Case report / Olgu sunumu

AN ACUTE DYSTONIA CASE INDUCED BY ADDITION OF QUETIAPINE WITH A SINGLE DOSE ON FLUOXETINE AND TRAZODONE

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Arrived: 08.08.2012, Accepted: 14.09.2012

ABSTRACT

A patient admitted with complaints of muscle contractions in neck, shoulder and arm which started recently after quetiapine administration. As a result the patient developed dystonia after adding a single dose of 12.5 mg/day quetiapine while taking trazodone and fluoxetine treatment. In this paper we take a look at the literature concerning quetiapine and dystonia. In this context it is warranted to be aware of combination therapy's side effects, including ones that are considered having a lower risk of extrapyramidal symptoms such as quetiapine.

Key words: *dystonia, extrapyramidal side effects, quetiapine*

NPACADEMY. 2012; 1(2):49-52

FLUOKSETİN VE TRAZODON KULLANIRKEN TEK BİR DOZ KETİYAPİN EKLENMESİYLE GELİŞEN BİR AKUT DİSTONİ OLGUSU

ÖZET

Bu yazıda ketiyapin başlanmasından sonra omuz, kol ve boyun bölgesinde kasılma yakınmasıyla gelen bir hasta sunduk. Sonuçta hasta fluoksetin ve trazodon kullanırken eklenen tek doz 12.5 mg/gün ketiyapin ile akut distoni geliştirmiştir. Bu yazıda olgumuzu literatüdeki ketiyapin ile gelişen distoni olguları ışığında gözden geçirdik. Ketiyapin gibi çok düşük ekstrapiramidal yan etki riski olan ilaçların bile kombinasyon tedavilerinde bu tip yan etkilere yol açabildikleri ve bu nedenle kombinasyon tedavisi yapılırken yan etkilere karşı dikkatli olunması gerektiği vurgulanmıştır.

Anahtar sözcükler: *Distoni, ekstrapiramidal yan etkiler, ketiyapin*

NPAKADEMİ. 2012; 1(2):49-52

INTRODUCTION

Dystonia refers to a movement disorder characterized by simultaneous involuntary contraction of agonist and antagonist axial and appendicular muscles.[1,2] Acute dystonia is a type of this disorder frequently developing secondarily as a reaction to some drugs and generally in the

early phases of treatment and sometimes even after a single dose of particular drug.[3]

Although connected to multiple etiologic factors, its pathophysiology has not been clarified.[4] Among risk factors are taking antipsychotic drugs for the first time, as well as taking highly potent and high doses, history of head trauma, anxiety, being an elderly woman and a young man.[3] Reported acute dystonia cases are frequently connected to conventional antipsychotic drugs usage, on the other hand limited dystonia case reports are connected to taking atypical antipsychotic and antidepressant agents.[5-10]

Most of the reported acute dystonia cases related to atypical antipsychotic drugs are related to risperidone, olanzapine, sertindol,[11] at the same time acute dystonia cases reported in relation to antidepressants, the effective component seems to be duloksetin, fluoxetine, citalopram, essitalopram and trazodone.[12] Among antidepressant agents dystonia as a side effect SSRI group drugs are more accountable.[12] Solely there are a few dystonia cases reported connected to quetiapine.[13-18]

Combined drug usage causes interactions such as increasing or decreasing effectiveness of pharmacologic agents, and in turn it is a well-known fact that many side effects are potentialized. Hereby, in the reported case we discussed a dystonia case in which dystonia emerged as a result of combined usage of antidepressant and atypical antipsychotic agents.

CASE REPORT

A 32 year old woman, admitted with complaints of muscle contractions in neck, shoulder and arm which started recently. The patient had admitted to psychiatry outpatients nearly three months ago with complaints of reluctance, crying spells, insomnia, deprivation of energy and motivation and anguish; therefore she was diagnosed as depressive disorder and fluoxetine (20 mg/day) and trazodone (50 mg/day) was given.

At thirtieth day of the treatment, she was partially improved but sleeplessness and depressive mood persisted, the doses were justified as fluoxetine (40 mg/day) and trazodone (100 mg/day). During the second month of therapy the patient kept the dose of fluoxetine as ordered, but decreased trazodone dose to 50 mg/day. After ten days she admitted with the main complaints of irritability, tenseness and arguing with people frequently and having problems with them easily; then quetiapine (12.5 mg/day) was added to her present therapy. Sixteen or seventeen hours after taking the first dose of quetiapine she felt mild pain and contraction on the right shoulder and neck, but she ignored. A day later, nearly eight hours later taking quetiapine (12.5 mg/day) dose she experienced contractions in her right shoulder, neck, arm and hand muscles so much, so that she tried to opened her fingers with the other hand's assistance in order to be able to write, she also mentioned that her neck bent towards right side and kept the position uninterruptedly.

