Neuropathic Pain: An Option Overview

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Presented at the 79th Annual Dalhousie Refresher Course, November 2005

What's the difference between standard pain and neuropathic pain?

Neuropathic pain results from a primary lesion or dysfunction of the nervous system, which differentiates it from the stimulation of pain receptors, as with nociceptive pain. Affecting only approximately 2% of Canadians, it can be a source of great distress in about 10% of longstanding diabetic patients and about 50% of patients with shingles.[1]

Unlike with the clearer role for analgesics in nociceptive pain, neuropathic pain can only rarely be attributed to a single mechanism, so efforts may need to be aimed at various levels of the nervous system and beyond.

What treatment options are available?

Pharmacologic management is usually first-line and generally starts with a trial of any of a number of adjuvant analgesics and, when appropriate, opioid analgesics. No single agent can guarantee success and trials of various agents from different classes (and potentially combinations of classes) may be required. A recent evidence-based study[2] of these medications has helped to clarify the choices from among the variety of drug classes. The management of peripheral etiologies has been further studied and is generally more successful than the management of central neuropathic pain.

Alma's Pain

- Alma has been dealing with breast cancer for over three years, and metastatic bone involvement for one year.
- The associated low-back pain has been well managed with long-acting and breakthrough opioids.
- Alma presents urgently to the ER with a two-day history of a "pins and needles" feeling in her right thigh that transformed overnight into excruciating paroxysms of pain.
- On examination, her right thigh is exquisitely sensitive to touch. She is in significant distress, with three to four paroxysms, each lasting less than 10 seconds, every five minutes. She looks as if she is being repeatedly "struck by lightening."

For more on Alma, go to page 92.

1. Anticonvulsants/antidepressants

Best studied are the anticonvulsants and the antidepressants, with both classes having shown activity in a variety of etiologies. Careful monitoring and titration to beneficial effect or to side-effects is necessary. Of the anticonvulsants, the lancinating pain of trigeminal neuralgia remains best served by carbamazepine, starting at 50 mg to 100 mg, daily, to a maximum of 200 mg, three times a day. Gabapentin, starting at 100 mg to 300 mg, daily, to a maximum of about 1,600 mg, three times a day, has

Neuropathic Pain: Etiologies

Peripheral

- Due to anatomic, chemical or biochemical damage to peripheral nerves:
  - Post-herpetic neuralgia
  - HIV-associated neuralgia
  - Trigeminal neuralgia
  - Tumour compression
  - Diabetic neuropathy
  - Sciatica
  - Post-operative/chemotherapy, radiation

Central

- Due to pathophysiologic changes in the brain or spinal cord:
  - Phantom limb pain
  - Post-stroke
  - Multiple sclerosis

Neuropathic Pain: Clinical Features

Three cardinal features:

- Dysaesthetic burning pain
- Paroxysmal lancinating pain
- Allodynia

Ask the patient about:

- Pain distribution
- Factors that exacerbate or improved pain

Look for:

- Sensory loss
- Hypersensitivity
- Motor/reflex changes

become a popular general choice, given its favourable side-effect profile.[3]

The antidepressants offer an established role for the tricyclics, but not the selective serotonin reuptake inhibitors, and this has been best studied in the treatment of diabetic neuropathy. There is no significant benefit between agents unless increased sedation with night dosing is desired with amitryptiline. Titration from 10 mg to 25 mg, daily, to upwards of 150 mg, daily, should be done slowly, as side-effects may impact upon a fairly narrow therapeutic window.

2. Antiarrhythmics

Other classes for potential use include antiarrythmics, in more resistant cases, that would call for specialist involvement. Topical agents should be considered first-line for localized symptoms. A compressive neuropathy may potentially rapidly improved through the use of systemic steroids.

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3. Opioids

There is a clear role for opioids in the management of neuropathic pain, especially in cases involving cancer where the patients frequently present with mixed pain syndromes. The decision to use opioids must be carefully weighed against the potential for tolerance, adverse effects and addiction in more chronic cases. The dosing and titration in neuropathic pain would be the same as for the management of nociceptive pain.

4. Non-pharmacologic approaches

Non-pharmacologic approaches[4] involve efforts directed not only at the nerve damage, but also at the person suffering from the associated pain. The

Neuropathic Pain: Common Treatment Options

Pharmacologic

- Adjuvant analgesics
  - Anticonvulsants: Carbamazepine, phenytoin, valproic acid, gabapentin
  - Tricyclic antidepressants: Amitryptiline, nortryptyline, desipramine
  - Others: Antiarrythmics (mexiletine, flecainide); topicals (lidocaine, EMLA, capsaicin); corticosteroids; NMDA antagonists (dextromethorphan, ketamine)
  - Opioids

Non-Pharmacologic

- Adjuvant
- Anesthetic
- Neurostimulatory
- Rehabilitation
- Surgical
- Psychologic

EMLA: Eutectic micture of local anesthetics

NMDA: N-methyl-D-asparate

Take-home message

- Neuropathic pain can be challenging to treat.
- No one drug or drug class can offer guaranteed success.
- First-line options include topical agents for very localized symptoms, an antidepressant or an anticonvulsant for general use, and combination with opioids for resistant cases or in cases of mixed pain, as with cancer.

More on Alma

- An urgent MRI confirms nerve root, not spinal cord, involvement.
- Pain management includes:
  - a bolus dose of dexamethasone intravenously, 16 mg and maintenance of the same dose daily by mouth;
  - start of gabapentin, 300 mg, twice daily and titrated quickly over four days to 600 mg, three times daily and titration of her same opioid as every four hour dosing with appropriate as-required doses.
- Alma gains satisfactory control over the paroxysms within 12 hours and is comfortable to undergo radiotherapy within two days. Her pain is, thereafter, well controlled with her opioid and continued dosing with gabapentin.

anesthetic options include focal nerve blocks and, in more extreme cases, intraspinal infusions of a combination of an opioid and a local anesthetic. Transcutaneous electric nerve stimulation units can provide initial benefit to many patients, but this is only sustained in a few. Surgical options are usually aimed at dealing with nerve compression or damage directly. Denervating a painful part may be possible through rhizotomy or cordotomy.

Rehabilitation may play a key role with physiotherapy, helping to manage any associated myofascial component, and occupational therapy helping to regain function without exacerbating pain. Cognitive approaches, such as hypnosis or distraction techniques, though not formally studied, may be considered, given the potential benefits and few risks.

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