Journal of Anaesthesia and Pain, 2022, Volume: 3, No.2: 26-30
https://jap.ub.ac.id

P-ISSN : 2722-3167
E-ISSN : 2722-3205

Review Article

Perioperative Application of 2% Lidocaine

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SUMMARY

Perioperative intravenous lidocaine (IVL) can help minimize opioid-related side effects that impede the postoperative recovery process. Neurological side effects were averaged at an 8 mg/kg dose, and cardiotoxicity side effects were reported at plasma values greater than 21 g/ml. Approximately 90% of lidocaine is converted to monoethylglycinexylidide (MEGX) in the liver via oxidative demethylation (dealkylation). Analysis of MEGX concentrations after lidocaine administration can be a method used to evaluate liver function. Perioperative intravenous lidocaine lowers discomfort, nausea, the duration of ileus, the need for opioids, and the length of time spent in the hospital after surgery. During injection, low blood concentrations can result in these symptoms, which may last for several hours or days after termination. Postoperative problems, such as pain and organ failure, can be caused by anti-inflammatory and pro-inflammatory components. Analgesic, anti-inflammatory, and anti-hyperalgesic are just some of the other effects of lidocaine. It also decreases the volume of the airways and the rate of breathing, prolongs the duration of exhalation, reduces the respiratory rate and tidal volume, also causes vasoconstriction at low concentrations and vasodilation at high concentrations. In clinical applications, lidocaine can prevent propofol injection pain, improve postoperative recovery, and play a role in various surgical procedures. Perioperative IVL application is proven to provide more benefits in various surgeries compared to other available anesthetic options. Very few studies have systematically analyzed the occurrence of side effects, and the quality of evidence is low.

Keywords: application , IVL, lidocaine, perioperative, anesthesia

Received: February 2022, **Revised**: April 2022, **Published**: May 2022
How to cite this article: FH Dewi, A Nugroho, FA Muttaqin. Perioperative application of 2% lidocaine. *Journal of Anaesthesia and Pain*. 2022:3(2): 26-30. doi:10.21776/ub.jap.2021.003.02.01

INTRODUCTION

First produced in 1943 and licensed for human use in Sweden in 1948, Lidocaine is a local anesthetic.[1] A growing body of evidence suggested that intravenous neuropathic blocking could alleviate the symptoms of peripheral neuropathy, hyperalgesia, and complex regional pain syndromes. Lidocaine is the only intravenous local anesthetic approved by the Food and Drug Administration (FDA). Lidocaine is one of the most commonly utilized medicines to reduce opioids and achieve opioid-free anesthesia.[2] IVL can reduce the side effects of using opioids that can hinder postoperative recovery.[3]

DISCUSSION

Pharmacokinetics

Traditional investigations of lidocaine's pharmacokinetic qualities have been based on IVL as an antiarrhythmic medication. Lidocaine plasma values of 1.4 g/ml to 6.0 g/ml are thought to be effective and safe for anesthesia. A lidocaine dose of 8 mg/kg, which corresponds to a plasma concentration of 15 g/ml, was found to increase the risk of seizures. Cardiotoxicity was identified as a side effect at more than 21 g/ml plasma values. [4,5]

Lidocaine's plasma concentration dropped by two following intravenous delivery, demonstrating that it is distributed to several organs in a compartmentalized fashion. As blood circulates through various organs in the body, it moves from the vascular compartment to the peripheral tissues (heart, lung, liver, and spleen) (muscle and adipose tissue). [4,6]

