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Perioperative Use of Intravenous Lidocaine

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CONCERN about opioid risks in the postoperative period¹ has spurred an increased interest in the use of nonopioid analgesic adjuncts. One drug of potential interest is IV lidocaine, which can be administered intra- 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 manipulation² and prevents airway reactivity on emergence in smokers. It also reduces anesthetic requirements by approximately one-third³ and may reduce neuropathic pain through inhibition of activity in injured afferent nerves.⁴

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.⁵ 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 1 μ M).⁶ 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 8.5 h, 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.⁷

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.⁸ 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).⁹

Surgery profoundly affects both pro- and anti-inflammatory systems in the body. The anti-inflammatory component tends to contribute to infections, whereas the proinflammatory component is involved in some

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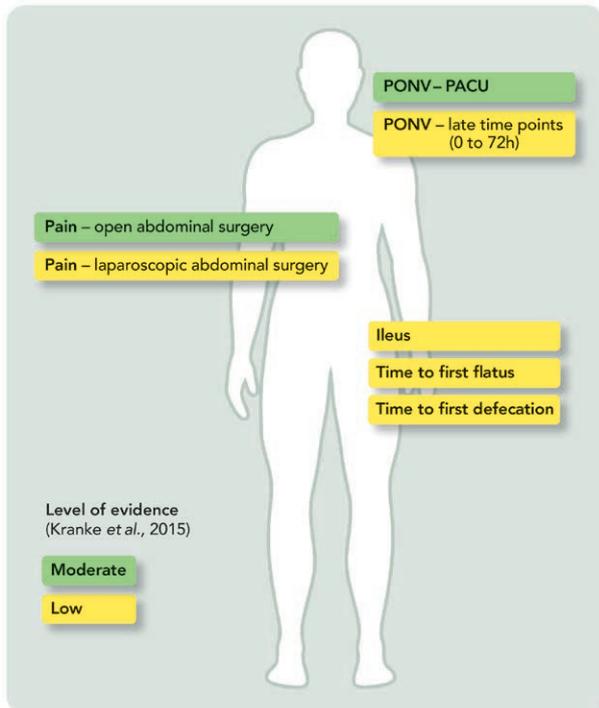


Figure 1. Effects of intravenous lidocaine. PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting.

postoperative complications (e.g., pain and ileus) and organ failure.¹⁰ 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.¹¹ 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,¹² and in patients with sterile inflammation, as occurs in trauma and surgery, PMN production of ROS is much greater than in healthy controls.¹⁰ 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).⁵ The underlying mechanism appears to be inhibition of a specific intracellular G-protein signaling molecule (G_q),¹³ 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.^{14–18} Although a majority of these trials are in patients undergoing open and laparoscopic abdominal procedures, data are available for other types of surgery.¹⁶

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 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ (after a bolus of 0 to 1.5 mg/kg), consistently improved postoperative pain scores in patients undergoing open or laparoscopic abdominal surgery.^{14–18} The Visual Analogue Scale (VAS) pain scores were decreased at rest and with activity 24 h after surgery.^{14,17,18} 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).¹⁶ 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.*¹⁹ 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.²⁰

On subgroup analysis, perioperative lidocaine infusion at rates greater than or equal to 2 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 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 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$.¹⁶ 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.¹⁶ 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.¹⁸

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.^{21,22} An older trial found lidocaine infusion to rank between thoracic epidural and opioid-based analgesia after colon surgery.²³

Table 1. A Summary of the Available Evidence

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

(Continued)

Table 1. (Continued)

