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Intravenous lidocaine in cancer-related neuropathic pain: case series

Lidocaína endovenosa en dolor neuropático relacionado con cáncer: serie de casos

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Abstract

Introduction

Administering systemic lidocaine has been shown to deliver effective analgesia for both cancer-related and non-cancer pain. Adverse effects and toxicity are rare with controlled administration.

Objective

To report the results obtained after the indication to manage with IV lidocaine infusion to control neuropathic pain flares in 9 cancer patients.

Methodology

Observational, descriptive, case series-type study. A search was conducted in the files of the Pain and Palliative Care Service of the National Cancer Institute - Instituto Nacional de Cancerología - in Bogotá. Patients over 18 years old diagnosed with cancer, who experienced high intensity neuropathic pain and with the cognitive ability to rate their pain in a numerical analogue scale (NAS), without any absolute contraindications for the use of IV lidocaine were included; patients were assessed between September 27 and November 21, 2019.

Results

9 patients experiencing a pain flare-up which was characterized as neuropathic were registered, of which 89 % had some improvement following the administration of an initial lidocaine bolus. After one hour, 60 % reported over 40% improvement in the initial NAS. After 24 hours all patients had experienced some improvement, with a reduction of 46% in the pain scale as compared to the baseline.

Conclusions

In this series of cases, the intravenous infusion of lidocaine as an option for the management of neuropathic pain flares seems to reduce pain intensity following the initial bolus administration.

Key words

Lidocaine; Intravenous infusion; Pain; Palliative care; Cancer; Anesthesiology.

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Resumen

Introducción: Se ha encontrado que la administración de lidocaína sistémica proporciona analgesia efectiva tanto en el dolor relacionado con cáncer como en el dolor no oncológico; se ha evidenciado que los efectos adversos y la toxicidad son raros en administraciones controladas.

Objetivo: Informar los resultados obtenidos luego de indicar el manejo con infusión de lidocaína endovenosa para control de crisis de dolor neuropático en 9 pacientes con cáncer.

Metodología: Estudio observacional descriptivo tipo serie de casos. Se realizó una búsqueda en la bitácora del Servicio de Dolor y Cuidados Paliativos del Instituto Nacional de Cancerología de Bogotá. Se incluyeron pacientes mayores de 18 años diagnosticados con cáncer, que cursaban con dolor neuropático de alta intensidad, con la capacidad cognitiva de calificar su dolor en una escala numérica análoga (ENA), sin contraindicaciones absolutas para uso de lidocaína endovenosa y que fueron valorados entre el 27 de septiembre y el 21 de noviembre de 2019.

Resultados: Se registraron 9 pacientes con crisis de dolor caracterizado como neuropático, de los cuales el 89 % tuvo algún grado de mejoría luego de la administración del bolo inicial de lidocaína. Pasada una hora, en el 60 % se observó una mejoría de más del 40 % de la ENA inicial. A las 24 horas, todos los pacientes experimentaron alguna mejoría, logrando una disminución en la puntuación del dolor según la ENA del 46 % en relación con la inicial.

Conclusión: En esta serie de casos, la lidocaína en infusión endovenosa se muestra como una opción para el manejo de las crisis de dolor neuropático, pues reduce la intensidad del dolor después del paso del bolo inicial.

Palabras clave: Lidocaína; Infusión intravenosa; Dolor; Cuidado paliativo; Cáncer; Anestesiología.

INTRODUCTION

Pain is a public health issue that disproportionately affects quality of life (1). The International Association for the Study of Pain defined neuropathic pain as pain resulting from central or peripheral nervous system injury often presenting in cancer patients (2,3). The epidemiological surveys indicate that a large proportion of patients with neuropathic pain do not get proper treatment, probably because of poor diagnostic accuracy and a lack of knowledge about effective drugs and their proper use (4). Some of these patients may be treated with tricyclic antidepressants, anticonvulsants, or antiarrythmia medications; however, with these medications symptoms improve over a few weeks and in a pain flare situation, a faster onset of action is required (4,5).

