





DOI: <https://doi.org/10.5554/22562087.e965>

Intravenous lidocaine infusion for the treatment of acute pain in the pediatric intensive care unit: case series

Infusión de lidocaína endovenosa para el tratamiento de dolor agudo en la unidad de cuidado intensivo pediátrico: serie de casos

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How to cite this article: Izquierdo LM, Moreno N, Ruiz S. Intravenous lidocaine infusion for the treatment of acute pain in the pediatric intensive care unit: case series. Colombian Journal of Anesthesiology. 2021;49:e965.

Abstract

Introduction: The use of intravenous lidocaine infusion has increased over the past decade as part of a multimodal approach to analgesia in adults; however, information about its safety and tolerability in the pediatric population is limited.

Methods: Acute pain management using lidocaine infusion in eleven patients treated in the pediatric intensive care unit.

Results: Five cases of postoperative abdominal pain and six cases of non-operative abdominal pain. Two cases were cancer patients affected by neutropenic colitis. Analgesic control achieved was good.

Conclusion: Lidocaine infusions are apparently a safe option for the management of acute pain, either post-operative or not, in the pediatric population.

Keywords: Lidocaine; pediatrics; postoperative analgesia; intensive care unit; multimodal analgesia.

Resumen

Introducción: El uso de la infusión de lidocaína endovenosa ha aumentado en la última década como parte de un enfoque analgésico multimodal en los adultos; sin embargo, se dispone de información limitada sobre su seguridad y tolerabilidad en la población pediátrica.

Métodos: Se presentan once casos de manejo de dolor agudo con lidocaína en infusión tratados en unidad de cuidado intensivo pediátrico.

Resultados: Cinco casos fueron postoperatorio abdominal y seis casos tenían dolor abdominal no postoperatorio. Dos pacientes tenían cáncer y cursaban con colitis neutropénica. El control analgésico alcanzado fue bueno.

Conclusión: Las infusiones de lidocaína parecen ser una opción segura para el manejo del dolor agudo ya sea posquirúrgico o no en la población pediátrica.

Palabras clave: Lidocaína; pediatría; analgesia postoperatoria; cuidado intensivo pediátrico; analgesia multimodal.

INTRODUCTION

Opioid medications are frequently used for pain management in pediatric intensive care units (PICU); however, they may be the source of adverse events, including respiratory failure (20-60%), postoperative nausea and vomiting (PONV) (25%), reduced gut motility, urinary retention, increased pain sensitivity, altered immune status and pruritus (2-10%) (1,2). One alternative to the use of opioids is Intravenous Lidocaine Infusion Therapy (IVLT). Because of its analgesic and anti-inflammatory properties, IVLT modifies the surgical injury-induced inflammatory response (3,4). Recent reviews confirm its use in videolaparoscopic abdominal surgery and in open surgery, highlighting its inclusion in protocols for enhanced recovery after surgery (ERAS) (4). Current evidence endorses its administration within the context of multimodal analgesia, based on its immune properties and action on surgical stress. Consequently, it is considered to be a necessary drug in modern perioperative management. Notwithstanding the fact that data in adults are promising, there is a paucity of evidence supporting the use of lidocaine infusions in the pediatric population (5-9).

In the context of insufficient data to confirm adequate doses and safe lidocaine levels in the pediatric population, this article presents six cases of successful use of IVLT in terms of safety and tolerability in patients treated with lidocaine infusion in the PICU.

CLINICAL CASES

All the cases documented in this report were collected in the PICU of the Military Hospital in Bogota, Colombia, between July 2019 and July 2020, and comprise patients with acute abdominal pain, distributed as follows: five postoperative cases and five non-surgical cases. Pain management was based on lidocaine infusion at a rate of 1 mg/kg/hour (8,9) for 24-48 hours, associated to the use of paracetamol 15 mg/kg. Li-

docaine bolus administration was not used. The FLACC and Wong Baker pain scales were applied and rescue opioids were used when the pain score was higher than 5.

