

# PALLIATIVE PEARLS

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## Intrathecal Opioid Therapy: A Patient Case & Overview November 2021

### PATIENT CASE

SH is a 65-year-old female with ovarian cancer recently admitted to hospice. She has a history of hypertension and GERD, is allergic to penicillin, and lives at home with her husband who is her primary caregiver.

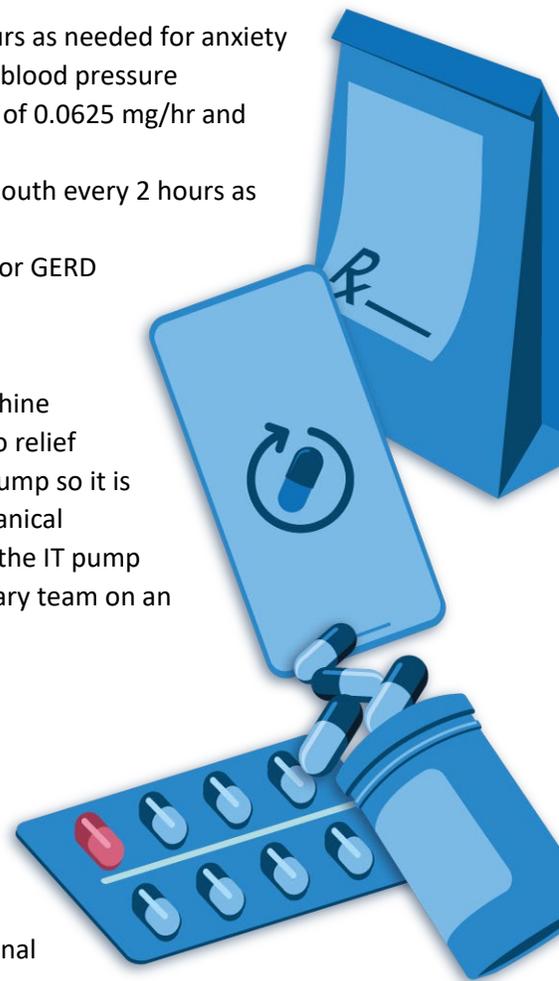
### MEDICATIONS

- Gabapentin (Neurontin®) 100 mg capsule; Take 2 capsules by mouth twice daily for neuropathic pain
- Lorazepam (Ativan®) 0.5 mg tablet; 1 tablet by mouth every 6 hours as needed for anxiety
- Lisinopril (Prinivil®) 10 mg tablet; 1 tablet by mouth every day for blood pressure
- Morphine continuous infusion; Infuse intrathecally at a basal rate of 0.0625 mg/hr and 0.01 mg every 20 minutes as needed for pain via infusion pump
- Hydromorphone (Dilaudid®) 1 mg/ml oral liquid: 1 ml (1 mg) by mouth every 2 hours as needed for pain
- Omeprazole (Prilosec®) 20 mg capsule; 1 capsule by mouth daily for GERD
- Senna 8.6 mg tablet; 2 tablets by mouth twice daily as needed for constipation

Prior to admission, SH was initiated on an implanted intrathecal (IT) morphine pump for uncontrolled visceral pain. Pain is currently uncontrolled with no relief following IT boluses. The clinician in the home is not familiar with the IT pump so it is unclear how many boluses SH has received. It is apparent there is a mechanical malfunction with the IT pump and it is not infusing. The plan is to consult the IT pump prescriber for care planning and to consult with the hospice interdisciplinary team on an interim solution to provide SH relief quickly.

