Abuse Of Tianeptine: A Case Report

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INTRODUCTION

Tianeptine is structurally similar to tricyclic antidepressants. However, it acts via serotonin and increases its uptake in cerebral tissue and platelets. It is an antidepressant agent that has a potential effect similar to SSRIs (selective serotonin reuptake inhibitors), which reduces stress-induced behavioral and physical effects through the hypothalamo-hypophysial axis (Malka et al. 1992). The anxiolytic efficacy profile of tianeptine is also similar to tricyclic and tetracyclic agents, and it was found that 37.5mg tianeptine has the equivalent anxiolytic effect of 20mg fluoxetine (Kasper and Olie 2002). It is metabolized in the liver without using the cytochrome P450 system. In studies on rats, it was shown that tianeptine has no direct effect on dopamine release or re-uptake (Mennini et al. 1988, Sacchetti et al. 1993). However, it was shown that after the administration of a single dose of tianeptine (12.5mg), the dopamine metabolite 3,4- dihydroxyphenilacetic acid (DOPAC) increases in the cerebral cortex and other regions of the brain (Sacchetti et al. 1993, Invernizzi et al. 1992). It was reported that using high doses of tianeptine in rats affects nerve cells temporarily without any prominent stimulating effect, stimulates muscular activity, and reduces sleep time. It was also reported that tianeptine improves attention and learning in rats (Labrid et al. 1992). There are some other studies reporting that tianeptine has effects on serotonin uptake, causes psychomotor stimulation in rats and cats, and has prominent cognitive influences (attention, memory, reasoning) (Invernizzi...
It was reported that the long-term use of tianeptine has no adverse effects on cognitive functions, psychomotor activity, cardiovascular function, sleep, and weight. Moreover, the most frequent initial adverse effects, which are nausea, vomiting, constipation, abdominal pain, vertigo, and sleep disturbance lessen as the treatment proceeds, and it has a low propensity for abuse (Wagstaff et al. 2001). Although there are findings about the risk of tolerance and abuse, there are few case reports about the excessive use of tianeptine. In initial reports, 16 abuse cases were detected with doses varying between 75-1875mg/day. In later years, 8 more cases with tianeptine abuse were reported (Leterme et al. 2003). In the case report of Guillem and Lepine (2003), the use of tianeptine was likened to the patient’s previous heroin dependence in terms of his experiencing physical and psychological wellbeing. It was reported that a tolerance, which resulted in an increase in consumption, developed after the first dose, that the user experienced a sensation of wellbeing, and that physical and psychological withdrawal symptoms were observed when the drug was withheld after one month when doses were not renewed.

In this case, tolerance, abuse, and the stimulating effect of tianeptine was observed in a patient who had a history of heroine dependence, multiple substance use, and had developed tolerance of tianeptine.

Case

K. Ç., a 34-year-old male patient who graduated from university and worked in the tourism sector for few months, consulted to our clinic with excessive daily use of tianeptine. In the psychiatric interview, it was learned that the patient had been hospitalized 3 previous times in our clinic and 4 other times in other clinics due to multiple substance use during the last 15 years. He had been a multiple substance user for 6 years before starting to use tianeptine. During the last 4 years, he used marijuana once every 3-4 months plus tianeptine every day, and was taking only tianeptine for the last year.

The patient began substance use 15 years ago with marijuana and alcohol; then he used marijuana 3-4 times/day and alcohol 140cl/day, 3 days a week. Six years later he began using heroin and cocaine together with alcohol and marijuana. The patient reported that he increased his heroin dose to 3-4gr/day (i.v. or nasally) after a 4-5-month period and also started using 0.5-1gr cocaine (nasally) within the same period. After 6 months he stopped taking cocaine, but continued to use heroin, marijuana, and alcohol, and complained about rhinorrhea, yawning, muscular pain, and severe cramps during this period.

Having used heroin and marijuana for two years, the patient received inpatient treatment in a hospital and abstained for a 5-month period after the treatment. During this period, he tried tianeptine on the advice of a friend who used tianeptine for its antidepressant effect. After the initial dose of 50mg, he experienced euphoria and increased physical energy; the patient then began to take tianeptine every two hours for a total of 375mg/day, beginning on the second day of use. Later, he began to take the drug at higher doses, eventually 3000mg/day, assuming that the higher doses might give him more pleasure. He then began to complain about pruritis, constipation, anorexia, weight loss, sleep disturbance, abdominal pain, dysuria, and impulsive behavior, but he continued to use tianeptine due to its more prominent satisfying effects. It was learned that the patient had no difficulty in getting the drug as it is sold without prescription, and that he worked only in temporary jobs and that his social life began to suffer.

