Zolpidem dependence

Insomnia has emerged as an important condition afflicting human population. Apart from behavioral intervention, hypnotics are often used for a short duration of time to manage insomnia. The earlier practice of using benzodiazepines routinely has come into disrepute due to various problems associated with their use, of which the addiction liability is an important one. Consequently, the use of non-benzodiazepine hypnotics such as zolpidem has increased enormously. Zolpidem is a short-acting imidazopyridine hypnotic that is an agonist at the gamma-aminobutyric acid A type (GABAA) receptor. It has been suggested that it acts selectively on alpha 1 subunit-containing GABA benzodiazepine (BZ1) receptors (contrary to classic benzodiazepines) presenting low or no affinity for other subtypes. Epidemiological and clinical data have generally concluded that the risk of dependence on zolpidem is low or minimal.

Some studies, however, have warned the physician against the routine use of zolpidem. Hajak et al., in their review of 36 published case reports on zolpidem dependence, have reported that the recommended dose of zolpidem in these cases exceeded by a factor of 8-120. Majority of the cases were reported in former drug or alcohol abusers and/or the patients had other recognizable psychiatric disorders. Other case series subsequently reported, however, do not report any association of zolpidem with other substance abuse; rather zolpidem abuse was associated with minor psychiatric disturbance. However there are no cases of zolpidem dependence reported from India. We are presenting a case of zolpidem dependence encountered in clinical practice.

Case history

A 31-year-old married male presented to the psychiatry outpatient facility of our institute with inability to stop zolpidem use. The patient had initially begun using alcohol in the form of spirits at 14 years of age at a party. He began regular use at weekends by 16 years of age. By 18 years of age after his employment as a sweeper in a hospital, he started using alcohol in company of his colleagues daily in the evening and also increased the consumption to about 180 ml of spirits. During bouts of heavy drinks in the evening he would develop tremors of hands, with anxiety and palpitations the next morning, which would be relieved by alcohol intake. Thus he started drinking in the morning and would consume about 360 ml of spirits throughout the day. He also started being absent from work because of constant drinking. He would not contribute to the family expenditure.

During a bout of severe drinking, the patient developed abdominal pain with vomiting. A diagnosis of acid peptic disease was made in the emergency department and treated accordingly. He was also referred to a psychiatrist for treatment of alcoholism. As part of detoxification the psychiatrist advised the patient to take oral diazepam 10 mg, t.d.s. However, the patient started using diazepam in dose of 40 to 50 mg per day to obtain high. During this time he had stopped use of alcohol. Diazepam use continued for 6 months. He had developed features of dependence on diazepam. After 6 months, the patient stopped diazepam use and resumed alcohol use following an altercation with family members. He continued to use alcohol in dependent pattern for 4 years till 2 years before. Following pressure from his family members, he left alcohol on his own without seeking treatment. He continued to remain free of alcohol or other substances till the time of presentation to the clinic.

Over the preceding 4 to 6 months before presentation to the clinic, the patient started having disturbances in onset of sleep along with frequent awakening at night without any features suggestive of psychiatric or medical illness. He approached the treatment centre wherein a detailed assessment was done. A diagnosis of primary insomnia was made after ruling out psychiatric and medical causes of sleep disturbance. Considering the past history of benzodiazepine dependence, the patient was prescribed zolpidem 10 mg/day as a hypnotic along with counseling regarding sleep hygiene. The patient was advised regular follow up, which he did not comply with.

Two months after prescribing zolpidem, the patient came to the outpatient clinic with complaints of intense anxiety, palpitations, tremulousness, restlessness and dysphoria over the prior two to three days. He reported that he had been using 30 tablets of 10 mg zolpidem/day in three divided doses over the preceding one month. He had gradually increased his intake from the prescribed dosage of 10 mg per day to the present dose of 300 mg/day. He claimed that he increased the dosage initially to ward off his insomnia; however he started enjoying the high produced by zolpidem and had to increase his dosage gradually in order to experience the same pleasure. He would develop withdrawal symptoms after a gap of 4 to 6 hours after intake of the drug. He could not work in the preceding 1 to 2 weeks due to the intense withdrawal symptoms and thus sought help.

The patient was hospitalized and assessed for physical problems associated with the use of high dose of zolpidem. Baseline investigations including hemogram, liver and kidney functions were normal. Electrocardiogram was normal. It was planned to detoxify the patient gradually with diazepam. However, the patient refused treatment and went against medical advice on the second day of admission.

Discussion

The case illustrates that zolpidem can be abused. As seen in this case, the phenomena of withdrawal, tolerance, and euphoria can also be experienced with zolpidem. In some cases,
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the dose of zolpidem abused could be very high, as in the present one, wherein the patient used about 30 times more than the prescribed dose, making it a total of about 300 mg of zolpidem per day. An important factor is that the patient was dependent on alcohol as well as diazepam in the past. Literature also supports the potential possibility of development of zolpidem dependence in such individuals. It has also been noted that at higher doses the effect of zolpidem becomes undistinguishable from benzodiazepines, which was true in our case too. Also noteworthy is that the patient had been abstinent on any drug for the past one and half years, after which he developed zolpidem dependence. This shows that one should always be extra careful in using the hypnotics currently available in such patient population, even after a long period of abstinence.

Conclusion

This case demonstrates that zolpidem is a potentially addictive drug that can be abused in very high doses especially in patients already dependent on other substances.

References


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