Levodopa – from Parkinson’s disease to restless legs?

By Dr Lisa Nissen

Restless legs syndrome (RLS) is a neurological disorder that is often described by patients as an uncomfortable and uncontrollable urge to move their legs. RLS occurs most frequently in middle-aged and older adults and is said to affect between 5–15% of the population. These symptoms are brought on by rest (sitting and lying down), are relieved by movement, and are worse at night or in the evening. RLS can have a significant impact on the quality of life of its sufferers, with the symptoms often affecting patients’ partners as well.

It is not surprising that RLS can lead to significant sleep disturbances. This disruption causing daytime fatigue, reduced concentration and memory, decreased motivation, confusion, anxiety, depression and reduced quality of life. Evidence suggests that idiopathic RLS may arise from subcortical brain dysfunction involving the dopaminergic system. This may result from a reduction in dopamine D2 receptor density or reduced postsynaptic dopamine levels. It is important that we recognize that RLS can be secondary to other disorders or conditions including: pregnancy, iron deficiency, diabetes and peripheral neuropathy. As a result, RLS can be an under-recognized condition particularly in the primary care.

There is no cure for RLS. However, if RLS symptoms are moderate to severe in intensity and are not due to an underlying reversible medical condition (e.g., iron deficiency) then drug treatment is usually used to relieve the symptoms with the aim of improving the quality of the patients’ sleep. Until fairly recently there were only a few medications approved specifically for RLS. However, there are a number of medications used for other conditions that are often used to treat RLS symptoms. These fall into four main groups: dopaminergic agents, sedatives, pain relievers, and anticonvulsants.

Some of the medications we have most commonly seen prescribed for RLS in the past are quinoline, dextroamphetamine, and amitriptyline. While they may provide limited relief for some patients, these medications may not be suitable for chronic use. Studies have shown that direct acting dopamine agonists, with their longer duration of action and reduced frequency of dose escalation and rebound may be a better therapy choice to these agents. These dopamine agonist include agent include newer agents like pramipexole and ropinirole and newer agents that have been developed specifically for RLS treatment. As well as older agents like pergolide, cabergoline and the grandfather of all levodopa.

A recent Cochrane review (2011) of levodopa for RLS showed that levodopa reduced symptom severity, improved sleep quality and quality of life, and improved periodic limb movement in sleep (monitored during polysomnography) compared to placebo when the results of nine clinical trials were reviewed. The most commonly reported side-effects of levodopa were nausea, although augmentation is a potential problem with all dopamine agonists in RLS.

However, the results of this review and the recent Cochrane review of dopamine agonists for RLS have given us greater insight into the role these medications can play in the management of this difficult condition.

Dosing information

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<th>Indication</th>
<th>Dosing</th>
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<tr>
<td>Restless legs syndrome</td>
<td>100 mg – 400 mg at night (given in combination with a peripheral dopa decarboxylase inhibitor (benzperazide or carbidopa)</td>
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<tr>
<td>Parkinson’s disease</td>
<td>300 mg – 2 g in divided doses daily (given in combination with a peripheral dopa decarboxylase inhibitor (benzperazide or carbidopa)</td>
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Useful references