Some studies describe controlling neuropathic pain flare-ups in cancer patients using IV lidocaine boluses. The systemic administration of lidocaine have been shown to be effective in providing analgesia both in cancer and non-cancer related pain. Moreover, the individual infusion of lidocaine results in extended analgesia hence allowing for reducing other analgesic agents and their associated toxicities (6); additionally, the adverse effects and toxicity are extremely rare in controlled perfusion (7).

Considering the significant impact on patients' quality of life, the objective of this study was to assess the response during neuropathic pain flare-ups in cancer patients treated with intravenous lidocaine.

METHODOLOGY

An observational, descriptive case series study was conducted in both male and female patients aged 18 years or older, diagnosed with cancer and experiencing a neuropathic pain flare, who were able to rate their pain using an analogue numeric scale, had no absolute contraindications for the use of intravenous lidocaine, and were hospitalized between September 27 and November 21, 2019.

A search was conducted in the files of the Pain and Palliative Care Service of Instituto Nacional de Cancerología, in Bogotá, Colombia. The data from 9 patients were recorded, including sociodemographic variables (age, sex) and clinical variables such as: the cancer diagnosis, the type of pain and intensity based on the numerical analogue scale (NAS) from 0 to 10, with 0-3 being mild pain; 4-7 moderate pain; and 8-10 severe pain. The pain data were collected before administering the lidocaine bolus, at the end of the administration and 24 hours after the start of the infusion. Additionally, any opioid salvage doses needed during the 24 hours following the administration of the lidocaine bolus were also recorded. The lidocaine bolus dose used, the number of rescue doses and the oral morphine equivalent dose (OMED) required in 24 hours after the completion of the lidocaine bolus were also recorded (Table 1).

The qualitative variables were described using absolute and relative frequencies. The quantitative variables were described as means. The Friedman's non-parametric

test was used, which is an extension of the Wilcoxon Signed-Rank test for paired ordinals.

This study was reviewed by the Ethics Committee of the National Cancer Institute, which approved the use of the data as reflected in Minutes N.° 009-2 of 2021. According to the local regulations, it was considered a risk-free study, collecting data from a secondary source.

RESULTS

Demographic variables

9 patients were included in the study with different cancer pathologies; the most frequent condition was cervical cancer, representing 33.3 %. The average age of the participants was 46.8 years (range: 23-68 years); 77.7 % (7) were females and 22 % (2) were males.

Clinical variables

The pain intensity was assessed using the numerical analogue scale (NAS), 100 % of the patients reported severe pain before administering the lidocaine bolus.

The pain assessment at the completion of the lidocaine bolus (duration of the bolus infusion: 30 minutes), resulted in 88.8 % of the patients rating pain as moderate and 11.1 % as severe. Additionally, pain assessment 1 hour after completion of the lidocaine bolus showed that 22.2 % were experiencing mild pain, 66.6 % moderate pain and 11.1 % severe pain. The 24-hour assessment after administering the lidocaine showed that every patient at some point experienced some pain relief; in the end, 78 % of the patients experienced a pain improvement of more than 50 % versus the baseline NAS. The average initial / final NAS reduction was 46 % (Table 2).

With regards to the need to use opioid rescue doses during the administration of lidocaine, only 2 patients had to use more than 2 rescue doses over the 24 hours of

Table 1. Demographic characteristics of the patients, lidocaine bolus dose and use of opioids.

Patient	Age	Gender	Pathology	Dose of the lidocaine bolus used (cm3/h)	Number of opioid rescue doses in 24 hours	OMED total rescue doses used (mg)
1	47	Female	Cervical cancer	5	3	30
2	68	Female	Cervical cancer	14	1	12
3	23	Female	Krukenberg tumor	9	1	5
4	55	Female	Cervical cancer	10	3	15
5	33	Male	Plasma cell leukemia	23	0	0
6	48	Female	Vulvar cancer	14	2	8
7	65	Female	Shoulder Leiomyosarcoma	16	2	24
8	33	Male	Sacral tumor	16	2	18
9	50	Female	Breast cancer	8	1	10

OMED: Oral morphine equivalent dose.
Source: Authors.

Table 2. Pain intensity follow-up over 24 hours.

