

# Acute Dystonic Reaction Associated with Increase in Trazodone Dose: A Case Report

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## ABSTRACT

Acute dystonic reaction associated with increase in trazodone dose: a case report  
Serotonergic drugs have been used for the treatment of various psychiatric disorders such as anxiety disorders, impulse control disorders and especially depression. Gastrointestinal system symptoms, weight changes and sleep disturbances are commonly observed side effects of serotonergic drugs. Drug-induced movement disorders are classically associated with dopamine receptor blocking agents, most notably typical and atypical antipsychotic medications. However, extrapyramidal side effects can also be seen with serotonergic agents, antiemetics, and opioid agonists. The most common extrapyramidal system symptoms are akathisia, dystonia, parkinsonism, and tardive dyskinesia. We describe a patient who developed an acute dystonic reaction after taking 100 mg trazodone and his symptoms resolved after receiving intra muscular anticholinergic treatment.

**Key words:** Dystonia, serotonergic system, trazodone

## ÖZET

Trazodon doz artışı ile ilişkili akut distonik reaksiyon: Bir olgu sunumu

Serotonerjik etkili ilaçlar başta depresyon olmak üzere, anksiyete bozuklukları, dürtü kontrol bozuklukları gibi farklı ruhsal hastalıkların tedavisinde kullanılmaktadırlar. Sık görülen yan etkileri arasında, gastrointestinal sistem belirtileri, kilo değişiklikleri, uyku bozuklukları yer almaktadır. İlaçla ortaya çıkan hareket bozuklukları klasik olarak dopaminerjik blokaj yapan ilaçlarla, özellikle de tipik ve atipik antipsikotiklerle ilişkili olarak görülmektedir. Bununla birlikte ekstrapiramidal sistem yan etkilerine serotonerjik ajanların, antiemetiklerin ve opioid agonistlerinin de neden olabildiği görülmektedir. En sık izlenen ekstrapiramidal sistem bulguları akatizi, distoni, parkinsonizm ve tardiv diskinezidir. Bu yazıda 100 mg trazodon almasının ardından akut distonik reaksiyon gelişen ve kas içi antikolinerjik ilaç uygulamasıyla belirtileri geçen bir hasta sunulmaktadır.

**Anahtar kelimeler:** Distoni, serotonerjik sistem, trazodon



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## INTRODUCTION

It has been thought that extrapyramidal system (EPS) side effects have emerged from an imbalance between acetylcholine and dopamine (1). The most common EPS symptom, which develops as a result of serotonergic drug intake is akathisia and apart from this acute dystonia, symptoms of Parkinsonism, tardive dyskinesia and tremor are also observed (2). In dystonia, muscular contractions are observed as involuntary, intermittent and continuous while the contractions in agonist and antagonist muscles develop in synchronization (3). Movement disorders generally develop due to

antipsychotic drug intake and they are observed more frequently with potent antipsychotics (1). On the other hand, it has been reported that with the intake of antidepressant, opioid, antiarrhythmic, anticonvulsant and antiemetic drugs in lower doses, EPS symptoms may also develop (4).

Serotonergic drugs may rarely cause EPS symptoms; but the mechanism of this side effect is not explained completely yet (2). Increase in the level of serotonin is known to suppress dopaminergic neurons (5). In the literature, the cases are most commonly related with fluoxetine in addition to those related with paroxetine, citalopram, escitalopram and sertraline (2).

In this presentation, emergence of acute dystonia in a patient who had been on venlafaxine 75 mg/day and trazodone 50 mg/day treatment for a year for depressive symptoms, right after venlafaxine was stopped and trazodone increased 100 mg/day at the same day, has been discussed.

## CASE

23 year-old, high-school graduate, single male has been doing his military service for 4 months and had worked as a hairdresser before his military service. He was diagnosed as major depressive disorder and his psychiatric treatment has been continued for 10 years at various intervals. During his military service, he applied to a psychiatry outpatient clinic with the complaints of sadness, emotional and social withdrawal, loss of interest and anhedonia. Venlafaxine XR 75 mg/day, which he had been on for the last year, was discontinued and bupropion 150 mg/day was started and trazodone 50 mg/day was prescribed. The next day the patient did not use venlafaxine or bupropion; however, he took one tablet of trazodone 100 mg for his difficulty in falling into sleep. He applied to the Emergency Service next morning with the complaint of contraction in his cervical muscle. His head was in extension position; he could not bring his no other symptoms including fever was present and this manifestation was developed for the first time; diseases of organic origin were abandoned. In his psychiatric evaluation, it was pointed out that he was worried and anxious because of the tonus in his muscles and because of the form his body had taken. He was describing depressive symptoms in the form of unhappiness, emotional and social withdrawal, with which he had been living for a while. Because the patient reported that he had been using alcohol and hashish irregularly before his military service, the possibility of malingering for providing sedative medicine was connoted. On the other hand, the fact that the patient stated that he had not experienced this kind of situation and stress causing incident before; his worried state; the questions he asked to figure out what happened to him rather than taking pills, made us abandon diagnosing him as malingering and conversion

disorder symptoms. The patient, who was evaluated as acute dystonia, was applied intramuscular biperiden 5 mg. Within half an hour after the treatment was carried out, it was observed that contractions stopped and did not recur. The medicines and pills the patient was on were discontinued and he was asked to apply the outpatient control 3 days later and it was learned that contractions did not recur. The treatment of the patient, whose outpatient follow-ups still continue, was regulated as mirtazapine 30 mg/day.

