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The role of lidocaine in perioperative pain and recovery management

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ABSTRACT

Pain control is crucial in surgical patients, being an essential part of enhanced recovery after surgery protocols. Lidocaine, an amide local anesthetic, was primarily used as an antiarrhythmic. It has analgesic, antihyperalgesic and anti-inflammatory effects, with various actions on cardiovascular, respiratory, and digestive systems. Lidocaine has been shown to also have antithrombotic, antimicrobial, and antitumoral effects. Numerous studies have reported its safe profile and role in managing perioperative pain after breast cancer, abdominal, genitourinary, gynecologic, obstetric, orthopedic, cardiothoracic, spine, thyroid, and upper airway surgery. Lidocaine, as part of multimodal analgesia, also shows promising results in ambulatory surgery. Therefore, the use of intravenous lidocaine in the perioperative period is mainly associated with better pain control, reduced opioid use, diminished incidence of postoperative nausea, vomiting, and ileus, and exhibits antithrombotic effects.

Keywords: surgery, acute pain, intravenous lidocaine, lidocaine`s sides effects

INTRODUCTION

Proper pain control during the perioperative period is a major cornerstone in surgical patients' management, being a part of enhanced recovery after surgery protocols [1]. In order to obtain that, various studies have shown that lidocaine infusion has a safe profile, and it is useful in pain control and opioid decrease in the perioperative period [2].

Besides pain control, due to its numerous pharmacological effects, lidocaine, as a short-acting amide local anesthetic, can prevent the occurrence of various complications in the postoperative period [3,4]. Over time, perioperative lidocaine administration has demonstrated its effectiveness in enhancing the recovery after surgery and reducing the complication rate. It also has an important role in controlling postoperative pain, shortening the hospital stay, and therefore the costs of medical care, and appears to increase surgical patient satisfaction and comfort after surgery [5,6].

KEY PHARMACOLOGICAL PROPERTIES OF LIDOCAINE

The molecular effect of lidocaine depends on its concentration [7]. Its effects are manifested through

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sodium and potassium channel blocking [8], interaction with acetylcholine receptor, 5-hydroxytryptamine (5HT-3 receptor) [9], blockage of calcium channels, and N-methyl-D-aspartate receptor [7]. It is an amide local anesthetic and was first used as an antiarrhythmic drug [10]. The beneficial effects of lidocaine in the perioperative period are obtained through intravenous infusion, which mimics the effects acquired when it is administered at the epidural level [11].

A. Analgesic and antihyperalgesic effects

The exact mechanism of lidocaine pain control during the perioperative period is not fully understood, and it seems to extend above sodium channel blocking [7]. Studies have shown the peripheral and central analgesic effects of lidocaine and its ability to suppress hyperalgesia [12-14].

B. Anti-inflammatory effects

Being an amide local anesthetic, at the injury site, lidocaine has the ability to suppress the activation and adhesion of leukocytes [15], inhibits the release of superoxide anions and interleukin 1 (IL-1) through neutrophils priming blocking [16,17], reduce neutrophil adhesion, endothelial hyperpermeability and therefore, the endothelial fluid leakage [18,19].

C. Cardiovascular effects

Lidocaine is used as an antiarrhythmic agent [10]. In doses used for an analgesic purpose, it has a minor cardiac effect, slightly decreasing the heart rate [20].

D. Respiratory effects

It is a weak respiratory depressant, with a peak effect of moderate magnitude at 2.5-3 minutes after bolus infusion [21]. Doses of 1-2 mg/kg of lidocaine are effective in laryngospasm prevention in case of general anesthesia and reduce the risk of fentanyl-induced cough appearance [22,23].

E. Digestive tract effects

Over time, intravenous lidocaine has shown an important role in favoring the resolution of postoperative ileus [24].

F. Antithrombotic, antimicrobial, and antitumoral effects

Like any local anesthetic, lidocaine inhibits platelet aggregation [25]. It also has some antimicrobial [26] and antitumoral properties [27].

MAJOR SIDE EFFECTS OF LIDOCAINE

Lidocaine, as a local anesthetic, which acts through blocking sodium and potassium channels, is associated with the potential risk of inducing so-called LAST (local anesthetic systemic toxicity). The main clinical manifestations in the case of LAST development are presented in Figure 1 [28-30]. It is considered that it is a molecule with greater safety margins and that neurological side effects are seen at doses of 8 mg/kg (plasma value of 15 µg/mL) and cardiac toxicity develops at plasma values > 21 µg/mL [10, 31].

