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Acute dystonia with concomitant use of amitriptyline and paroxetine

Abstract

Amitriptyline and paroxetine are antidepressant agents useful for the treatment depressive disorders. Antidepressant induced extrapyramidal symptoms represent an under recognised but important clinical entity as it can adversely impact treatment adherence. Cases of acute dystonia have been reported with selective serotonin reuptake inhibitors but there are only few cases reporting dystonia on amitriptyline. To add to this literature, we report a case of middle aged female who developed dystonia on amitriptyline while already being treated with paroxetine. So, it is warranted to be aware of combination therapy's side effects.

Keywords: Antidepressive Agents. Depressive Disorder. Extrapyramidal Symptoms. Serotonin Uptake Inhibitors.

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Introduction

Movement disorders refer to a group of diseases of central nervous system (CNS) that involve neurodegeneration of the basal ganglia, cerebellum, or both. The various types of psychotropic agents such as antipsychotics, mood stabilisers, anticonvulsants, and antidepressants can induce movement disorders. The classic neuroleptic induced movement disorders are primarily mediated by the impact on dopamine 2 (D2) receptors located in the extrapyramidal tract.[1]

The fifth edition of the Diagnostic and Statistical of Manual of Mental Disorders lists eight categories of medication induced movement disorders. It includes: 1) Neuroleptic induced parkinsonism, 2) Neuroleptic malignant syndrome, 3) Medication induced acute dystonia, 4) Medication induced acute akathisia, 5) Medication induced tardive dyskinesia, 6) Medication induced postural tremor, 7) Antidepressant discontinuation syndrome, 8) Other medication induced movement disorder.[2]

Acute dystonia occurs in up to ten per cent of patients and characterised by abnormal positioning of the head and neck, spasm of jaw muscles, impaired swallowing, speaking or breathing, thickened or slurred speech, tongue protrusion or dysfunction, deviated eyes in any direction, and abnormal positioning of limbs or trunk.[3] Extrapyramidal symptoms (EPS) have been reported with different classes of antidepressants and can develop with short-term or long-term use.[4] The selective serotonin reuptake inhibitors (SSRI) are used to treat an array of disorders such as depression, anxiety, posttraumatic stress disorder, phobia, obsessive-compulsive disorder, and panic disorder. Due to fewer side effects and better tolerability than tricyclic antidepressants (TCA) and monoamine oxidase (MAO) inhibitors, the SSRIs have become most widely prescribed antidepressants.[5] A number of case reports suggested the risk of EPS with SSRIs.[6] The studies also reported that SSRIs were more common offenders in producing EPS than non-SSRI antidepressants.[7,8] The review of literature reported that TCA induced EPS are infrequent.[7]

Combined drug usage may cause pharmacokinetic interaction and in turn many side effects are potentialised. Here we report a case of 32 years old women who developed dystonia as a result of combined usage of paroxetine and amitriptyline.

Case report

A 32 years old female presented in the emergency department of Acharya Vinoba Bhave Rural Hospital at Sawangi (Meghe), Wardha, Maharashtra, India with the complaints of deviation

of angle of mouth, slurring of speech, and up rolling of eyeballs for last two days and admitted in the critical care unit. She was diagnosed as major depressive disorder before three years and on regular treatment from psychiatry unit as per the informant and available records. She was receiving paroxetine 12.5 mg/day and propranolol 40 mg/day. Despite good drug compliance she had relapse of symptoms in the form of dizziness, worry, shivering of hands and feet after around one year; so, the dose of paroxetine was increased to 25 mg/day with complete remission. Again she developed symptoms on regular treatment, so amitryptiline 25 mg/day was added and its dose was raised to 50 mg/day after seven days, which she was receiving for last two and half months from current presentation.

There was no past history suggestive of similar symptoms, physical illness, or substance use; no history of psychiatric illness in the family. The patient was hospitalised in the critical care unit, thoroughly assessed, and diagnosed as drug induced acute dystonia. All medications that she was receiving were stopped and managed with injection promethazine hydrochloride 25 mg intravenous. She showed complete improvement of symptoms over a period of five hours. Laboratory tests including whole blood count, liver function tests, and routine biochemical tests revealed no abnormalities. She was discharged on the fifth day and advised for regular follow up. In view of relapse of depressive symptoms on the 14th day, she was started on paroxetine 12.5 mg/day which was raised to 25 mg/day after three days. She reported significant improvement on same treatment and no recurrence of dystonia symptoms.

Discussion

The first published case reports related to antidepressants induced EPS date back to the 1950s.[9] During the 1970s, a variety of TCA induced EPS were reported.[7,10,11] The EPS reported with TCA monotherapy include akathisia, dyskinesia, dystonia, and rabbit syndrome.[9-20] Only few cases of amitriptyline induced acute dystonia have been noted in adults, ascribed to drug interactions, overdose, and/or long term therapy.[18,19,21] These symptoms appear to be dose related.[7] Previous reports suggested that EPS were more common in females than males.[22,23] Vandel *et al.*[8] reported that these symptoms respond to antiparkinsonian agents and reduction in the TCA dose. Advancing age, female sex, and pharmacokinetic interaction by cytochrome P450 2D6 (CYP2D6) inhibition of concurrent drugs appear to be risk factors for EPS.[7,22-24]

The plausible mechanism of antidepressant associated EPS include the inhibitory modulation of dopaminergic function in the nigrostriatal pathways, the reciprocal balance between dopaminergic, serotonergic, noradrenergic, or cholinergic activity, and CNS synaptic potentiation of serotonin and/or norepinephrine through inhibition of transporters or inhibition of their degradation by MAO. The striatal inhibition of dopaminergic functions by serotonin, the receptor occupancy studies of serotonin, the receptor polymorphism and CYP2D6 phenotypes all lend credence to various hypothesis presented.[25-32]

In our case report, the causal relationship between acute dystonia and amitriptyline is based on: 1) close temporal correlation between drug administration and onset of the symptoms, 2) improvement following drug withdrawal and addition of anticholinergic agent, 3) exclusion of other possible causes, and 4) no recurrence of symptoms after the drug was discontinued. The patient was already receiving paroxetine, and after two and half months of adding amitriptyline, symptoms of dystonia occured. Review of literature reported that in 23% of cases, EPS developed in 32 to 90 days of treatment initiation; and the coadministered medication with SSRI may cause interaction responsible for the emergence of EPS.[4,22] This suggests that in this case, dystonia developed as a result of combined paroxetine and amitriptyline usage.

As a result this case made us consider that amitriptyline in low dose, previously reported to have less EPS, may develop acute dystonia, or especially when combined with the other psychopharmacological agents, may increase the risk. So, clinicians must be aware of side effect potential of antidepressants in low doses especially in combination therapy and patients should be monitored.

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