Managing Refractory Nerve Pain

By Dr Tim Hucker, Pain Specialist

Neuropathic pain is a common problem in Australia, affecting about 8% of adults[1]. The prevalence of such a problem ranges enormously with the aetiology. For instance, it affects a quarter of people with Diabetes and is even more prevalent in HIV.

In addition, the effect of pain is substantial, often associated with significant compromise in patient's function, mood and relationships.

In this, the second of two factsheets, we move on to consider pain management options when first line treatment of neuropathic pain has failed.

In 2019 a collaboration of pain specialists from differing backgrounds published a very useful algorithm for the management of neuropathic pain.[2] This follows a 6-step treatment protocol whereby a patient, accurately diagnosed with neuropathic pain, would have trialled in steps 1-3 at least one anti neuropathic agent from the well-known families of anti-neuropathics. In all likelihood, prior to referral to a specialist most patients would have trialled a combination of them and/or Tramadol.

This factsheet covers steps 3-6 from specialist referral onwards and the treatment steps a patient would likely undergo. Underpinning all of this is the essential component of multidisciplinary team care that runs concurrently with all neuropathic pain management.

Step 3: Following specialist referral

The two main options in step 3 are atypical anti-neuropathics or interventional therapies.

- **Atypical anti-neuropathics.** Under this banner are medications such as the SSRI's, anticonvulsants such as Phenytoin and the NMDA antagonists. Whilst it varies between specialty, few pain specialists are likely to use the anticonvulsants.
- **NMDA antagonists.** Many pain specialists use ketamine infusions as part of their treatment algorithm. In most cases, patients are admitted to hospital for a period of approximately a week for the purpose of effectively desensitising the overly sensitised NMDA receptor. Sensitisation via the NMDA receptor (for which ketamine is an antagonist) is a feature of chronic neuropathic pain. The results of this vary considerably from patient to patient and consensus on dose targets, duration of infusion etc still remains debated.
- **Interventional therapies.** There are a number of very simple, day case type procedures that can be considered at this step. Whilst the evidence remains limited, some would argue that trialling simple options prior to the more invasive steps would be a reasonable approach. Examples include pulsed radiofrequency procedures. In these, a peripheral nerve, dorsal root ganglion or autonomic ganglion has an electrical current applied after sensory testing. This current is non ablative, and produces analgesia by inducing a neuroimmunomodulatory change in the sensitised nerve producing analgesia without causing any loss of nerve function.

In common with much of pain medicine, greater study of options in this step is required. However, consideration of these, before heading down to step 4 if the pain is still refractory is worthwhile.

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Step 4: Neuromodulation (usually spinal cord stimulation)

A number of different bodies internationally have reported on the use of spinal cord stimulation (SCS) for neuropathic pain. The Faculty of Pain Medicine in Australia for instance, reports indications likely to respond as failed back surgery syndrome, refractory angina pectoris, complex regional pain syndrome and neuropathic pain secondary to peripheral nerve damage. They considered conditions that may respond to include - pain associated with peripheral vascular disease, brachial plexopathy (without avulsion), axial pain after surgery, intercostal neuralgia and other peripheral neuropathic syndromes. [3]

Other countries such as the U.K's NICE (national institute of health and care excellence) recommend neuromodulation as a treatment option for all chronic pain conditions of neuropathic origin with a VAS (pain score) >50/100. [2]

- **Patient selection.** The success of SCS is critically dependant on patient selection. In short, the right patient in the right frame of mind, with the right condition at the right time. All patients should have time taken to understand the process, ensure there are no psychological contraindications and have realistic expectations prior to the trial plus clear markers of success considered.
- **Process-trial phase.** In almost all cases, a trial of stimulation is undertaken. This is a two-week process (after a day case procedure) where the two stimulator leads are sited epidurally, are externalised and connected to a programmer. In conjunction with a rep from the manufacturer, the patients are monitored closely and programming adjusted to get maximal coverage of pain area.
- **Preparation for implant.** If the trial is deemed successful – eg. 70% pain relief, improved functional goals and opioids reduced in the trial, then a patient is likely to be offered an implant. Again, a patient should be well prepared for this process as the follow up post implant is time consuming for the patient and clear informed consent is required.
- **Implant and post.** In the implant stage – essentially the trial is repeated but this time the leads are connected to an IPG. Similar to a pacemaker, this is the battery and controller for the stimulator and often sited under the skin in the upper buttock. After wound healing the patient is programmed to obtain the same benefits found in the trial. Most systems are rechargeable through the skin and last around 10 years.

Step 5: Low-dose Opioid medication

Opioid medications have increasingly been listed lower and lower down the paradigms for neuropathic pain management. A full discussion of their use, or not to use, is outside the remit of this sheet. It is unusual though to see them sited as low as 5th line treatments. However, debate continues into their perceived lack of efficacy and the dangers of long term opioid use. Whether third, fourth or fifth line it is as imperative to obtain informed consent for long term opioid therapy as if it is a procedure.

Factors to consider in consent:

- Lack of efficacy. In a Cochrane review from 2017, the conclusion was that of a lack of evidence to support or refute morphine as efficacious in any neuropathic condition. [4]
- Side effects. The short-term side effects of opioid use are well documented, long term side effects are often less considered though. These include hypogonadism, osteoporosis and immune dysfunction.
- Compliance with treatment. Monitoring the treatment and its efficacy should be set out at the beginning after a trial phase. Various options to consider include opioid risk assessment and contract prior to commencement.

Step 6: Targeted drug delivery

The final step included in this algorithm is targeted drug delivery. Essentially this is an intrathecal catheter connected to a refillable pump usually pocketed in the anterior abdominal wall. The goal is to deliver analgesics, principally opioids, to their site of action at the dorsal horn of the spinal cord. Delivery at this site means that effective doses can be reduced often by factors of a hundred times less. Not only is the goal analgesia but a significant side effect reduction due to this highly reduced dosing.

Currently, intrathecal pump implantation for pain is only undertaken in some centres in Australia. At present at Northern Beaches Hospital this can be undertaken for intractable cancer pain in conjunction with palliative care, but is not for chronic non-cancer pain.

References:

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