### NEURAXIAL THERAPY OVERVIEW

Pain in advanced disease is commonly managed with oral or parenteral medications such as NSAIDs, corticosteroids, and opioid analgesics. A small subset of these patients, often with cancer, do not respond to or are intolerant to therapy via these routes and may require a more targeted approach. Neuraxial opioid therapy is targeted therapy and refers to the administration of opioids into the spaces surrounding the spinal cord, such as the epidural space or the intrathecal space.<sup>1</sup>



Neuraxial delivery permits analgesia to be restricted to fewer dermatomes, which may be an advantage in some patients.<sup>2</sup> Dermatomes are areas of skin, each of which is connected to a single spinal nerve root. The spinal cord has 31 segments giving rise to 31 spinal nerves, which are composed of 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal spinal nerve. Dermatomes exist for each of these spinal nerves, except the first cervical spinal nerve.<sup>3</sup>

## **Epidural Space**

Three layers of connective tissue surround the spinal cord: the dura mater which is the outermost layer, the arachnoid mater, and the pia mater which is the innermost layer. The epidural space is outside the dura mater, and contains blood vessels, nerve roots, fat, and connective tissue.<sup>1</sup> Drugs administered epidurally may be given as a single injection or as a continuous infusion via an indwelling catheter.<sup>4</sup> The medication is distributed by diffusion through the dura mater into the cerebrospinal fluid (CSF) then to the spinal cord or nerve roots, by vascular uptake by the vessels in the epidural space into systemic circulation and, lastly, via uptake by the fat in the epidural space, creating a drug depot from which the drug can eventually enter the CSF or the systemic circulation.<sup>5</sup>

## **Intrathecal Space**

The arachnoid mater and pia mater are separated by the subarachnoid (i.e., intrathecal) space, which contains CSF, arteries, and veins.<sup>6</sup> A catheter placed in the intrathecal space has the advantage of having more direct access to the CSF and spinal drug receptor sites. Lower doses of medication can be used compared with epidural delivery leading to better pain control and possible lower adverse effects. It is important to note that only preservative-free medications can be used for intrathecal administration.<sup>1,4</sup>

The remainder of this overview will focus on the intrathecal route of administration.

## **Considerations Before Initiating Intrathecal Opioid Therapy**

### **General<sup>2</sup>**

- Medical status of the patient
- Goals of care
- Availability of professional support (i.e., referral to a specialist to evaluate the feasibility and appropriateness of neuraxial therapy)
- Availability of family support
- Cost

### **Indications for Intrathecal Drug Therapy<sup>7</sup>**

- Axial neck or back pain (not a surgical candidate)
- Failed back surgery syndrome
- Abdominal/pelvic pain (visceral, somatic)
- Extremity pain (radicular, joint)
- Complex regional pain syndrome
- Trunk pain (postherpetic neuralgia, post-thoracotomy syndromes)
- Cancer pain (direct invasion and chemotherapy-related)

- Analgesic efficacy with systemic opioid delivery complicated by intolerable side effects

## Risks of Intrathecal Drug Therapy<sup>2,8,9</sup>

- Respiratory depression
- Infection of the meninges or surrounding tissues
- Potential dislodgement, either movement of the catheter tip or complete removal, from the neuraxial space, resulting in opioid withdrawal
- Catheter tip inflammatory mass formation, or granuloma (common with long-term use)
- Rare: bleeding, spinal cord injury

## Trial of Efficacy<sup>8,9</sup>

- Prior to starting a neuraxial therapy, a trial to evaluate efficacy of a medication or combination may be performed via a single shot administration or a short-term infusion, either epidural or intrathecal
- A trial may not be necessary for patients already tolerating the same drug by a different route

## INTRATHECAL MEDICATIONS

Opioids are the most used agents, often as monotherapy. Medications include:<sup>8,9</sup>

- Morphine 0.1-0.5 mg bolus (max for opioid naive: 0.15 mg), then 0.1–0.5 mg/day
- Hydromorphone 0.025-0.1 mg bolus (max for opioid naive: 0.04 mg), then 0.01–0.15 mg/day
- Fentanyl 15–75 mcg bolus (max for opioid naive: 25 mcg), then 25-75 mcg/day

Combining opioids with other agents achieves a synergistic effect and may reduce the required dose of opioid. Medications include the following:<sup>4,8,10</sup>

