Intravenous lidocaine for acute pain: an evidence-based clinical update

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Key points
- I.V. lidocaine is a potent anti-inflammatory, anti-hyperalgesic, and gastrointestinal pro-peristaltic drug.
- Level 1 evidence from gastrointestinal surgery demonstrates decreased pain scores, opioid analgesic consumption, and side-effects.
- I.V. lidocaine is a useful acute pain adjunct to achieve enhanced recovery after surgery outcomes.
- Patients may show particular benefit when they have acute hyperalgesia, when opioids are not effective in treating acute pain, or both.
- Our acute pain service experience confirms that with careful patient selection, appropriate monitoring, and nursing policies, lidocaine infusions may be safely continued for several days after operation.

Poorly controlled acute pain remains one of the most undesirable consequences after surgery. Despite increased awareness and widespread efforts to address this, reports continue to estimate that a significant number of patients undergoing surgery experience moderate to severe pain, with a majority of them expressing dissatisfaction with their pain management.

Advances in multimodal analgesia have largely replaced conventional opioid monotherapy, but continued reliance on opioids to manage postoperative pain may at least partly explain the inadequacy of conventional acute pain management.

Almost 30 yr ago, the well-known ‘WHO Step Ladder’ was introduced and has since become a widely accepted concept for rational pain management. This concept has had a major impact on developing the current rationale for the management of acute pain by introducing the concept of multimodal analgesia, highlighting the importance of determining pain severity, encouraging step-wise pain management, and suggesting a wider role for adjuvant agents. Even the origins of the more current concept of opioid-sparing analgesia can probably be traced back to this WHO Step Ladder.

The role of analgesic adjuvants in perioperative pain management, notably ketamine, lidocaine, and the gabapentinoids, continues to be explored. In most situations, the use of these drugs allows for further significant decrease in the requirement or reliance on opioids for adequate pain management. While clinical research in the past two decades has supported the use of these adjuvant drugs in the management of postoperative pain, their exact positioning within the original WHO Step Ladder paradigm continues to evolve. We believe that the use of some of these adjuvants should be based on the identification of pronociception which often presents as hyperalgesia. This understanding of the role of pronociception, often independent of severity and coexisting with surgical postoperative pain is, in our opinion, a very important addition to the concept of the original WHO step ladder.

In our experience, adoption of this modification improves the safety and outcomes of acute pain management. Anti-hyperalgesia therapies (e.g. ketamine, lidocaine, clonidine, and pregabalin) have demonstrated decreases in pain scores, opioid analgesic consumption, and opioid side-effects. Within this group of analgesic adjuvants, lidocaine is unique in that it has been shown to improve important enhanced recovery after surgery (ERAS) outcomes—early ambulation and feeding, early fitness for discharge, and increased patient satisfaction.

Lidocaine is a widely available and commonly used local anaesthetic. When administered i.v., it demonstrates anti-hyperalgesic properties that improve acute postoperative pain...

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management. In this review, we will briefly discuss the pharmacology of i.v. lidocaine, explore the evidence for its use, and share our experience with its use for acute pain management.

Understanding the pharmacology

Lidocaine is an amide-type local anaesthetic that exerts its pharmacological action through the block of sodium channels in neural tissues, thereby interrupting neuronal transmission. This action is best demonstrated when the drug comes directly in contact or in the vicinity of neural tissues. The systemic effects of lidocaine are also probably or at least partially, related to this mechanism.4 The exact mechanism by which i.v. lidocaine provides systemic analgesia remains largely unknown. Published and ongoing research is continuing to support the use of i.v. lidocaine in acute pain management and is also offering some further insights into its mechanisms of action.5–12

An excellent review of the pharmacology of lidocaine has been published elsewhere.4 In summary, the early clinical evidence for the analgesic effects of i.v. lidocaine came from its use in chronic neuropathic pain where the clinical benefit has been established. Basic science studies and further work in animal models suggest that the systemic effect of lidocaine occurs predominantly in damaged and dysfunctional nerves, where it prevents depolarization of the neuronal membranes. There is also some suggestion that systemic lidocaine may also reduce and/or prevent the neo-proliferation of active sodium channels and block their spontaneous firing, especially in traumatized and scarred tissues. In acute pain, i.v. lidocaine demonstrates significant analgesic, anti-hyperalgesic, and anti-inflammatory properties. It also reduces sensitivity and activity of spinal cord neurones (central sensitization) and decreases N-methyl-D-aspartate receptor-mediated post-synaptic depolarization. Other studies have additionally demonstrated a clinically relevant decrease in systemic inflammatory markers in patients receiving lidocaine perioperatively.6–8