Type of Surgery	References	Bolus	Infusion	Duration	Results	Evidence
Ambulatory	McKay <i>et al.</i> 2009 ⁴¹	1.5 mg/kg	2 mg · kg ⁻¹ · h ⁻¹	Before induction to end surgery	Decreased pain PACU, faster discharge	Moderate: small benefit, limited number of studies
	De Oliveira <i>et al.</i> 2012 ⁴²	1.5 mg/kg	2 mg · kg ⁻¹ · h ⁻¹	Before induction to end surgery		
Multilevel spine	Farag <i>et al.</i> 2013 ⁴³	No bolus	2 mg · kg ⁻¹ · h ⁻¹	Induction to PACU discharge (maximum 8 h)	Decreased pain score, improved quality of life 1 and 3 months PO	Moderate: small benefit in one study
Cardiac	Insler <i>et al.</i> 1995 ⁴⁴	1.5 mg/kg	30 µg · kg ⁻¹ · min ⁻¹	After induction to 48 h in ICU	No effect on pain scores or opioid consumption	No support from limited number of studies
	Wang <i>et al.</i> 2002 ⁴⁵	1.5 mg/kg bolus and 4 mg/kg to CPB priming solution	4 mg/min	Opening of pericardium to end surgery	Decreased PO cognitive dysfunction	
	Mathew <i>et al.</i> 2009 ⁴⁶	1 mg/kg	4 mg/min for 1 h, 2 mg/min for second h, 1 mg/min to end	After induction to 48 h PO		
Laparoscopic renal	Wuethrich <i>et al.</i> 2012 ⁴⁷	1.5 mg/kg	2 mg · kg ⁻¹ · h ⁻¹ , then 1.3 mg · kg ⁻¹ · h ⁻¹ PO	Induction to 24 h PO	None	No support from single small study
Abdominal hysterectomy	Bryson <i>et al.</i> 2010 ⁴⁸	1.5 mg/kg	3 mg · kg ⁻¹ · h ⁻¹	Before induction to skin closure	None	No support from two small studies
	Grady <i>et al.</i> 2012 ⁴⁹	1.5 mg/kg	2 mg · kg ⁻¹ · h ⁻¹	Induction to 24 h PO		
Hip arthroplasty	Martin <i>et al.</i> 2008 ⁵⁰	1.5 mg/kg	1.5 mg · kg ⁻¹ · h ⁻¹	30 min before incision to 1 h PO	None	No support from single small study

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 h^{15,18} 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—lightheadedness, 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,⁵¹ 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 otolaryngology⁴¹; 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

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.⁴⁴ Lidocaine was administered as a 1.5-mg/kg bolus followed by an infusion rate of 30 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ 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.^{45,46} Wang *et al.*⁴⁵ 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.*⁴⁶ could only confirm this (in a secondary analysis) for low doses of lidocaine in the nondiabetic 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.⁴⁰ 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.⁵⁰ 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,⁵⁵ 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.⁴³ 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

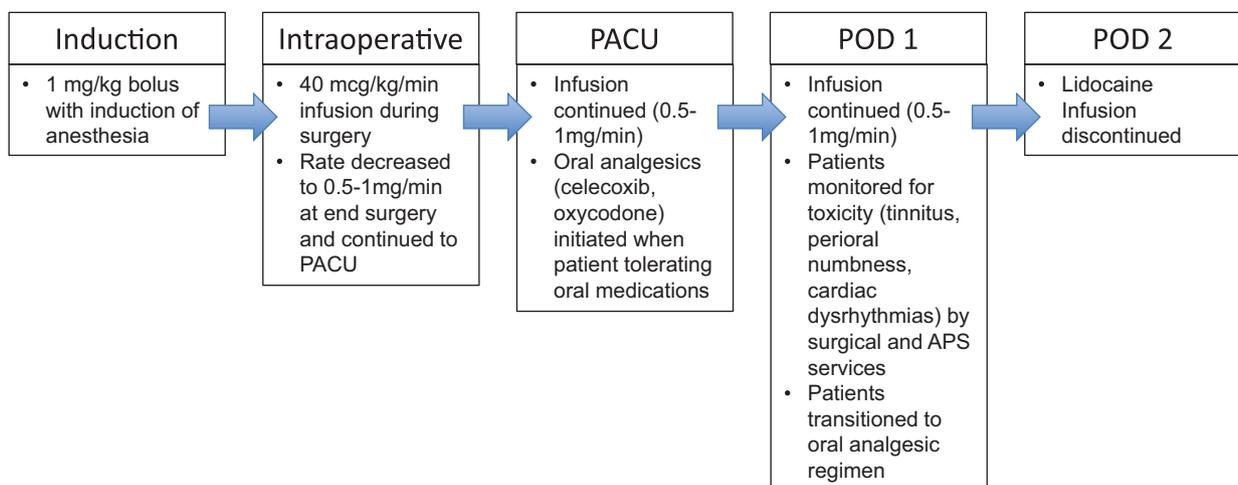


Figure 2. Representative protocol for use of intravenous lidocaine for perioperative analgesia. APS = acute pain service, PACU = postanesthesia care unit; POD = postoperative day. Adapted from University of Virginia Enhanced Recovery After Surgery (ERAS) Protocol for Colorectal Surgery.

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.

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Competing Interests

The authors declare no competing interests.

