

## Expanding your anaesthetic technique: an overview on the efficacy of using a lidocaine infusion as part of a balanced anaesthetic

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### Summary

This article is intended to provide a review of the use of lidocaine as part of a balanced anaesthetic technique. Lidocaine has many properties that make it useful as an adjunct to anaesthesia. It is used routinely at the University of Virginia and other centers in the US and Europe, and we have successfully used it in the management of neurosurgical cases in Africa.

In this review, we will discuss the clinical use of intraoperative intravenous lidocaine. Additionally, we will describe the method for its use and will identify potential situations where intravenous lidocaine may be of benefit to you in your anaesthetic practice.

Lidocaine is relatively inexpensive and safe to administer. We hope this review will educate you about the benefits of using lidocaine beyond its traditional role, and enable you to use lidocaine safely in your anaesthetic practice.

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### INTRODUCTION

Lidocaine (lignocaine) is an amide local anaesthetic. Local anaesthetics were first discovered in the 19th century when cocaine was isolated from cocoa leaves. Cocaine was used medically for the first time in 1884 as a topical anesthetic, and was used intrathecally for the first time in 1885. Lidocaine was subsequently developed in 1943. Lidocaine acts primarily via sodium channel blockade, but also has other actions, such as inhibition of G-protein receptors and NMDA receptors. It is metabolized primarily by the liver and is excreted by the kidneys in the form of active metabolites and unchanged drug. It has analgesic, anti-hyperalgesic and anti-inflammatory properties.<sup>1,2</sup>

Lidocaine was used initially in the management of arrhythmias. It subsequently was found to be effective as a topical anesthetic and in the administration of regional and neuraxial anesthesia. But lidocaine has utility beyond these uses and new applications are being studied around the world. Specifically, it can be used as an adjunct to general anesthesia when administered as an intravenous infusion. When used in this manner, it has been shown to reduce the minimum alveolar concentration (MAC) of volatile anesthetics. It can help reduce postoperative pain and opioid consumption in patients undergoing specific types of surgery. It also can help reduce postoperative ileus, in part due to its opioid sparing effects. Finally, the use of intra-operative lidocaine infusions can potentially lead to a reduction in thrombosis, cognitive dysfunction and airway irritability in certain populations of patients.

- Lidocaine infusions reduce minimum alveolar concentration (MAC) of volatile anesthetics
- Lidocaine infusions decrease postoperative pain, opioid consumption, and duration of ileus
- Lidocaine infusions may reduce postoperative risk of thrombosis, cognitive dysfunction and airway irritability in certain populations of patients

### BENEFITS OF INTRAVENOUS LIDOCAINE

#### Minimum alveolar concentration

General anaesthesia is usually performed with volatile anesthetics, often supplemented with intravenous opioids, and sometimes with regional anesthesia for the prevention and treatment of pain. Unfortunately, the use of volatile anesthetics is often associated with decreases in blood pressure, which can be particularly pronounced in hypovolemic patients or those with cardiac disease. Hence, approaches that would reduce the requirement for volatile anaesthetics would be helpful.

Intravenous lidocaine, when given as a bolus prior to the start of surgery followed by a continuous intravenous infusion, has been shown to reliably reduce the MAC of volatile anaesthetics. For example, one study demonstrated that the addition of intravenous lidocaine as an adjunct to anesthesia with nitrous oxide and halothane reduced MAC by 10-28 %.<sup>3</sup> We showed that intravenous lidocaine resulted in a 35% reduction in sevoflurane end-tidal concentration required to maintain hemodynamic stability. Animal studies have shown even greater reductions in MAC with the use of intravenous lidocaine.<sup>4</sup> Taken together, these studies indicate that the use of a lidocaine infusion intraoperatively probably reduces MAC by approximately 30%. This effect of intra-operative intravenous lidocaine infusions makes lidocaine useful for nearly all types of surgical procedures if the desired endpoint is a reduction in MAC. This may be particularly useful to avoid the undesired effects of specific anesthetic or to reduce cost when more expensive inhaled anesthetics are used.

- An intravenous lidocaine infusion during surgery can reduce the MAC of volatile anesthetics by approximately 30%

#### Postoperative pain, opioid consumption, and ileus

As anesthetists, one of our biggest challenges relates to the prevention and management of postoperative pain in our patients. While opioids are the mainstay of postoperative analgesia, their use can be associated

with a variety of adverse effects, including respiratory depression, sedation, and postoperative nausea and vomiting, ileus, and urinary retention. Furthermore, opioids have been shown to be tumor promoting and can potentially put the patient undergoing surgery for cancer resection at risk for cancer recurrence or metastasis. These side effects can be detrimental to the recovery of the patients we are intending to help and can significantly impact morbidity and mortality. Adjuvant medications can help to reduce the amount of opioids that our patients require.