The dose of i.v. lidocaine necessary for analgesia in the perioperative period is 1–2 mg kg⁻¹ as an initial bolus followed by a continuous infusion of 0.5–3 mg kg⁻¹ h⁻¹. The most widely reported and clinically effective dose range appears to be from 1 to 2 mg kg⁻¹ h⁻¹. Lidocaine has a high hepatic extraction ratio and its metabolism depends not only on hepatic metabolic capacity, but also on hepatic blood flow. A continuous infusion (without a bolus) will take 4–8 h to achieve a steady-state plasma concentration (Fig. 1). On discontinuation after prolonged infusion, the plasma levels decrease rapidly (Fig. 2). The context-sensitive half-time after a 3 day infusion of lidocaine is ∼20–40 min, and there is no accumulation over time in healthy individuals. Monoethylglycinexylidide (MEGX) and glycinexylidide (GX) are the two major metabolites of lidocaine. MEGX has similar convulsant and anti-arrhythmic potency as lidocaine. However, MEGX is rapidly metabolized by the liver to GX. MEGX has also been shown to decrease the clearance of lidocaine. GX has significantly less activity than lidocaine and is both metabolized and excreted by the kidney. MEGX has been known to cause toxicity in patients with cardiac failure and GX known to accumulate in patients with renal failure.

Despite the well-described safety profile in numerous clinical trials, it must be reiterated that systemic lidocaine has a very narrow therapeutic index; central nervous system (CNS) toxicity occurs (>5 µg ml⁻¹) slightly above the therapeutic plasma level (2.5–3.5 µg ml⁻¹). The factors that influence the plasma concentration of free lidocaine include the dose and rate of injection, acid-base status, hypercapnia and hypoxia, low plasma protein levels, and diminished hepatic or renal function. Very rarely do patients actually have a hypersensitivity, idiosyncrasy, or diminished tolerance to systemic lidocaine that is independent of the above-
mentioned factors. In our experience, lidocaine toxicity is almost always a result of an iatrogenic error in dose, delivery, or infusion pump programming.

The progression of clinical presentation in lidocaine toxicity often follows a well-described course and closely mirrors the increasing plasma concentration. When the plasma concentration of lidocaine exceeds 5 µg ml⁻¹, patients will first exhibit CNS symptoms of toxicity. This begins ~6 µg ml⁻¹ and is quite definite at 10 µg ml⁻¹. In awake patients, these CNS symptoms follow an almost predictable progression. It begins with numbness of the tongue, metallic taste, a feeling of light headedness, and then complaint of tinnitus. Visual disturbances then progress to muscle twitching, unconsciousness, and seizure development. If undetected or untreated, this will proceed into coma, and the patient will probably suffer a respiratory arrest, cardiovascular collapse, or both. In clinical practice, the more common complaints as systemic lidocaine approaches toxic levels are sedation, sleepiness, light-headedness, relaxation, euphoria, unreality, and ‘flying and drunkenness’. Toxicity with lidocaine results in cardiovascular system (CVS) signs in awake patients far less frequently than CNS symptoms for two reasons. First, lidocaine itself is less cardioxious than the lipophilic bupivacaine. Secondly, and probably more importantly, these CVS events occur when the serum levels exceed 10 µg ml⁻¹, which is well above that necessary to exhibit CNS toxicity (5–6 µg ml⁻¹). These CVS signs include negative inotropy (greater in patients with conduction problems or after myocardial infarction), effects on conduction (prolonged PR interval and QRS duration, sinus tachycardia, sinus arrest, and partial or complete atrio-ventricular dissociation), and effects on vascular tone (where hypertension often precedes hypotension). Once again, these effects are potentiated by acidosis, hypercapnia, and hypoxia which in turn worsen myocardial depression; increase arrhythmias; and can prove to be fatal.