In admission, her general appearance seemed anxious; head deviated to right and right arm pressed to the body in a fixed position. She was conscious, co-operation perfect, time, place and personal orientation were intact. Her affect was anxious and irritable. Her speech was minimized and her attention was directed to the body due to contractions. In physical examination palpation revealed firmness on the right side of the neck, arm and hand muscles and also flexion and extension. Since this condition was interpreted as acute extrapyramidal side effect secondary to the drug, it was evaluated in the Simpson Angus Scale (SAS) and the degree of dystonia was found out to be 9.

Our patient had received radioactive iodine prior six years because of Grave's Disease and was on thyroxin (100 microgram/day) now. Laboratory tests including thyroid function tests, whole blood count, routine biochemical tests, and blood calcium levels revealed no abnormalities. Brain Magnetic Resonance Scans also showed to be normal. Since there was no other medical condition to explain this clinical picture, we accepted acute dystonia, induced by quetiapine and 5 mg biperiden was administered via intramuscular route. Contractions and tenseness relieved in about 20 minutes. And then Quetiapine was ceased and biperiden (4 mg/day/orally) was started for a period of one week.

After one week, she did not complain of pain. Though the patient had not received biperiden

orally, rigidity and contractions of muscles were absent and SAS score was zero. We decided fluoxetine (20 mg/day) and trazodone (25 mg/day) were maintained.

DISCUSSION

The evidence for medication-induced acute dystonia is abundant. The mechanism of acute dystonia in humans is still unclear, but the connection between the serotonergic and dopaminergic systems seems to play a major role. In addition some tests performed with primates, such as application of intrastrial acetylcholine, carbachol or antipsychotic agents showed an increase in strial release of acetylcholine; which in turn induced dystonia.

In central dopaminergic systems two main reactions develop against dopaminergic blockage. The acute and short lasting reaction is the increase in dopamine's turnover. This is in keeping with the development of clinical period of acute dystonia. During this period blood drug level is not stable; it increases and more importantly it decreases rapidly. Secondly, slower and long acting one is the "post synaptic receptor super sensitivity".[19] These two factors constitute basic principles of "mismatch" hypothesis. According to this hypothesis due to increased strial dopamine release induced by "increased turnover" blockade postsynaptic receptors in inconsistent and unbalanced way. As antipsychotic levels fall down this blockades dissapear, and causes development of acute dystonia.[20,21]

The symptoms of medication-induced acute dystonia usually occur within hours to several days of starting, increasing or decreasing the dose of medication; severity usually decreases with rest and relaxation.[22] The appearance period of quetiapine induced dystonia and its relation with dose show differences in related reports.[13-18] Generally when there appears to be no organic defect in the base with quetiapine induced dystonia cases the dose is approximately 400-600mg/day with a duration of 2-4 weeks,[14,15] but in the presence of a defect in the base (such as Parkinson's Disease, head trauma) a very low dose such as 12.5 mg and a very short time,[13] or rather high dose and a very short period of time dystonia is induced.

In this patient, the rapid onset of neck and arm-forearm-neck symptoms within 12-18 hours of an augmentation of 12.5 mg quetiapine once a day suggests that the patient may have been sensitized by the initial trial of fluoxetine and trazodone with quetiapine augmentation. In our case, this condition could be due to only low dose of quetiapine, but also could be related to latent effect of perused antidepressants inducing dystonia. Because, while usually associated with antipsychotics, antidepressants may also cause changes in dopamine, either an increase (directly) or a decrease (possible indirectly through serotonin receptors that inhibit dopamine pathways) resulting in movement disorders.[23]

Increased serotonergic neurotransmissions inhibition of the dopaminergic neurons at the ventral tegmental area.[24] Also there are theories about noradrenergic or probable serotonergic modulation of the cholinergic pathways[25] and calcium channel blockers inhibition theory.[26] These suggest that; serotonergic fluoxetine or trazodone,[27] which is shown to block calcium channels, alone or together are responsible from dystonia, because there are cases of dystonia with trazodone and fluoxetine.[28-30]

On the other hand CYP 3A4 trazodone takes part in destruction of quetiapine and specially fluoxetine inhibits quetiapine, so quetiapine blood levels increase and may trigger dystonia.[31] In addition, contribution of another fact to these possible three mechanisms is the variation of CYP 450 3A4 enzymes among individuals. This variation is related to genetic factors in a rate of %85.[32]

As a result, this case made us consider that quetiapine, previously reported to have least extrapyramidal side effects, may induce acute dystonia, or especially combined psychopharmacological agents when used with quetiapine may increase acute dystonia risk.

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