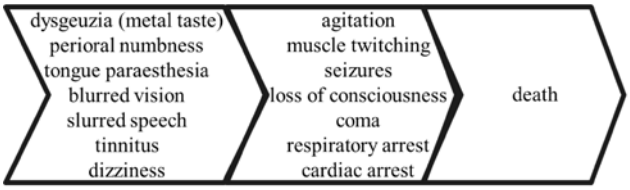

FIGURE 1. *Local Anesthetic Systemic Toxicity*

WEBEIL ET AL. *showed in a systemic review that the administration of intravenous lidocaine to control perioperative pain is not associated with major adverse events [32].*

PERIOPERATIVE USE OF LIDOCAINE

The main beneficial effects of intravenous lidocaine use in surgical patients are pain control, opioid consumption reduction, the reduction in postoperative nausea, vomiting, and postoperative ileus incidence [33-35]. It appears that using lidocaine, as part of multimodal analgesia control, leads to a reduction in hospital stay length [36].

Currently recommended dosage targets the administration of an initial bolus of 1,5-2 mg/kg 10 minutes prior to anesthesia induction, followed by the infusion of 1,5-2 mg/kg/hr for 24 hours in the postoperative period [28,37].

A. Breast surgery

It is well known that high-risk operations, like breast cancer surgery, can lead to chronic postoperative pain development in 10% of cases, further decreasing the life of this subgroup of patients [38]. Grigoras et al. reported that the perioperative use of intravenous lidocaine has a safe profile and decreases the incidence of chronic or persistent postsurgical pain (PPSP) [39]. Another trial, including 148 patients, showed that perioperative lidocaine infusion for patients with mastectomy is associated with decreased incidence of postoperative pain at 3 and 6 months follow-ups [40].

A meta-analysis written by Chang et al. presented that the intravenous lidocaine use in patients undergoing breast surgery is not associated with acute pain control in the first 3 days after surgery, but with the reduction in total analgesic consumption at 72 hours and subjects exhibited a lower risk of developing chronic pain (3-6 months after surgery) [41].

B. Abdominal surgery

Dai et al. published a report about 115 patients undergoing gastrointestinal tumor surgery and showed that intravenous lidocaine administration in the perioperative period is associated with reduced acute postoperative pain and increased patient comfort. At the same time, it accelerated the gastrointestinal function recovery [7].

An important meta-analysis by Marret et al. highlighted that lidocaine use in patients with abdominal

surgery reduces the pain 24 hours after surgery, reduces the postoperative ileus duration and the nausea and vomiting episodes incidence, shortening the hospital stay length [42]. In another analysis, Ventham et al. showed that, after laparoscopic surgery, lidocaine infusion is associated with decreased opioids requirements, improved postoperative pain scores in the first 24 hours, lower incidence of nausea or vomiting, and the patients were able to resume oral feeding more rapidly [43].

C. Genitourinary surgery

In the case of radical prostatectomy, studies have shown that the intravenous administration of lidocaine reduces the pain scores in the postoperative period, decreases opioid consumption, and reduces general hospitalization [36].

A study regarding the use of lidocaine in 64 subjects undergoing laparoscopic renal surgery reported no benefits for this intervention [44].

D. Gynecologic and Obstetric surgery

There are various reports that do not support the perioperative use of intravenous lidocaine in needing total abdominal hysterectomy due to the lack of evidence supporting the benefits of this intervention [45, 46].

E. Orthopedic surgery

Perioperative intravenous lidocaine appears to better control the acute pain in case of ankle dislocation [47].

A study by Martin et al. showed no benefits of perioperative lidocaine infusion in terms of superior pain control or rapid recovery after total hip arthroplasty [48].

F. Thoracic and upper airway surgery

A recent study published by Wang et al. showed that intravenous infusion of lidocaine (2 mg/kg within 10 minutes before starting anesthesia + 2 mg/kg/hr until the end of the surgery) can improve the perioperative recovery status and pain scores, reduce intraoperative opioid use, and decrease the risk of postoperative nausea and vomiting development. It also favours the rapid postoperative recovery of patients undergoing upper airway surgery [47].

Cui et al. showed that perioperative intravenous lidocaine use is associated with improved pain scores and reduced opioid consumption 6 hours after surgery [48].

