



Why not?

Patients with advanced cancer may exhibit complex pain syndromes and can develop pain that is completely or partially refractory to opioids. How to help such patients is a recurring theme in palliative care and frequently requires innovative multidisciplinary approaches. This article describes a joint initiative between The Ottawa Hospital Regional Cancer Centre and The Ottawa Hospital Pain Clinic to adapt intravenous lidocaine infusion — a technique normally used only in hospital acute care settings — to home care for a terminal cancer patient suffering from severe neuropathic pain. All other options for managing this patient's pain had been exhausted, and once her pain was controlled, she expressed a strong desire to be at home. To make living at home with a continuous lidocaine infusion possible, a multidisciplinary group developed new policies and procedures and conducted education sessions with all the caregivers involved. The protocol that was developed has been successfully employed to help an increasing number of patients at The Ottawa Hospital.

OPTIONS FOR MANAGEMENT OF INTRACTABLE PAIN

Continuous lidocaine infusion in the home

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Pain is a complex physiologic process that involves a variety of mechanisms within the peripheral, central and autonomic nervous systems. The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”

Moreover, “pain is always subjective and each individual learns the application of the word through experiences related to injury in early life.”¹ An important type of pain, neuropathic pain, has been defined by the International Association for the Study of Pain as “initiated or caused by a primary lesion or dysfunction in the nervous system.”¹ This type of pain frequently presents a challenge to clinicians in selecting effective analgesics. Depending on where the lesion or dysfunction occurs within the nervous system, neuropathic pain can be peripheral or central in origin. The term neuropathic pain represents a diverse group of syndromes including brachial plexopathy, spinal cord compression and nerve root impingement. Many patients have difficulty describing pain that arises from nerve injury, but may describe it as burning, shooting or shock-like. Such pain is often accompanied by numbness, allodynia and hyperpathia.² Patients may also describe their pain as deep and aching — which can be confused with somatic or nociceptive pain. Some identifying markers of neuropathic pain include redness, swelling, temperature changes (hot or cold), loss of hair, and muscle, motor and sensory deficits.³

Recent consensus statements and reviews have presented algorithms for managing neuropathic pain.^{4,6} Neuropathic pain frequently responds to treatment with coanalgesics that block nerve conduction via sodium and calcium channels, such as tricyclic antidepressants, anticonvulsants and antiarrhythmic agents. Refractory neuropathic pain is also treated with opioids

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and with pharmacologic agents that block N-methyl-D-aspartate receptors (NMDA-R) such as methadone, dextromethorphan and ketamine.

When standard therapy fails, innovative and creative solutions need to be employed. Lidocaine is an amide local anesthetic and sodium channel blocker that has proven effectiveness in the treatment of acute and chronic neuropathic pain in patients with diverse diagnoses.⁷ Traditionally, intravenous lidocaine has been given as an intermittent bolus dose and has provided pain relief lasting from hours to months.⁷⁻⁹ Its mechanism of action may involve the blockade of sodium channels and the reduction of ectopic electric discharges from damaged nerve fibres.¹⁰

OTTAWA HOSPITAL'S FIRST CASE OF LIDOCAINE INFUSION FOR PAIN

In March 2004, the Ottawa Hospital Pain Clinic was asked to become involved in the challenging case of a woman with severe neuropathic pain who had undergone all standard pain relief procedures. She had been diagnosed with metastatic breast cancer 13 years ago and was confronted with increasing pain related to a right brachial plexopathy and massive lymphedema. Due to the location of her tumours her pain experience was considerable; a necrotic tumour had invaded her chest wall as well as her brachial plexus. Her pain was unrelenting despite application of the World Health Organization's 3-step ladder approach to pain management^{11,12} and adequate trials of tricyclic antidepressants, anticonvulsants, intravenous opioids, ketamine and methadone. She developed significant toxicities from these medications. The most worrying toxicities included deep somnolence, confusion, hallucinations, myoclonic jerking and ataxia, without reasonable pain control. She was either deeply somnolent or awake and in excruciating pain. Despite the extent of her locally invasive disease, there were no metastases in major organs and her life expectancy was estimated to be approximately 6 months. The team felt strongly, however, that she was at increased risk of dying from her pain and/or its treatment.

