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CASE REPORT

Using Benzodiazepine Detoxification and Cognitive Behavioral Psychotherapy in the Treatment of a Patient with Generalized Anxiety Disorder Comorbid with High-dose Zolpidem Dependence

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In recent years, literature has shown that zolpidem dependence is not uncommon in the clinical practice, but there is no standard guideline for treatment of zolpidem dependence. Benzodiazepine detoxification has been widely used for alcohol detoxification, which is also an inhibitory substance. We would like to share the experience of benzodiazepine detoxification and cognitive behavioral psychotherapy in a patient with high-dose zolpidem dependence comorbid with generalized anxiety disorder.

Key words: Benzodiazepine detoxification, cognitive behavioral therapy, zolpidem dependence

INTRODUCTION

Zolpidem, known as a nonbenzodiazepine hypnotic agent, is useful for treating insomnia.[1] It can bind to the α1-containing g-aminobutyric acid $(GABA)_A$ receptors with high affinity but low or no affinity to those α2, α3, or α5 $GABA_A$ receptors.[2] Due to its selectivity in binding, as we known, it has strong hypnotic effect with weak muscle relaxant, anxiolytic, and anticonvulsant effect.[3] The previous review studies revealed that zolpidem has low or minimal dependence risk epidemiologically.[4,5] Nevertheless, growing evidence showed that zolpidem has the potential for abuse and dependence.[6]

A few studies mentioned the psychotherapy effect to treat zolpidem dependence,[7] and there was no standard guideline for treatment of zolpidem dependence. However, we have a lot of clinical experiences in the management of alcohol dependence, which is also an inhibitory substance dependence disorder. We would like to share the experience of treating a high-dose zolpidem dependence patient successfully with benzodiazepine detoxification and cognitive behavioral therapy (CBT), which is frequently used in the alcohol dependence.

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CASE REPORT

Mr. H was a 23-year-old man who just graduated from a college. He had circadian phase shift during the college life and slept less and less since the 3rd year in the college. He could only sleep 4–6 h since then and felt fatigue easily at day time. He went to one local clinic and the general practitioner prescribed zolpidem 10 mg before bedtime for him, but the hypnotic effects decreased several months later. He turned out to buy the zolpidem in illegal pharmacy dispensers because the previous general practitioner refused to prescribe higher dosage. Four months later, he had to use 60–100 mg zolpidem every night; moreover, he took it at daytime for relaxing. Soon, he found that he could not afford it because he had to take 60–100 tablets (10 mg per tablet) of zolpidem every single day. He came to our psychiatric department, and we prescribed lorazepam 2 mg and clonazepam 2 mg every night for replacing zolpidem. After 1 month therapy, Mr. H still used 40–60 tablets of zolpidem every day and was suggested admission.

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After he was admitted under the diagnosis of zolpidem dependence without other substance abuse or dependence, zolpidem was stopped at once and we replaced it by lorazepam 2 mg q.i.d and clonazepam 4 mg every night. No withdrawal symptoms (tremor, palpitation, sweating, or seizure) emerged during hospitalization. We decreased 25% of the medication dosage every week, and the detoxification therapy was done smoothly 4 weeks later. Mr. H was discharged after completing the detoxification.

During the hospitalization, we found that he had been having difficulty in facing his father's authority with consequent anxiety and also met the diagnoses of generalized anxiety disorder and cluster B personality traits. After discussing with him and his family, we performed CBT instead of antidepressant for him. CBT was conducted 1 h weekly by the psychologist for him with a 10-week program to decrease his difficulty of facing authority, including his father in the outpatient department. Mr. H stopped any hypnotic after 2-year follow-up and could make effective communications with his father.

DISCUSSION

According to previous literature, there were different reasons causing zolpidem dependence. Some patients feel anxiolytic effect and others get strong sedation effect and euphoria.[8,9] Some people might even misuse zolpidem to extremely high dose (400–1000 mg per day) which could cause death or seizure if withdrawal syndrome happened suddenly.[10] Obviously, there must be discreet reasons making some addictive people use hundreds of times of usual dosage of zolpidem.

It was reported that we could treat high-dose zolpidem dependence patients with long-acting benzodiazepines, such as diazepam.[11,12] However, there was no standard guideline for treatment of zolpidem dependence. We used the alcohol abstinence experiences to treat zolpidem dependence, which is also a central nervous system depressant. During detoxification, benzodiazepines are used as substitution of cross-tolerant drugs to prevent progression from minor alcohol withdrawal symptoms to major ones.[13,14] Lorazepam is one of the most frequently used benzodiazepines. The possible biomechanism is that zolpidem might lose its selectivity on $GABA_A$ receptor and exert the same pharmacological effects as classical benzodiazepines or alcohol.[15]

A few studies mentioned the psychotherapy effect to treat zolpidem dependence.[7] Darker *et al*. performed two meta-analyses showing that CBT plus taper is effective only in the short-term (3-month period) in reducing benzodiazepine use and insufficient evidence to support the use of motivational interviewing to reduce benzodiazepine use.[16]

We suggest that all the high-dose zolpidem dependence patients have to be admitted during abstinence due to safety issue. Besides the zolpidem dependence, it is necessary to find out whether the patient has psychiatric comorbidity, such as mood disorder, anxiety disorder, or other substance dependence. Combining medication and psychological therapy for an addictive patient is effective, and motivation interviewing can reduce the extent of substance abuse.[17,18] In this case, we found some dynamic factors and forced Mr. H to face the anxiety and weakened his dependent behavior. We share this case with abstinence from zolpidem successfully under alcohol abstinence model, that is, combination of benzodiazepine detoxification and cognitive behavioral psychotherapy. We hope it is helpful for other similar patients.

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Conflicts of interest

There are no conflicts of interest.

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