G. Spine and thyroid surgery

In a study reported by Farag et al., including 160 adult patients undergoing spinal surgery, the infusion of lidocaine 2 mg/kg/hr showed good outcomes regarding postoperative pain control [49].

Apparently, in subjects with thyroid surgery, the intravenous administration of lidocaine only controls the pain in the first 4 hours after surgery, but decreases the opioid consumption and reduces the levels of systemic C-reactive protein [50].

H. Ambulatory surgery

In the first 24 hours after ambulatory surgical procedures performance (plastics, urology, gynecology, general surgery, minor orthopedics), the infusion of lidocaine reduces the opioid consumption and decreases the pain scores, but has no influence on nausea and vomiting incidence, nor on discharge time [51].

CONCLUSIONS

This article offers a brief overview of key pharmacological properties of lidocaine, its analgesic and systemic effects, the major side effects of intravenous administration, and the perioperative use of this molecule in controlling pain in various types of surgical interventions. There are various reports about the safety and efficacy of lidocaine infusion in multimodal analgesic management of surgical patients, along with other beneficial systemic effects. Numerous current clinical trials aim to study the role of this molecule in acute and chronic pain, highlighting its importance.

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REFERENCES

1. Nimmo SM, Foo IT, Paterson HM. Enhanced recovery after surgery: pain management. *Journal of surgical oncology.* 2017 Oct;116(5):583-91.
2. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. *JAMA surgery.* 2017 Jul 1;152(7):691-7.
3. Dai YE, Jiang R, Su W et al. Impact of perioperative intravenous lidocaine infusion on postoperative pain and rapid recovery of patients undergoing gastrointestinal tumor surgery: A randomized, double-blind trial. *Journal of Gastrointestinal Oncology.* 2020 Dec;11(6):1274.
4. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery. *Drugs.* 2010 Jun;70(9):1149-63.
5. Baral BK, Bhattarai BK, Rahman TR et al. Perioperative intravenous lidocaine infusion on postoperative pain relief in patients undergoing upper abdominal surgery. *Nepal Med Coll J.* 2010 Dec 1;12(4):215-0.
6. Xie C, Wang Q, Huai D. Intravenous Infusion of Lidocaine Can Accelerate Postoperative