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References

- Weinger MB, Lee LA, Lorri A; for the Anesthesia Patient Safety Foundation: No patient shall be harmed by opioid-induced respiratory depression. Anesthesia Patient Safety Foundation Newsletter, 2011
- Hamill JF, Bedford RF, Weaver DC, Colohan AR: Lidocaine before endotracheal intubation: Intravenous or laryngotracheal? ANESTHESIOLOGY 1981; 55:578–81
- Kaba A, Laurent SR, Detroz BJ, Sessler DI, Durieux ME, Lamy ML, Joris JL: Intravenous lidocaine infusion facilitates acute rehabilitation after laparoscopic colectomy. ANESTHESIOLOGY 2007; 106:11–8; discussion 5–6
- Kirillova I, Teliban A, Gorodetskaya N, Grossmann L, Bartsch F, Rausch VH, Struck M, Tode J, Baron R, Jänig W: Effect of local and intravenous lidocaine on ongoing activity in injured afferent nerve fibers. Pain 2011; 152:1562–71
- Hollmann MW, Herroeder S, Kurz KS, Hoenemann CW, Struemper D, Hahnenkamp K, Durieux ME: Time-dependent inhibition of G protein-coupled receptor signaling by local anesthetics. ANESTHESIOLOGY 2004; 100:852–60
- Inoue R, Suganuma T, Echizen H, Ishizaki T, Kushida K, Tomono Y: Plasma concentrations of lidocaine and its principal metabolites during intermittent epidural anesthesia. ANESTHESIOLOGY 1985; 63:304–10
- Barrevelde A, Witte J, Chahal H, Durieux ME, Strichartz G: Preventive analgesia by local anesthetics: The reduction of postoperative pain by peripheral nerve blocks and intravenous drugs. Anesth Analg 2013; 116:1141–61
- Krause KH, Demareux N, Jaconi M, Lew DP: Ion channels and receptor-mediated Ca²⁺ influx in neutrophil granulocytes. Blood Cells 1993; 19:165–73; discussion 173–5
- Biella G, Sotgiu ML: Central effects of systemic lidocaine mediated by glycine spinal receptors: An iontophoretic study in the rat spinal cord. Brain Res 1993; 603:201–6
- Leliefeld PH, Wessels CM, Leenen LP, Koenderman L, Pillay J: The role of neutrophils in immune dysfunction during severe inflammation. Crit Care 2016; 20:73
- Hollmann MW, Durieux ME: Local anesthetics and the inflammatory response: A new therapeutic indication? ANESTHESIOLOGY 2000; 93:858–75
- Rabinovici R, Bugelski PJ, Esser KM, Hilleagass LM, Griswold DE, Vernick J, Feuerstein G: Tumor necrosis factor-α mediates endotoxin-induced lung injury in platelet activating factor-primed rats. J Pharmacol Exp Ther 1993; 267:1550–7
- Hollmann MW, McIntire WE, Garrison JC, Durieux ME: Inhibition of mammalian Gq protein function by local anesthetics. ANESTHESIOLOGY 2002; 97:1451–7
- Sun Y, Li T, Wang N, Yun Y, Gan TJ: Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: A meta-analysis of randomized controlled trials. Dis Colon Rectum 2012; 55:1183–94
- Marret E, Rolin M, Beaussier M, Bonnet F: Meta-analysis of intravenous lidocaine and postoperative recovery after abdominal surgery. Br J Surg 2008; 95:1331–8
- Kranke P, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, Eberhart LH, Poepping DM, Weibel S: Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. Cochrane Database Syst Rev 2015; 7: CD009642
- Vigneault L, Turgeon AF, Côté D, Lauzier F, Zarychanski R, Moore L, McIntyre LA, Nicole PC, Fergusson DA: Perioperative intravenous lidocaine infusion for postoperative pain control: A meta-analysis of randomized controlled trials. Can J Anaesth 2011; 58:22–37
- McCarthy GC, Megalla SA, Habib AS: Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: A systematic review of randomized controlled trials. Drugs 2010; 70:1149–63
- Koppert W, Ostermeier N, Sittl R, Weidner C, Schmelz M: Low-dose lidocaine reduces secondary hyperalgesia by a central mode of action. Pain 2000; 85:217–24
- McNicol ED, Tzortzopoulou A, Cepeda MS, Francia MB, Farhat T, Schumann R: Single-dose intravenous paracetamol or propacetamol for prevention or treatment of postoperative pain: A systematic review and meta-analysis. Br J Anaesth 2011; 106: 764–75

