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Original Research Paper

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CASE REPORT: ALPRAZOLAM WITHDRAWAL DELIRIUM WITH PSYCHOSIS

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ABSTRACT Benzodiazepines are widely acknowledged to be addictive, and withdrawal symptoms can occur after 4–6 weeks of continuous use. One third of long-term user's experience problems on dosage reduction or withdrawal. We present a case of reversible delirium with brief psychotic episode following withdrawal of alprazolam in an otherwise healthy middle age man, in the absence of cardinal withdrawal symptoms. physicians and psychiatrist should be aware that the short-acting benzodiazepine alprazolam, can present as delirium with reversible brief psychotic episodes after 24-48 hours of discontinuation, in the absence of cardinal withdrawal symptoms as outlined in the DSM-5 and should be considered as a diagnosis, after excluding other possibilities.

KEYWORDS : Alprazolam, withdrawal, delirium, psychosis

INTRODUCTION

Benzodiazepines are widely acknowledged to be addictive, and withdrawal symptoms can occur after 4–6 weeks of continuous use (1,2). One third of long-term user's experience problems on dosage reduction or withdrawal (3). Documented cases of sedative, hypnotic, or anxiolytic withdrawal delirium are highlighted by autonomic instability, as well as particular physical examination findings that characterise the suspected diagnosis. We present a patient with alprazolam withdrawal delirium, who had measurable signs of withdrawal in form of delirium with psychosis.

Case report

Mr X, a 45-year-old male, was brought to the psychiatry emergency in march 2020, referred from medical emergency for the evaluation of altered mental status following withdrawal of alprazolam 3-4 days prior to the day of reporting to hospital. Previously, he was self-medicating himself taking alprazolam around 10-12 mg daily for his chronic complain of decreased sleep from past 3-4 years. The dose of alprazolam had gradually increased to the present dose. Mr X exhibited disinhibited behaviour, agitation, aggression, violence, not recognising family members, misidentification and suspiciousness. He also had persecutory delusions involving harm both to the family and self. After presenting to the emergency department, Mr X had altered consciousness, not oriented to time, place and person, poor attention and concentration, impaired immediate and recent memory, impaired judgement and absent insight. There was no significant precipitating factor (head injury, convulsions, tremors, fever etc). There was no history of any previous psychiatric illness of patient or his family. Mr X's wife, the primary caregiver, stated that she noticed, when Mr X was denied taking or decreased the dose of alprazolam tablets, his behaviour exhibited periods of wakefulness, agitation, restlessness, aggression and verbalised threats to harm himself and his family.

There is no significant medical, surgical, personal and family history contributing to present illness. No history of alcohol and any other substance intake was reported.

Mr X's vital signs were within normal limits; his physical examination was unremarkable. Results of extensive laboratory work, including electrolytes, renal and liver function tests, and complete blood counts, were within normal limits. The urine toxicology screen was negative for amphetamines, cannabis, hallucinogens, benzodiazepines, cocaine and opiates. A diagnosis of alprazolam withdrawal delirium and brief reversible psychosis (DSM-5 criteria for sedative, hypnotic, or anxiolytic withdrawal) was established. Diagnostic features of sedative, hypnotic, or anxiolytic withdrawal are highlighted by 2 or more symptoms including "autonomic hyperactivity (e.g. increases in heart rate, respiratory rate, blood pressure, or body temperature, along with sweating), tremors of the hands, insomnia, nausea, irritability, sometimes accompanied by vomiting, anxiety, and psychomotor agitation(4). We present a case of reversible delirium with brief psychotic episode following withdrawal of alprazolam in an otherwise healthy middle age man. Our case shows that sedative, hypnotic, or anxiolytic withdrawal delirium can occur in the absence of cardinal withdrawal symptoms.

The course of his illness was around 28-30 days, during which he improved gradually with delirium getting resolved first followed by psychosis and was stabilised on tablet clonazepam for sleep disorder. Alprazolam withdrawal delirium and brief psychosis is reversible and can be treated with use of long-acting benzodiazepines. In this case, we used clonazepam to control symptoms of alprazolam withdrawal delirium and psychosis.

DISCUSSION

Alprazolam's misuse potential stems from its unique pharmacokinetic properties of rapid absorption, low lipophilicity, and short half-life (t1/2), and pharmacodynamic properties of high potency and more severe withdrawal symptoms occurring after a shorter period of use. Compared with diazepam, alprazolam is less lipophilic, thus having a smaller volume of distribution, and is less protein-bound at 68%, compared with 98% for diazepam, meaning its faster metabolism and shorter duration of action would increase its abuse liability more so than of diazepam (5).

In addition to its pharmacological properties which may contribute to its increased misuse potential, alprazolam uniquely affects the dopaminergic function in the striatum similarly to stimulants. The striatum is a heterogeneous structure connected to dopaminergic reward circuitry, receiving input from the prefrontal cortex and ventral tegmental area to guide behavioural output, including motor planning, decision-making, motivation, and reward. Most drugs involved in misuse or addiction consistently lead to dopamine release in the striatum (6,7,8). Alprazolam is a high-potency triazolobenzodiazepine and half-life of alprazolam is

much shorter (8–16 hours), with no accumulation of oxidative metabolites. Once the drug is discontinued, thus triggering severe withdrawal symptoms due to rapidly eliminated alprazolam. The triazole ring may also play a role in the metabolism of alprazolam (5).

Data available on PubMed, there are 4 published cases of alprazolam withdrawal delirium, all 4 patients experienced autonomic instability in the presence of delirium and brief reversible psychosis (9,10,11,12). Alprazolam is one of the most commonly prescribed drugs by psychiatrists, physician and other practicing doctors. It is available by name of Xanax, alprax etc. It is one of the commonly over the counter sold drug making it easily to be acquired. All these factors contribute to increase the 'abuse liability' of Alprazolam.

CONCLUSION

In conclusion, physicians and psychiatrist should be aware that the short-acting benzodiazepine alprazolam, can present as delirium with reversible brief psychotic episodes after 24-48 hours of discontinuation, in the absence of cardinal withdrawal symptoms as outlined in the DSM-5 and should be considered as a diagnosis, after excluding other possibilities. The easy availability, short acting and addiction potential makes alprazolam a potential substance of drug abuse.

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