Interdisciplinary team meetings were held to strategize the treatment options available. Neuraxial interventions with opiates and local anesthetics were considered but the painful area to block extended from C4 to T8 and might not be satisfactorily covered with an epidural infusion. In addition, ongoing chemotherapy placed her at increased risk of intrathecal or epidural infections. With all options for pain relief exhausted, we considered treatment with intravenous lidocaine.

The patient was transferred from the oncology ward to the Pain Clinic for a trial of intravenous lidocaine as a bolus dose. The Brief Pain Inventory (BPI), which incorporates a 0-10 scale with 0 being no pain and 10 being the worst possible pain, was used to assess her pain.¹³ The patient's pain score prior to the infusion was 10/10. In a monitored setting and receiving supplemental oxygen, she was pre-treated with intravenous midazolam 1.5 mg. A dose of 1.5 mg/kg of intravenous lidocaine was given over 2 minutes and this was followed by 3.5 mg/kg over 30 minutes, for a total dose of 5 mg/kg. She tolerated the procedure well,

and rated her post-infusion pain at 0/10. However, within 60 minutes following the completion of the lidocaine bolus dose, the pain returned to pre-infusion scores of 10/10. At that time the treating anesthesiologist decided to initiate a continuous infusion of 1.5 mg/kg/hour because of her dramatic improvement with the bolus dose of lidocaine. Within an hour, her pain score returned to 0/10, her cognition improved substantially and the doses of fentanyl and ketamine were reduced by 50%. The patient continued to have satisfactory pain control and a special exception was made to the current hospital policy that intravenous lidocaine could be administered only in a monitored setting. She was transferred back to the oncology unit after 6 hours of uneventful cardiac monitoring in the Pain Clinic. Within 48 hours she was walking with the help of her husband, and expressed a desire to go home.

OVERCOMING ORGANIZATIONAL BARRIERS

A strategy and new policies were required to allow this patient to stay on the ward and eventually return home with the continuous intravenous lidocaine infusion. On an urgent basis, we had to overcome enormous hospital procedural and policy challenges to ensure safe nursing, medical and patient care practices. While it was apparent to all that the patient was benefiting tremendously from her infusional lidocaine, the staff had understandable anxiety about this novel treatment as it contravened the current hospital policy of constant cardiac monitoring during infusion of lidocaine. However, since the indication for the use of lidocaine in this context was not to correct cardiac arrhythmia, the patient was not eligible for admission to the cardiac care unit. As noted above, a special exception was made by hospital administration to allow lidocaine to be given without cardiac monitoring while she was cared for on the oncology ward until a new policy could be developed to allow continuous infusion on the wards without monitoring.

To allay anxiety, the palliative nurse specialist and pharmacist provided education to the staff, patient and family members, often on a one-to-one basis. The staff gained knowledge of common side effects and drug interactions (See box, page 37).

We suspect that one episode of drug interaction related to lidocaine occurred. During hospitalization the patient developed oral thrush and was treated with oral fluconazole. Soon afterwards, she developed vivid hallucinations which abated after the fluconazole was stopped. This may have been related to lidocaine toxicity of the central nervous system. Unfortunately, serum lidocaine assays were not available within the hospital so the samples were sent to an out-of-town laboratory. Since the turnaround for results was 3-4 weeks, we had to rely on clinical signs of lidocaine toxicity such as twitching, somnolence and blood pressure changes. In addition, the lidocaine level needed to be sampled from a site separate from the infusion (because lidocaine adherence to tubing results in artificially high levels).

Consensus guidelines were set with regard to the acceptable interval for taking vital signs and the timing for obtaining serum lidocaine levels, as there is limited published literature to guide timing of lidocaine levels for long-term use.

With this treatment proving highly successful in reducing the patient's pain, the treating doctors and nurses felt that this procedure might benefit others. With hospital approval, a committee was formed to develop the policy and procedures for long-term administration of intravenous lidocaine.¹⁴ The committee members included our anesthesiologist, pharmacists, nurse educator and palliative care nurse specialist and palliative care physicians.