An important clinical correlate of the i.v. lidocaine toxicology— as long as the patients are awake (or are easily aroused from sleep) and remain communicative, it is the subtle CNS symptoms and signs that precede major complications and they should therefore be carefully sought after by the nursing staff (Table 1). A corollary to this concept—cardiac signs will be the primary presentation if the CNS symptoms have been missed. And a caveat to the safety of i.v. lidocaine—decreased dosing and continuous cardiac monitoring is required in patients with cardiac, hepatic, or renal dysfunction and in those who are deeply sedated or anaesthetized—usually in the operating theatres, recovery units, or in the intensive care unit (ICU).

Evaluating the evidence

Perioperatively, when i.v. lidocaine is administered as a continuous infusion at clinically relevant doses (1–2 mg kg⁻¹ h⁻¹), it usually results in plasma concentrations that remain below 5 µg ml⁻¹. Lidocaine at this plasma level is adequate to attenuate sympathetic responses, decrease pain, and demonstrate a significant volatile anaesthetic and opioid-sparing effect. This use of lidocaine for up to 24 h has been widely reported to show a significant decrease in pain, reduce analgesic requirements along with a faster return of intestinal function, and overall reduction in side-effects.

Rimbäck and colleagues published one of the earliest clinical trials with i.v. lidocaine. They had previously observed that intraperitoneal lidocaine reduced the incidence of postoperative ileus and wanted to determine if this was a local or systemic effect of the drug. They enrolled 30 patients undergoing open cholecystectomy who were given radio-opaque markers to swallowing before their surgery. They observed that the patients randomized to i.v. lidocaine treatment (100 mg bolus followed by 3 mg min⁻¹ for 24 h) showed significant recovery in bowel motility that was confirmed by serial radiographs. These patients also had less pain, opioid requirements, and recovered faster. The investigators suggested that i.v. lidocaine reduced ileus and/or enhanced gut function recovery through one or more of five mechanisms—excitatory effect on gut smooth muscle (direct), reduced pain and opioid requirements (indirect), block of sympathetic reflexes, reduced catecholamine production, and an anti-inflammatory effect.

Groudine and colleagues randomized patients undergoing open radical prostatectomy to receive placebo or lidocaine (bolus 1.5 mg kg⁻¹ followed by 3 mg min⁻¹ continued until 60 min after skin closure). They confirmed the safety of this regimen by estimating the plasma concentrations to remain within the therapeutic range (1.3–3.7 µg ml⁻¹). They reported a significant reduction in opioid analgesic requirements, decreased pain scores with greater satisfaction, and earlier return of bowel activity in the patients receiving lidocaine. They also noted that on the third postoperative day, when the surgical drains were being removed, most patients receiving lidocaine had either passed flatus or had a bowel movement, were ambulant, and had progressed to a full diet. These patient outcomes mentioned above are exactly those sought by many ERAS protocols and this study highlighted the possible important role played by i.v. lidocaine in achieving clinically relevant ERAS outcomes.

The effect of intraoperative lidocaine administration is sustained beyond its infusion period and continues into the postoperative period. This study confirmed that patients receiving lidocaine had decreased analgesic requirements and pain scores that became more prominent 36 h after the lidocaine infusion had been terminated.

As other ERAS protocols become more widely adopted and meticulously implemented, the impact of single modalities or interventions become more difficult to define, demonstrate, or prove. Kaba and colleagues’ study showed that i.v. lidocaine can play an important role even in a standardized colorectal ERAS protocol. They randomized 45 patients undergoing laparoscopic colon resections to receive placebo or i.v. lidocaine (bolus of 1.5 mg kg⁻¹ followed by 2 mg kg⁻¹ h⁻¹ for 24 h). Other than decreasing pain scores, analgesic consumption, and side-effects well beyond the duration of lidocaine infusion, they observed two other important findings. When titrated with a depth of anaesthesia monitor, patients receiving lidocaine required a significantly lower MAC of volatile anaesthetic agent. More importantly, these patients had a significant improvement in their dynamic pain scores. In other words, while the pain scores at rest were no different, on mobilization, deep breathing, and coughing, the patients receiving lidocaine were able to perform better than those receiving a standard opioid-based analgesic protocol.

