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Case Report

Fluoxetine-induced tardive dyskinesia in a patient with Parkinson's disease

Raidoo DM. Fluoxetine-induced tardive dyskinesia in a patient with Parkinson's disease.

Background: This is a report of a 66-year-old male with Parkinson's disease (PD), depression and anxiety who developed tardive dyskinesia (TD) while on fluoxetine.
Methods: The patient underwent psychiatric, neurological and neuroimaging examination.
Results: The patient's neuroimaging examination was normal, his psychiatric assessment revealed depression and anxiety, and his neurological evaluation diagnosed only mild PD. The patient's TD resolved when fluoxetine was discontinued and recurred upon re-exposure.
Conclusion: This case shows that fluoxetine as monotherapy can be associated with TD especially in patients with concomitant PD. Clinicians must be aware of this side-effect and monitor for features of TD due to antidepressants that are often used to treat comorbid depression in patients with PD.

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Introduction

Tardive dyskinesia (TD) is an uncommon side-effect of selective serotonin reuptake inhibitors (SSRIs) (1). When SSRIs are prescribed to male patients over 55 years old, there is a moderate risk of akathisia and Parkinsonism but a lower risk of TD (1). I report the development of TD attributed to fluoxetine which had successfully treated both a mood disorder due to Parkinson's disease (PD) with a major depressive-like episode, and an anxiety disorder due to PD with generalised anxiety features.

Case presentation

A 66-year-old male was seen by the urgent care psychiatrist for an 18-month history of feeling increasingly tense and anxious, with lack of ambition and constant worrying. Written informed consent was obtained from the patient for publication of this case report. He ruminated about having PD, his inability to work as much as he used to and its possible financial consequences. He also reported feeling depressed, not having much motivation and losing 25 pounds in the last 6 months. His terminal insomnia had improved with trazodone 50 mg prescribed by his primary care provider 4 months earlier. He stated that he was not able to walk and move as fast as earlier and had episodes of tremor involving both hands. He indicated that all of these symptoms were affecting his ability to work as an independent contractor. He denied any suicidal thoughts, psychotic symptoms or any prior psychiatric history. He denied using street drugs, was a non-smoker, drank two cups of coffee a day and no more than two beers few days a week. He reported that his mother had both PD and depression. His general medical examination, blood counts and metabolic parameters were normal. He was started on fluoxetine 20 mg and scheduled for outpatient follow-up with psychiatry and neurology.

His neurological evaluation, 1 week later, reported mild intermittent tremor especially on the left side, mildly abnormal gait with slightly decreased arm swing on the left side, slightly brisk knee reflexes rated as 3+ bilaterally, slow movements, a lower voice and a negative pull back test. Brain magnetic resonance imaging (MRI) with and without contrast showed no midline shift, neoplasm, haemorrhage, infarct, demyelination or hydrocephalus. He was

diagnosed as early stage PD and started on a therapeutic trial of carbidopa/levodopa 25/100 TID.

During his follow-up with outpatient psychiatry, his fluoxetine was increased in increments of 10 mg/day every 6–8 weeks to treat ongoing symptoms of depression and anxiety. At his follow-up visit 6 months after, the fluoxetine was initiated and currently at 50 mg daily, he reported no side-effects, and that his anxiety and ruminations were better but his mood was still 'a little depressed', so the fluoxetine was increased to 60 mg daily. After 6 weeks, he reported that his anxiety was fine, mood was 'a lot better' but he had noticed tightening of his jaw muscles and difficulty swallowing for several hours each day starting 1 h after his morning dose of fluoxetine. As he had no orofacial dyskinetic or choreiform movements or other adverse effects, his fluoxetine was maintained at its current dose. After 6 weeks, he presented with chewing and lateral jaw movements and twisting movements of the tongue, but no tongue protruding, lip puckering or facial grimacing and apart from bilateral hand tremor at rest there were no choreoathetoid movements of the limbs or trunk. Despite his reluctance, he was instructed to stop the fluoxetine immediately and return to the clinic in 1 week. Four days after stopping the fluoxtetine, the oral dyskinetic movements (ODM) stopped so he restarted the fluoxetine at 20 mg because he felt 'tense, anxious and depressed'. At his follow-up visit 3 days later, he reported a 'happier' mood, a 'little worse' anxiety but no tightening of the jaw muscles, difficulty swallowing or ODM but he did continue to have intermittent tremor of his hands. We discussed other treatment options for his anxiety, but he wanted to continue the fluoxetine 20 mg. At his follow-up 2 weeks later he reported improved mood and anxiety but again had chewing and lateral jaw movements and tremor of the tongue with a score of 5 on the abnormal involuntary movement scale (AIMS). A diagnosis of TD was made on the basis of medication exposure for over 3 months, 'positive' criteria for the disorder, involvement of the tongue, abnormal movements present for at least 4 weeks and absent during sleep that the patient was aware of and causing him mild distress (2). The fluoxetine was switched to venlafaxine sustained action 37.5 mg for 1 week and 75 mg thereafter. At his 2 week follow-up the TD had remitted (AIMS score of 1), his anxiety was 'okay' but his mood was 'a little depressed'. He was afraid that an increase in venlafaxine may precipitate the TD but was willing to try a 10 000 lux phototherapy lamp for 1 h each morning throughout winter. In early spring he stopped using the phototherapy lamp and his anxiety and depression remained in remission without resurgence of the TD.