Adverse effects were measured clinically, with continuous heart rate, blood pressure and arterial oxygen saturation monitoring. Moreover, nurses checked the patients regularly for the presence of dizziness, metal taste sensation, visual disorders, or evidence of neurologic decline using the Glasgow scale. It is important to highlight that no child received sedation during lidocaine infusion administration because most of these symptoms could not have been detected with the patient under general anesthesia or sedation. Bradycardia was observed in one patient but no objective serum measurements were obtained; however, bradycardia was resolved upon discontinuation of the lidocaine infusion. There were no altered liver or renal tests in any of the patients, with albumin levels being within normal ranges in all cases. Metabolic acidosis was present in all cases upon admission and was addressed within the first 24 hours. There were no other findings that could have affected the bioavailability or clearance of the drug.

Publication of this case series was approved by the Research Ethics Committee of the Central Military Hospital, as stated in Minutes No. 14 dated April 9, 2020. The baseline characteristics of the patients are summarized in Table 1.

DISCUSSION

This small sample of patients showed that intravenous lidocaine for postoperative and non-operative pain management was well tolerated. Patients were older than 2 years of age, and mean age was 9.2 years. Adverse events were experienced by 9%, but symptoms were typically mild and resolved promptly. Only 3 patients needed a change in dose and added opioids.

Acute pain in the PICU is one of the biggest challenges for pediatric intensive care physicians faced with cases of postoperative or non-operative bowel inflammation.

The inflammatory response that occurs after major abdominal surgery is very significant for patients and physicians, and during the perioperative period (1,10,11). Excess perioperative stimulation of the inflammatory and hemostatic systems may give rise to postoperative ileus, ischemia-reperfusion and hypercoagulation syndromes - such as deep vein thrombosis - and exaggerated inflammatory response to pain, with impaired gastrointestinal motility. This results in prolonged length of stay and delayed initiation of enteral feeding. Consequently, modulating the inflammatory response may dampen the severity of those complications (1,3,4).

The administration of anesthetic and analgesic drugs through lumbar epidural puncture is currently used in the pediatric population to achieve an analgesic effect and reduce the response to intense surgical stress (3,4); however, there are inherent risks to the insertion of a peridural catheter that may give rise to complications, particularly in this population groups. In these cases, IVLT may be used as a safe and effective strategy to improve perioperative outcomes in pediatrics (7,11).

The results observed in this case series were similar to those reported by Gibbons et al. (8) who found a 35% association between lidocaine infusions used for refractory pain in cancer patients and adverse effects, in particular neurologic effects such as paresthesias. In this case series, no evidence was found of side effects such as blurred vision, nausea, confusion, tinnitus or metallic taste, as was the case in a study by Lemming et al. (9). In this series, the dose used to achieve adequate analgesia was 1 mg/kg/hour, as compared with other studies (8-11) which used doses higher than 1 mg/kg/hour. Abdominal pain was controlled in all patients with a 24-hour infusion, and the addition of paracetamol was sufficient as multimodal analgesia. In general terms, opioid sparing was significantly higher and played a key role in early enteral feeding initiation (24-48 hours).

Adequate dosing and safe lidocaine levels in the pediatric population are still unclear. Therapeutic plasma levels and IVLT duration for the treatment of acute pain

TABLE 1. Patient characteristics.

Patient	Age in years	Diagnoses	Postoperative	Type of surgery: Open vs. Laparoscopic	Use of drains	Time of adverse effect or improvement (1 mg/kg/hour)	Adverse events	Other analgesic agents	Consciousness status (Glasgow)	Oxygenation system
1	10	Neutropenic colitis, acute lymphocytic leukemia relapse	No	None	No	24 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
2	6	Appendicitis surgery	Yes	Open	Orogastric tube	24 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
3	11	Gut perforation surgery	Yes	Open	Ileostomy	24 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
4	14	Systemic pain, T-cell lymphoma patient	No	None	No	24 hours	No pain relief, paresthesias	Morphine, paracetamol	15/15	Ambient: 0.21 %
5	8	Abdominal sepsis, colitis	No	None	No	19 hours	Bradycardia	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
6	2	Intestinal invagination surgery	Yes	Open	Orogastric tube	24 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
7	11	Appendectomy	Yes	Open	Orogastric tube	24 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
8	11	Splenectomy	Yes	Open	Orogastric tube	24 hours	No pain relief	Morphine, paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
9	5	Acute pancreatitis	No	None	Orogastric tube	24 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min
10	17	Pancreatitis with pancreatic pseudocyst	No	None	Orogastric tube	24 hours	Two doses of morphine	Two doses of morphine	15/15	Low-flow nasal cannula 1 Lt/min
11	7	Neutropenic colitis, acute lymphocytic leukemia relapse	No	None	No	48 hours	None	Paracetamol	15/15	Low-flow nasal cannula 1 Lt/min