At least two studies have compared i.v. lidocaine with thoracic epidural analgesia. Kuo and colleagues’ studied patients undergoing open colonic resections and randomized them into three groups—epidural, i.v. lidocaine, and placebo. While patients with epidurals had better pain relief, lower opioid consumption, earlier return of bowel function, and lesser production of cytokines than i.v. lidocaine during the 72 h after colonic surgery, the i.v. lidocaine group was better in all respects than the control group. This study, while confirming thoracic epidural analgesia as the ‘gold standard’ for open surgery, suggested that i.v. lidocaine may offer a useful alternative, especially when epidurals are contraindicated, refused, or fail. In 2011, Wongyingsinn and colleagues compared i.v. lidocaine with epidural analgesia for....
Table 1 Summary of the Ottawa Hospital Policy for i.v. lidocaine

<table>
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<th>Stage</th>
<th>Treatment</th>
<th>Monitoring</th>
<th>Comments</th>
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| Preparation    | The initial dose is administered in a clinical area where continuous cardiac monitoring, non-invasive AP, pulse oximetry, and resuscitative equipment/cardiac arrest cart is available | • Assess clinical status, vital signs, and pain scores at rest and with activity  
  • The patient or healthcare professional may also complete a Brief Pain Inventory (BPI) and/or DN4 questionnaire  
  • Weight—If patient’s BMI is more than 30, use ideal body weight (IBW) | The physician must be available to remain in attendance with the patient for at least 15 min after administration of the lidocaine bolus |
| Initiation     | Bolus dose i.v. lidocaine = 1.5 mg kg\(^{-1}\) given slow i.v. push over 2–4 min followed by infusion (see below) | • Assess pain q 15 min until pain is stable, or as determined by the physician  
  • Continuous visual patient monitoring during first 20 min after initiation of infusion, and then as per physician’s orders  
  • Oxygen saturation, AP, and heart rate: q30 min for 1 h, then as per physician’s orders  
  • Side-effects—sedation score: None—fully awake, alert. Mild—occasionally drowsy, easily aroused. Moderate—frequently drowsy; easily roused, drifts off to sleep during conversation. Severe—somnolent; difficult to arouse, minimal or no response to stimuli  
  Sleep—normal sleep; easily aroused, RR> 10 and even, not shallow  
  • ECG monitoring may be carried out at the discretion of the attending physician  
  • Administer midazolam 1–2 mg i.v. p.r.n. if patient develops twitching, or tremors  
  • Observe for signs of toxicity including twitching, tremors, or seizures Hypertension may be an early warning sign of toxicity  
  • The most common symptoms of toxicity include sedation, tinnitus, metallic taste, and perioral numbness  
  • These symptoms usually disappear with cessation of the infusion for 1–2 h and resumption of the infusion at a decreased rate  
  • Other signs of toxicity include respiratory depression, dizziness, confusion, blurred vision, double vision, visual hallucinations, bradycardia, hypotension, and agitation  
  • Page/call APS stat if patient develops any signs or symptoms of toxicity and/or if there is no change in pain scores and analgesic consumption | • In patients with co-morbidities or at the discretion of the physician, the bolus dose can be reduced or infusion duration may be increased (given over 1 h)  
  • If the patient develops symptoms or signs of toxicity, further treatment can be adjusted or avoided |
| Infusion       | • Usual range for a lidocaine infusion is 0.5–2 mg kg\(^{-1}\) h\(^{-1}\).  
  • The usual starting dose is 1 mg kg\(^{-1}\) h\(^{-1}\).  
  • This infusion can be increased or decreased by 0.25–0.5 mg kg\(^{-1}\) h\(^{-1}\) based on clinical response (pain scores) or signs of toxicity  
  • Allow 8 h for steady-state serum levels to be achieved before making dosage adjustments | • Observe for signs of toxicity including twitching, tremors, or seizures Hypertension may be an early warning sign of toxicity  
  • These symptoms usually disappear with cessation of the infusion for 1–2 h and resumption of the infusion at a decreased rate  
  • Other signs of toxicity include respiratory depression, dizziness, confusion, blurred vision, double vision, visual hallucinations, bradycardia, hypotension, and agitation  
  • Page/call APS stat if patient develops any signs or symptoms of toxicity and/or if there is no change in pain scores and analgesic consumption | • On the APS, routine serum lidocaine level testing is not necessary  
  • However, in the event of life-threatening symptoms that may be attributed to lidocaine toxicity, serum lidocaine levels should be drawn and sent for analysis  
  • These symptoms may include: hypotension, abrupt/severe change in the level of consciousness, bradycardia  
  • In all these cases, the lidocaine infusion must be stopped immediately |
| Infusion       | • Lidocaine infusion for APS patients may be discontinued at the discretion of attending anaesthesiologist once bowel recovery is underway and oral analgesics are both tolerated and sufficient for pain control | • Patients may experience a sudden reduction in their pain scores and opioid analgesic requirements in the first 24 h after starting lidocaine  
  • Continue to optimize multimodal analgesia  
  • Anti-hyperalgesic medications (e.g. pregabalin) may be required to replace or supplement i.v. lidocaine  
  • On the APS, routine serum lidocaine level testing is not necessary  
  • However, in the event of life-threatening symptoms that may be attributed to lidocaine toxicity, serum lidocaine levels should be drawn and sent for analysis  
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  • In all these cases, the lidocaine infusion must be stopped immediately |