After intravenous administration, lidocaine builds up in the pancreas, pituitary, thyroid, and adrenal medulla cells. Lidocaine is primarily metabolized in the liver. About 90% of lidocaine is oxidatively deethylated (dealkylation) in the liver became monoethylglycinexylidide, which is then further deethylated to glycinexylidide. Once hydrolyzed to xylidine, the major metabolic waste in urine, it is then oxidized to 4-hydroxy-xylidine. [3,4] When the drug concentration was 10 g/ml, the plasma concentration of protein-bound lidocaine was 40%, and when the drug concentration was 3 g/ml, it was 90%. At any given lidocaine concentration, binding fractions are determined by postoperative alpha-1-acid glycoprotein (AAG) plasma levels. 1.0-1.5 mg/kg intravenous bolus loading is recommended,

followed by 50 g/kg/minute (3.0 mg/kg) for the first hour. For the second hour 25 g/kg/minute (1.5 mg/kg) is recommended, and 12 g/kg/minute (0.75 mg/kg) for the third hour until 22 hours. The dose decrease to 0.6 g/kg/minute (0.35 mg/kg) for 24 to 48-hour period of. [4,7]

Pharmacodynamics

Intravenous lidocaine can relieve pain and nausea during surgery, and shorten the treatment duration. Compared to placebo, IVL reduced 24-hour opioid intake by 10 mg morphine equivalent, which correlated with superior recovery scores. Using intravenous perioperative fluids (IVL) reduced postoperative ileus (average of eight hours), nausea and vomiting (PONV) (ten to twenty percent) and shortened hospital stays by eight hours and up to eight twenty-four hours. Low blood concentrations during infusion can result in these symptoms, which may last for several hours or days after termination. Because lidocaine remains long after the medication has been metabolized to non-biologically active amounts, this mechanism happens.[3,4]

Sodium channel blocking is unlikely to be the mechanism here; as usual, blood levels block during perioperative only a small percentage of neuronal sodium channels, plus polymorphonuclear granulocytes (PMNs) do not express sodium. Systemically block excitatory responses in spinal cord-wide neurons via a mechanism that may involve strychnine-sensitive glycine receptors. [3,4]

Clinical Application

IVL has several advantages in its application as perioperative management. This study will discuss some of the clinical applications of 2% lidocaine.

1. *Preventing the pain of propofol injections*
   To induce anesthesia, propofol is utilized. Despite this, one of propofol's drawbacks is the excruciating pain it causes when it is administered. In adults, 37.9 percent of patients reported having high-intensity pain, and in children, 15.6 percent. Prostaglandin E2 and bradykinin, which release mediators that excite afferent nerve terminals, might produce pain immediately after a propofol injection, but they can also cause pain later. [8]
   When propofol is injected, the mechanism of lidocaine's pain-blocking impact on blood vessels is still a mystery. It is also a weak solution of free base cations. In combination with propofol, it could lower the pH. [3]

2. *Improve post-surgery recovery*
   IVL helps to alleviate pain in the first 24 hour post surgery. Abdominal surgery was the area where the greatest impact was felt. Opioid use is related to reduced pain as well. A decrease of hospital treatment duration, postoperative nausea at baseline and >24 h, and the need for opioids during surgery and in the postoperative period were all observed secondary outcomes. Postoperative ileus was less common (RR = 0.37) because of the reduction in this risk. Moreover, the risk of nausea without vomiting was decreased (RR = 0.72). [9,10]

3. *Abdominal surgery*
   For open surgery or abdominal laparoscopy, intravenous lidocaine of 1.5 to 3 mg/kg/hour after a bolus of 0 to 1.5 mg/kg reduces the visual analog scale (VAS). Twenty-four hours after surgery, VAS values fell at rest and while engaging in physical activity. Open abdominal surgery had a VAS reduction of 0.7 and laparoscopic surgery a reduction of 1.1.[11]
   In the first 72 hours following abdominal surgery, the morphine intake of 40 patients was reduced by 35%. 1.6 points reduced the VAS, and morphine consumption was reduced by 30% in the first four hours following surgery as a result of this reduction in opioid use. [11]
   Reduced postoperative pain, opiate use, and opiate-related side effects were all observed following laparoscopic removal of a patient's cholecyst (PONV, ileus, and pruritus). Results on pain intensity, postoperative opiate needs, and the average hospital stay were significant in intra-abdominal prostatectomy. Excessive postoperative opiate use and length of stay were reduced following a nephrectomy if 1.5 mg/kg IVL administration followed by an 1 mg/kg/hour intraoperative infusion and 24 hours post-operatively. [3]

