Intravenous Lidocaine for Opioid-Resistant Pain Control in Metastatic Breast Cancer

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Abstract

A fifty-one-year-old woman presented with pain related to metastatic breast cancer. The palliative care team was consulted for acute pain management intervention. At home, she was taking methadone for pain control. However, shooting pains down her legs had progressed to an unmanageable level, to the point where she was confided to bed. She was admitted to the hospital and was started on a hydromorphone PCA without complete pain control. Intravenous lidocaine was trialed and significantly improved the patient's pain and decreased the need for other opioid medications. After these results, she was started on a lidocaine drip without side effects noted.

Keywords: Cancer; Intravenous Lidocaine; Metastatic Breast Cancer

1. Background

Untreated pain is a distressing phenomenon for physicians, patients and society. It takes a toll on the economy, costing an estimated \$560 - 635 billion annually in health care costs and lost productivity [1]. Managing pain is a challenge for many physicians and patients to find the right balance of benefits and risks. Currently opioids are the most commonly used analgesia for moderate to severe acute pain, however, this is not risk free [2]. Opioid use has been associated with increased post-operative complications including respiratory depression, nausea, vomiting and gastrointestinal slowing [2]. Additionally, there is a growing opioid addiction epidemic growing in this country. In general, there has been a growing trend in healthcare to find other mechanisms of pain relief. Moreover, when opioids fail to manage a patient's pain, other options must be explored. One of these options is intravenous lidocaine, which has been shown to be effective in treating opioid-refractory cancer pain [2]. This treatment was

reported for pain management as early as 1962 by Bartlett and Hutaserani, however there is still not much written on its efficacy or indications [3].

2. Case Presentation

A 51 year old female presented with metastatic estrogen-receptor positive, progesterone-receptor positive, HER-2 positive, pleomorphic lobular carcinoma of her left breast, diagnosed six months prior. An initial MRI found metastasis to the lumbar spine and a T12 compression fracture. She chose to explore alternative therapies for a short course, and then was treated with tamoxifen and leuprolide. However, her pain continued to worsen, compelling her to enroll in hospice for pain management. This included palliative radiation to the sacrum and thoracic spine, which provided temporary pain relief. After a short time though, she presented to our hospital for uncontrolled pain, concerning for progressive metastatic disease.

The pain was located in her lower back and was triggered by movement with shooting pains down both legs. No muscle weakness, changes in sensation, or focal neurologic deficits were present, but walking was impaired by pain. On physical exam, she was unable to lift her legs without shooting pain and spasms. Upper extremity strength was 4/5 and lower extremity strength was 3/5. The patient was in excruciating pain and rated it as a 201/10.

3. Treatment

Prior to hospitalization for pain control, she was taking 15 milligrams of methadone every 6 hours with hydromorphone (Dilaudid) as needed for breakthrough pain. She had tried 50 microgram/hour fentanyl patches in the past, but this was discontinued due to the cost. On presentation, she was started on a hydromorphone PCA, 25 mg of nortriptyline nightly, and 5 mg of baclofen three times a day. On day 2 of hospitalization, methadone was decreased to every 8 hours due to drowsiness. On day 3, she reported continued pain despite extensive courses of opioid pain medications. On exam, she was unable to get out of bed due to the shooting pains down her legs when moving them. At this time, IV lidocaine was proposed.

A trial of lidocaine was given to assess pain response. For this, 100 milligrams of IV lidocaine was administrated over a half hour. At baseline, she was unable to lift legs without shooting pain and spasms. She reported some decreased range of motion of upper extremities when lifting arms to head with rare shooting pain down neck. Upper extremity strength was 4/5 and lower extremity strength was 3/5. At 15 minutes, she was able to lift her legs while laying down without pain or muscle spasms. At 30 minutes, she reported a complete resolution of pain. She was able to sit up unassisted on the side of the bed, then stand and walk with the assistance of a walker. The patient's overall pain was significantly improved and she rated it as a 2/10. She had full range of motion of upper extremities without pain. Upper extremity strength was 5/5 and lower extremity strength was 5/5. After the trial, her heart rate increased while standing to (96->142) but returned to baseline when she returned to bed (95). Blood pressure remained

unchanged during the trial. No adverse effects were reported including no seizures, no changes in mental status, no nausea or vomiting.