Note: Serum lidocaine levels take several days or weeks to be reported and are therefore of limited usefulness for APS patients  
• Mild sedation or other mild symptoms of lidocaine toxicity (peri-oral numbness, heavy tongue, tinnitus) should not require lidocaine blood level testing  
• Mild to moderate sedation can be secondary to lidocaine or opioids  
• Typical duration of infusion is 12–72 h, but may be extended at the discretion of APS physician to achieve bowel recovery and opioid-sparing pain control
I.V. lidocaine for acute pain

It has been well described that postoperative pain remains incompletely controlled in some settings and increased understanding of its mechanisms is required. It is well known that opioids are effective in treating acute pain when it is predominantly nociceptive in nature. More recently, it has been appreciated that opioids themselves can cause hyperalgesia—opioid-induced hyperalgesia. It is also known that patients undergoing certain procedures develop acute neuropathic pain and opioids are not effective in blunting this “pronociception.” Acceptance of this concept is vital to the understanding of the role of i.v. lidocaine in the management of acute pain. This concept is based on the well-known fact that opioids and anti-hyperalgesics (ketamine, lidocaine, and pregabalin) act on opposing sides of the nociception–pronociception paradigm.

When a patient is identified as having or being at risk of developing acute hyperalgesia, we recommend the use of anti-hyperalgesic medication such as i.v. lidocaine, ketamine, or gabapentinoids. The objective diagnosis of acute neuropathic pain can be made using Bouhassira’s widely accepted DN4 questionnaire.

We strongly believe that i.v. lidocaine plays an important role as an analgesic adjunct when used to block or treat acute hyperalgesia. We have additionally taken advantage of its versatility, easy availability, low cost, and wide familiarity of use and have observed significant clinical benefit that outweighs the potential risks from its use that encouraged us to standardize this protocol and widen its availability.

In 2009, the acute pain service (APS) of our tertiary level university hospital implemented a protocol for the use of lidocaine infusions for perioperative pain management (summarized in Table 1). This protocol allowed for the continuous infusion of i.v. lidocaine in the surgical wards without continuous ECG monitoring. We audited the first 3 yr of this protocol implementation and after research and ethics board approval, completed a retrospective quality assurance study in 2013. Patients receiving i.v. lidocaine for pain management by APS physicians were identified from the pharmacy database for the 3 yr period between September 2009 and August 2012. During this period, 169 patients received lidocaine; of which, 102 patients were analysed with complete data. The patients were 52% male with mean age 53 yr (range 18–89 yr). The indications for i.v. lidocaine are divided between laparotomy and other gastrointestinal surgeries (49%), spinal surgery (16.7%), trauma (12.7%), amputations (6.9%), hysterectomies (5.9%), other orthopaedic surgeries (3.9%), and others (4.9%). The duration of lidocaine infusion was 2–3 days for ~75% of the patients. Preoperative chronic pain and chronic opioid use were present in 50 and 35.3% of all patients, respectively. A bolus dose (mean dose of 1.34 mg kg\(^{-1}\) and range 0.75–2.5 mg kg\(^{-1}\)) was used in 95% of our patients. The lidocaine infusion dose ranged between 0.5 and 2 mg kg\(^{-1}\) h\(^{-1}\). Eleven percent of patients received i.v. lidocaine after failure of epidural analgesia in bowel surgeries. Mild side-effects and/or signs of toxicity were reported in six patients—the infusion was stopped for four and reduced for two patients. For ~40% of patients, lidocaine was started as an adjuvant after failure of the initial plan in controlling pain. In these patients, there was a significant (20–25%) reduction in opioid consumption within 24 h. When comparing the decrease in pain scores, patients receiving i.v. lidocaine showed a clinically relevant improvement in dynamic pain when compared with rest pain, which has been reported elsewhere by studies done by Kopert and colleagues and Kaba and colleagues.

