Diabetic neuropathy is one of the most common microvascular complications of diabetes and is associated with significant morbidity worldwide. The prevalence of neuropathy is estimated to be about 8% in newly diagnosed patients and greater than 50% in patients with longstanding disease [1]. Different classification systems for diabetic neuropathy exist and clinically it can be broadly divided into sensorimotor neuropathy (associated with pain, paraesthesia and sensory loss), cardiovascular autonomic neuropathy (which may contribute to myocardial infarction, malignant arrhythmia and sudden death), gastrointestinal autonomic neuropathy (associated with gastroparesis) and genitourinary autonomic neuropathy (linked with sexual dysfunction and neurogenic bladder) [2]. This is a broad subject and the focus of this brief commentary will be the treatment options for this common diabetic complication.

Currently, no drug has been shown in trials to prevent diabetic neuropathy. The Eurodiab Insulin-Dependent Diabetes Mellitus study found that suboptimal glycemic control was associated with the development of diabetic peripheral neuropathy in a large cohort of more than 3,000 people with Type 1 Diabetes [3]. Therefore intensive diabetes therapy is recommended in patients with diabetic neuropathy. The prevention of cardiovascular autonomic neuropathy depends on diabetes therapy and the focus of this brief commentary will be the treatment options for this common diabetic complication.

Combination therapy with two or more agents has also been explored, but unfortunately there are too few controlled studies on the efficacy of combining drugs. Therefore there are currently no recommendations for combination therapy.

Non-pharmacological approaches are limited and have not been conclusively proven to be effective. Various forms of electrical stimulation have been used to manage pain including percutaneous electrical nerve stimulation and frequency-modulated electromagnetic neural stimulation [5]. Evidence for the benefits of acupuncture in treating neuropathy is limited, but one small trial (in 45 subjects with painful neuropathy) reported an improvement in pain when compared with sham treatment [9]. Emerging therapies for diabetic neuropathy

### Table 1. Treatment options for painful diabetic peripheral neuropathy.

<table>
<thead>
<tr>
<th>Class</th>
<th>Medication</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic Anti-depressants</td>
<td>Amitriptyline, Desipramine, Imipramine, Nor-riptyline</td>
<td>Inhibition of reuptake of serotonin and/or norepinephrine, block of sodium channels, anticholinergic</td>
</tr>
<tr>
<td>GABA Analouges</td>
<td>Gabapentin, Pregabatin</td>
<td>Decreases release of glutamate, norepinephrine, and substance P with ligands on voltage-gated calcium channels</td>
</tr>
<tr>
<td>Serotonin Norepinephrine reuptake inhibitors</td>
<td>Duloxetine, Paroxetine, Venlafaxine</td>
<td>Inhibition of both serotonin and norepinephrine reuptake</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Carbamazepine, Lamotrigine, Oxcarbazepine, Sodium valproate, Topiramate</td>
<td>Inhibition of voltage-gated sodium channels, resulting in reduced peripheral nerve excitability</td>
</tr>
<tr>
<td>Topical analgesics</td>
<td>Capsaicin 0.0075%, Lidocaine 5% patch</td>
<td>Desensitization of epidermal nociceptors and blocking nerve conduction</td>
</tr>
<tr>
<td>Analgetic opiates</td>
<td>Morphine, Oxycodone, Tramadol</td>
<td>μ-Receptor agonism, inhibition of norepinephrine and serotonin reuptake</td>
</tr>
<tr>
<td>Aldose reductase inhibitor</td>
<td>Epalrestat</td>
<td>Inhibition of enzyme associated with hyperglycemia linked ischemic nerve injury</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>α-Lipoic acid</td>
<td>Antioxidant</td>
</tr>
</tbody>
</table>

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**Table 1.** Treatment options for painful diabetic peripheral neuropathy.
include treatment based on endothelial progenitor cells [10] and mesenchymal stem cells[11] although these options are currently in the experimental stage.

In summary, the treatment of diabetic neuropathy involves both prevention (through better glycemic control) as well as pain relief through a number of different classes of drugs. Although treatment options are currently limited, it is hoped that ongoing research will reveal new therapeutic targets in treating this frequently occurring and challenging complication of diabetes.

References


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