>No support from limited number of studies</td>
</tr>
<tr>
<td></td>
<td>Wang et al. 2002</td>
<td>1.5 mg/kg bolus and 4 mg/kg to CPB priming solution</td>
<td>4 mg/min</td>
<td>Opening of pericardium to end surgery</td>
<td>Decreased PO cognitive dysfunction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mathew et al. 2009</td>
<td>1 mg/kg</td>
<td>4 mg/min for 1 h, 2 mg/min for second h, 1 mg/min to end</td>
<td>After induction to 48 h PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparoscopic renal</td>
<td>Wuehrich et al. 2012</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg⁻¹ · h⁻¹, then 1.3 mg · kg⁻¹ · h⁻¹ PO</td>
<td>Induction to 24 h PO</td>
<td>None</td>
<td>No support from single small study</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>Bryson et al. 2010</td>
<td>1.5 mg/kg</td>
<td>3 mg · kg⁻¹ · h⁻¹</td>
<td>Before induction to skin closure</td>
<td>None</td>
<td>No support from two small studies</td>
</tr>
<tr>
<td>Hip arthroplasty</td>
<td>Grady et al. 2012</td>
<td>1.5 mg/kg</td>
<td>2 mg · kg⁻¹ · h⁻¹</td>
<td>Induction to 24 h PO</td>
<td>None</td>
<td>No support from single small study</td>
</tr>
<tr>
<td></td>
<td>Martin et al. 2008</td>
<td>1.5 mg/kg</td>
<td>1.5 mg · kg⁻¹ · h⁻¹</td>
<td>30 min before incision to 1 h PO</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

CPB = cardiopulmonary bypass; ICU = intensive care unit; PACU = postanesthesia care unit; PO = postoperative; PONV = postoperative nausea and vomiting.
Perioperative lidocaine infusion may be beneficial in the bariatric population, as these patients may be highly sensitive to the respiratory depressant effects of opioids. In patients undergoing bariatric surgery, lidocaine infusion reduced 24-h opioid consumption by 10 mg morphine equivalents compared to placebo, which correlated with improved quality of recovery scores.32

In addition to improving analgesia, perioperative lidocaine infusion shortens the duration of postoperative ileus by an average of 8 h15,18 and decreases the incidence of postoperative nausea and vomiting (PONV) by 10 to 20%.15,17 It seems likely that these benefits are due, in part, to opioid-sparing effects. However, studies reporting reductions in opioid consumption but no effect on PONV suggest that there is not a simple causal relationship.41 Perioperative lidocaine infusion reduces the length of hospital stay by an average of 8 h and up to 24 h.14,15,17,18

Toxicity from perioperative lidocaine infusion (e.g., neurologic changes—light-headedness, dizziness and visual disturbances,41 and cardiac dysrhythmias23) is exceedingly rare.15,17,18 Drowsiness was reported in 2 of 18 patients who received perioperative lidocaine infusion for abdominal surgery.51 There are anecdotal reports that patients who receive perioperative lidocaine appear to be more sleepy during emergence from anesthesia. Lidocaine has been shown to blunt sympathetic responses to tracheal extubation,53 and it is the authors’ bias that the apparent delayed awakening results from patients being less responsive to the endotracheal tube. Perioperative lidocaine has been shown not to affect time to PACU discharge.41

Given the available evidence, the use of perioperative lidocaine infusion may have value for patients undergoing open and laparoscopic abdominal procedures, including colectomy, cholecystectomy, and appendectomy, with benefits including a small but significant reduction in opioid consumption, ileus duration, and post-PONV. It reduces the length of hospital stay after colorectal surgery and may be useful for enhanced recovery.52 Perioperative lidocaine infusion may be an effective alternative for patients for whom neuraxial analgesia is contraindicated.21

Genitourinary Surgery
In patients undergoing radical retropubic prostatectomy, perioperative lidocaine infusion decreased postoperative pain scores by two-thirds and reduced opioid consumption in the PACU by 50%.35 First flatus occurred 33% earlier, and length of hospital stay was reduced by 1 day. Lidocaine infusion improved the 2-min walking test performance in patients undergoing laparoscopic prostatectomy.34 Perioperative lidocaine infusion may have value for patients undergoing radical prostatectomy. In contrast, lidocaine infusion was not shown to be of benefit in a small study of patients undergoing laparoscopic renal surgery.47

Gynecologic and Obstetric Surgery
Two trials investigated the use of perioperative lidocaine infusion in patients undergoing total abdominal hysterectomy. There was no difference between lidocaine and placebo in the primary outcomes (length of hospital stay48 or 6-min walk distance49) or secondary outcomes (pain scores, opioid consumption, PONV, recovery, and fatigue scores) for either study. These studies do not support the use of perioperative lidocaine infusion for patients undergoing total abdominal hysterectomy. Interestingly, there may be a benefit of lidocaine for patients undergoing laparoscopic gynecologic procedures, as discussed for ambulatory surgery below.

