A case of Zolpidem dependence successfully detoxified with gabapentin

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ABSTRACT

An elderly female patient with Zolpidem dependence, who was successfully detoxified using Gabapentin is reported. Gabapentin may be considered as an alternative in the detoxification of non-benzodiazepine hypnotics.

Key words: Gabapentin, non-benzodiazepine dependence, Zolpidem

INTRODUCTION

Zolpidem is a short acting, non benzodiazepine hypnotic, a member of the imidazopyridine class. Its mechanism of action shares much in common with benzodiazepines as it is active at the central benzodiazepine receptors (sometimes called the omega ‘w’ receptors).[1] This receptor is a sub-unit of the GABA-A receptor and Zolpidem binds preferentially to the w1 receptor. Therefore, it has been proposed that it lacks benzodiazepine like side effects, having minimum abuse and dependence potential.[2] This selectivity for w1 receptors however is lost at higher than standard hypnotic dosages, and thus Zolpidem acts like any other benzodiazepine.[3,4] The tolerance producing potential of Zolpidem was found to be the same as that of benzodiazepines and tolerance was found to develop in some people in just a few weeks, at doses of 30-120 mg above the recommended dose.[5]

Various cases of Zolpidem dependence have been reported. However, till date, there is no consensus as regards the medication to be used in the detoxification.

We present a case report of an elderly female patient who developed dependence to Zolpidem over a period of 8 months and was successfully detoxified with Gabapentin.

CASE REPORT

Mrs. M.C., 72-year-old female, received a prescription for Tab Zolpidem 10 mg per day as a treatment for insomnia. She gradually increased the number of tablets and would take Zolpidem even during the day as it increased her efficiency to carry out work done earlier. Over an 8 month period, the use escalated to 300 mg per day following which she was noted to be sleeping most of the time during the day, and would not attend to her routine household chores. If she was denied the tablets, she would become irritable on minimal provocation, would complain of feeling weak, along with decreased energy and ability to carry out work done earlier and would also develop tremulousness of hands and feet along with craving for Tab. Zolpidem. In view of the above symptoms, patient was taken to a private psychiatrist. She was initiated on 6 mg of Tab Clonazepam per day and the dose of Zolpidem was reduced to 150 mg per day over a period of 28 days. However, the craving persisted and hence she was referred to this hospital.

On mental status examination at admission, patient was found to be anxious with increased psychomotor activity, ill-sustained concentration, and dysphoric mood along with tremors of outstretched hands.

On physical examination, no gross abnormality was noted except for pallor and blood pressure of 180/110 mm Hg.
Routine blood investigations and chest X-ray were within normal limits. ECG showed evidence of right bundle branch block.

She was started on a daily dose of Cap Gabapentin which was initiated at 300 mg one in the morning and two tablets at night, and gradually increased by 100 mg every fifth day to the dose of 1200 mg per day and Tab Zolpidem was reduced by 15 mg every third day. Patient was successfully detoxified over a period of 30 days. At discharge, the dose of Gabapentin was reduced to 600 mg per day which was tapered over a month. The patient was followed up after a fortnight of stopping Tab Gabapentin and was found to be asymptomatic.

DISCUSSION

During the last decade, non BZD hypnotic, Zolpidem was considered to be a novel solution for the treatment of insomnia as it was suggested that it maintained the beneficial characteristics of BZDs as far as the reduction of sleep latency and sleep maintenance are considered, without having their side effects.

It was suggested that Zolpidem lacked anxiolytic, anticonvulsant, and muscle relaxant action and hardly caused memory impairment and more importantly minimal abuse and dependence potential.[6]

Several recent publications have highlighted that the abuse potential of Zolpidem was underestimated. A systematic review based on Medline literature search identified 36 cases of Zolpidem dependence. Both sexes and all age groups were involved to a similar extent.[7,8]

In extreme cases, dose increase reached a factor of 30-120 mg above the recommended dose. In our case, patient used the drug to cope with everyday activities thereby receiving anxiolytic action from it. This is discrepant with the suggested reliability of Zolpidem for alpha 1 subunits of GABA receptors which are claimed to be responsible only for sedative activity.

