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Case Report / Olgu Sunumu

Tianeptine Addiction: A Case Report

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ABSTRACT

Tianeptine addiction: a case report

Common clinical problems associated with antidepressant therapy, are usage of a lower dose than recommended and cessation of the drug prematurely by the patients themselves. Withdrawal symptoms have been known for a long time, but other features of addiction, such as tolerance and compulsive drug use are very rare. The neurobiological properties of tianeptine involve a dynamic interplay between numerous neurotransmitter systems. The effects of tianeptine on the glutamatergic system can provide a key action in the cascade of events triggered by this compound and its antidepressant efficacy. In this article, with particular emphasis on the effects of tianeptine on the glutamatergic system, the abuse potential of the drug was explained through a case with "Tianeptine addiction" diagnosis.

Key words: Addiction, antidepressant, tianeptine

ÖZET

Tianeptin bağımlılığı: Bir olgu sunumu

Antidepresan kullanımıyla ilgili olarak, genellikle rastlanan klinik problemler, hastanın ilacı söylenenden daha düşük dozda alması ve istenilenden daha erken tedaviyi sonlandırmasıdır. Antidepresanlarla çekilme belirtilerinin olması uzun zamandır bilinen bir bilgidir fakat tolerans ve kompulsif ilaç kullanımı gibi bağımlılığın diğer özellikleri oldukça nadirdir. Tianeptinin nörobiyolojik özellikleri, birçok nörotransmitter sisteminin dinamik etkileşimini içermektedir. Glutamaterjik sistem üzerine etkilerinin, bu molekülün tetiklediği olaylar zincirinde ve antidepresan etkinliğinde anahtar role sahip olduğu düşünülmektedir. Bu makalede de, "tianeptin bağımlılığı" tanısı konmuş olan bir vaka üstünden tianeptinin kötüye kullanılma potansiyeli özellikle glutamaterjik sistem üzerine olan etkileri üstünde durularak açıklanmaya çalışılmıştır.

Anahtar kelimeler: Bağımlılık, antidepresan, tianeptin

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INTRODUCTION

It is common knowledge that antidepressants can cause withdrawal symptoms, however other properties of addiction such as developing tolerance and compulsive drug use are very rare (1,2). The usually seen clinical problems are; usage of a lower dose than recommended and cessation of the treatment before the planned time by the patient. Pharmacodynamics of most antidepressants and the absence of an acute euphoria or "high" after taking the medication theoretically eliminate the possibility of addiction.

Addiction can be defined as a syndrome characterized by compulsive substance abuse. It is generally accepted that the antidepressant drugs do not cause addiction; however there are studies in the literature that challenges this idea. Haddad's review on antidepressant addiction (3) searched through all the literature in English for antidepressant addiction, starting from 1963. The study reported 21 cases which satisfy the substance abuse criteria of American Psychiatric Association (APA) DSM-IV in antidepressant addiction.

Even though tianeptine has been proven to be efficient in depression, monoamine hypothesis cannot explain this efficiency. Because in contrast to SSRIs (selective serotonin reuptake inhibitors), tianeptine actually increases the reuptake of serotonin. As a matter of fact, tianeptine contributed to our understanding of complex central mechanisms triggered by antidepressants and depression etiology. In the literature, there are a few case reports with tianeptine addiction (4-6). In this article, we wanted to explain the abuse potential of tianeptine and its effect on glutamatergic system through a case diagnosed with "tianeptine addiction".

CASE

A 28-year old male patient admitted to our clinic with complaints of high-dosage tianeptine usage and difficulty in quitting the drug usage. The patient had complaints of social withdrawal, disturbances of sleep and appetite and crying 10 years ago, following his parents' divorce. Patient was then referred to psychiatry unit and diagnosed with depression and treated with venlafaxine 75 mg/day. However, patient did not comply with the treatment because of nausea and dizziness complaints. Then the patient was switched to escitalopram 10 mg/day and benefited from this therapy, but ended the treatment because of side effects. In the next 3 years, patient had no psychiatric complaints but after the 3 years, patient had complaints of social anxiety, social withdrawal and avoidance, thoughts of self-worthlessness and social function loss and he seeked for treatment. In that term, patient was prescribed tianeptine 12.5 mg 3 times a day. He reported that he really benefited from the treatment, saying he became much more optimistic and happy, and experienced very few side effects compared with his previous antidepressant experiences, and there was a big difference in his mood when he took the drugs and when he did not. He also reported that he felt worthless and weak-willed when he did not take the medication and confident and comfortable when he did. On the other hand, the patient started to lose these effects on the 4th month of treatment. When he wanted to give up the medication, he had complaints of sweating, hot flashes on hands and feet, extreme weakness, dryness in mouth, anxiety and fear. He then took another tablet and like this, he increased the dosage up to 750 mg/day. Patient said that even though he took very high doses for the desired effect, this high dosage caused a loss of appetite, intestinal gas and a frequency in urination. The patient started to spend all his money on the medication and takes 10-15 pills before going to a social event or a job interview. He had thoughts of not getting the job or friends abandoning him if he did not take the medication. His drug cessation attempts did not last more than 3 days. When he had withdrawal symptoms, he started using tianeptine again. Patient wanted to give up this drugabuse with his own will and admitted to our clinic.