Almost half of our patients underwent intra-abdominal surgical procedures. Spine and trauma surgery accounted for another 27.4% of our i.v. lidocaine usage. In the spinal surgery population, there is a higher incidence of chronic pain, neuropathic symptoms, and chronic opioid usage that make lidocaine an ideal perineural analgesic adjunct. Our trauma population often have multiple injuries that preclude the use of regional anaesthesia techniques. Patients with rib fractures have also shown significant benefit from lidocaine infusions.

To study the safety of these prolonged infusions, we have used a three-compartment model with age, height, and weight.

laparoscopic colonic resections in a standardized ERAS protocol. They reported no difference in postoperative pain intensity, early mobilization, dietary intake, duration of hospital stay, and post-operative complications between groups. This study confirms that even in well-established protocols, for laparoscopic colorectal surgery, i.v. lidocaine can ensure the same ERAS outcomes as continuous epidural infusions.

Lidocaine may also be useful as an adjunct to treat postoperative ileus. Many of the above-mentioned clinical trials have suggested that lidocaine may have an indirect effect on gut motility by decreasing pain, opioid analgesic requirements, and sympathetic block. A remarkable case series reports the use of i.v. lidocaine in the management of ileus secondary to spinal cord injury. These authors report that in patients with ileus (duration 4–10 days), after a serious spinal cord injury refractory to conventional medical management, five out of seven of these patients experienced resolution of their ileus with a lidocaine infusion of 10–20 h duration. This finding suggests that lidocaine may have a more direct effect on the gut than previously considered. It is our opinion that i.v. lidocaine may prove to be the drug of choice in the management of postoperative ileus, although further controlled studies are necessary to confirm this.

Beyond the colorectal and abdominal surgery literature, the role of i.v. lidocaine has been evaluated in other surgical models with mixed results. Farag and colleagues published a clinical trial that evaluated the contribution of i.v. lidocaine in 116 patients undergoing complex spinal surgery. They reported that patients receiving i.v. lidocaine (2 mg kg\(^{-1}\) h\(^{-1}\) from induction to 8 h after operation) had a significant (10–20%) reduction in pain scores and a 25% reduction in opioid consumption at 48 h. This intervention also led to a significant improvement in overall recovery for these patients. I.V. lidocaine has also been described to be beneficial in patients with chronic pain after spinal cord injury, a well-known pain model with notoriously few effective treatment options.

The use of i.v. lidocaine in other models of acute pain has produced less consistent results—for example, patients undergoing hip arthroplasty, hysterectomy, and some other procedures did not demonstrate a clinical or statistically significant analgesic benefit from this drug. Despite these results, studies examining i.v. lidocaine in experimental ischaemic pain in volunteers, post-amputation stump pain, and in the prevention of persistent pain after breast surgery continue to provide encouraging results. We expect more trials in a wide variety of surgical models to be performed and reported in due course.

Until this date, there have been at least six published systematic reviews with meta-analyses (Level 1 evidence) for the perioperative use of i.v. lidocaine. Sun and colleagues published a clinical trial that evaluated the contribution of i.v. lidocaine in 116 patients undergoing complex spinal surgery. They reported that patients receiving i.v. lidocaine (2 mg kg\(^{-1}\) h\(^{-1}\) from induction to 8 h after operation) had a significant (10–20%) reduction in pain scores and a 25% reduction in opioid consumption at 48 h. This intervention also led to a significant improvement in overall recovery for these patients. I.V. lidocaine has also been described to be beneficial in patients with chronic pain after spinal cord injury, a well-known pain model with notoriously few effective treatment options.