SOURCE. Authors.

are not well defined, although the optimal therapeutic range for the treatment of acute pain appears to be between 1 and 1 y 5 µg/mL. Bolus administration of 2 mg/kg and a continuous infusion of 2 to 5 mg/kg/hour have been shown to reach plasma levels of 1 to 4 µg/mL; lidocaine has a half-life of approximately 100 minutes and

linear pharmacokinetics (4). Toxic plasma levels of lidocaine are considered to exist at > 6 µg/mL, while the first signs of local anesthetic systemic toxicity (LAST) will manifest as perioral numbness, metallic taste, tinnitus, visual and hearing disorders, paresthesias, nausea, dizziness and drowsiness. Given the short half-life, LAST

symptoms are easily reversed with a lower rate of infusion or discontinuation of the lidocaine infusion (3,5).

In infants under 6-7 months of age, liver metabolism is immature, plasma levels of acid glycoprotein α-1 are low, which increases free circulating lidocaine and, consequently, the risk of toxicity (4).

Case studies described in pediatrics (8,9) have used lidocaine infusion at doses ranging between 0.5 and 2 mg/kg/hour, with varying results in terms of adverse effects. IVLT doses used for pain relief are usually in the range of 1 to 2 mg/kg/hour. At this infusion rate, plasma levels are usually under 3-5 µg/mL, but awake patients may complain of confusion, perioral numbness, dizziness or sedation (3,4).

Although IVLT is currently used more frequently in our PICU, it is not yet part of postoperative care in general, except in abdominal surgery. Adverse effects were mild, occurred in very few patients and were reverted with dose lowering or infusion discontinuation; however, adverse event assessments were limited by the subjectivity of the intensive care physicians and the nurses working the shifts. There was often a delay between onset of symptoms and medical assessment, resulting in symptom resolution by the time the patient was assessed. IVLT could be a valuable option for abdominal pain treatment in pediatrics and a tool to consider in cases in which regional techniques, either neuroaxial or peripheral, are contraindicated.

This study being a case series with no control group or the possibility of having objective measurements of plasma lidocaine levels has limitations. It is considered innovative in that it shows that IVLT can be used as an additional option in the PICU for multimodal analgesic management in the context of acute postoperative or non-operative abdominal pain. Further evidence needs to be gathered in pediatrics by means of prospective studies that assess the clinical effectiveness of lidocaine in the treatment of postoperative pain, as well as its effect on the use of opioid-based therapies.

CONCLUSION

IVLT can be a safe option for postoperative and non-operative pain management as part of multimodal analgesia in the pediatric population. Moreover, opioid sparing in

patients with postoperative abdominal pain may work in favor of positive outcomes, such as early enteral feeding and a lower rate of secondary adverse events.

ETHICAL RESPONSIBILITIES

Approval by the ethics committee

The Central Military Hospital research ethics committee authorized publication of this case series, as stated in Minutes No. 14 of April 9, 2020.

Human and animal protection

The authors declare that the procedures performed were in accordance with the ethical standards of the responsible human experimentation committee and with the World Medical Association and the Declaration of Helsinki.

Data confidentiality

The authors declare having followed the institutional protocols regarding patient data disclosure.

Right to privacy and informed consent

The authors declare that no patient data appear in this article. The authors obtained the informed consent from the patients and/or subjects referred to in this article. The relevant documents are kept by the corresponding author.

ACKNOWLEDGEMENTS

Authors' contributions

LMI: Original project conception, study planning, data collection, interpretation of the results, initial manuscript drafting, final manuscript approval.

NM: Study planning, data collection, final manuscript drafting, final manuscript approval.

SR: Study planning, data collection, and final manuscript approval.

Assistance for the study

None declared.

Funding and sponsorship

None declared.

Conflict of interest

None declared.

Submissions

None declared.

Acknowledgement

The authors are grateful to all the staff of the Central Military Hospital Intensive Care Unit in Bogotá, Colombia, for their well-know support in the publication of this case series.

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