The use of intravenous lidocaine infusions intraoperatively has been studied in a variety of surgeries including open and laparoscopic abdominal surgery, orthopedic surgery, cardiac surgery, head and neck surgery and ambulatory surgery. Analysis of these data shows a benefit of intravenous lidocaine infusions by reducing postoperative pain and opioid consumption, and reduction of ileus, in patients undergoing abdominal surgery.<sup>2,5</sup>

In a recent review article, McCarthy et al, reviewed 16 randomized controlled trials evaluating the use of perioperative intravenous lidocaine infusions for improving postoperative analgesia and enhancing recovery of bowel function. These trials involved 764 patients, 395 patients receiving intraoperative lidocaine and 369 control patients. Patients undergoing open and laparoscopic abdominal surgery were found to have significant reductions in postoperative pain intensity and opioid consumption. Specifically, pain scores were reduced at rest and with cough and movement up to 48 hours postoperatively. Additionally, opioid consumption was reduced by up to 85% in lidocaine-treated patients when compared to controls. Unfortunately these results were not consistent with all types of surgery. No such benefit was shown in patients undergoing tonsillectomy, total hip arthroplasty, or coronary artery bypass surgery.<sup>2</sup>

At this time, it is unclear why lidocaine was ineffective in the prevention of pain in all types of surgery; however, lidocaine has been shown to alleviate visceral pain in animal models by reducing visceromotor reflexes and evoked and spontaneous activity of neurons excited by colorectal distention.<sup>6</sup> This may explain why lidocaine infusions are more effective at reducing pain in patients undergoing abdominal surgery.

In addition to improvement in postoperative pain and a reduction in postoperative opioid consumption, studies have also shown that intraoperative lidocaine infusions have led to a reduction in postoperative ileus.<sup>2,5,7</sup> In the analysis mentioned above, lidocaine infusions resulted in an earlier return of bowel function, with first flatus occurring up to 23 hours earlier and first bowel movement occurring up to 28 hours earlier.<sup>2</sup> Postoperative ileus has many potential complications. It can lead to nausea, vomiting, increased pain and a prolonged hospital stay. It can also lead to a delay in the time to oral intake, which is vital to the recovery of patients who have undergone surgery.

This beneficial effect of intravenous lidocaine on ileus can be partially explained by the reduction in opioid requirements in patients undergoing surgery. Opioids are known to cause ileus, prolonging intestinal transit time. Additionally, lidocaine has been shown to have a direct excitatory effect on intestinal smooth muscle. Lidocaine

prevents several nerve reflexes that are activated upon entering the parietal peritoneum, which leads to inhibition of the gut. Lidocaine has also been shown to block the sympathetic innervation of the bowel leading to increased parasympathetic tone, which promotes gut motility.<sup>8</sup>

- Intravenous lidocaine infusions have been shown to reduce postoperative pain and opioid consumption in patients undergoing abdominal surgery
- Intravenous lidocaine infusions have not been shown to decrease postoperative pain and opioid consumption in patients undergoing head and neck surgery, orthopedic surgery or cardiac surgery
- Intravenous lidocaine infusions can lead to a reduction in ileus postoperatively, specifically in patients undergoing abdominal surgery

### Other potential benefits of IV lidocaine

Aside from the benefits of MAC reduction, decreased postoperative pain, decreased opioid need postoperatively, and quicker recovery of bowel function, intravenous lidocaine infusions have other potential benefits for your patient. These include a reduced risk of developing thrombosis (blood clots), cognitive impairment, and airway irritability.

It has been found that epidural administration of local anesthetics reduces the risk of developing venous thrombosis postoperatively.<sup>9</sup> While this effect is multifactorial, the risk of developing thrombosis is partially reduced by systemic administration of local anesthetics. This is likely due to the fact that local anesthetics, like lidocaine, have a profound anti-inflammatory effect.<sup>10</sup> Intravenous lidocaine has been shown to be highly effective in preventing thrombosis after orthopedic surgery.<sup>11</sup> While lidocaine infusions can help prevent the development of thrombosis, they do not increase the risk of bleeding. Therefore, they are safe to use intraoperatively because they reduce your risk of developing a blood clot without increasing your risk of bleeding after surgery.