- Bupivacaine 0.5-2.5 mcg bolus, then 1-4 mg/day
  - Local anesthetic drug that exerts its effect by sodium channel blockade, inhibiting the action potential in the dorsal horn of the spinal cord
- Ziconotide 1–5 mcg bolus, then 10-20 mcg/day
  - Calcium channel blocker specific to the neuronal calcium channels that regulates synaptic transmission in nociceptive neurons
- Clonidine 5–20 mcg bolus, then 20-100 mcg/day
  - Alpha-2 adrenergic agonist that modulates pain transmission by depressing the release of neurotransmitters

The 2017 Polyanalgesic Consensus Conference (PACC) report provides recommendations on intrathecal drug infusion for cancer or other terminal condition-associated pain based upon literature review and conference member consensus. The evidence is strongest for the following indications and respective medications:<sup>2,9</sup>

- Localized nociceptive or neuropathic pain:
  - Ziconotide
  - Morphine
  - Fentanyl
  - Hydromorphone
  - Morphine or fentanyl or hydromorphone plus bupivacaine
  - Morphine or fentanyl or hydromorphone plus clonidine
  - Morphine or fentanyl or hydromorphone plus ziconotide
- Diffuse nociceptive or neuropathic pain:
  - Ziconotide
  - Morphine
  - Hydromorphone
  - Morphine or hydromorphone plus clonidine
  - Morphine or hydromorphone plus bupivacaine
  - Morphine or hydromorphone plus ziconotide

## CONVERSION FROM NEURAXIAL ROUTE TO PARENTERAL OR ORAL

There are no definitive guidelines however one set of conversions is frequently referenced:<sup>1,6,11</sup>

- 300mg oral morphine equals
- 100mg parenteral morphine equals
- 10mg epidural morphine equals
- 1mg intrathecal morphine

## ASSESSMENT AND RECOMMENDATION

For managing SH's immediate needs and uncontrolled pain, the care team agrees on an oral pain regimen. The number of boluses from IT morphine is unknown and oral hydromorphone has not been used recently. Using the current daily dose of IT morphine prescribed, we apply the 300:100:10:1 (PO:IV:EPIDURAL:IT) conversion as follows:

- Morphine IT at 0.0625 mg/hr continuously would be a daily dose of 1.5 mg IT
- Using a 1:300 (IT morphine:oral morphine), the morphine oral equivalent is 450mg/day
- Using a 25:5 conversion (oral morphine:oral hydromorphone), the oral hydromorphone equivalent is 90 mg/day
- Hydromorphone 1 mg/ml oral liquid is already in the home:
  - Recommendation: 15 ml (15 mg) by mouth every 4 hours around the clock with 10 ml (10 mg) by mouth every 2 hours as needed for pain
- If the supply of hydromorphone in the home is low, consider an oral regimen with morphine 20mg/ml concentrate as this product has a quick onset and more readily available at local pharmacies:
  - Recommendation: 3.75 ml (75 mg) by mouth every 4 hours around the clock with 2.25 ml (45 mg) by mouth every 2 hours as needed for pain

Long-term considerations depending on intrathecal pump status and patient goals of care:

- Morphine LA 230 mg by mouth every 12 hours with Morphine 20mg/ml; 2.25 ml (45 mg) by mouth every 2 hours as needed for breakthrough pain
- Transdermal fentanyl 100 mcg/hr patch; apply 2 patches (200 mcg/hr) topically every 72 hours with Morphine 20mg/ml; 2.25 ml (45 mg) by mouth every 2 hours as needed for breakthrough pain
- Morphine IT 1.5 mg/day is equivalent to Morphine IV 150 mg/day
  - Infuse 6.25 mg/hr continuously with a 1.5 mg bolus every 15 minutes as needed for breakthrough pain
- Morphine IV 150 mg/day is equivalent to Hydromorphone IV 30 mg/day
  - Infuse 1.25 mg/hr continuously with a 0.4 mg bolus every 15 minutes as needed for breakthrough pain

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