Rabbit Syndrome Likely Induced by Escitalopram: A Case Report

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Abstract

Objective: As reports of rabbit syndrome (RS) unrelated to antipsychotic medications have appeared, antidepressants, especially serotonin reuptake inhibitors (SSRIs), have been pointed as offenders producing RS. The induction of RS by SSRIs has been thought to be a consequence of serotonergically mediated inhibition of the dopaminergic system. We present a case of escitalopram-induced RS to increase awareness of this problem. **Case Summary:** A 35-year-old male, diagnosed with moderate depressive disorder, was started on escitalopram 10 mg/day along with clonazepam 0.5 mg at night on an outpatient basis. Personal and family history was not significant for any medical or psychiatric disorder, including movement disorders. **Results:** Three months after the initiation of escitalopram, the patient started complaining of abnormal trembling perioral movements, which increased on tasks involving focusing. A computed tomography scan of the brain revealed normal findings. With a diagnosis of drug-induced RS, escitalopram was stopped and 2 mg/day trihexyphenidyl was started. The patient reported complete improvement in 20 days. Trihexyphenidyl was stopped and sodium valproate 400 mg was started for irritability. **Conclusions:** Escitalopram can induce RS. This effect suggests that, for some patients, escitalopram has neuropsychiatric effects similar to those of a dopamine-blocking antipsychotic drug. Besides stopping medication, some patients may require medications temporarily to relieve symptoms.

Keywords

adverse drug reactions, affective disorders, adult medicine, antidepressants, anticonvulsants

Introduction

Rabbit syndrome (RS) is a distinct extrapyramidal syndrome (EPS), described by Villeneuve,¹ characterized by involuntary, rapid, fine, rhythmic movements along the vertical axis of mouth, occurring at a frequency of around 5 Hz. It is limited exclusively to the oral and masticatory muscles, without the involvement of tongue. While old, RS is believed to occur in approximately 2% to 5% of patients chronically treated with first-generation antipsychotic drugs (APDs).^{1,2} Recently, reports of RS induced by second-generation APDs have been reported.^{3–6} However, of particular interest is RS unrelated to APDs exposure.^{7–9} To date, only sparse reports of antidepressant drug (ADD) induced RS have been reported in the literature.^{10–12} We would like to report a case of RS induced by 10 mg per day of escitalopram, and it resolved completely with discontinuation of escitalopram and addition of trihexyphenidyl (THP).

Case Report

A 35-year-old male presented to psychiatry outpatient clinic with complaints of sadness of mood, irritability, decreased interest in previously pleasurable activities, restlessness, lethargy, and sleep disturbances of 2 months duration. There was no history of any medical or psychiatric illness in the past.

Personal and family histories were noncontributory. General physical examination and neurological examination were normal. Mental status examination revealed decreased psychomotor activity, depressed affect, ideas of hopelessness and worthlessness with insight present. A diagnosis of Depressive Disorder, Moderate was made. He was started on escitalopram 10 mg per day along with clonazepam 0.5 mg at night. Follow-up after 10 days reported subjective improvement in depressive symptoms and biological functions. The same treatment was continued. Regular follow-up revealed overall improvement in all the symptoms except irritability. However, after 3 months of regular treatment, the patient complained of abnormal trembling perioral movements. The patient reported that movements increased whenever he was under any kind of stress. Detailed evaluation at this time did not reveal any past history of movement disorder, head injury, fits, or drug use/abuse. Examination revealed abnormal perioral movements that worsened with tasks involving motor performance or demanded concentration. No abnormal

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tongue movements were observed. No Parkinsonian sign or dystonia was observed. Routine blood investigations, ophthalmological examination, as well as computed tomography of head were within normal limits. After excluding other causes, diagnosis of escitalopram-induced Rabbit Syndrome was made. Escitalopram was stopped and THP 2 mg per day was added. Follow-up after 10 days reported improvement in RS. However, as irritability persisted, sodium valproate 400 mg per day was added. Subsequently the patient reported improvement in irritability also and his abnormal movements also disappeared. THP was discontinued 20 days after initiation and the patient was maintained on sodium valproate 400 mg per day and clonazepam 0.5 mg per day with sustained improvement in symptoms over a period of 5 months of follow-up. Naranjo Probability Scale applied retrospectively revealed a score of 5, pointing to a "Probable" drug reaction.

Discussion

Prevalence of EPS with antidepressants is unclear, with estimates of 1 to 1000 in users of selective serotonin reuptake inhibitors (SSRIs).¹³ RS is a distinct form of EPS. In particular, a relatively recent review reported 3 cases of EPS with escitalopram, one each of oculogyric crisis, dystonia, and RS. FDA adverse drug reporting system reported escitalopram to be implicated in 7% of cases of EPS.¹⁴ Recently, a case of parkinsonism induced by escitalopram was reported.¹⁵

The pattern of movement in RS contrasts tardive dyskinesia (TD), another form of oral dyskinesia, in which the tongue is involved in making slower and less regular movements. Similar to TD, the movements of RS increase in situations of fatigue and anxiety. Different from other types of oral dyskinesias, such as buccolingual and buccolinguo-masticatory syndromes, RS cannot be suppressed voluntarily by the patient.¹⁶ RS can be associated with drug-induced parkinsonism and TD.^{2,17,18} RS symptoms are similar to Parkinson's symptoms in their persistence during stage 1 non-REM sleep, whereas a cessation of symptoms is observed in the same situation with TD.

Risk factors for RS include middle and old age, female sex, and history of brain damage.^{10,19,20} However, no risk factor was present in our case.

RS may appear during treatment with neuroleptic medications or after discontinuation of such medicines. The mechanisms triggering RS are believed to be similar to those involved in the pathogenesis of the neuroleptic-induced Parkinsonian syndrome.²⁰ In fact, RS may be due to a hypercholinergic state resulting from the neuroleptic blockade of dopaminergic neurons in the extrapyramidal system. This would explain the response of RS to anticholinergic drugs.^{17,21}

ADDs through potent inhibition of serotonin uptake may cause RS through serotonin-mediated inhibition of

dopaminergic neurotransmission in basal ganglia. A SPECT study of ADD (imipramine) induced RS revealed decreased basal ganglia perfusion while the movement disorder was present and a return to normal perfusion when RS resolved.¹⁰

In our case, RS began 3 months of start of escitalopram and improved with THP 2 mg per day for 10 days and stoppage of escitalopram. Previous case report of escitalopram-induced RS reported RS to occur soon after starting drug and responded only to its discontinuation. Favorable response to THP in cases of RS has been previously reported in the literature.^{22,23}

To conclude, RS is a distinct form of EPS that can be induced by escitalopram. One should consider the possibility of antidepressant-induced RS/movement disorders/EPS in patients presenting with abnormal movements. Further studies are warranted to estimate the frequency and risk factors of RS in patients treated with antidepressant drugs for effective understanding and management of these complex conditions. Clinicians need to be aware of movement disorders with escitalopram for effective management.

Declaration of Conflicting Interests

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