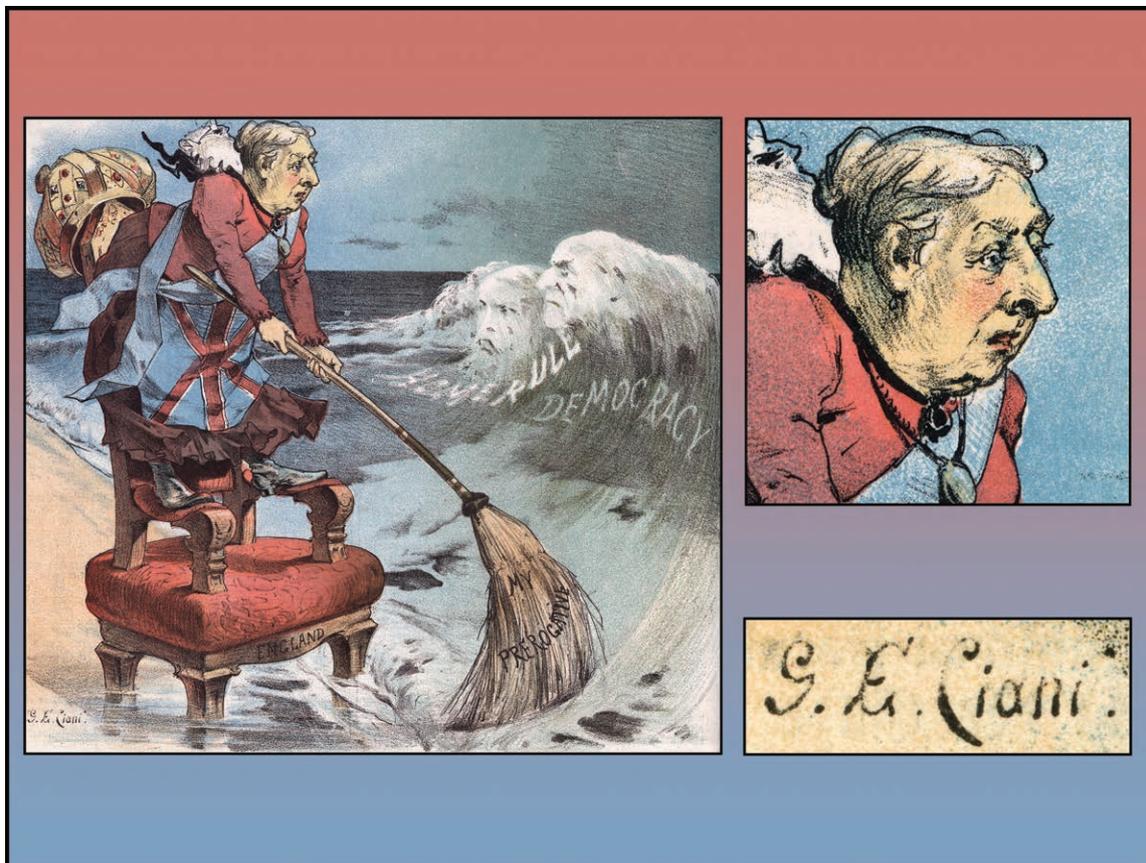
21. Swenson BR, Gottschalk A, Wells LT, Rowlingson JC, Thompson PW, Barclay M, Sawyer RG, Friel CM, Foley E, Durieux ME: Intravenous lidocaine is as effective as epidural bupivacaine in reducing ileus duration, hospital stay, and pain after open colon resection: A randomized clinical trial. *Reg Anesth Pain Med* 2010; 35:370–6
22. Terkawi AS, Tsang S, Kazemi A, Morton S, Luo R, Sanders DT, Regali LA, Columbano H, Kurtzborn NY, Durieux ME: A clinical comparison of intravenous and epidural local anesthetic for major abdominal surgery. *Reg Anesth Pain Med* 2016; 41:28–36
23. Kuo CP, Jao SW, Chen KM, Wong CS, Yeh CC, Sheen MJ, Wu CT: Comparison of the effects of thoracic epidural analgesia and i.v. infusion with lidocaine on cytokine response, postoperative pain and bowel function in patients undergoing colonic surgery. *Br J Anaesth* 2006; 97:640–6
24. Herroeder S, Pecher S, Schönherr ME, Kaulitz G, Hahnenkamp K, Friess H, Böttiger BW, Bauer H, Dijkgraaf MG, Durieux ME, Hollmann MW: Systemic lidocaine shortens length of hospital stay after colorectal surgery: A double-blinded, randomized, placebo-controlled trial. *Ann Surg.* 2007; 246:192–200
25. Koppert W, Weigand M, Neumann F, Sittl R, Schuettler J, Schmelz M, Hering W: Perioperative intravenous lidocaine has preventive effects on postoperative pain and morphine consumption after major abdominal surgery. *Anesth Analg.* 2004; 98:1050–5, table of contents
26. Baral BK, Bhattarai BK, Rahman TR, Singh SN, Regmi R: Perioperative intravenous lidocaine infusion on postoperative pain relief in patients undergoing upper abdominal surgery. *Nepal Med Coll J.* 2010; 12:215–20
27. Wongyingsinn M, Baldini G, Charlebois P, Liberman S, Stein B, Carli F: Intravenous lidocaine versus thoracic epidural analgesia: A randomized controlled trial in patients undergoing laparoscopic colorectal surgery using an enhanced recovery program. *Reg Anesth Pain Med.* 2011; 36:241–8
28. Tikuišis R, Miliauskas P, Samalavičius NE, Žurauskas A, Samalavičius R, Zabulis V: Intravenous lidocaine for postoperative pain relief after hand-assisted laparoscopic colon surgery: A randomized, placebo-controlled clinical trial. *Tech Coloproctol.* 2014; 18:373–80
29. Lauwick S, Kim DJ, Michelagnoli G, Mistraretti G, Feldman L, Fried G, Carli F: Intraoperative infusion of lidocaine reduces postoperative fentanyl requirements in patients undergoing laparoscopic cholecystectomy. *Can J Anaesth.* 2008; 55:754–60
30. Saadawy IM, Kaki AM, Abd El Latif AA, Abd-Elmaksoud AM, Tolba OM: Lidocaine vs. magnesium: Effect on analgesia after a laparoscopic cholecystectomy. *Acta Anaesthesiol Scand.* 2010; 54:549–56
31. Kim TH, Kang H, Choi YS, Park JM, Chi KC, Shin HY, Hong JH: Pre- and intraoperative lidocaine injection for preemptive analgesics in laparoscopic gastrectomy: A prospective, randomized, double-blind, placebo-controlled study. *J Laparoendosc Adv Surg Tech A.* 2013; 23:663–8