Animal studies have demonstrated that lidocaine has neuroprotective properties.<sup>12</sup> Lidocaine has been found to attenuate cognitive dysfunction in rats receiving general anesthesia with isoflurane.<sup>13</sup> Likewise, lidocaine infusions can reduce postoperative opioid requirements.<sup>2,7</sup> Opioids can increase the risk of postoperative cognitive dysfunction, especially in elderly patients.<sup>14</sup> Additionally lidocaine has been found to reduce postoperative pain in patients undergoing abdominal surgery.<sup>2,5,7</sup> Pain is also a risk factor for postoperative cognitive dysfunction. Therefore, it is hypothesized intravenous lidocaine infusions can reduce the risk of postoperative cognitive dysfunction in patients, potentially due to its neuroprotective effects, opioid sparing properties and impact on pain reduction.

Lidocaine has been found to be a potent inhibitor of the cough reflex.<sup>15</sup> Studies have demonstrated that intravenous lidocaine can decrease reflex bronchoconstriction in asthmatics.<sup>16,17</sup> This is likely secondary to neural blockade of vagal reflex pathways. Smokers are

also prone to reflex bronchoconstriction. Endotracheal intubation can be especially stimulating to **asthmatics** and to **smokers** placing both populations of patients at risk of airway hyperactivity. At UVA we routinely use intravenous lidocaine infusions to help **mitigate** airway hyperactivity in both **asthmatics** and **smokers**.

- Intravenous lidocaine infusions may reduce the risk of developing a blood clot
- Intravenous lidocaine may infusions reduce the risk of postoperative cognitive dysfunction
- Intravenous lidocaine infusions may reduce airway hyperactivity in smokers and asthmatics

### WHEN SHOULD YOU CONSIDER USING INTRAVENOUS LIDOCAINE?

So far, much has been said about the benefits of using an intravenous lidocaine infusion as an adjunct to general anaesthesia. We have seen that intravenous lidocaine infusions can reduce MAC of Halothane by 30%. They can reduce postoperative pain, opioid consumption and ileus in patients undergoing open or laparoscopic abdominal surgery. They can probably reduce the risk of thrombus formation in nearly all patients due their anti-inflammatory effects. Additionally they may reduce the risk of developing postoperative cognitive dysfunction and they may reduce airway hyperactivity in certain patients such as smokers and asthmatics.

Thus, intravenous lidocaine infusions can have measureable benefit. Given these benefits, when might you consider using one to supplement your anaesthetic?

In our practice, we **typically use** an intravenous lidocaine infusion as an adjunct to anaesthesia in patients undergoing **all open and laparoscopic abdominal** surgeries who do **not** have an **epidural**. Often, an epidural is not used due to the preference of the surgeon or patient factors that make an epidural contraindicated, like coagulopathy, systemic infection, or patient refusal.

We also use intravenous lidocaine infusions in cases where we want to limit the amount of volatile anaesthetics we are providing or in cases where we are providing total intravenous anaesthesia and we would like to limit the amount of propofol or opioid that we are administering. Situations where you might want to **limit** the amount of **volatile anaesthetics** include patients with a **cardiomyopathy**, or patients who may **not tolerate** a **reduction** in systemic vascular resistance caused by volatile anaesthetics, such as those with severe **peripheral vascular disease** or **cerebral ischemia**. Additionally, by limiting the amount of volatile anaesthetic required, the use of lidocaine may help reduce the cost of safely providing anaesthesia.

### HOW TO USE INTRAVENOUS LIDOCAINE IN YOUR PRACTICE

Typically, a **lidocaine infusion that provides 30-40mcg.kg<sup>-1</sup>.min<sup>-1</sup> or 1.8-2.4mg.kg<sup>-1</sup>.h<sup>-1</sup>** is necessary to reach a serum lidocaine concentration necessary to benefit the patient. As a general rule of thumb, providing an **infusion of 3mg.min<sup>-1</sup>** in patients weighing **more than 80kg** and **2mg.min<sup>-1</sup>** in patients between **50-80kg** is appropriate. Often, it is beneficial to provide a **1-2mg.kg<sup>-1</sup> bolus**

**prior** to initiating the infusion. Generally, we run the infusion from the **onset** of anaesthesia, **prior** to surgical **incision**, until the **end** of the **procedure**. The infusion can be administered **postoperatively** (for example in the recovery room), but should **only** be done so under **close supervision**.