Drawing on others' experience

There are many publications examining the effect of intravenous lidocaine on neuropathic pain and it has been the subject of a recent Cochrane meta-analysis.^{7,15,16} A literature search identified limited case studies reporting success with continuous infusional lidocaine. Brose and Cousins¹⁷ discuss 3 patients who were successfully treated with subcutaneous lidocaine, with 1 patient having the infusion for 6 weeks. Thomas et al report good results for 6 inpatient hospice patients treated with continuous infusion of lidocaine.¹⁸ Likewise, Ferrini describes success in treating terminally ill patients with continuous intravenous lidocaine administered at home.¹⁹ In keeping with the literature findings, our institution's policy statement identified the criteria for administering lidocaine infusion for palliative pain control: this treatment is considered only in patients who have had an adequate trial of parenteral opioids and oral antineuropathic coanalgesics, and can only be prescribed by anesthesiologists and/or palliative care physicians.¹⁴

IN THE COMMUNITY

While policies were being developed and caregivers trained, the patient remained in hospital and was treated throughout with the lidocaine infusion. After 12 days of successful pain control she was discharged home with her infusion continuing. Education and information was essential, not only for the patient and her family, but also for the community healthcare providers including visiting nurses, palliative physicians and emergency room staff should the patient require emergency services.¹⁹ Our hospital pharmacist composed a letter of information outlining side effects and drug interactions.¹⁹ As well, communication and decision-making responsibilities were defined. The challenges in the community reflected the same anxieties as those expressed by the staff in the hospital setting. These concerns were amplified by the fact that the medical director for home care services was away on vacation; therefore a decision to involve home care nurses in this treatment could not be made until his return. In the meantime, the patient had already returned home; tasks such as changing the bags of lidocaine, taking serum lidocaine levels and pain assessments became the responsibility of the palliative care nurse specialist in the cancer clinic. With the return of the medical director, the home care nursing services willingly took on those responsibilities in the community. Regularly scheduled appointments with the oncologist, anesthesiologist and palliative care team were arranged to monitor pain, side effects and serum lidocaine levels.

During our visits to the patient's home, she expressed delight with her treatment and her ability to remain at home.


Lidocaine toxicity, side effects and drug interactions²⁰

- Signs of lidocaine toxicity include twitching, tremors, seizures, tinnitus, perioral numbness, drowsiness, metallic taste, somnolence, respiratory depression, dizziness, confusion, blurred vision, double vision, visual hallucinations, bradycardia > 20%, hypotension > 20% and agitation. Hypertension can be an early warning sign of toxicity, followed by hypotension.
- Excessive sedation may occur, due to either lidocaine or opioid toxicity: patients may experience a sudden reduction in opioid requirements in the first 24 hours after starting lidocaine.
- Lidocaine is metabolized in the liver by the cytochrome P450 enzyme system (CYP450). Drug interactions related to the induction or inhibition of CYP450 do not seem to affect lidocaine. Drugs that adversely affect hepatic blood flow can be expected to raise the plasma concentration of lidocaine, including the following:
 - phenytoin
 - beta-blockers
 - antibiotics: ciprofloxacin, norfloxacin, erythromycin, clarithromycin
 - antifungals: fluconazole, itraconazole, ketoconazole
 - antidepressants: fluoxetine, fluvoxamine, sertraline, citalopram, paroxetine
 - others: valproic acid, bromocriptine, cimetidine, diltiazem, methadone, nifedipine, verapamil

She was able to attend and help her daughter prepare for her wedding. She had also found renewed interest in her decorative painting hobby and other such activities. Our courageous patient continued intravenous lidocaine treatment until her death 5 months later. Since then, 11 more patients have benefited from the continuous infusional lidocaine treatment that she helped us develop. Several of these also received their treatment at home.

This treatment succeeded thanks to a truly multidisciplinary approach to a complex pain management situation. The passion of those who advocated for this unconventional approach to pain management has made a big difference in the lives of several families. Consideration of infusional lidocaine is now incorporated into the pain management armamentarium for selected patients in the Ottawa area. The chief lessons learned from this case were to never give

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up on the quest for symptom relief, to seek expert opinion and to learn from our experiences through policy development and ongoing education so that others may benefit in the future. 

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Disclosure

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