Early Recovery in Patients Undergoing Surgery for Obstructive Sleep Apnea. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2021;27:e926990-1.
7. Van Der Wal SE, Van Den Heuvel SA, Radema SA et al. The in vitro mechanisms and in vivo efficacy of intravenous lidocaine on the neuroinflammatory response in acute and chronic pain. *European journal of pain.* 2016 May;20(5):655-74.
8. Butterworth JF, Strichartz GR. Molecular mechanisms of local anesthesia: a review. *Anesthesiology.* 1990 Apr 1;72(4):711-34.
9. Arias HR. Role of local anesthetics on both cholinergic and serotonergic ionotropic receptors. *Neuroscience & Biobehavioral Reviews.* 1999 Oct 1;23(6):817-43.
10. Weinberg L, Peake B, Tan C, Nikfarjam M. Pharmacokinetics and pharmacodynamics of lignocaine: A review. *World Journal of Anesthesiology.* 2015 Jul 27;4(2):17-29.
11. Inoue R, Suganuma T, Echizen H et al. Plasma concentrations of lidocaine and its principal metabolites during intermittent epidural anesthesia. *Anesthesiology.* 1985 Sep 1;63(3):304-10.
12. Devor M, Wall PD, Catalan N. Systemic lidocaine silences ectopic neuroma and DRG discharge without blocking nerve conduction. *Pain.* 1992 Feb 1;48(2):261-8.
13. Jaffe RA, Rowe MA. Subanesthetic concentrations of lidocaine selectively inhibit a nociceptive response in the isolated rat spinal cord. *Pain.* 1995 Feb 1;60(2):167-74.
14. Kawamata M, Watanabe H, Nishikawa K et al. Different mechanisms of development and maintenance of experimental incision-induced hyperalgesia in human skin. *The Journal of the American Society of Anesthesiologists.*2002;97(3):550-9.
15. Caracas HC, Maciel JV, de Souza MM, Maia LC. The use of lidocaine as an anti-inflammatory substance: a systematic review. *Journal of dentistry.* 2009 Feb 1;37(2):93-7.
16. Peck SL, Johnston RB, Horwitz LD. Reduced neutrophil superoxide anion release after prolonged infusions of lidocaine. *Journal of Pharmacology and Experimental Therapeutics.* 1985 Nov 1;235(2):418-22.
17. Sinclair R, Eriksson AS, Gretzer C et al. Inhibitory effects of amide local anaesthetics on stimulus-induced human leukocyte metabolic activation, LTB4 release and IL-1 secretion in vitro. *Acta anaesthesiologica scandinavica.* 1993 Feb;37(2):159-65.
18. Schmidt W, Schmidt H, Bauer H et al. Influence of lidocaine on endotoxin-induced leukocyte-endothelial cell adhesion and macromolecular leakage in vivo. *The Journal of the American Society of Anesthesiologists.* 1997 Sep 1;87(3):617-24.
19. Piegeler T, Votta-Velis EG, Bakhshi FR et al. Endothelial barrier protection by local anesthetics: ropivacaine and lidocaine block tumor necrosis factor-α–induced endothelial cell Src activation. *Anesthesiology.* 2014 Jun;120(6):1414-28.
20. Lieberman NA, Harris RS, Katz RI et al. The effects of lidocaine on the electrical and mechanical activity of the heart. *The American journal of cardiology.* 1968 Sep 1;22(3):375-80.
21. Goodman NW, Stratford N. Effect of iv lignocaine on the breathing of patients anaesthetized with propofol. *British journal of anaesthesia.* 1995 Nov 1;75(5):573-7.
22. Qi X, Lai Z, Li S et al. The efficacy of lidocaine in laryngospasm prevention in pediatric surgery: a network meta-analysis. *Scientific reports.* 2016 Sep 2;6(1):1-8.
23. Gecaj-Gashi A, Nikolova-Todorova Z, Ismaili-Jaha V, Gashi M. Intravenous lidocaine suppresses fentanyl-induced cough in Children. *Cough.* 2013 Dec;9(1):1-4.
24. Harvey KP, Adair JD, Isho M, Robinson R. Can intravenous lidocaine decrease postsurgical ileus and shorten hospital stay in elective bowel surgery? A pilot study and literature review. *The American journal of surgery.* 2009 Aug 1;198(2):231-6.
25. Borg T, Modig J. Potential anti-thrombotic effects of local anaesthetics due to their inhibition of platelet aggregation. *Acta anaesthesiologica scandinavica.* 1985 Oct;29(7):739-42.
26. Johnson SM, Saint John BE, Dine AP. Local anesthetics as antimicrobial agents: a review. *Surgical infections.* 2008 Apr 1;9(2):205-13.
27. Chamaraux-Tran TN, Piegeler T. The amide local anesthetic lidocaine in cancer surgery—potential antimetastatic effects and preservation of immune cell function? a narrative review. *Frontiers in Medicine*. 2017 Dec 20;4:235.
28. Foo I, Macfarlane AJ, Srivastava D et al. The use of intravenous lidocaine for postoperative pain and recovery: international consensus statement on efficacy and safety. *Anaesthesia.* 2021 Feb;76(2):238-50.
29. Neal JM, Barrington MJ, Fettiplace MR et al. The third American Society of Regional Anesthesia and Pain Medicine practice advisory on local anesthetic systemic toxicity: executive summary 2017. *Regional Anesthesia & Pain Medicine.* 2018 Feb 1;43(2):113-23.
30. Donald MJ, Derbyshire S. Lignocaine toxicity; a complication of local anaesthesia administered in the community. *Emergency medicine journal.* 2004 Mar 1;21(2):249-50.
31. DeToledo JC. Lidocaine and seizures. *Therapeutic Drug Monitoring.* 2000 Jun 1;22(3):320-2.
32. Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. *The Lancet*. 2019 Apr 13;393(10180):1537-46.
33. Beaussier M, Delbos A, Maurice-Szamburski A, Ecoffey C, Mercadal L. Perioperative use of intravenous lidocaine. *Drugs.* 2018 Aug;78(12):1229-46.
34. Dunn LK, Durieux ME. Perioperative use of intravenous lidocaine. *Anesthesiology.* 2017 Apr;126(4):729-37.
35. Bakan M, Umutoglu T, Topuz U et al. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Revista brasileira de anestesiologia. 2015 May;65:191-9.
36. Groudine SB, Fisher HA, Kaufman RP et al. Intravenous lidocaine speeds the return of bowel function, decreases postoperative pain, and shortens hospital stay in patients undergoing radical retropubic prostatectomy. *Anesthesia & Analgesia.* 1998 Feb 1;86(2):235-9.
37. Weibel S, Jelting Y, Pace NL et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults. *Cochrane Database of Systematic Reviews*. 2018(6).
38. 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. *British journal of anaesthesia.* 2016 Jun 1;116(6):770-83.
39. Grigoras A, Lee P, Sattar F, Shorten G. Perioperative intravenous lidocaine decreases the incidence of persistent pain after breast surgery. *The Clinical journal of pain.* 2012 Sep 1;28(7):567-72.
40. Kendall MC, McCarthy RJ, Panaro S et al. The effect of intraoperative systemic lidocaine on postoperative persistent pain using Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials criteria assessment following breast cancer surgery: a randomized, double-blind, placebo-controlled trial. *Pain Practice.* 2018 Mar;18(3):350-9.
41. Chang YC, Liu CL, Liu TP et al. Effect of perioperative intravenous lidocaine infusion on acute and chronic pain after breast surgery: A meta-analysis of randomized controlled trials. *Pain practice.* 2017 Mar;17(3):336-43.
42. Marret E, Rolin M, Beaussier M, Bonnet F. Meta-analysis of intravenous lidocaine and postoperative recovery after abdominal surgery. *Journal of British Surgery.* 2008 Nov;95(11):1331-8.
43. Ventham NT, Kennedy ED, Brady RR et al. Efficacy of intravenous lidocaine for postoperative analgesia following laparoscopic surgery: a meta-analysis. *World Journal of Surgery.* 2015 Sep;39(9):2220-34.
44. Wuethrich PY, Romero J, Burkhard FC, Curatolo M. No benefit from perioperative intravenous lidocaine in laparoscopic renal surgery: a randomised, placebo-controlled study. *European Journal of Anaesthesiology| EJA.* 2012 Nov 1;29(11):537-43.
45. Grady MV, Mascha E, Sessler DI, Kurz A. The effect of perioperative intravenous lidocaine and ketamine on recovery after abdominal hysterectomy. *Anesthesia & Analgesia.* 2012 Nov 1;115(5):1078-84.
46. Bryson GL, Charapov I, Krolczyk G et al. Intravenous lidocaine does not reduce length of hospital stay following abdominal hysterectomy. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie.* 2010 Aug;57(8):759-66.