There was no history of previous substance addiction or abuse. The patient's main complaint was that he could not give up "tianeptine" and he was hospitalized for "tianeptine addiction". First, tianeptine was stopped and diazepam 20 mg/day was started in order to control anxiety and withdrawal symptoms. Patient's lab results (Complete blood count, routine biochemical markers, and liver, kidney and thyroid function tests) were within the normal range. On the second day of patient's hospitalization, patient showed symptoms of excessive hunger, xerostomia, nausea and hot flashes. In a week, those complaints subsided. Diazepam dosage was lowered and finally stopped. Patient was discharged and paroxetine 20 mg/day was started for "tianeptine addiction" and "social phobia". In the follow-up interviews, he had no complaints regarding tianeptine and he did not use tianeptine anymore. But his social phobia continued, so paroxetine dose was increased to 30 mg/day.

DISCUSSION

The main characteristic of addiction is the compulsive usage of the substance being abused. Both DSM-IV and ICD-10 emphasize the compulsive usage of the substance and continuation of substance usage despite all the problems associated with the substance, in the diagnosis of addiction. In this case, patient was diagnosed with "tianeptine addiction" because of the presence of tolerance, withdrawal symptoms, uncontrolled substance usage and failed cessation attempts.

In the studies on antidepressant abuse and their addiction potential, the authors mainly emphasize the warning signs of previous alcohol and substance abuse (5). However, even though in most of the cases which satisfy the addiction criteria has a history of alcohol/substance abuse and/or Axis II personality disorders, there are a few cases that did not have either of them such as in our case (4,7).

The efficiency and tolerability of tianeptine was

clearly shown on depression patients (8). Tianeptine's mechanism of action made us question the fast monoamine modulation hypothesis in antidepressant efficiency. Tianeptine triggers the cellular adaptation steps that show antidepressant effect. One of the most important steps triggered by tianeptine is the phosphorylation of glutamate receptor sub-types (9). Reagan et al's (10) study reported that tianeptine modulates the neurostimulation of neurons by NMDA receptors in basolateral and central cores of amygdala.

There are many interactions between glutamatergic and dopaminergic systems that affect the results of psychostimulant drugs. The studies that investigate the trans-synaptic and intracellular mechanisms of interaction between glutamate-dopamine due to stimulant exposure help us to understand the pathophysiology of stimulant abuse on both cellular and molecular level (11). Striatum, the main central nervous system part that is responsible for action and movement, is richly innervated with glutamatergic and dopaminergic cells. Psychostimulants such as amphetamine and cocaine change the glutamatergic and dopaminergic transmissions, causing behavioral changes in animal subjects (12).

When the pharmacology of stimulants such as cocaine is reviewed, the importance of glutamate in addition to dopamine in substance abuse development can also be seen (12). Glutamatergic neurons that go to dopaminergic nerve bodies and synapses start from hippocampus, amygdala and cortex. Glutamatergic agonists were shown to increase the dopamine secretion when applied to dopaminergic nerve body or synapses. In addition, the increased excitement of neurons in striatum following stimulant exposure was connected to the activation in corticostriatal glutamatergic pathways (11).

Except for a few cases in the literature, antidepressants are generally accepted as non-addictive (13-15). Even in those cases, the most important reason for antidepressant addiction is reported to be the psychostimulant effect. Tianeptine's neurobiological properties include dynamic interactions of many neurotransmitter systems. It's thought that the effects of this molecule on the glutamatergic system play a key role in the chain of events that is triggered by it as well as its antidepressant effect. This effect of tianeptine on glutamate might play a role in its psychostimulant, thus addictive effect.

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