At our institution we have **premixed** lidocaine infusion bags, which contain **8% lidocaine**. Every milliliter (ml) in these bags contains 80mg of lidocaine. It may be difficult for you to obtain premixed lidocaine infusion bags; however, you can make one with the resources available to you.

For instance, if you have **lidocaine 2%** available at your institution then you can mix **30ml of lidocaine** with **70ml of normal saline** to give you a solution containing **6mg.ml<sup>-1</sup>**. If your patient is 85kg and you would like to run an infusion at 3mg.min<sup>-1</sup> then you would run your infusion at **0.5ml.min<sup>-1</sup>** or **30ml.h<sup>-1</sup>**. This mixture would provide you with a little over **3 hours of intravenous lidocaine**.

If you only have lidocaine 1% at your institution and you want to use a 1 liter bag then you would mix 100ml of lidocaine 1% with 900ml of normal saline to give you a solution containing 1mg.ml<sup>-1</sup> of lidocaine. If your patient is 65kg and you would like to run an infusion at 2mg.min<sup>-1</sup> then you would run your infusion at 2ml.min<sup>-1</sup> or 120ml.h<sup>-1</sup>. This mixture would provide you with over 8 hours of intravenous lidocaine.

Making a lidocaine infusion is easy and relatively **inexpensive** compared to many of the drugs that we use in anaesthesia. It is important however to know the concentration of lidocaine that you are working with and the amount of medication that you are delivering. This is important because there is a risk of developing local anesthetic toxicity if you make the solution improperly or deliver it inappropriately.

It is important to remember that the **toxic dose of lidocaine is considered to be 4.5mg.kg<sup>-1</sup>** and this should not be exceeded in a single dose due to the risk of local anesthetic toxicity. We do not advocate for the use of a lidocaine infusion in patients weighing less than 50kg due to the risk of local anesthetic toxicity. Signs of local anesthetic toxicity include **slurred speech, peri-oral numbness, a metallic taste in the mouth**, seizures and eventually cardiovascular collapse. This can be difficult to identify in patients under general anaesthesia and often it is not recognized until more serious consequences are realized.

It is unlikely that your patients will have local anaesthetic toxicity if you use the doses that we have recommended. However, if local anesthetic toxicity is suspected, discontinue the lidocaine infusion immediately. Notify the surgeon and perform advanced cardiac life support paying special attention to the airway, breathing and circulation. Maintain oxygenation, ventilation and support the blood pressure. Provide chest compressions if necessary. Seizures can be treated with benzodiazepines, barbiturates or even propofol. In addition to advanced cardiac life support, **Intralipid 20%** has been shown to help in situations where severe lidocaine toxicity, suggested by seizures and cardiovascular collapse, is suspected. If you have **Intralipid 20%**, a **bolus of 1.5ml.kg<sup>-1</sup>** is recommended **followed by an infusion of 0.25-0.5ml.kg<sup>-1</sup>.min<sup>-1</sup> for 60 minutes**. Further information can be found about the use of Intralipid at **LipidRescue.org**.

- In patients >80kg we recommend a lidocaine infusion of 3mg.min<sup>-1</sup>
- In patients 50-80kg we recommend a lidocaine infusion of 2mg.min<sup>-1</sup>
- For safety reasons do not use a lidocaine infusion in patients under 50kg
- Prior to the start of the infusion we recommend an intravenous bolus of lidocaine of 1.5-2mg.kg<sup>-1</sup>
- Start the infusion immediately after the start of anesthesia before the surgical incision
- Discontinue the infusion at the end of the procedure
- While a lidocaine infusion will help reduce postoperative pain and opioid consumption, you should still administer opioids for pain

## CONCLUSION

When used appropriately, intravenous lidocaine infusions have been shown to be beneficial to patients undergoing general anaesthesia for surgery. The use of an intravenous lidocaine infusion can be used to reduce the MAC of volatile anaesthetics in an effort to reduce the amount of volatile anaesthesia administered. An intravenous lidocaine infusion can also be used in patients undergoing abdominal surgery to reduce postoperative pain, opioid consumption and ileus in patients who do not have an epidural. Lidocaine infusions may additionally reduce the risk of developing a thrombus, postoperative cognitive dysfunction or airway hyperactivity.

We routinely use lidocaine infusions at our institution to supplement general anaesthesia. We hope that this review has provided you with the knowledge and tools to be able to use intravenous lidocaine infusions in your practice.

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