32. De Oliveira GS Jr, Duncan K, Fitzgerald P, Nader A, Gould RW, McCarthy RJ: Systemic lidocaine to improve quality of recovery after laparoscopic bariatric surgery: A randomized double-blinded placebo-controlled trial. *Obes Surg* 2014; 24:212–8
33. Kim TH, Kang H, Hong JH, Park JS, Baek CW, Kim JY, Jung YH, Kim HK: Intraperitoneal and intravenous lidocaine for effective pain relief after laparoscopic appendectomy: A prospective, randomized, double-blind, placebo-controlled study. *Surg Endosc.* 2011; 25:3183–90
34. Lauwick S, Kim DJ, Mistraretti G, Carli F: Functional walking capacity as an outcome measure of laparoscopic prostatectomy: The effect of lidocaine infusion. *Br J Anaesth* 2009; 103:213–9
35. Groudine SB, Fisher HA, Kaufman RP Jr, Patel MK, Wilkins LJ, Mehta SA, Lumb PD: Intravenous lidocaine speeds the return of bowel function, decreases postoperative pain, and shortens hospital stay in patients undergoing radical retroperitoneal prostatectomy. *Anesth Analg* 1998; 86:235–9
36. Terkawi AS, Durieux ME, Gottschalk A, Brenin D, Tiouririne M: Effect of intravenous lidocaine on postoperative recovery of patients undergoing mastectomy: A double-blind, placebo-controlled randomized trial. *Reg Anesth Pain Med* 2014; 39:472–7
37. Terkawi AS, Sharma S, Durieux ME, Thammishetti S, Brenin D, Tiouririne M: Perioperative lidocaine infusion reduces the incidence of post-mastectomy chronic pain: A double-blind, placebo-controlled randomized trial. *Pain Physician* 2015; 18:E139–46
38. Choi SJ, Kim MH, Jeong HY, Lee JJ: Effect of intraoperative lidocaine on anesthetic consumption, and bowel function, pain intensity, analgesic consumption and hospital stay after breast surgery. *Korean J Anesthesiol.* 2012; 62:429–34
39. Grigoras A, Lee P, Sattar F, Shorten G: Perioperative intravenous lidocaine decreases the incidence of persistent pain after breast surgery. *Clin J Pain* 2012; 28:567–72
40. Cui W, Li Y, Li S, Wang R, Li J: Systemic administration of lidocaine reduces morphine requirements and postoperative pain of patients undergoing thoracic surgery after propofol-remifentanyl-based anaesthesia. *Eur J Anaesthesiol* 2010; 27:41–6
41. McKay A, Gottschalk A, Ploppa A, Durieux ME, Groves DS: Systemic lidocaine decreased the perioperative opioid analgesic requirements but failed to reduce discharge time after ambulatory surgery. *Anesth Analg* 2009; 109:1805–8
42. De Oliveira GS Jr, Fitzgerald P, Streicher LF, Marcus RJ, McCarthy RJ: Systemic lidocaine to improve postoperative quality of recovery after ambulatory laparoscopic surgery. *Anesth Analg* 2012; 115:262–7
43. Farag E, Ghobrial M, Sessler DI, Dalton JE, Liu J, Lee JH, Zaky S, Benzel E, Bingaman W, Kurz A: Effect of perioperative intravenous lidocaine administration on pain, opioid consumption, and quality of life after complex spine surgery. *ANESTHESIOLOGY* 2013; 119:932–40