47. Sin B, Gritsenko D, Tam G et al. The use of intravenous lidocaine for the management of acute pain secondary to traumatic ankle injury: a case report. *Journal of Pharmacy Practice.* 2018 Feb;31(1):126-9.
48. Martin F, Cherif K, Gentili ME et al. Lack of impact of intravenous lidocaine on analgesia, functional recovery, and nociceptive pain threshold after total hip arthroplasty. Anesthesiology. 2008 Jul;109(1):118-23. doi: 10.1097/ALN.0b013e31817b5a9b. PMID: 18580181; PMCID: PMC2728117.
49. Wang Q, Ding X, Huai D et al. Effect of intravenous lidocaine infusion on postoperative early recovery quality in upper airway surgery. *The Laryngoscope.* 2021 Jan;131(1):E63-9.
50. Cui W, Li Y, Li S et al. Systemic administration of lidocaine reduces morphine requirements and postoperative pain of patients undergoing thoracic surgery after propofol–remifentanil-based anaesthesia. *European Journal of Anaesthesiology| EJA*. 2010 Jan 1;27(1):41-6.
51. Farag E, Ghobrial M, Sessler DI et al. Effect of perioperative intravenous lidocaine administration on pain, opioid consumption, and quality of life after complex spine surgery. *Anesthesiology.* 2013 Oct; 119(4):932-40.
52. Choi KW, Nam KH, Lee JR et al. The effects of intravenous lidocaine infusions on the quality of recovery and chronic pain after robotic thyroidectomy: a randomized, double-blinded, controlled study. *World Journal of Surgery.* 2017 May;41(5):1305-12.
53. McKay A, Gottschalk A, Ploppa A et al. Systemic lidocaine decreased the perioperative opioid analgesic requirements but failed to reduce discharge time after ambulatory surgery. *Anesthesia & Analgesia.* 2009 Dec 1;109(6):1805-8.