In obstetrics, perioperative lidocaine infusion was associated with smaller increases in heart rate and blood pressure and lower maternal plasma cortisol concentrations compared with placebo in patients undergoing general anesthesia for elective cesarean section.53 There was no difference in neonatal Apgar score or acid–base status, suggesting that lidocaine may blunt maternal stress to surgery without ill effects on the neonate. However, no clear outcome benefits have been demonstrated, and additional studies are necessary to evaluate the safety and efficacy of perioperative lidocaine infusion in the obstetric population. At this time, the available evidence does not support its routine use in this patient population.

Breast Surgery
In patients undergoing breast surgery, there is no difference between perioperative lidocaine or placebo infusion on total morphine consumption, pain scores, duration of hospital stay, PONV, return of bowel function, and patient satisfaction in the immediate postoperative period.36,37,54 However, despite this lack of short-term benefit, lidocaine infusion does provide beneficial long-term effects, specifically a reduced incidence of chronic postsurgical pain at 3 and 6 months after mastectomy—one of few demonstrations of long-term benefits associated with perioperative lidocaine infusions (also see Spine Surgery).37,39 Perioperative lidocaine infusion therefore may be considered for patients undergoing mastectomy.

Ambulatory Surgery
Perioperative lidocaine infusion reduced pain scores and PACU opioid requirements in patients undergoing ambulatory procedures that included general surgery, endocrine, breast, gynecology, urology, plastics, minor orthopedic, and minor otolaryngology; however, this difference did not persist at 24 h after surgery. There was no difference in incidence of PONV or time to discharge compared to placebo. In another trial, patients undergoing ambulatory laparoscopic surgery who received lidocaine intraoperatively were discharged 26 min faster and required less opioid medication after discharge, which was correlated with better quality of recovery scores.42

Perioperative lidocaine infusion may provide benefit for patients undergoing ambulatory surgery procedures in order to reduce opioid requirements and facilitate recovery and discharge. Considering the difference in effect in various

Anesthesiology 2017; 126:729-37

Copyright © 2017, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.
surgical populations, it seems likely that different subgroups of outpatients also will have varying responses, but this has not been investigated.

**Cardiothoracic Surgery**

Studies have not shown a difference in postoperative pain or in opioid or benzodiazepine consumption after coronary artery bypass grafting surgery in patients who received lidocaine infusion versus placebo intraoperatively. Lidocaine was administered as a 1.5-mg/kg bolus followed by an infusion rate of 30 μg · kg⁻¹ · min⁻¹ until 48 h postoperatively. A limitation of this study is that lidocaine was not added to the cardiopulmonary bypass pump volume, thus effective doses may not have been achieved during cardiopulmonary bypass. Subsequent studies used higher doses of lidocaine (4 mg/min) intraoperatively; however, the endpoint of these studies was postoperative cognitive dysfunction rather than pain. Wang et al. showed that lidocaine reduced the incidence of postoperative cognitive dysfunction after cardiac surgery when administered as a bolus of 1.5 mg/kg followed by a 4-mg/min infusion, with 4 mg/kg lidocaine added to the cardiopulmonary bypass priming solution. A subsequent study by Mathew et al. could only confirm this (in a secondary analysis) for low doses of lidocaine in the non-diabetic cardiac surgery population. The available evidence does not support the use of perioperative lidocaine infusion for cardiac surgery patients.

Perioperative lidocaine infusion was shown to be of benefit in patients undergoing thoracic surgery, where it reduced pain scores and opioid consumption in the PACU and up to 6 h after surgery. Based on this single study, lidocaine may have value for patients undergoing thoracic surgery who are not candidates for neuraxial analgesia.

**Hip Surgery**

In patients undergoing total hip arthroplasty, there was no difference in pain scores or morphine consumption at 24 or 48 h with perioperative lidocaine infusion (1.5 mg/min) compared to placebo. In addition, there was no difference in functional outcomes, including pressure pain threshold, area of hyperalgesia, or maximum degree of hip flexion. It is unclear why these results are so different from the benefits observed in, e.g., bowel surgery. Blood levels of inflammatory mediators have been shown to be higher after abdominal surgery than after less invasive procedures, and perioperative lidocaine infusion may be less effective for procedures such as total hip arthroplasty, which are possibly less invasive and cause a limited degree of inflammation. Although based on a single (but high-quality) study, the current evidence suggests that the use of perioperative lidocaine infusion for hip surgery may not improve outcomes.