4. Outcome and Follow-Up

Following the response to the trial, a lidocaine drip was started at 1 mg/kg/hr. Methadone was decreased to 15 milligrams twice daily. As the day when on she reported slight increase in pain and lidocaine drip was increased to 1.135 mg/kg/hr. She was transferred to a community hospital, with a plan to continue increasing lidocaine dose as necessary with a maximum of 2 mg/kg/hr. In the 48 hours prior to the lidocaine infusion, her total methadone dose was 90 mg with 81.23 mg of hydromorphone delivered via PCA. In the 48 hours following lidocaine initiation, opioid use significantly decreased. Total methadone given was 60 mg with 33.65 mg of hydromorphone delivered via PCA.

	24-hour methadone dosage	24-hour hydromorphone PCA requirement
Relative to starting lidocaine drip (24 hr periods)		
2 days before	45 mg	60.39 mg
1 day before	45 mg	20.84 mg
1 day after	30 mg	9.65 mg
2 days after	30 mg	24 mg

Table 1: Treatment of methadone and hydromorphone PCA dosage.

5. Discussion

Lidocaine modulates pain through its analgesic and anti-inflammatory effects [2]. It works on neuronal cell membranes to interrupt pain by blocking a voltage-gated sodium channel [4]. Lidocaine patches are a commonly used in long-term pain management treatment, however IV lidocaine is a much less used intervention [5]. Intravenous lidocaine has been suggested as a treatment for opioid resistant pain. It has been shown in studies to be effective at treating refractory cancer pain, complex regional pain syndrome, neuropathic pain syndromes, traumatic or post-herpetic peripheral nerve injury, and surgical pain [2,5]. A 1986 placebo-controlled study found IV lidocaine significantly improved chronic pain in 78% of participants, with effects lasting 2 hours to 25 days [6]. Lidocaine also has been shown to reduce opioid consumption [2]. A double-blind study by Terkawi et al. found a decrease in chronic post-surgical pain in breast cancer patients after IV lidocaine infusion [7]. A double-blind, randomized trial by Sharma et al. found increased analgesic effects up to 9 days after infusion in chancer pain patients [8].

Dosage for IV lidocaine has been studied as well. The dosage selected in this case was based off the MUSC Palliative guidelines for IV lidocaine use. Following this guide, an initial trial of 100 milligrams of IV lidocaine was

administrated over a half hour was given as a predictor of effectiveness before starting the lidocaine drip. Following success of the trial, 1mg/kg/hr of lidocaine was started and increased as needed. Studies have found that 1.33–3 mg/kg/hour IV lidocaine dosage achieved goal plasma concentrations of 2–5 µg/mL [2].

Side effects of lidocaine treatment must also be considered. One study found one side effect reported in 52% of patients [2]. Side effects of IV lidocaine include dizziness, sedation, tinnitus, seizures and arrhythmias [4]. Other less serious side effects include, metallic taste, tremor, try mouth, insomnia and allergic reactions [4].

Given the great costs to all parties involved of unmanaged pain, physicians should be aware of alternative pain medications to opioids, especially in cases where opioids are not fully effective. The use of this medication should be trialed before it is started for long-term use. Finally, use of IV lidocaine can cause serious side effects which should be recognized and managed appropriately. Overall, IV lidocaine is a under used pain medication and an effective alternative to opioids for some patients.

6. Learning Points/Take Home Messages

- Intravenous lidocaine should be considered as a pain management alternative to opioids.
- A trial of lidocaine should be performed to test pain response.
- Serious side effects including sedation, seizures and arrhythmias should be monitored.

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