The Ottawa experience

It has been well described that postoperative pain remains incompletely controlled in some settings and increased understanding of its mechanisms is required. It is well known that opioids are effective in treating acute pain when it is predominantly nociceptive in nature. More recently, it has been appreciated that opioids themselves can cause hyperalgesia—opioid-induced hyperalgesia. It is also known that patients undergoing certain procedures...
as covariates (Kuipers and colleagues) to simulate the pharmacokinetics of a prolonged infusion.19 This was done for two doses of infusions—1 and 2 mg kg\(^{-1}\) h\(^{-1}\). We have found that without an initial bolus, the levels of lidocaine increase gradually over 4 h and then stabilize at ~8 h (Fig. 1). They remain stable over the next few days in the models and then rapidly decline upon discontinuation of the infusion (Fig. 2). We find this pharmacokinetic model reassuring and in keeping with our current clinical practice. Other investigators have reported up to 14 days of continuous infusion without toxicity.20

**Practical application**

Valid and continued training of the nursing staff is of vital importance to the safe and successful implementation of this protocol. On the surgical wards, i.v. lidocaine may be used, but standard resuscitative equipment should be available for immediate use. The immediate in-house availability of the APS team during the daytime and on-call anaesthesia team after hours ensures round the clock support of the nursing staff.

An important caveat remains; that the initiation of this therapy is clearly defined as requiring the anaesthetist in attendance and to be commenced in a monitored setting. Most of our patients receiving i.v. lidocaine after operation have received a bolus (1–2 mg kg\(^{-1}\) to maximum of 100 mg over 1 min) as part of their anaesthetic induction. The remaining patients have the lidocaine commenced while they are awake in the postoperative period in the post-anaesthetic care unit or PACU, with a similar bolus dose given over 2–4 min. The infusion is started immediately after the bolus, both during the anaesthetic and in PACU at a rate of 1 mg kg\(^{-1}\) h\(^{-1}\). In the awake patient, this rate can be adjusted upwards to 1.5 or 2 mg kg\(^{-1}\) h\(^{-1}\). The lidocaine infusions are run for 2–3 days and can be reduced again to 1.5 or 1 mg kg\(^{-1}\) h\(^{-1}\) depending on the benefit. All patients will also receive our standardized multimodal analgesia APS protocols. When the patient leaves the PACU to the surgical ward, a protocol is printed and attached to the patient chart. For patients on i.v. lidocaine, we ensure careful bedside monitoring (Table 1) by the nursing staff, meticulous and regular follow-up by the APS team along with proper handover and communication between them and the surgical teams.

In 2009, the Ottawa Hospital implemented a formal protocol (Nursing Policy #2-397/2009) to guide the administration of i.v. lidocaine for acute pain management on the standard surgical wards (Table 1). We summarize our experience with i.v. lidocaine and focus on patient safety factors:

(i) **Patient selection:** Patients who may benefit from i.v. lidocaine are summarized in Table 2. I.V. lidocaine may have adverse effects on cardiac conductivity, myocardial contractility, and precipitate partial or grand mal seizures. Hence, caution is warranted in patients with history of any degree of heart block, heart failure, or seizure disorder. Impaired liver and renal function or drug interactions may also impair lidocaine clearance; hence, this needs to be carefully considered. A thorough list of potential drug interactions and medical conditions that place patients at increased risk was listed in the formal policy.

(ii) **Regional anaesthesia techniques:** I.V. lidocaine is contraindicated when other regional anaesthesia techniques are concurrently used, especially where bolus or large doses of any local anaesthetic are administered. Examples include epidural, plexus blocks, and TAP blocks. I.V. lidocaine infusion can be initiated 4–8 h after the last epidural or regional catheter bolus, TAP block, and is best initiated in these situations without a bolus dose. In the case of a failed epidural, as long as the epidural infusion was stopped without an epidural bolus (test dose), i.v. lidocaine can be initiated immediately—again without a bolus dose. Individual patient factors may also need consideration in all these situations and extended monitoring may be justified.

(iii) **Physician and nursing factors:** I.V. lidocaine may only be ordered by anaesthetists—all nurses on the wards where this treatment modality is to be implemented should be educated regarding the policy and procedures associated with i.v. lidocaine for acute pain management.

(iv) **Maintenance of i.v. lidocaine on the standard ward:** when i.v. lidocaine therapy is started in theatre, a critical care area such as PACU or ICU, therapeutic levels (2.5–3.5 μg ml\(^{-1}\)) may be maintained on the standard ward with no need for continuous ECG monitoring. Assessments of level of sedation, and so on are done as per i.v. PCA standards—however, ECG monitoring, \(S_\text{aO}_2\), and arterial pressure (AP) measurement device should all be immediately available.