## DISCUSSION

People who are thought to be having acute dystonia symptoms, should also be investigated whether he/she suffers from tetanus, Wilson's disease, encephalitis, hypocalcemia, catatonia, conversion disorder or malingering (2). Since symptoms, which would direct us to abovementioned diagnoses, were not confronted in this patient, it was decided that he suffered from drug-induced acute dystonia. Etiopathogenesis of movement disorders, which develop after drug intake, can not be explained completely (6). Movement disorders are the problems, which are associated with dopaminergic system and they are often confronted in the practice of psychiatry due to antipsychotic drug intake (4). Reduction of dopamine level, which occurs as a result of connecting antipsychotics to D2 receptors in nigrostriatal pathway, is thought to be responsible for EPS symptoms (7). It has been reported that EPS symptoms could also develop due to the intake of serotonergic antidepressants, antiarrhythmics causing calcium channel blockage and antiemetics (4). Although it is not always acute dystonia, which is among the symptoms; upon discontinuation of venlafaxine, there are notifications related to the occurrence of discontinuation symptoms like tremor, dysarthria, akathisia, tension, increased heart rate, throwing up, headache, feeling of imbalance (8,9).

In the case, which is presented here, acute dystonia occurred when the patient did not take venlafaxine and trazodone although he had been on venlafaxine 75 mg/day and trazodone 50 mg/day for the last year. No symptoms were experienced in the meantime. He only

took one tablet of trazodone 100 mg once and the next day acute dystonia developed in his cervical muscles. It is known that dystonia may develop as a withdrawal symptom of serotonergic antidepressants (10). Dystonia was thought to be related to dose increase of trazodone instead of discontinuation of venlafaxine, because in the past there were periods of several weeks during which the patient had not use both of the medications, but no dystonia was observed. Also the patient had a contractions after he had taken one tablet of trazodone 100 mg, longer-acting swinging was enabled by the usage of venlafaxine in XR form, no other discontinuation symptoms were observed after dystonia had developed, complaints were cured rapidly and did not recur after biperiden treatment.

In the literature, there are two cases in which acute dystonia developed due to trazodone intake. In the first case, acute dystonia developed on the 12<sup>th</sup> day after the dose of trazodone had been increased to 400 mg (11). In the other case, it was reported that acute dystonia observed 2 weeks after the dose of trazodone had been increased to 50 mg/day (7). There was also no case of tardive dyskinesia reported with trazodone (5).

Trazodone has generally antagonistic effect on serotonergic receptors in particular 5-HT<sub>1A</sub>, 5-HT<sub>1C</sub> and 5-HT<sub>2</sub>. Having active metabolite, M-chlorophenylpiperazine is a strong serotonin modulator (12). Therefore, trazodone acts both like a serotonin agonist and an antagonist. Among the other mechanisms of action, there are pre-synaptic alpha 2 and post-synaptic alpha 1 adrenergic receptors as well as H1 histaminergic receptor blockage. It is also known that it connects T type calcium channels (12).

Although mechanism of movement disorders due to serotonergic drugs is not explained completely, variety of opinions has been suggested. Serotonergic intakes, which come to dopaminergic neurons in nigrostriatal pathways, have inhibitor characteristics. For this reason, it is obvious that increase in the serotonergic concentration will create suppression on

dopaminergic system (6). It is thought that increasing arousal in 5HT<sub>2A</sub> receptors in basal ganglions may also create EPS symptoms (6). Agonistic effects of trazodone on serotonergic system may cause this kind of dystonia. It is reported that the effect of trazodone on calcium channels may also be related with acute dystonia (5). Venlafaxine is a serotonin and norepinephrine reuptake inhibitor; its half-life is between 5-11 hours with o-methylvenlafaxine, its active metabolite. The discontinuation of venlafaxine, change in the level of serotonin and norepinephrine affects dopaminergic swinging and may cause movement disorders (13).

It is observed that dystonia, which occurs due to antidepressant intake, is seen within the weeks or the next days after the dose has been increased or drug intake has started. In the case presented here, dystonia was observed several hours after the patient, who was on trazodone 50 mg/day, had taken one tablet of trazodone 100 mg once. This also supports the opinion that after the serotonergic arousal exceeds a certain level; it interacts with nigrostriatal dopaminergic system (6).

In the treatment of EPS symptoms, which occur as a drug side effect, anticholinergic drugs like biperiden, diphenhydramine, benzotropine are used and after the treatment, most of the time, recovery is observed within 30 minutes. In some cases repetition of the drug dose is required and a long term treatment is rarely needed (2). In our case, healing was observed once intramuscular biperiden 5 mg had been applied and in the follow-ups it was observed that dystonia did not recur.

Because of their high efficiency rates and since they have fewer side effects, serotonergic agents are the drugs, which are used frequently. In addition to their frequent side effects, it should also be considered that movement disorders may occur therefore dose should not be increased unless necessary and treatment should be carried out with the minimum dose, which provides general well-being.

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