The patient’s medical history was unremarkable, except for eczema and an ileus operation that he had a year earlier. In his psychiatric history, there were two suicide attempts within two years; one attempt with wrist cutting and other attempt with amitriptyline overdoses, and the patient had reanimation treatment for amitriptyline intoxication in the intensive care unit. It was detected that the suicide attempts were impulsive and occurred during periods when he was angry with his family. His family history revealed there were primary and secondary relatives who have had alcohol abuse, depression, and convulsive seizures. The patient declared that he used tianeptine the day before his hospitalization and that he had distress and insomnia during the first five days of his hospitalization. The patient spent 10 days in the detoxification unit and received only 8mg/day hydroxyzine; after-
wards, he was accepted into the therapy program based on both his desire and an evaluation of his motivation for therapy. He completed the 28-day in-patient therapy program. His biochemical and hematological analyses were in the normal range and his EEG was also normal. According to the DSM-IV criteria, he was diagnosed with multiple drug dependence-full remission, because of his history of repetitive use of three different substances (marijuana, heroin, cocaine) at larger amounts than intended, spending excessive time using the substances, disruption in his social and occupational activities, and not using any substance within last 12 months. He was also diagnosed with other drug abuse (tianeptine) because of his use of tianeptine at high doses for a year, and the amount of effort he put into obtaining and using the substance, while experiencing a reduction in his social and occupational activities.

DISCUSSION

The efficacy of tianeptine in alcohol abuse and dependence treatment has been documented (Favre et al. 1997); however, to the best of our knowledge, no has been published about its efficacy in the treatment of dependence of substances other than alcohol. It was stated that there is no evidence that use of tianeptine protects brain metabolism against the effects of psychosocial stress (Czeh et al. 2001) nor that users develop physical dependence (Wilde and Benfield 1995). It was reported that patients who were former heroin addicts did not increase the dose of tianeptine themselves during their treatment of 1-2 months (Delalleau et al. 1988). It was shown that a single dose of 337.5mg tianeptine has only insignificant and temporary adverse effects and is well tolerated at high doses (Ansseau et al. 1992).

It was reported that the treatment of a depressed patient with 1875mg/day tianeptine for a minimum of 7 months caused no severe or toxic effects and revealed psychostimulating effects at higher doses (Vandel et al. 1999). Moreover, the undesirable adverse effects, which are seen at higher doses, such as nausea, vomiting, abdominal pain, weight loss, anorexia, and constipation, were reported to be seen initially and to disappear later. The stimulating effects experienced by this patient, such as euphoria and increased physical energy, are similar to those experienced by our patient. In the present case, it was interesting that the stimulating effect of tianeptine was pleasant, tolerable at high doses, and there was need to increase the dose to achieve the same effect.

It was stated in the case reports of Leterme et al. (2003) that five subjects used tianeptine at different doses (varying between 87.5-2612.5mg) and psychostimulating effects were observed in all of them. In four of these five subjects, who were diagnosed with tianeptine abuse, benzodiazepine dependence was also reported, and the subjects declared (hypothesized) that they had to use sedatives to counterbalance the stimulating effect of higher doses of tianeptine. It was also mentioned that sedatives other than benzodiazepines (meprobamate, hydroxyzine etc.) might be preferred because they can be easily acquired. Although their contribution to the increase of paradoxical effects is less, the other reason for their preference is the fact that withdrawal from them is easier than that of benzodiazepines.

Although differing from the results of some studies about the usage of tianeptine at higher doses (Kasper and Olie 2002, Czeh et al. 2001, Wilde and Benfield 1995, Delalleau et al. 1998), the stimulating effect of tianeptine was mentioned, in particular, in other case reports about the abuse of tianeptine (Guillem and Lepine 2003, Vandel et al. 1999). Symptoms like muscular pain and feeling cold, which were reported during drug withdrawal, (Guillem and Lepine 2003) were not detected in our case; however, discomfort and distress were encountered. Treatment with tianeptine may be risky in terms of high-dose use and tolerance development in patients with substance dependence (Guillem and Lepine 2003, Leterme et al. 2003, Vandel et al. 1999). The literature also includes reports about addiction to antidepressants that have amphetamine-like effects, such as amineptine and tranylcypromine (Guillem and Lepine 2003).

Abuse or dependence of tianeptine is an important issue in patients who have histories of alcohol or substance abuse, and the efficacy of its treatment with this population requires further investigation.
REFERENCES


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