Zolpidem has been suggested to have selective activity on GABA A receptors with alpha 1 subunits, opposite to BZDs which do not present selectivity and bind to alpha 2, 3, and 5 subunits.

Alpha 1 subunit containing receptors are located in most regions of the brain and it is presumed that their activation has hypnotic action. Alpha 2 subunit receptors are enriched in amygdala, the region that strongly contributes to anxiolytic action of benzodiazepines.

Zolpidem was believed to have low affinity for alpha 2 and 3 receptors therefore having minor anxiolytic action and minimal activity on memory function.

Our patient reported anxiolysis after using Zolpidem. It is possible that the drug in high doses such as that taken by this patient could induce this effect by losing its selectivity and acting also on alpha 2, 3, and 5 subunit containing GABA A receptors.

In our patient we have used Gabapentin in the treatment of Zolpidem dependence.

Gabapentin has been used efficiently to assist or treat alcohol withdrawal, management of cocaine dependence as well as benzodiazepine dependence and detoxification.[9‑12]

Gabapentin lacks shortbacks of BZDs in treatment of any drug dependence. It is eliminated via renal mechanisms which may be of particular utility in patients with hepatic dysfunction. It does not interact with liver enzymes thus decreasing the risk of pharmacokinetic interactions. It has no direct effect on the GABA receptors or transporters, it is shown to increase GABA turnover in various regions of the brain. It binds to subunits of the L-type calcium channels and increases the synthesis and non-synaptic release of GABA in the brain. Moreover, it may influence the synthesis of glutamate.[13] It has been hypothesized that gabapentin, through its GABAergic activity, may restore the feedback inhibition from the nucleus accumbens after alteration through repeated drug use.[14]

In addition to its increasingly corroborated efficacy in the treatment for alcohol detoxification, cocaine dependence as well as benzodiazepine dependence gabapentin seems to become a promising alternative in non-benzodiazepine detoxification, for non-benzodiazepine monodependence as well as for patients with multiple drug abuse.

CONCLUSION

Gabapentin may be a compound worth screening as a potential treatment for Zolpidem detoxification. The possible effectiveness of Gabapentin in the detoxification of dependence producing substances warrants further investigation by systematic and well designed studies.

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Announcement

The Executive Committee of Bombay Psychiatric society (BPS) is pleased to announce the launch of its revamped website www.bombaypsych.org. The website has a new section on awareness and education for patients, family members, and the public in general.

This is an attempt to reach out to people who are misled into either avoiding Psychiatric help, or prematurely dropping out of treatment. Mental health related myths and misconceptions, based on socio-cultural influences get limited attention in day to day clinical work. These influences are often not anticipated or are not a clinician’s priority. Such issues are often addressed by lay advisors (nonmedical & unqualified); and can lead to immense damage to the credibility of our profession, and create numerous obstacles in the management of psychiatric disorders. We have included such issues, and general information about mental health in the form of frequently asked questions (FAQs). Answers to these FAQs in English, Hindi, Marathi and Gujarati (4 most used languages in Mumbai) ensure that almost the entire population of Mumbai is covered. Except for some geo-cultural differences these would be useful all over the country.

A website has now become one of the most practical means of mass communication. Computer access and literacy are no longer major hurdles. A computer literate person can access this website himself, and can help his fellow citizens to do so. Presently, BPS members are provided with printed slips and stickers to make their patients aware of the website. Other options are being explored. We are sharing this model of public education to maximise its utilization, and for feedback of fellow IPS members.

Dr. Malay Dave  Dr. Shobha Nair  Dr. Sanjay Bagadia
Web Editor  Hon. Secretary  President (2012-13)