4. *Genitourinary surgery*
   IVL lowered pain intensity by two-thirds and decreased narcotic usage in the post anesthesia care unit (PACU) by 50% in radical retropubic prostatectomy. IVL improves the two minute walking test in laparoscopic prostate surgery. One day was shaved off the stay because the first flatus occurred 33% earlier than expected. IVL does not affect the outcome of laparoscopic kidney surgery. [4]

5. *Obstetric and gynecological surgery*
   When compared to a control group, elective cesarean sections undergoing perioperative IVL had higher pulse and blood pressure. However it has lower plasma cortisol. Neonatal APGAR ratings did not differ across groups. To summarize, IVL is a safe and effective in reducing postoperative stress in women after cesarean birth surgery. [4]

6. *Breast surgery*
   In the first 72 hours following breast surgery, intravenous morphine lowers discomfort. 3-6 months following surgery, they have a decreased chance of developing persistent pain. [4]

7. *Outpatient surgery*
   In patients undergoing outpatient procedures, perioperative intravenous lidocaine reduces PACU pain scores and the need for opioids, but not in PONV and patients discharge. [4]

8. *Cardiothoracic surgery*
   Up to 48 hours after coronary artery bypass, a bolus of 1.5 mg/kg and then 30 g/kg/min infusion made no meaningful difference in postoperative pain. Lidocaine was not used in the bypass pump's volume, and it is possible that an effective dose was not attained in this trial. Postoperative cognitive impairment was lessened but not eliminated. Using IVL in thoracic surgery minimizes the need for pain medication and opiate use after the procedure. [4,12]

9. *Pelvic surgery*
   During pelvic surgery, there is no difference in pain intensity or morphine intake after 24 or 48 hours in

patients who had total hip arthroplasty with IVL at a 1.5 mg/minute dose. Compared to less invasive treatments, post-abdominal surgery had greater inflammatory mediators in the blood. As a result of IVL's ineffectiveness poor, the total hip arthroplasty process, which is minimally invasive, this phenomena can be explained. [4,13]

10. *Spine surgery*
Postoperative fentanyl usage and pain intensity were reduced, while the quality of recovery was improved. [3,14]

11. *Neurosurgery*
IVL reduces pain intensity with limited duration. IVL 1.5 mg/kg regulate blood and intracranial pressure elevation in the same amount as a bolus injection of 1.5 mg/kg esmolol for neurosurgical patients. [3,15]

12. *Thyroid surgery*
Pain and postoperative opiate use decreased after thyroid surgery, and C-reactive protein levels dropped. In the first four hours after surgery, the effects are minimal. [3]

13. *Health-related advantages*
Other intraoperative pharmacodynamic effects of IVL can be seen. IVL can decrease the cerebral hemodynamic response to airway manipulation. A 1.5-2 mg/kg IVL injection, 2-3 minutes before laryngoscopy can reduce systolic catecholamine, blood pressure, mean arterial pressure, and heart rate during intubation and extubation. To the same amount as sevoflurane and propofol. In adult patients, IVL minimizes the need for hypnotic medications during anesthesia by up to one-third. Additionally, the use of intraoperative opiates was reduced by up to 50%. As the dose of IVL increases, it consistently lowers the bispectral index (a measure of anesthetic depth). [3]

Table 1. Available evidences of the use of lidocaine [4]

