Guest Editorial

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Perioperative intravenous lidocaine: Crossing local boundaries and reaching systemic horizons

Lidocaine is a widely used amide-type local anesthetic and Class 1b antiarrhythmic drug. In addition to its anesthetic and antiarrhythmic effects, lidocaine has important analgesic, antinociceptive, immuno-modulating, and anti-inflammatory properties.[1] Systemic lidocaine infusion has been used as an analgesic adjunct for the management of acute perioperative pain in many clinical settings.[2] Systemic lidocaine is also effective in obtunding the sympathetic response to laryngoscopy,[3] in reducing the pain of propofol injection,[4] prevention of postoperative airway complications[5] and also for the treatment of chronic neuropathic pain.[6]

The opioid sparing effect of lidocaine is supported by a high level of evidence.[7] This effect can be of great use particularly in obese patients with obstructive sleep apnea, where there is an increased risk of sedation and severe respiratory depression with opioid use. Enhanced Recovery After Surgery (ERAS) protocols recommend intravenous lidocaine as a component of opioid-sparing multimodal analgesia, particularly after major gastrointestinal surgery. In 2015, a Cochrane review was published, which included 45 trials, compared to the effect of continuous perioperative lidocaine infusion with epidural analgesia in adults undergoing general anesthesia. The results suggested that the lidocaine infusion was equally effective in the reduction of postoperative pain, expedited gastrointestinal recovery time, reduced postoperative nausea/vomiting, reduced opioid usage, and a reduction in hospital length of stay.[8]

Intravenous infusion of lidocaine has been shown to be as effective as epidural bupivacaine in reducing ileus duration, hospital stay, and pain after open colon resection.[9] Hence, in patients where perioperative epidural analgesia is contraindicated, intravenous infusion of lidocaine could also be considered as an alternative intervention to modulate the postoperative inflammatory responses.[10] ERAS guidelines for colorectal surgery also recommends the use of continuous infusion of intravenous lidocaine intraoperatively whenever thoracic epidural anesthesia is contraindicated. Under careful monitoring, it can be continued in the postoperative period also to provide analgesia.[11] On discontinuation after prolonged infusion, the plasma levels decrease rapidly [Figure 1].[12] 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.[12] It has been shown that intravenous lidocaine infusion causes a significant reduction in inflammatory mediators which has implications in not only the return of bowel function but also thrombosis, post-operative myocardial infarction, and sepsis.[13] Systemic administration of lidocaine tends to decrease interleukin-1 (IL-1), tumour necrosis factor-alpha (TNF-α), intercellular adhesion molecule-1 (ICAM-1), mucosal COX-2 (cyclooxygenase-2), and plasma

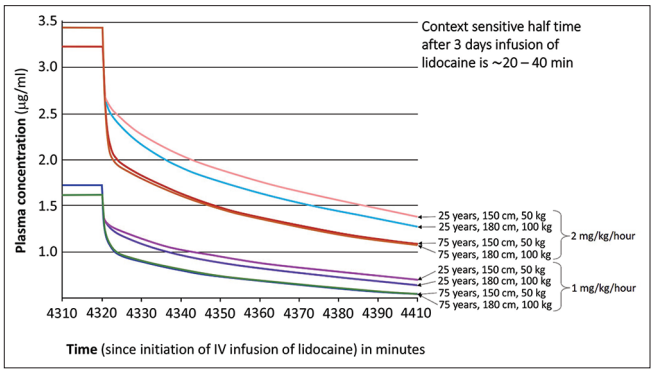

Figure 1: Pharmacokinetic profile of intravenous lidocaine (without a bolus) after discontinuation of infusion in 4 types of patients groups with two infusion rates of 2 mg/kg/hour and 1 mg/kg/hour. Age 25 years, Weight 50 kg, Height 150 cm. Age 25 years, Weight 100 kg, Height 180 cm. Age 75 years, Weight 50 kg, Height 150 cm. Age 75 years, Weight 100 kg, Height 180 cm

prostaglandin E2. *In vitro* studies have demonstrated the modulatory effect of lidocaine on potassium channels, calcium channels, G-coupled protein receptors, N -methyl-D-aspartate (NMDA) receptors, and the glycinergic system. Such mechanisms are thought to contribute to the anti-neuroinflammatory effects of lidocaine and may explain its clinical benefits in the management of acute and chronic pain.[14]

Pharmacokinetics: The aim of an intravenous lidocaine infusion is to achieve a therapeutic steady-state concentration while minimizing systemic toxicity. The usual dose recommended is a bolus of 100 mg before the incision and then 1-2 mg/kg/hour continuous infusion, which is the same as given to treat premature ventricular contractions. At this infusion rate, plasma concentration remains below 5.0 μ/mL, which is adequate for most of its clinical effects. Achieving and maintaining this level can be dependent on patient comorbidities, age, and other factors that should be considered on a patient-by-patient basis.[15] 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.[12] Lidocaine is metabolized in the liver by the cytochrome P450 system forming numerous key active metabolites, which are predominantly excreted by kidneys.

Safety and side effects: Lidocaine has a long-proven track record for safety as intravenous medication. Though it has been very well tolerated, it is important to check for any contraindications before starting the infusion [Table 1].[12] Very few minor symptoms like light-headedness, dizziness, tinnitus, or metallic taste were reported after intravenous use for pain control, and that also resolve soon after discontinuation of the infusion. Some practitioners report delayed emergence among patients receiving lidocaine infusion which could be attributed to the blunting of airway reactivity to the endotracheal tube.[16] Serious side effects, such as neurologic changes and cardiac toxicity, are exceedingly rare.

Table 1: Contraindications for lidocaine infusion

Sensitivity or allergy to lidocaine
Significant heart disease (2nd or 3rd Degree heart block)
Severe cardiac failure (Ejection fraction <20%)
History of Adams-Stokes, Wolff-Parkinson-White Syndrome or Active dysrhythmia
Concurrent treatment with Class I Antiarrhythmics or Amiodarone
Severe hepatic impairment (Bilirubin >1.46 mg/dl)
Severe renal impairment (<30 mL/min/1.73 m^2 or End-stage renal disease)
History of uncontrolled seizure
Acute porphyria

Khezr MB *et al*. have demonstrated that the use of intravenous lidocaine infusion during spinal anesthesia for cesarean section produced increased sedation.[17] Lidocaine is recommended only if there is a clear need and the benefit outweighs the risk. Lidocaine has been shown to cross the placenta by simple passive diffusion and can cause varying degrees of fetal and neonatal toxicity. After lidocaine administration, the maternal total plasma concentration will be higher as compared to the fetus, however, free lidocaine concentrations will remain the same in both mother and fetus.[18] This can lead to alterations of the central nervous system, peripheral vascular tone, and cardiac function in the fetus. Thus, fetal heart rate should be monitored continuously. This drug may also delay labor and lead to diminished muscle strength in the new-born for the first few days of life.[19]

To conclude, the growing interest in the ERAS concept has inspired the use of intravenous lidocaine for the management of perioperative pain. Defining the roles of intravenous lidocaine in various other clinical settings is necessary to maximize its clinical benefits such as anti-inflammatory, immune-modulating, and anti-cancer effects so that it can be safely applied to routine clinical practice.

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