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Escitalopram-induced extrapyramidal symptoms

Sir,

Serotonin-specific reuptake inhibitors (SSRIs) are widely used for a variety of clinical conditions due to their relatively safe side-effect profile. Among the various classes of antidepressants, SSRIs are the common offenders producing extrapyramidal symptoms (EPSs). The incidence of EPS is high with escitalopram (12%) followed by sertraline (11%), paroxetine (10%), and fluoxetine (8%).[1] The SSRIs produces reversible or irreversible motor disturbances through pathophysiological changes in basal ganglion motor system by altering the dopamine receptors postsynaptically.[2]

A 34-year-old female presented with complaints of sadness of mood, crying spells, feeling lonely, decreased interest in day-to-day activities, lethargy and disturbed biological functions for the last 6 months. Her past and family history and personal history was noncontributory. General and systemic examination was within normal limits. Mental status examination revealed decreased psychomotor activity, depressed affect, depressive cognitions with well-preserved insight. A diagnosis of moderate depressive disorder was made, and she was started on escitalopram 10 mg/day along with clonazepam 0.5 mg at night time. She was maintaining well and escitalopram 10 mg was continued for the next 18 months as per patient's request. 18th month, she presented with complaints of slurring of speech, drooling of saliva, decreased bodily movements, and slowness in walking. Neurological examination revealed bradykinesia, cogwheel rigidity, dysarthric speech, and tremor of hands. Routine biochemical tests and head MRI, EEG were done and were found to be normal. No history of any other drug use/abuse, head injury, seizures, fever or movement disorder was reported. A diagnosis of escitalopram-induced acute extrapyramidal syndrome was made after excluding other possible causes. Escitalopram was immediately discontinued, the patient was reassured, and trihexyphenidyl 2 mg bid was started. Follow-up after 2 weeks reported significant improvement. Subsequently trihexyphenidyl was stopped and dothiepin 50 mg/day was started to control the depressive symptoms. The patient was followed-up for the next 6 months without any symptom recurrence. The Naranjo probability scale applied retrospectively revealed a score of 6, pointing to a "probable" drug reaction.

The data for escitalopram-induced EPS is rare except in few cases.[3,4] The potential risk factors for EPS induced by antidepressants are advancing age, female gender, preexisting extrapyramidal disorder, other concurrent neuroleptic medications and pharmacokinetic interaction through CYP2D6 inhibition.[1] Other than the female gender, none of these risk factors were present in our patient. Researchers have extrapolated a link between antidepressant-induced EPS and the CYP2D6 phenotype. On analyzing the risk factors for these reactions during treatment with SSRIs, including the CYP2D6 phenotype, serotonin, and dopamine transporter and receptor polymorphisms, it was noted that the risk of EPS with SSRIs seemed to increase with advanced age and the presence of the A1 allele of the dopamine D2 receptor gene Taq1A.[5]

Being a young patient, the possibility of young-onset parkinsonian disease was considered in which, family history of parkinsonism is an important risk factor.[6] Our patient's history was not significant for

either parkinsonism or any other movement disorder. In rat models of EPS induced by SSRIs, a specific effect on tyrosine hydroxylase, which is a speed-limiting enzyme of dopamine synthesis in substantia nigra has been reported. Tyrosine hydroxylase synthesis was significantly decreased by SSRIs in substantia nigra, and the serotonin transporter (SERT) inhibition can activate microglia and alter the regulation of tyrosine hydroxylase, the rate-limiting enzyme for dopamine biosynthesis, and these changes may play a role in mediating the EPS associated with SERT inhibitors.[7]

Drug-induced parkinsonism (DIP) may represent a preexisting vulnerability to future Parkinson's disease. Treatment of DIP involves discontinuation of the offending drugs, which usually promotes remission of the parkinsonian syndrome within a short time, although parkinsonism may sometimes persist and require dopaminergic treatment. One atypical feature in our patient was that compared to previously reported cases where EPS developed few weeks after initiation of escitalopram, in the index patient EPS developed only 2 years after starting escitalopram. However, the EPS was reversed after a short course of anticholinergic treatment. The reason for late onset of EPS needs further exploration. This is an attempt to create an awareness of drug-induced EPS as adverse reaction in patients taking escitalopram even after months or years of therapy so that timely recognition can prevent such adverse effects.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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