## AUGMENTATION IN RESTLESS LEG SYNDROME: MANAGEMENT CHALLENGES

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Augmentation is defined as an increase in symptom severity despite (mostly dopaminergic) treatment. Alternatively, there can be an earlier onset of symptoms in the afternoon by at least 4 hours and/or a shorter latency of symptoms at rest, or a spread of symptoms to previously unaffected body parts. Augmentation is the paradoxical worsening of Restless Leg Syndrome (RLS) symptoms after prolonged RLS treatment that typically occurs in 10-68% of patients who underwent sustained treatment with dopamine agonists, usually after 3-10 years of effective management. Excess postsynaptic desensitization of dopamine 2 (D2) receptors in the substantianigra and putamen with prolonged intermittent dopaminergic stimulation is assumed to be the cause of augmentation, while the exact process is unknown. Smaller dosages of longer-acting dopaminergic agonists, such as ropinirole and pramipexole, are expected to reduce the risk of augmentation; of these agonists, rotigotine has the lowest risk of augmentation due to its longest half-life. Levodopa and other shorter-acting dopaminergic agonists have the greatest chance of producing enhancement when used consistently. The current recommendations for management include stopping the offending substance, improving sleep quality and habits, adding \( \text{a}2\text{\text{\text{m}}}\) medicines, or starting opioid therapy, but the latter two options carry a high risk of side effects. The binding sites for the gabapentinoid medications pregabalin and gabapentin are represented by the á2ä-2 and á2ä-1 proteins. Because gabapentin enacarbil has fewer negative effects than regular gabapentin, the FDA has approved it for treatment in RLS. Patients who have developed resistance to first-line RLS treatments can also benefit from low-dose opioid medicines, especially when combined with dopamine agonists. For the majority of individuals, low-dose opioid medicines continue to effectively treat symptoms of refractory RLS over a 2-year follow-up period. The most often given opioid was methadone. Methadone has replaced oxycodone ER as the usual treatment for patients who are refractory to opioids. Its lengthy half-life, once-daily dosage, and lack of euphoric effects make it significantly less likely to be abused. This was the result of a big clinical trial involving opioids. Given its distinct pharmacological profile, aripiprazole, a dopamine receptor partial agonist (DRPA), may offer a further alternative for managing augmentation in RLS.

Keywords: Augmentation in Restless Leg Syndrome, Restless Leg Syndrome

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