44. Insler SR, O'Connor M, Samonte AF, Bazaraal MG: Lidocaine and the inhibition of postoperative pain in coronary artery bypass patients. *J Cardiothorac Vasc Anesth* 1995; 9:541–6
45. Wang D, Wu X, Li J, Xiao F, Liu X, Meng M: The effect of lidocaine on early postoperative cognitive dysfunction after coronary artery bypass surgery. *Anesth Analg* 2002; 95:1134–41, table of contents
46. Mathew JP, Mackensen GB, Phillips-Bute B, Grocott HP, Glower DD, Laskowitz DT, Blumenthal JA, Newman MF: Neurologic Outcome Research Group (NORG) of the Duke Heart Center: Randomized, double-blinded, placebo controlled study of neuroprotection with lidocaine in cardiac surgery. *Stroke* 2009; 40:880–7
47. Wuethrich PY, Romero J, Burkhard FC, Curatolo M: No benefit from perioperative intravenous lidocaine in laparoscopic renal surgery: A randomised, placebo-controlled study. *Eur J Anaesthesiol* 2012; 29:537–43
48. Bryson GL, Charapov I, Krolczyk G, Taljaard M, Reid D: Intravenous lidocaine does not reduce length of hospital stay following abdominal hysterectomy. *Can J Anaesth* 2010; 57:759–66
49. Grady MV, Mascha E, Sessler DI, Kurz A: The effect of perioperative intravenous lidocaine and ketamine on recovery after abdominal hysterectomy. *Anesth Analg* 2012; 115:1078–84
50. Martin F, Cherif K, Gentili ME, Enel D, Abe E, Alvarez JC, Mazoit JX, Chauvin M, Bouhassira D, Fletcher D: Lack of impact of intravenous lidocaine on analgesia, functional recovery, and nociceptive pain threshold after total hip arthroplasty. *ANESTHESIOLOGY* 2008; 109:118–23
51. Wallin G, Cassuto J, Högström S, Lindén I, Faxén A, Rimbäck G, Hedner T: Effects of lidocaine infusion on the

sympathetic response to abdominal surgery. *Anesth Analg* 1987; 66:1008–13

52. Thiele RH, Rea KM, Turrentine FE, Friel CM, Hassinger TE, McMurry TL, Goudreau BJ, Umapathi BA, Kron IL, Sawyer RG, Hedrick TL: Standardization of care: Impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. *J Am Coll Surg* 2015; 220:430–43
53. El-Tahan MR, Warda OM, Diab DG, Ramzy EA, Matter MK: A randomized study of the effects of perioperative i.v. lidocaine on hemodynamic and hormonal responses for cesarean section. *J Anesth* 2009; 23:215–21
54. Choi E, Lee H, Park HS, Lee GY, Kim YJ, Baik HJ: Effect of intraoperative infusion of ketamine on remifentanyl-induced hyperalgesia. *Korean J Anesthesiol* 2015; 68:476–80
55. Naito Y, Tamai S, Shingu K, Shindo K, Matsui T, Segawa H, Nakai Y, Mori K: Responses of plasma adrenocorticotropic hormone, cortisol, and cytokines during and after upper abdominal surgery. *ANESTHESIOLOGY* 1992; 77:426–31

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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.)

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