Surgery	References	Bolus	Infusion	Time administration	Outcome	Evidence
Ambulatory	McKay et al., 2009	1.5 mg/kg	2 mg/kg/h	Before induction to end surgery	Decreased pain PACU, faster discharge	Moderate: small benefit, a limited number of studies
	De Oliveira et al., 2012	1.5 mg/kg	2 mg/kg/h	Before induction to end surgery		
Multilevel spine	Farag et al., 2013	No bolus	2 mg/kg/h			Moderate: small benefit, a limited number of studies
Cardiac	Insler et al. 1995	1.5 mg/kg	30 mg/kg/h	After induction to 48 h in ICU	No effect on pain scores or opioid consumption	No support from a limited number of studies
	Wang et al., 2002	1.5 mg/kg bolus and 4 mg/kg to CPB priming solution	4 mg/min	Opening of the pericardium to end surgery	Decreased PO cognitive dysfunction	
	Mathew et al. 2009	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 et al., 2012	1.5 mg/kg	2 mg/kg/h then 1.3 mg/kg/h PO	Induction to 24 h PO	None	No support from a single small study
Abdominal hysterectomy	Bryson et al., 2010	1.5 mg/kg	3 mg/kg/h	Before induction to skin closure	None	No support from two small studies
	Grady et al. 2012	1.5 mg/kg	2 mg/kg/h	Induction to 24 h PO		
Hip arthroplasty	Martin et al. 2008	1.5 mg/kg	1.5 mg/kg/h	30 min before incision to 1 h PO		No support from a single small study
Thoracic	Cui et al., 2010	No bolus	33 mg/kg/h	Induction to skin closure	Decreased pain and opioid consumption	Moderate: small benefit in one study

Breast	Terkawi et al. 2014 and 2015	1.5 mg/kg	2 mg/kg/h	Induction to 2 h after surgery	Decreased incidence of chronic pain at 3 and 6 months	Moderate: small benefit, a limited number of studies
	Choi et al. 2012	1.5 mg/kg	1.5 mg/kg/h	30 min before incision to skin closure	No effect on pain scores, opioid consumption, or PONV	
	Grigoras et al. 2012	1.5 mg/kg	1.5 mg/kg/h	Before induction to 60 min after skin closure		
Prostate	Lauwick et al., 2009	1.5 mg/kg	2 mg/kg/h	Induction to end surgery	Decreased pain, opioid consumption, ileus duration, and length of hospital stay	Moderate: small benefit, a limited number of studies
	Groudine et al. 1998	1.5 mg/kg	1.5 mg/kg/h	Before induction to 60 min after skin closure		
Laparoscopic abdominal	Colectomy Kaba et al. 2007	1.5 mg/kg	2 mg/kg/h during surgery, 1.33 mg/kg/h PO	Induction to 24 h PO	Decreased pain scores and opioid consumption; duration of ileus	Strong: benefit was shown in multiple studies or meta-analyses
	Wongyingsinn et al., 2011	1.5 mg/kg	2 mg/kg/h during surgery, 1 mg/kg/h PO	Before induction to 48 h PO		
	Tikuišis et al., 2014	1.5 mg/kg	2 mg/kg/h during surgery, 1 mg/kg/h PO	Before induction to 24 h PO		
	Cholecystectomy Lauwick et al., 2008	1.5 mg/kg	2 mg/kg/h	Induction to end surgery		
	Saadawy et al., 2010	2 mg/kg	2 mg/kg/h	Before induction to end surgery		
	Gastrectomy Kim et al., 2013	1.5 mg/kg	2 mg/kg/h	Preoperative to end surgery		
	De Oliveira et al., 2014	1.5 mg/kg	2 mg/kg/h	Before induction to end surgery		
	Appendectomy Kim et al., 2011	1.5 mg/kg	2 mg/kg/h	Two minutes before induction to end surgery		
Open abdominal	Colorectal Kuo et al., 2006	2 mg/kg	3 mg/kg/h	30 min before ending surgery	Decreased pain scores and opioid consumption; decreased nausea, duration of ileus, and length of hospitalization	Strong: benefit was shown in multiple studies or meta-analyses
	Herroeder et al. 2007	1.5 mg/kg	2 mg/min	Before induction to 4 h PO		

