

FAST FACT AND CONCEPT #98 INTRATHECAL DRUG THERAPY FOR PAIN

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Background Intrathecal (IT) drug delivery can be an invaluable adjunct in the management of severe and refractory pain. While most of the evidence supporting the use of IT pain pumps in palliative care settings has been largely based on case series and consensus statements, one prospective randomized clinical trial of cancer patients with refractory pain, suggested that IT drug delivery may have better analgesia, less opioid-related side effects, and longer survival compared with oral opioids.

Candidates for IT drug therapy: Appropriate patient selection is important to optimize the safety and effectiveness of IT therapy. Candidates for IT pumps should have:

- An established diagnosis of severe chronic pain classified as neuropathic, nociceptive, or mixed;
- Pain refractory to oral analgesics or are intolerant to oral analgesics;
- Failed or are not a candidate for nonpharmacologic or surgical treatments;
- Pain that is below the neck and ideally focal in location.

Because multiple psychosocial factors can influence a patient's pain perception as well as their ability to manage a pump once implanted, a psychological evaluation should be considered for patients being evaluated for IT implantation.

Epidural vs. Intrathecal Analgesia IT analgesia is distinguished from epidural analgesia by catheter location within the neuraxis (see *Fast Fact #85*). In the former, the catheter lies within the subarachnoid space, where small quantities of medication have direct access to spinal drug receptor sites. In the latter, larger doses of medication (necessitated by epidural fat and vascular uptake) must diffuse across the dura to reach these receptors.

There are no published guidelines on when to use the IT versus epidural route. In general, implantable IT pumps are reserved for patients with a life expectancy > 3 months. Potential disadvantages of IT relative to epidural techniques may include: lack of reprogramming/refilling capabilities near the patient's home, payor constraints, infusion volumes too great for an implantable pump, and the need for frequent patient controlled analgesia. Potential advantages of IT – relative to epidural – techniques are:

- Superior analgesia in the presence of epidural pathology (e.g. metastatic disease, radiation fibrosis, vertebral compression), widespread pain, and pain poorly responsive to high-dose epidural therapy.
- Ease of catheter placement, particularly in the presence spinal pathology.
- Fewer catheter problems such as catheter migration, fibrosis, or tip occlusion.
- Lower dose requirements may reduce side effects and lower drug costs.

Choice of System There exists a spectrum of IT system options – from a simple, percutaneous catheter/external pump to a totally implanted system. Life expectancy, performance status, and available professional expertise may also guide which system is selected. A trial of IT analgesia may be done to assess response to therapy and proper patient selection prior to implantation of a pump. Programmable pumps are often used and can allow patients to administer bolus doses for breakthrough pain.

Drug Choice Arner and Arner (1985) demonstrated the following relative responsiveness of pain mechanisms to intraspinal opioids: continuous somatic pain > continuous visceral > intermittent somatic > intermittent visceral > neuropathic > cutaneous (ulcers or fistulas). First line treatment for somatic pain syndromes includes a single agent opioid (most often morphine or fentanyl) or ziconotide (a selective voltage-gated calcium channel blocker with a sole FDA indication as an analgesic in IT pumps). Bupivacaine or ziconotide may be added in combination with an opioid as second line therapy. For neuropathic pain, morphine with bupivacaine or ziconotide alone is recommended. Second line therapy may include a change to hydromorphone alone or the addition of clonidine.

Complications and Side Effects Complications may occur from a) the procedure (e.g. post-spinal headache), b) medications (e.g. opioid-related respiratory depression, sedation, urinary retention, pruritis), and c) hardware (e.g. catheter kinking/disconnection/dislodgement, infection, granuloma formation at the catheter tip). Major contraindications to IT catheter placement include coagulopathy, infection at catheter insertion site, and sepsis.

Ziconotide use has been associated with increased suicidality, worsening of mood disorders, confusion, somnolence, dizziness, and new onset psychosis. Frequency of adverse effects may be attenuated by slow titration. Patients receiving ziconotide should be closely monitored for psychological side effects. Ziconotide should be avoided in patients with pre-existing psychosis.

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