



Letter to the Editor

Vagus Nerve Stimulation: A Potential in the Treatment of Restless Legs Syndrome

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Restless Legs Syndrome/Willis-Ekbom Disease (RLS/WED) is a chronic neurosensory disorder that is characterized by a strong urge to move, accompanied by an uncomfortable paraesthesia in the legs which may affect up to 15 percent of adult people in industrialized countries [1]. KA Ekbom coined “restless legs”, and wrote in his thesis from 1945, that many patients with RLS suffer from severe pain, so they need to have prescribed an opioid to have relief of their suffering [2].

Restless legs syndrome is a puzzling disease, mostly because of the uncertainty of its etiology. There seems to be a genetic component, but it is also known that RLS/WED may be caused by other underlying pathologies and is treated by remedying those conditions. Another highly researched area in the quest to find an etiology and treatment for RLS/WED is the brain dopamine system; until now, dopaminergic medication was considered the first line of treatment for RLS/WED that is not caused by other underlying factors.

Recently, the American Academy of Sleep Medicine (AASM), due to the risk of augmentation syndrome associated with the use of dopamine agonists, suggests against the standard use of these drugs, except in special cases. The recommended drug treatments for RLS include calcium channel alpha 2-delta ($\alpha 2\delta$) receptor ligands, opioids and iron supplementation when indicated [3]. This represents a substantial challenge, as dopamine agonists remain the most frequently prescribed agents for RLS, and the $\alpha 2\delta$ receptor ligands are prescribed “non-label” and affected by serious side effects has for example risk of addiction [4]. Pending greater clarity in therapeutic algorithms, alternatives to conventional drugs are being actively sought.

A female patient, aged 40 years, suffering from very severe RLS/WED since childhood was treated with three pharmaca in this

context, a dopamine agonist, a calcium channel alpha 2-delta ($\alpha 2\delta$) receptor ligand and an opioid with very reduced efficacy. She was also several times treated with iron iv due to low ferritin values. She visited my department and told that she purchased a device (Nurosyl, Parasymp Ltd, UK) a device operating with transauricular vagus nerve stimulation (taVNS) transcutaneously with an application on the ear. She had used the device during for about 30 minutes per day. Before using the VNS device, she wanted to record the RLS severity by measuring by using the International Restless Legs Scale (IRLS), a 10-item questionnaire developed by the International Restless Legs Syndrome Study Group (IRLSSG) [5]. Each question has five response options, ranging from “0” to “4”. Hence, the total score can range from “0” to “40”, indicating “no symptoms” to “very severe symptoms”, respectively.

This patients IRLS scores was 33 before she started treatment, and reduced to 21 after 2 months treatment. The patient did not notice any side effects. During the treatment period she had discontinued all the drugs she used before she initiated treatment with taVNS. However, the fact, that the patient noticed reduction of her symptoms already after 2 months of treatment would indicate that the placebo efficacy might be large.

Transcutaneous, transauricular vagus nerve stimulation was introduced in the treatment of severe drug resistant epilepsy for more than twenty-five years ago, and then it also has spared to be used in other disease and conditions such severe depression and in pain [6,7].

The literature on taVNS in RLS is scarce. Merkl and collaborators published in 2007 the first case with RLS and an efficacy by using taVNS. Recently, Hartley et al reported a substantial effect on RLS-symptoms in 15 pharmacoresistant patients treated with taVNS over 6 months [8,9].

Multiple side effects of the recommended drugs, such as emerging problems of augmentation, motivate further research on alternative

treatments of this common ailment.

Overall, non-invasive electrical neuromodulation of the vagus nerve appears to represent a biologically plausible and scientifically motivated approach in RLS. However, well-designed, sham-controlled clinical trials with objective outcome measures and systematic dose optimization are required to clarify the clinical role of these interventions.

Conflict of Interests: The author declares no conflict of interest.

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