Swenson et al., 2010	No bolus	1-3 mg/min	Before induction to return of bowel function
Abdominal Koppert et al., 2004	1.5 mg/kg	5 mg/kg/h	30 min before incision to 1 h PO
Baral et al. 2010	1.5 mg/kg	1.5 mg/kg/h	30 min before incision to 1 h PO

PACU: Post-anesthesia care unit; PO: Peroral; ICU: Intensive care unit

SUMMARY

Perioperative IVL application is proven to provide more benefits in various surgeries compared to other available anesthetic options. Very few studies have systematically analyzed the occurrence of side effects, and the quality of evidence is low. In conclusion, no significant side effects of perioperative systemic lidocaine concerning the general administration protocol.

ACKNOWLEDGMENT

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CONFLICT OF INTEREST

None

REFERENCES

1. Weinberg L, Peake B, Tan C, Nikfarjam M. Pharmacokinetics and pharmacodynamics of lignocaine: A review. *World J Anesthesiol*. 2015;4(2):17-29.
2. Yang X, Wei X, Mu Y, Li Q, Liu J. A review of the mechanism of the central analgesic effect of lidocaine. *Medicine*. 2020;99(17).
3. Beaussier M, Delbos A, Maurice-Szamburski A, Ecoffey C, Mercadal L. Perioperative use of intravenous lidocaine. *Drugs*. 2018;78(12):1229-1246.
4. Dunn LK, Durieux ME. Perioperative use of intravenous lidocaine. *Anesthesiology*. 2017;126(4):729-737.
5. Chrousos GP, Katzung B, Trevor A. *Basic and clinical pharmacology*. Adrenocorticosteroids Adrenocortical Antagon 13th ed; McGraw-Hill Med New York, NY, USA. Published online 2015.
6. Hashemian AM, Zamani Moghadam Doloo H, Saadatfar M, et al. Effects of intravenous administration of fentanyl and lidocaine on hemodynamic responses following endotracheal intubation. *Am J Emerg Med*. 2018;36(2):197-201. doi:10.1016/j.ajem.2017.07.069
7. Kurabe M, Furue H, Kohno T. Intravenous administration of lidocaine directly acts on spinal dorsal horn and produces analgesic effect: An in vivo patch-clamp analysis. *Sci Rep*. 2016;6:26253. doi:10.1038/srep26253
8. Euasobhon P, Dej-arkom S, Siriussawakul A, et al. Lidocaine for reducing propofol-induced pain on induction of anaesthesia in adults. *Cochrane Database Syst Rev*. 2016;(2): CD007874
9. Kranke P, Jokinen J, Pace NL, et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane database Syst Rev*. 2015;(7):CD009642. doi:10.1002/14651858.CD009642.pub2
10. Weibel S, Jokinen J, Pace NL, et al. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *Br J Anaesth*. 2016;116(6):770-783. doi:10.1093/bja/aew101
11. 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(11):1183-1194. doi:10.1097/DCR.0b013e318259bcd8
12. Wood KB, Li W, Lebl DR, Ploumis A. Management of thoracolumbar spine fractures. *Spine J*. 2014;14(1):145-164. doi:10.1016/j.spinee.2012.10.041
13. Li WX, Luo RY, Chen C, et al. Effects of propofol, dexmedetomidine, and midazolam on postoperative cognitive dysfunction in elderly patients: A randomized controlled preliminary trial. *Chin Med J (Engl)*. 2019;132(4):437-445. doi:10.1097/CM9.0000000000000098
14. Bizimungu R, Alvarez S, Baumann BM, et al. Thoracic Spine Fracture in the Panscan Era. *Ann Emerg Med*. 2020;76(2):143-148. doi:10.1016/j.annemergmed.2019.11.017
15. Wick JB, Sivaganesan A, Chotai S, et al. Is there a preoperative morphine equianalgesic dose that predicts ability to achieve a clinically meaningful improvement following spine surgery?. *Neurosurgery*. 2018;83(2):245-251.