(v) **Dose:** The usual rate of i.v. lidocaine therapy is 1 mg kg\(^{-1}\) h\(^{-1}\). Acceptable range is 0.5–2 mg kg\(^{-1}\) h\(^{-1}\). Need for continuation of therapy to be assessed on a daily basis.

(vi) **Initiation of i.v. lidocaine therapy:** Patients with ASA status I or II with no concern for adverse effect or drug interactions with i.v. lidocaine may be considered for initiating therapy on the standard wards. Consider portable continuous ECG, \(S_\text{aO}_2\), and AP monitors during loading dose and for 15 min after. The anaesthetist may administer 1.5 mg kg\(^{-1}\) (total max. of 100 mg) i.v. by intermittent bolus over 4 min. The anaesthetist should stay in attendance for 15 min after loading dose completed.

(vii) **High-risk patients:** Less healthy patients (especially elderly, obese, and those with hepatic and renal dysfunction) are at risk for respiratory depression in the first few hours after initiation of lidocaine treatment, secondary to the

### Table 2 Summary of indications for i.v. lidocaine

<table>
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<tr>
<th>Intraoperative</th>
<th>Alternative to regional anaesthesia</th>
<th>Postoperative</th>
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<tr>
<td>1. Epidural—contraindicated or failed</td>
<td>Acute pain with pronociception (hyperalgesia)</td>
<td>1. Epidural—inadequate or failed</td>
</tr>
<tr>
<td>2. Laparoscopic converted to open</td>
<td></td>
<td>2. Laparoscopic converted to open</td>
</tr>
<tr>
<td>3. Trauma—burns, degloving, crush injury</td>
<td></td>
<td>3. Trauma—burns, degloving, crush injury</td>
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<tr>
<td>4. Rib, clavicle, or sternal fractures</td>
<td></td>
<td>4. Rib, clavicle, or sternal fractures</td>
</tr>
<tr>
<td>5. Prevention or treatment of ileus</td>
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<td>5. Prevention or treatment of ileus</td>
</tr>
</tbody>
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opiods administered before initiation of lidocaine therapy. It may be reasonable to initiate and continue the i.v. lidocaine therapy in a higher dependency monitored area like PACU, step-down unit, or ICU. Once the dose of lidocaine has been titrated, they should remain closely monitored for 4–8 h for the plasma concentrations to stabilize. The titration of therapy and level of care needs to be individualized to the patient needs.

(viii) Equipment and drug administration concerns (bags, pumps, and connectors): Use 250 ml commercially supplied bags of a standard 0.4% lidocaine solution. Ensure the bags are well labelled in their stock area and must avoid mistaking for 500 ml i.v. bags. It is preferable to use an i.v. administration pump with preprogrammed settings (0.4% and 250 ml) from a drug library for i.v. lidocaine—once i.v. lidocaine is chosen, only the patient’s weight and dose (in mg kg\(^{-1}\) h\(^{-1}\)) need to be inputted. Programming of the pump is performed by the primary bedside nurse and cross-checked by another nurse before initiation. There must be protection against the possibility for gravity free-flow of the i.v. lidocaine. This is easily achieved by only administering the i.v. lidocaine via the side-port of a PCA Y-connector that has an anti-free-flow valve (often referred to as an anti-siphon valve) built into the Y-connector.

Conclusion

The concepts of multimodal analgesia and its therapeutic options in the management of acute postoperative pain are still evolving. Identification of acute hyperalgesia is an important concept that improves the safety and efficacy of acute pain management. I.V. lidocaine is a useful option in the prevention and/or treatment of acute hyperalgesia. The benefits of perioperative i.v. lidocaine infusions have been confirmed with good quality evidence; these include decreases in pain scores, analgesic consumption, and side-effects with improvements in ERAS outcomes. We are also able to attest to the safety of i.v. lidocaine infusions for postoperative pain on standard surgical wards, provided a well-established APS protocol is followed.

Declaration of interest

None declared.

MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at [https://access.oxfordjournals.org](https://access.oxfordjournals.org) by subscribers to BJA Education.

Podcasts

This article has an associated podcast which can be accessed at [http://www.oxfordjournals.org/podcasts/bjaed_intravenous_lidocaine_vol_16_issue_9.mp3](http://www.oxfordjournals.org/podcasts/bjaed_intravenous_lidocaine_vol_16_issue_9.mp3).

References