Patient	NAS before start of the bolus	NAS at the endo of the bolus	NAS 1 hour after completing the bolus	NAS 24 hours after the bolus administration	% reduction in initial/ final NAS
1	8	5	3	4	50 %
2	8	5	5	8	0
3	8	5	5	4	50 %
4	8	7	7	7	12.5 %
5	8	7	7	4	50 %
6	8	6	7	4	50 %
7	9	7	5	4	56 %
8	9	8	10	3	67 %
9	10	7	3	3	70 %
Average NAS	8.4	6,3	5,7	4,5	46,4 %

NAS: Numerical Analogue Scale for measuring pain intensity.
Source: Authors.

observation. Over the course of the observation period, significant differences were found in at least two follow-up groups. In the paired comparisons (using Hold-adjusted Wilcoxon) significant differences were only found between the NAS before the start of the bolus and the NAS at the completion of the bolus (30 minutes) (p = 0.049).

DISCUSSION

There was a significant improvement in pain intensity in this case series, before and after the lidocaine bolus; however, at some point during treatment, 100 % of the patients reported a reduction in pain intensity. There were no complications in any of the patients and the reason was probably the adequate follow-up in each patient during the administration of the lidocaine bolus.

The first description about the use of a local intravenous anesthetic agent as analgesic was published over 60 years ago (8), in 1948, when Löfgren and Lundqvist introduced lidocaine for the first time (9). Although the primary use of local anesthetic agents is achieving anesthesia in a specific area, it has been shown that systemic administration has been successful in the treatment of chronic pain (10); however, the intravenous administration of these agents has become a widespread practice (8).

Physiologically, the analgesic effect of lidocaine may be due to the NaV1.8 and NaV1.9 sodium channels block of sensitive peripheral neurons. This cell membrane block prevents the passage of sodium and potassium ions through the nerve receptors, and hence their conduction (7, 9,11). However, there are other mechanisms involved as well in the lidocaine-induced analgesia (2), such as the direct or indirect interaction with different receptors and nociceptive transmission pathways – muscarinic agonists, glycine inhibitors, endogenous opioid release and adenosine triphosphate, decreased production of excitatory amino acids, neurokinins and thromboxane A2— (1,12).

Multiple regimens have been described. Typically, a bolus IV dose of between 1-5 mg/kg is administered over 15 to 60 minutes, depending on the dose. The time described until achieving analgesia ranges from 1-45 minutes. If the patient responds to the initial bolus, the current IV therapy or the subcutaneous infusions may be administered for days and even months, depending on the response (13).

The studies by Ferrante et al. are examples of the improvement in neuropathic pain using lidocaine. They found a complete pain relief in 10 out of 13 patients, assessing them using the McGill pain questionnaire, before and after receiving the IV lidocaine infusion, showing a significant analgesic effect (14).

The limitations of this study are primarily the small sample size and the variability of the patients' characteristics, with a limited ability to strongly infer causality.

In conclusion, the analgesic control achieved in the study patients was considerable after the initial bolus and very high at some point during the follow-up; no adverse effects were documented with the medication. All patients treated were undergoing multimodal pain management and with different doses of opioids, which could have influenced the analgesic control achieved. In this case series, lidocaine as an IV infusion is an option for the management of neuropathic pain flares, primarily reducing pain intensity after the administration of the initial bolus.

ETHICAL RESPONSIBILITIES

Informed consent

This study was approved by the Research Ethics Committee of the Instituto Nacional de Cancerología, at the meeting held on April 28, 2021, as evidenced under Minutes N.° 009-21 of the MetricsMed Platform.

Protection of humans and animals

The authors declare that no experiments were conducted in humans or animals for this research project.

Confidentiality of the data

The authors declare that they adhered to the institutional protocols on the publication of patient data.

Right to privacy

The authors declare that no patient data have been disclosed in this article.

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Contributions by the authors

DSCD: Planning of the study, data collection, literature search, interpretation of the results, initial drafting of the manuscript, initial correction of the manuscript, final draft.
DSB: Adaptation of the study, literature search, initial draft of the manuscript, final draft.
BMMA: Planning of the study, interpretation of the results final draft of the manuscript, and final approval.

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Conflict of interests

The authors have no conflict of interests to disclose.

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