

FLUOXETINE INDUCED EXTRAPYRAMIDAL SYMPTOMS : CASE REPORTS

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ABSTRACT

This case report describes the induction of extrapyramidal symptoms with fluoxetine, which is reported to be a rare phenomenon. A dopamine blockade at the nigrostriatal level primarily mediated by serotonin has been proposed as the probable mechanism.

Key Words : Fluoxetine, extrapyramidal symptoms

In recent years there have been several case reports of extrapyramidal symptoms as a result of treatment with fluoxetine (Tate, 1989; Lipinski et al., 1989; Fallon & Liebowitz, 1991; Steur, 1993; Arya, 1994; Coutler & Pillans, 1995). The symptoms noted include bradykinesia, cogwheel rigidity and akathisia. Extrapyramidal symptoms develop in patients while being treated with fluoxetine or the baseline extrapyramidal symptoms are reported to have worsened. As fluoxetine is a commonly used and well-tolerated antidepressant, looking into this rare and intriguing side effect is worthwhile. Clinically, one runs the risk of losing the patients due to suicide because of this distressing side-effect or noncompliance. We report two cases of fluoxetine-induced extrapyramidal symptoms and possible mechanisms responsible for the induction of these side-effects are discussed.

CASE 1

Mr. A, a 25 year-old male reported to our hospital with a major depressive episode for two weeks. He had a manic episode one year before and was treated successfully elsewhere. In the outpatient department he was started on fluoxetine 20 mg daily. Five days later he reported with severe restlessness and inability to

sit at ease in one place for any length of time. He had severe disturbance in sleep and marked reduction in appetite. Subjectively he was expressing fearfulness without any reason. Detailed physical examination revealed significant cogwheel rigidity, bradykinesia, reduce eye blinking and mask like face with akathisia. He had not received any other medication for this episode but for fluoxetine. As the emergence of such side-effects may be linked to fluoxetine it was immediately stopped and lithium 900 mg per day with amoxapine 50 mg daily was started. After three days he was much better with significant reduction in depression and had no extrapyramidal symptoms including akathisia. The same medication was continued further and he remained well.

CASE 2

Mr. AH was a 19 year-old male, admitted in our hospital with one year history of depressive syndrome. He also had significant trichotillomania with trichophagia for the same period. He was started on fluoxetine increased up to a maximum dosage of 60 mg per day. Due to inadequate response fluoxetine was potentiated with lithium. Following this he started showing the features of hypomania, so fluoxetine was reduced to 20 mg per day and

haloperidol 10 mg per day was started. With this regime he developed severe side effects for which trihexyphenidyl 4 mg per day was added. A gradual improvement was noticed and during discharge there was remarkable improvement in hypomanic and compulsive symptoms. Next few months he came regularly for follow up and was maintaining well. There after he stopped visiting the hospital.

After nine months he was readmitted with florid manic symptoms and significant compulsive symptoms like trichotillomania and trichophagia for which haloperidol 10 mg per day and fluoxetine 20 mg per day was started. Within six days he developed akathisia and pseudoparkinsonism. Haloperidol was immediately stopped and trihexyphenidyl 4 mg per day was added and continued for one week. Within few days he became completely free from extrapyramidal symptoms. Because of the distressing compulsive symptoms, fluoxetine was increased to 40 mg per day. Two weeks after this he had recurrence of extrapyramidal symptoms with severe bradykinesia, cogwheel rigidity, tremor and facial flattening. After stopping the fluoxetine, within one week, he completely recovered from extrapyramidal symptoms. Subsequently, due to repeated mania-like episodes and poor drug compliance he was started on depot injection flupenthixol (40 mg i.m. every three weeks). With this regimen he is maintaining well and is coming for follow up regularly.

DISCUSSION

The mechanism by which fluoxetine, a primary serotonergic inhibitor induces or worsens the extrapyramidal side effect is still speculative. Opler (1991) proposed a three-neuronal model of extrapyramidal motor system by which dopaminergic, cholinergic and gabaergic agents can have effects on the extrapyramidal system. In this model the major input into the basal ganglia is the inhibitory dopamine nigrostriatal tract, second neuron is the excitatory cholinergic interneurone and third neuron

represents major inhibitory gabaergic flow. The blockade of dopamine tract causes disinhibition of the second neuron and subsequently increased firing of gabaergic neurons that inhibit the voluntary motor system observed clinically as bradykinesia. However, this model does not explain the role of serotonergic agents in the extrapyramidal system. Hamilton & Opler (1992) postulated a "four neuronal model" in which they added a first neuron that is serotonergic arising from raphe nucleus causing inhibition in the firing of nigrostriatal tracts and, therefore, capable of producing extrapyramidal effects. There has been evidence for the presence of serotonergic projection from the raphe nucleus to substantia nigra (Azmita, 1978). The extrapyramidal system has rich innervation of serotonergic fibres. Pharmacological evidence showed that serotonergic antagonists like cyproheptadine and methysergide could relieve the catalepsy induced by neuroleptics in rodents (Carter & Pycock, 1977). Fluoxetine has also been reported to inhibit the catecholamine synthesis in dopamine rich areas of forebrain, hippocampus and striatum (Baldessarini & Marsh, 1990). This serotonin-induced inhibition of dopamine neurons may result in decreased stimulation of dopamine with consequent extrapyramidal symptoms.

The cases in this report show the occurrence of severe pseudo parkinsonian symptoms and akathisia with fluoxetine. Neither of them reported suicidal ideation that is contrary to the previous reports (Teicher et al., 1990; Rothschild & Locke, 1991; Tueth, 1994). A possible reason could be the detection of side effects early in treatment, and immediate intervention hindered the evolution of suicidal ideation as a response to the feeling of akathisia. From reports in literature and the cases in this report, it appears that fluoxetine may be associated with extrapyramidal reactions. Furthermore, because of its potent inhibitory effect on hepatic oxidative metabolism, the potential for increased levels

of concomitant psychotropic medicines and increased side effects that may include extrapyramidal symptoms, should be borne in mind.

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