Restless Legs Syndrome and Schizophrenia
A Case Report

To the Editors:

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estless legs syndrome (RLS), with a prevalence of 10% of the general population, is characterized by an urge to move the legs that is usually accompanied by or occurs in response to uncomfortable and unpleasant sensations in the legs. It may be idiopathic or secondary to pregnancy, low ferritin levels, uremia, and neurological disorders. Because RLS is associated with a dopaminergic dysregulation, dopamine agonists can treat RLS, whereas antipsychotic drugs, which are dopamine antagonists, can worsen it. Hence, the treatment of RLS in patients with schizophrenia is a matter of concern.

We report a case of complete recovery of idiopathic RLS in a patient with schizophrenia, after treatment with the antipsychotic drug amisulpride. The patient provided written informed consent for anonymized publication of her data.

A 36-year-old woman was admitted for the first time in the psychiatry department for positive and negative psychotic symptoms (PANSS total score = 112; positive score = 29, negative score = 33, general psychopathology score = 50), leading to a diagnosis of schizophrenia (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) that was never treated before. An idiopathic RLS was also diagnosed based on the Restless Legs Syndrome scale (IRLS score of 31). She described uncomfortable and unpleasant sensations in the legs like burning feelings. Moreover, she had impetuous need to move legs in the evening that was relieved by movements and associated sleep disturbances. These symptoms were present since the end of adolescence and were stable over time. Akathisia, a frequent symptom in patients with schizophrenia treated with antipsychotics, was excluded here because the symptoms had begun before antipsychotic treatment and were present only in the evening (Barnes Akathisia Rating Scale global score = 0). The RLS was considered idiopathic because no neurological disorder, uremia (4.2 mmol/L; reference range, 2.6–8.1), and pregnancy (beta-hCG < 2 UI/L) were evidenced; ferritin (160 μg/L; reference range, 20–200) and renal function (glomerular filtration rate CKD-EPI = 111 mL/min/1.73 m²; reference range, 90–120) were in the reference range. The RLS had never been treated before. No abnormal involuntary movement was evidenced.

Risperidone (3 mg/d) was prescribed but discontinued after 2 weeks because of worsening of RLS. Indeed, after risperidone treatment, the uncomfortable sensations increased in intensity and frequency and extended to the arms. Thus, liquid haloperidol (11 mg/d) was introduced. This compound was chosen because the hallucinations were severe and because oral solution is available and could facilitate adequate dose management. However, haloperidol was stopped after 3 weeks because of extrapyramidal symptoms (Simpson Angus Scale score = 0.9) and akathisia (Barnes Akathisia Rating Scale global score = 4). Thus, amisulpride, a benzamide antipsychotic with a low risk of neurological symptoms, was chosen (dose up to 600 mg/d). A substantial recovery of RLS was observed after 2 weeks (IRLS score = 16), along with improvement of psychotic symptoms (PANSS total score = 40; positive score = 7, negative score = 14, general psychopathology score = 19). Interestingly, the patient stopped amisulpride for 3 days (because of bacterial conjunctivitis that she attributed to her treatment), leading to a worsening of RLS (IRLS score = 31). Restless legs syndrome improved after the reintroduction of amisulpride (400 mg/d) and recovered completely after one more week of treatment (IRLS score = 1).

Of note, the anticholinergic drug trospamine (20 mg/d) was prescribed during 4 days to treat acute dystonia related to risperidone treatment. No effect on RLS was observed. Benzodiazepine treatments were also used during hospitalization to treat acute anxiety symptoms. No change in RLS symptoms intensity was observed during introduction, dosage decrease, or benzodiazepine withdrawal.

The positive effect of amisulpride on RLS was unexpected; however, its specific pharmacodynamic profile could explain this effect. First, the amisulpride effect on D2 receptors depends on its dose and concentration; it is a D2 receptor antagonist at high concentrations and a dopaminergic D2 agonist in low concentrations (explained by presynaptic action on D2/D3 autoreceptors). Second, amisulpride has antidopaminergic effects selectively in the mesolimbic area (leading to antipsychotic effects), whereas it could have dopaminergic agonist effects in the other areas including spinal area. Third, spinal prodopaminergic effects induce antinoceptive effects in RLS. So it could make sense that amisulpride, via dopaminergic agonist effects in the spinal area, could improve RLS. Because the improvement of RLS with amisulpride was unexpected, we did not systematically conduct polysomnography or suggested immobilization test before and after treatment. These tests could be useful to assess periodic limb movements during sleep and wake (frequently associated with RLS) and to add more precision in the assessment of RLS severity and outcome after treatment. So we recommend to perform these tests for future patients with RLS before and after initiation of amisulpride treatment.

This case report is relevant because the RLS prevalence in patients with schizophrenia treated with antipsychotics is doubled, as compared with healthy controls. It suggests that amisulpride could be a useful antipsychotic medication for patients with schizophrenia and RLS.

ACKNOWLEDGMENTS

Drs Colle and Boichot have contributed equally to this work.

AUTHOR DISCLOSURE INFORMATION

Romain Colle, Flavien Boichot, Erwan Bouteiller, Céline Elie-Lejeubvre, Patrick Hardy, Céline Verstuyft, and Emmanuelle Corruble declare no conflict of interest. Denis J. David: Lundbeck; Roche and Servier.

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