The adverse drug reaction probability scale indicated a probable relationship between the fluoxetine and the patient's TD (3). Throughout the period of treatment, he was concurrently given trazodone 50 mg for insomnia and carbidopa/levodopa 25/100 without dose adjustments. The patient denied taking any other prescription or over the counter medication or herbal products.

Discussion

In this patient with no prior antipsychotic use, the temporal relationship between the development of TD 6 months after fluoxetine was initiated and the remission of these movements when fluoxetine was discontinued suggests that the TD was induced by fluoxetine. Also, the re-emergence of symptoms following re-exposure establishes a stronger causal relationship between fluoxetine and TD. Although there are several reviews of antidepressant-induced extrapyramidal symptoms (EPS) that implicate fluoxetine as the SSRI most commonly associated with EPS, the incidence of SSRI-induced TD appears to be low (1,4–7). In their review, Gill et al. found that although there are a number of cases of akathisia, parkinsonism and dystonia associated with various antidepressant classes, there were only nine cases of reversible dyskinesia due to fluoxetine and one each due to paroxetine, sertraline and fluvoxamine (5). The most recent case-control study of spontaneous reports of EPS associated with SSRIs over a 14-year period in the Netherlands also found more reports of parkinsonism and dystonia and relatively few cases of dyskinesia, of which six were due to paroxetine and one each due to fluvoxamine and fluoxetine (1). Some of the cases of TD associated with fluoxetine described the classic bucco-lingual-masticatory syndrome that resolved when fluoxetine was discontinued and abnormal movements of the extremities were absent (8,9). This is similar to the symptom pattern in our patient.

Some of the risk factors that have been identified for developing movement disorders secondary to SSRIs include concomitant or prior use of antipsychotics, prior history of drug-induced EPS, advanced age and PD (1,4). Our patient had never been on neuroleptics; he was in his mid-60s and did have PD. There is one case report of an increase in finger tap scores when a patient with PD was prescribed fluoxetine (10). Also, in a small study of cabergoline for patients with PD, five patients from the placebo group were prescribed fluoxetine for depressive symptoms, and two of these five had an increase in their parkinsonian disability (11). Our patient did not experience an increase in his tremor or develop any other parkinsonian symptom. His jaw muscle

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tightening and swallowing difficulty were probably mild dystonia. Both of these symptoms resolved when the fluoxetine was discontinued. Any reports of TD due to fluoxetine in a patient with PD could not be found.

Although TD was described in the 1950s, its mechanism is poorly understood. It has traditionally been associated with older antipsychotics that block dopamine receptors in the central nervous system. It is believed that this chronic blockade subsequently induces a supersensitivity of the dopamine receptors in the striatum of individuals susceptible to developing TD (12). Patients with genetically abnormal dopamine-2 and dopamine-3 receptors were found to present a greater likelihood towards the emergence of TD (13). The mechanism of SSRI-induced EPS is postulated to the antidopaminergic effect of serotonin in the striatum (14). The low dopamine in the striatum of this patient with PD may have been a risk factor for the fluoxetine-induced TD. Other potential contributors are the ability of trazodone and levodopa to increase serotonin levels and dyskinesia symptoms. Levodopa-induced dyskinesia is a well-recognised entity seen in some patients treated with higher doses of levodopa for many years (15). There is evidence from murine studies that low dose trazodone can enhance dopaminergic neurotransmission in the basal ganglia (16) and thereby induce movement disorders although these are rarely reported with clinical use of trazodone (17). As this patients' TD resolved while he was still taking trazodone and levodopa, they are less likely to have been the causative agents but should, nevertheless, be considered.

Medication-induced movement disorders affect compliance, psychosocial and occupational function (18) and can induce suicidal ideation (19–21). Although the patient in our case reported only mild distress from the TD and denied thoughts of suicide, these are important reasons for clinicians to be aware of the relatively uncommon side-effect of EPS associated with SSRIs, a commonly used medication, especially in patients that have predisposing factors such as the PD in this patient. In these patients, clinicians should avoid activating antidepressants (fluoxetine, paroxetine and citalopram) that have been shown in murine studies to increase midbrain dopamine (22). A recent review of antidepressant-induced EPS showed that venlafaxine accounted for the least number of movement disorders (1). Also, although venlafaxine inhibits serotonin re-uptake at all doses, the low dose used in this patient may have prevented the change in striatal dopamine levels that were produced by the former fluoxetine.

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