Intravenous lidocaine in cancer-related neuropathic pain: case series

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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.
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 anti-arythmia 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 (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 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>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Gender</th>
<th>Pathology</th>
<th>Dose of the lidocaine bolus used (cm³/h)</th>
<th>Number of opioid rescue doses in 24 hours</th>
<th>OMED total rescue doses used (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>Female</td>
<td>Cervical cancer</td>
<td>5</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>Female</td>
<td>Cervical cancer</td>
<td>14</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>Female</td>
<td>Krukenberg tumor</td>
<td>9</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>Female</td>
<td>Cervical cancer</td>
<td>10</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>Male</td>
<td>Plasma cell leukemia</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>48</td>
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<td>Vulvar cancer</td>
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<td>16</td>
<td>2</td>
<td>24</td>
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<tr>
<td>8</td>
<td>33</td>
<td>Male</td>
<td>Sacral tumor</td>
<td>16</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>Female</td>
<td>Breast cancer</td>
<td>8</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

OMED: Oral morphine equivalent dose.

Source: Authors.

<table>
<thead>
<tr>
<th>Patient</th>
<th>NAS before start of bolus</th>
<th>NAS at the end of the bolus</th>
<th>NAS 1 hour after completing the bolus</th>
<th>NAS 24 hours after the bolus administration</th>
<th>% reduction in initial / final NAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>50 %</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>50 %</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>12.5 %</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>4</td>
<td>50 %</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>6</td>
<td>7</td>
<td>4</td>
<td>50 %</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>7</td>
<td>5</td>
<td>4</td>
<td>56 %</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>8</td>
<td>10</td>
<td>3</td>
<td>67 %</td>
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<tr>
<td>9</td>
<td>10</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>70 %</td>
</tr>
</tbody>
</table>

Average NAS: 8.4

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 \( (9) \).

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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REFERENCES


