Type 2 Diabetes – Neuropathy

Usual Presentation: Begins in feet and progresses proximally; often symmetrical but may present atypically. Symptoms include chronic or undulating pain, numbness and tingling, burning or occasionally shooting or stabbing pain.

Prevention and Treatment of Neuropathic Pain Syndrome is as follows:
- Maintain glycemic control.
- Promote smoking cessation and or alcohol cessation or reduction.
- Consider alpha lipoic acid 600mg daily (OTC supplement).

Goal of therapy is to reduce symptoms by approximately 50%.

Non-Prescription Therapy
Consider alpha lipoic acid 600mg daily which is more effective than vitamin B therapy.

Prescription therapy

1st Line - Tricyclic Antidepressants (TCA) (Amitriptylline, Nortriptylline, Desipramine) are efficacious and low cost; consider contraindications.

2nd Line – If first line doesn’t work use Calcium Channel Modulators (Gabapentin, Pregabalin) OR Serotonin Norepinephrine Reuptake Inhibitors (SNRI) (Venlafaxine, Duloxetine)

3rd Line – Last line of treatment is long acting Opioids (Morphine, Tramadol).

Common reasons for treatment failure:
- Dose is too low.
- Inadequate trial; requires 2 to 8 weeks of treatment to observe symptom reduction.
- Pt expecting elimination of symptoms; treatment reduces symptoms approximately a 50%.
- Incorrect diagnosis; if in doubt, refer to pain specialist or neurologist.
- If patient does not respond or has adverse effects, change the medication class.
- If patient has some but inadequate relief, raise the dose then consider adding or changing medications.
The following tables present information about the medications, dose, side effects, other benefits and cautions for using medications to treat neuropathy.

**Table 1. 1st Line Medications - Tricyclic Antidepressant (TCA)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline</td>
<td>25-150mcg daily</td>
<td>May help with sleep disorders</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>25-150mcg daily</td>
<td>Less sedating, less anticholinergic</td>
</tr>
<tr>
<td>Desipramine*</td>
<td>25-150mcg daily</td>
<td>Less sedating, less anticholinergic</td>
</tr>
</tbody>
</table>

* Drug not included in IHS National Core Formulary

**Side effects** of first line medications may include: sedation, dry mouth, blurred vision, weight gain, urinary retention.

**Other benefits** may include: improvement of depression and insomnia.

**Caution:** personal or family history of dysrhythmia or sudden cardiac death, glaucoma, suicide risk, seizure disorder; caution autonomic neuropathy (may cause orthostatic sx) - get standing Blood Pressures.

**Table 2. 2nd Line Medications - Calcium Channel**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabapentin*</td>
<td>100-1,200mg TID</td>
</tr>
<tr>
<td>Pregabalin*</td>
<td>50 – 200mg TID</td>
</tr>
</tbody>
</table>

* Drug not on IHS National Core Formulary

**Side effects:** sedation, dizziness, peripheral edema

**Other benefits:** improvement of insomnia, fewer drug interactions.

**Caution:** cardiac disease, glaucoma, suicide risk, seizure disorder.

**Table 3. Other 2nd Line Medications - Serotonin Norepinephrine Reuptake Inhibitors (SNRI)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine* (Effexor®)</td>
<td>75-225 mg daily; starting dose: 37.5mg</td>
</tr>
<tr>
<td>Duloxetine* (Cymbalta®)</td>
<td>60 mg daily; starting dose: 30mg</td>
</tr>
</tbody>
</table>

*Drug not on IHS National Core Formulary

**Side effects:** sedation, dry mouth, blurred vision, weight gain, urinary retention

**Other benefits:** improvement of depression and insomnia

**Caution:** renal insufficiency; do not stop abruptly - taper dose
Table 4. 3rd Line Medications – Long Acting Opioids

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine* (MS Contin®) (or other long acting opioids)</td>
<td>Start at low dose and titrate gradually</td>
</tr>
<tr>
<td>Tramadol* (Ultram®)</td>
<td>Start at low dose and titrate gradually</td>
</tr>
</tbody>
</table>

* Drug included in the IHS National Core Formulary

**Side effects:** sedation, nausea, constipation (always prescribe stool softener)

**Caution:** abuse, suicide risk, short action-opioids not recommended for long term treatment.

**Combination therapy is not well studied:** some evidence exists for the combination of gabapentin and nortryptilline. Caution with drug interactions (e.g. serotonin syndrome risk with tramadol and many antidepressant meds).

If above medications are not efficacious, contraindicated, or if intolerable adverse events occur, may consider:

- Bupropion* (Wellbutrin®)
- Topiramate* (Topamax®)
- Citalopram* (Celexa®)
- Paroxetine* (Paxil®)
- Topical capsaicin* (for localized pain)
- Topical lidocaine*(for localized pain)*

*Drug not included in the IHS National Core Formulary

**References:**