

Restless Leg Syndrome

The most common condition you have never heard of

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What is Restless Leg Syndrome?

Willis-Ekbom disease, also known as Restless Leg Syndrome (RLS), is a neurological disorder that causes an involuntary urge to move legs and feet, accompanied by a crawling sensation which worsens during times of rest and inactivity (1). When asking people who suffer with RLS, they make it clear that the discomfort they feel every day is far more torturous than the pins and needles sensation we have all experienced. An astonishing 10% of adults in the UK are affected by RLS, meaning you are likely to know someone who suffers from this illness (2). Yet the source of this disease is still idiopathic (3) and current pharmacological treatments are of limited therapeutic value. As someone whose mum battles with RLS I am aware of the immense impact this illness has on all aspects of life and therefore how vital more research and awareness could be for sufferers.

What causes RLS?

The mechanism behind RLS is still not fully understood, however current studies recognise a strong association between this disease and iron deficiency (3). This may explain why a quarter of pregnant women acquire RLS, as mild anaemia is typical during pregnancy. However, RLS is still prevalent between both sexes and amongst all ages. Furthermore, research has also shown that abnormalities in the neurotransmitter dopamine are involved in RLS pathogenesis (4). This study aimed to develop an understanding of the use of dopamine receptor agonist cabergoline in targeting D2 receptors and found that cabergoline has profound benefits in relieving symptoms and therefore suggests that these receptors are involved in the mechanism of RLS. Disruptions in the dopamine pathway results in involuntary movement of the lower limbs, and in some cases these symptoms can progress to the whole body.

Life with RLS

Life with RLS can be tiresome, disruptive and lonely. As this illness affects people during times of inactivity, it is classified as a sleep disorder (5) and periodic limb movements of sleep (PLMS) is a symptom expressed by more than 80% of RLS patients, with twitching or jerking limb movements occurring up to every 15 to 40 seconds.

RLS patients can suffer with significant sleep deprivation and therefore feel exhausted during the day. As a result of extreme tiredness, patients experience social isolation where activities such as sit-down meals, cinema trips, reading and even working are disrupted (6). As these everyday tasks become incredibly difficult, RLS patients can be left depressed and isolated. This is reflected by statistics that show a significantly higher risk of self-harm in RLS patients than those that do not have this disease (7).

Coping mechanisms

With limited pharmacological treatments, RLS patients experiment with different coping mechanisms that work for them. When experiencing an episode of irritation, a distraction is often used in an attempt to psychologically resist the urge to twitch. Some patients use extreme methods such as self-harm to numb an area of discomfort. Having asked an RLS patient what their personal coping mechanisms are, they stated that listening to loud music with earphones at night helps to relieve symptoms. There is currently no study that has researched this psychological phenomenon, but the loud music may work as a distraction to provide short-term relief. They have also found drinking tonic water helps to ease irritation. This may be due to the presence of quinine (an anti-malaria agent). Quinine tablets are available in the UK and for recent years have been used to treat nocturnal leg cramps (8). However, this particular RLS patient found that tonic water was only beneficial for a limited amount of time before its effects become futile. A recent channel 5 documentary followed RLS patients to deepen our understanding of how people cope with this disease. They found many patients attempt to gain a feeling of numbness by taking strong painkillers and sleeping tablets such as codeine (6). However, in doing so patients expose themselves to accidental overdose as taking more of a drug does not boost its therapeutic outcome, it only increases their adverse effects. Overall, current coping mechanisms have been discovered by patients through trial and error and do not have much scientific study to fully understand their method of action but have shown to be beneficial to individual RLS patients for short-term relief.

Pharmacological Treatment

With more research into the pathogenesis of RLS, the future may see more successful drug development in this



Figure 1. RLS affects 10% of adults in the UK.

area. Currently therapeutic treatment for regular RLS symptoms is to prescribe dopamine agonists, for example, ropinirole, pramipexole and rotigotine skin patches, that are able to boost levels of neurotransmitters in the brain (9). A study was conducted to determine if cabergoline (a dopamine receptor agonist) can be used as a long-term drug for RLS patients based on its safety and efficacy values (4). It found that patients had a beneficial response to cabergoline as their sleep satisfaction levels increased as well as relieving symptoms during the day. The study analysed 302 RLS patients by monitoring the effects of cabergoline over a period of 26 weeks. A titration period determined an optimal dose of 1.5 mg, which was taken for the subsequent 181 days and the beneficial effects of the drug was displayed consistently throughout this time. The study discovered mild adverse effects of cabergoline relating to the gastrointestinal system and central nervous system. These effects included nausea, dizziness, fatigue and headaches. 78.8% of participants experienced at least one of these adverse effects during the experiment but as these symptoms are not classed as severe, the drug was determined as safe to use and well-tolerated by most patients. Cabergoline was successful in improving sleep in 85.7% of people that took part in the study and more than 68.1% of participants stated that they were completely relieved of all RLS symptoms during day and night, therefore showing cabergoline to have a high efficacy. Although the study failed to identify the pathogenesis of RLS, it can be understood that there is some benefit in targeting dopamine receptors, D2, which may help to improve future understanding of RLS mechanisms and drug development. In total, this research concluded cabergoline to be a safe drug and beneficial in relieving symptoms experienced by patients with idiopathic RLS. However, this treatment is not currently licensed for use in RLS in the UK.

If symptoms of RLS are only felt occasionally, levodopa is rarely prescribed as it poses the risk of worsening symptoms (10). Gabapentin and pregabalin, which can also be used to treat epilepsy, are used to reduce the neuropathic pain associated with RLS, as it uses a similar mechanism to dopamine and can reduce pain sensations. However, these anticonvulsant drugs are less potent than dopamine agonists and also come with an array of adverse effects such as neuropathic pain, pruritus and can potentially worsen RLS (11).

Opioids, such as codeine, are prescribed as a final option when patients are unresponsive to all other painkillers. Opioids require careful observation to avoid addiction or accidental overdose but have been successful in providing short-term relief amongst patients (6). Finally, cannabidiol (CBP) and cannabis has been used by patients and has shown success in its ability to numb restless legs. It is difficult to say if the mechanism of cannabis works by targeting receptors that switch off RLS or if it works as a distraction. However, controversy over the legalisation and pharmacological benefits prevent the widespread use of cannabis. There is currently a lack of randomised control trials to investigate the benefit-risk ratio of medicinal cannabis. Despite this, cannabis based products are available for medical use in the UK, where specialists can prescribe these using their clinical judgement on a case-by-case basis (12).

Overall, current pharmacological treatment offers no curative options and current medicines are contraindicated which limits the number of RLS patients who can benefit from them. Hence future research has potential to expand the availability of RLS drugs and increase their beneficial outcomes.

In conclusion, it is evident that future research is essential in order to gain a greater understanding of RLS and develop more effective medical treatments. This research will help improve the quality of life for many people in the UK. To support RLS patients, visit the RLS-UK charity website to help raise awareness and funding for future RLS discovery.

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