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Assessment and Pharmacological Management of Neuropathic Pain

By Dr Tim Hucker, Pain Specialist

Neuropathic pain is a common problem in Australia, affecting approximately 8% of adults.[1] The prevalence of such a problem ranges enormously with the aetiology, but can be extremely high. For instance, a quarter of people with diabetes and even higher proportion with HIV experience neuropathic pain. The effect of pain is substantial, often associated with significant compromise in patient's function, mood and relationships.

In 2019 a collaboration of pain specialists from differing backgrounds published a very useful algorithm for the management of neuropathic pain. [2] This algorithm would be a very reasonable approach when faced with the patient with "nerve pain" and uses a 6-step treatment protocol with the consistent coexisting theme of multidisciplinary team care running alongside it, eg. sleep hygiene, psychological management etc.

There are some provisos and recommendations to be considered in following this path. In the first of two fact sheets we will concentrate on the first line to third lines of treatment in the algorithm, which, broadly speaking, make up the pharmacological options. The second fact sheet addresses the interventional options if treatment is proving intractable.

Prior to even the first step, it is crucial to maintain a high index of suspicion for neuropathic pain and diagnosing accurately. A number of different pain scoring systems can be used, but probably the most navigable is the DN-4.

The DN-4

This is a simple ten point tool (yes=1 point), where a score of 4 or more equates to a diagnosis of neuropathic pain with relatively good specificity and sensitivity. It is administered easily bedside with two questions from history taking and two on a simple examination using only cotton wool and a toothpick, for instance.

History	Yes	No
1. Does the pain have one or more of the following characteristics		
Burning	☐	☐
Painful cold	☐	☐
Electric shocks	☐	☐
2. Is the pain associated with one or more of the following symptoms		
Tingling	☐	☐
Pins and needles	☐	☐
Numbness	☐	☐
Itching	☐	☐

Examination	Yes	No
3. Is the pain located in an area where the physical examination may reveal one or more of the following characteristics.		
Hypoaesthesia to touch (reduced sensation of cotton wool)	☐	☐
Hypoaestheisa to pinprick (less sensation of the toothpick)	☐	☐
4. In the painful area, can the pain be caused or increased by		
Brushing	☐	☐

First to third line therapy

First line therapy is a 4-6 week trial of the medications grouped into TCA's, SNRI's, Gabapentinoids and Topical treatments.

Provisos and recommendations:

- **Trial time.** If often takes longer than the advised 4-6 week period to ensure that these medications, all of which have a reasonable list of side effects, can be started low and uptitrated. Amitriptyline, for instance, is often started at too high a dose for the patient and the side effects are too off-putting for them to consider restarting at a lower dose.
- **Uptitration.** Often starting at 10mg Amitriptyline for 5 days then 20mg for 5 days etc is a useful compromise to allow patients to get to an optimal dose. Similarly for Gabapentin, trialling at 300mg od for 5 days, then bd for 5 days etc can be more acceptable.
- **Choice of agent.** Choosing between each is often personal preference, however certain cases require targeting. Diabetic peripheral neuropathy and post herpetic neuralgia, for instance, are much better managed with Duloxetine than the other antineuropathics.
- **Choice of Gabapentinoid.** The pendulum that swung ten years or so ago to Pregabalin appears to be swinging back to Gabapentin. This may relate to Gabapentin having a greater anti-spasmodic profile or being more titrateable as a 3 times a day medication with individual doses ranging from 100mg to 900mg.
- **TCA swap.** If Amitriptyline is too sedating, try a like-for-like dose swap to Nortriptyline
- **Topical Lignocaine.** Often profoundly effective for profound skin allodynia such as in post herpetic neuralgia. Now available over the counter as Nervoderm and patches can be cut to shape to make up for the expense. It does not appear to work for the "negative" type of neuropathic pain, i.e. when skin findings are of numbness rather than sensitivity
- **Other topical agents.** Usage of the other topicals is complicated. For instance, high dose Capsaicin 8% is considered in this algorithm, however tolerability at this dosing is a considerable issue
- **Agent rotation.** Prior to step 2 it would be worth instituting a swap if one medication is intolerable and trialling that for 4-6 weeks prior to second line treatment.

Second line therapy

The next line of treatment, predicated on an exacerbation of pain or inadequate response to first line, recommends use of Tramadol or combining the first line therapies and again running on a 4-6 week trial.

Provisos and recommendations:

- Beware the interaction list of Tramadol
- Tapentadol may be of similar value in this line of treatment. The reality is both Tramadol and Tapentadol are Opioids, with all the same issues of the more traditional opioids.
- Combining first line therapies would be in the form of Gabapentinoid plus TCA or SNRI, not usually combining the TCA and SNRI options.
- If mood disorder is profound and neuropathic pain uncontrolled, involving a psychiatrist by now is useful to enable the neuropathic treatment switch without mood compromise

Third Line Therapy

Prior to instituting third line treatment, the algorithm advises specialist referral. The recommendations in the third line phase are for medications (SSRI's, Anticonvulsants, NMDA antagonists) or the use of interventional treatment.

Provisos and recommendations:

- Referral at this stage is recommended, although it would be worthwhile maintaining a low threshold for referral earlier, if concerns over severity and or treatment resistance exist
- Many pain specialists would avoid the SSRI group of medications for neuropathic pain and likely reconsider other options from steps 1 or 2
- Topirimate is frequently used for headache or facial pain where there are neuropathic features.
- Whilst Ketamine may be useful in this group, challenges with prescribing and formulating may make this practically difficult

Conclusion

Obtaining a good prognosis for new onset neuropathic pain relies on early and accurate assessment and rapidly instituting management.

Management in the new onset case, starts with pharmacological options that should be started early and uptitrated from low doses due to medication side effects. Where single agents fail, broadly speaking the approach is to move to combined recommended therapies, before considering the lower evidenced remedies and moving to an interventional approach with a pain specialist.

References:

1. Murnion B, Neuropathic pain: current definition and review of drug treatment. Aust Prescr 2018;41:60-3
2. Bates D et al, A comprehensive algorithm for Management of Neuropathic pain. Pain Medicine, 20, 2109, S2-S12