**Spine Surgery**

Perioperative lidocaine infusion was found to reduce pain scores in patients undergoing major spine surgery and was noninferior compared with placebo with regards to postoperative opioid consumption. At 1 and 3 months after surgery, patients who had received lidocaine reported significantly improved quality of life, as measured by the Acute Short-Form 12 Health Survey. Based on the results that show both short- and long-term benefits, perioperative lidocaine infusion may provide value for patients undergoing major spine surgery.

**Conclusion**

Current studies and meta-analyses of these studies show that perioperative lidocaine infusion is indeed effective but suggest that its clinical effectiveness may vary by surgical procedure (table 1). However, no obvious mechanistic reason exists why effectiveness would differ between relatively similar procedures (e.g., open prostatectomy vs. hysterectomy), and these perceived differences may instead result from study design or sample size.

---

**Figure 2.** Representative protocol for use of intravenous lidocaine for perioperative analgesia. APS = acute pain service, PACU = postanesthesia care unit; POD = postoperative day. Adapted from University of Virginia Enhanced Recovery After Surgery (ERAS) Protocol for Colorectal Surgery.
considerations. Perioperative lidocaine infusion reduces postoperative pain and speeds return of bowel function in several types of open abdominal and laparoscopic procedures. In open prostatectomy, thoracic procedures, and major spine surgery, it has been shown to decrease postoperative pain and opioid consumption and to improve functional outcome. In breast surgery, it may help to prevent development of chronic postsurgical pain. Data for other types of surgery are limited, but at this time, no benefit has been shown in patients undergoing total abdominal hysterectomy, total hip arthroplasty, or renal surgery.

Perioperative lidocaine infusion may be a useful analgesic adjunct in enhanced recovery protocols. Lidocaine infusion was used in an enhanced recovery protocol for patients undergoing open and laparoscopic colorectal surgeries (representative protocol shown in fig. 2), which showed benefits in pain scores, opioid consumption, length of hospital stay, and other outcomes.21,22 Perioperative lidocaine infusion may also be considered for enhanced recovery procedures for other types of surgery where the available evidence suggests that there may be a possible benefit and minimal risk of neurologic and cardiac side effects. Although accumulation of lidocaine is a concern with continuous infusion, at doses used in the studies cited here, plasma concentrations remain well below the toxic level (5 µg/ml) even after 24 h.3,19,35 Toxicity from perioperative lidocaine infusion is exceedingly rare but may present with symptoms of tinnitus, perioral numbness, and cardiac dysrhythmias. Monitoring plasma lidocaine levels may be considered in patients at increased risk for lidocaine toxicity such as those with abnormal liver or kidney function or those who cannot be queried about symptoms of lidocaine toxicity.

**Research Support**

Support was provided solely from institutional and/or departmental sources.

**Competing Interests**

The authors declare no competing interests.

**Correspondence**

Address correspondence to Dr. Dunn: Department of Anesthesiology, University of Virginia Health System, P. O. Box 800710, Charlottesville, Virginia 22908. lak3r@hscmail.mcc.virginia.edu. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY’s articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

**References**


2. Hamill JF, Bedford RF, Weaver DC, Colohan AR: Lidocaine before endotracheal intubation: Intravenous or laryngotra-


8. Krause KH, Demaurex N, Jaconi M, Lew DP: Ion channels and receptor-mediated Ca2+ influx in neutrophil granulo-


13. Hollmann MW, McIntyre WE, Garrison JC, Durieux ME: Inhibition of mammalian Gq protein function by local anes-
thetics. ANESTHESIOLOGY 2002; 97:1451–7


Copyright © 2017, The American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

From Chloroform to Home Rule: Queen Victoria Rides One Wave and Resists Another

An American humor magazine, Puck, covered its February 18, 1886 issue with a political cartoon signed by its artist, G. E. Ciani (born c. 1847, signed below right). In “Her Resolute Opposition” (left), the illustrator depicts a determined Queen Victoria (1819 to 1901, close up above right) struggling to sweep back the tide of public sentiment. At that time, the Irish Parliamentary Party of Charles Parnell (1846 to 1891) had tipped Parliamentary balance away from the Conservatives of Lord Robert Cecil Salisbury (1830 to 1903) and toward the Liberals of William Gladstone (1809 to 1898). Cartoonist Ciani depicts the visages of Parnell and Gladstone cresting the waves of “Home Rule” and “Democracy,” respectively, as they crash by Salisbury to face the monarch’s broom of “Prerogative.” This is nearly 33 yr after Victoria “swept” in aristocratic acceptance and then public enthusiasm for chloroform analgesia and anesthesia during childbirth. (Copyright © the American Society of Anesthesiologists’ Wood Library-Museum of Anesthesiology.)

George S. Bause, M.D., M.P.H., Honorary Curator and Laureate of the History of Anesthesia, Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.