

# Antidepressant, Anticonvulsant Treatment for Peripheral Neuropathic Pain

Differentiate the cause of painful neuropathy before prescribing pain treatment.

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**N**o matter what the underlying cause – thyroid disorders, diabetes or neurological problems – patients with painful neuropathy will come to their podiatrist seeking treatment. It is important that the clinician perform a complete work up in order to select the proper medication and treatment.

I recently presented information about antidepressant and anticonvulsant treatment for diabetic neuropathy at the 2005 Annual Scientific Meeting of the American Podiatric Medical Association in Orlando. There I said that physicians must first differentiate between metabolic and anatomic causes of peripheral neuropathic pain. Metabolic causes generally consist of endocrine disorders. Examples of anatomic causes of include herniated disc or Morton's neuroma.

Differentiating between the two causes allows appropriate treatment. If a patient has a herniated disc, for example, he or she may need a referral to a neurologist, a neurosurgeon or a physiotherapist. Metabolic disease must be treated as such.

Then determine if the neuropathy is causing pain and/or numbness. Is there a loss of motor function? If there are motor function problems, then there is possible damage to the entire neuron; not necessarily the case in diabetic neuropathy.

## ANTIDEPRESSANTS

**Tricyclic.** The two classes of pharmaceuticals used to manage peripheral neuropathic pain are antidepress-

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sants and anticonvulsants (Table 1). Amitriptyline (Elavil, Merck for AstraZeneca) is a tricyclic antidepressant that has been widely prescribed for peripheral neuropathy. In fact, it is more popularly used for this indication than for its psychiatric indication. Nortriptyline is another member of this class.

Patients who take large doses of tricyclic antidepressants often say they have dry mouth or cannot urinate properly. When medications in this category do not work for severe pain, clinicians will often increase the doses. Unfortunately, upping the dosage just increases the side effects and not necessarily the beneficial outcome.

**Selective serotonin reuptake inhibitors.** Another class of antidepressants used to treat neuropathic pain is selective serotonin reuptake inhibitors (SSRIs). Some of these agents are effective in pain management and some are not. The classic original SSRI is fluoxetine (Prozac, Eli Lilly and Company). A study conducted by the National Institutes of Health a number of years ago showed that while fluoxetine may be a good antidepressant, it is a poor drug choice for treating neuropathic pain.

Venlafaxine (Effexor, Wyeth) is an SSRI that is used with

**TABLE 1. PHARMACEUTICALS  
FOR NEUROPATHIC PAIN**

Antidepressants	Anticonvulsants
amitriptyline	gabapentin
nortriptyline	pregabalin
fluoxetine	
venlafaxine	
duloxetine	

some success for the treatment of pain.

The newest SSRI on the market for pain treatment is duloxetine (Cymbalta, Eli Lilly and Company). It is pharmacologically similar to venlafaxine, although there are some advancements. Some of its advantages are that it raises serotonin levels as well as the norepinephrine levels. The original SSRIs just work on serotonin. It also has fewer side effects than venlafaxine.

I recommend that you not start with the therapeutic dosage with any of these drugs. Start with smaller doses to make sure that the patient does not have any side effects and up-titrate.

Although some internists have added the antidepressant bupropion (Wellbutrin, GlaxoSmithKline) to duloxetine with good results, there is not enough solid literature on its use with duloxetine.

### SIDE EFFECTS

Some patients who have used duloxetine have reported being overly jumpy and agitated, however some have reported feeling overly lethargic. The choices are to continue treatment and see if the side effects go away, lower the dosage temporarily or discontinue the medication.

As with any psychiatric drug, you have to carefully manage patients, especially if they have a history of suicidal ideations or if they are taking other medications for clinical depression. You must be very frank with patients and ask personal questions about their mental health.

Nausea and headache are also possible side effects with antidepressants and are in fact more pronounced with venlafaxine and less pronounced with duloxetine. There is also the possibility that antidepressants do not work in some patients.

### ANTICONVULSANTS

The most commonly prescribed anticonvulsant for neuropathic pain is gabapentin (Neurontin, Pfizer). It can be used for any kind of neuropathic pain; it does not work for arthritic pain. Gabapentin is well tolerated, and it controls pain well.

One problem with gabapentin is that it can be sedat-

ing. The best way to manage this is to start with very small amounts and gradually build up until a therapeutic level is reached. Gabapentin can also lead to suicide in those with a history of suicidal ideation, so be sure to do a complete patient history.

I have found in my practice that if I use physical medicine in combination with gabapentin – such as electrostimulation or Anodyne Therapy – I can use a lower dosage of the drug. Once again, this drug can lead to suicide in those with a history of suicidal ideation. Do your history and ask the pertinent questions. Don't be ashamed.

Gabapentin is a very short-acting drug; it may only last between 4 to 6 hours. It must be given in broken up dosages, such as 600 mg, 4 times a day. Be sure to counsel patients not to drive or operate heavy machinery when they first start taking the drug.

Gabapentin is not Food and Drug Administration-approved for treating peripheral neuropathy pain. However, it is fine to prescribe any drug for other indications, as long as there are no contraindications.

### NEWLY AVAILABLE

A new drug is now on the market that is pharmacologically related to gabapentin. It is called pregabalin (Lyrica, Pfizer). One advantage is that it can be taken three times a day. The dosage can be varied – within limits – to the severity of the symptoms.

What if your patient is taking gabapentin, amitriptyline, nortriptyline or another drug that is controlling their neuropathic pain? Do you switch to duloxetine because it is newer and has a more specific indication? The answer is: No.

These drugs do not cure peripheral diabetic neuropathy. However, they are palliative medications used to restore a patient's quality of life, eliminate pain and enable them to better function. Because the drugs are not cures, if one is working well for that patient – even though a new drug came out – my recommendation is not to switch.

In summary, there are three excellent pharmaceuticals that we use to control neuropathic pain. There are variants of these medications on the market as well. Judicious use of these medications can make a major contribution in the way pain associated with peripheral neuropathy is managed. ■

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