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Review

## Misuse of Alprazolam as 'kutta goli' among the youth and school children in the Malegaon city of India

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### ABSTRACT

The drug Alprazolam was approved by the United States Food and Drug Administration in 2003 to treat panic disorder and anxiety. Approval was granted to Upjohn UK Limited, a pharma company. Due to its euphoria, mania, drowsiness, and amnesia effects, it has the most misuse liability and addiction property. According to a Times of India report, the illegal sale of Alprazolam tablets continues in the textile town of Malegaon, Nashik District, Maharashtra, India. Last year, the Food and Drug Administration booked 23 people and recovered Alprazolam tablets close to 90,000 INR. The Alprazolam tablet is a scheduled drug and is supposed to be sold only on the prescription of doctors however it is sold illegally in Malegaon city by the code names like 'kutta goli'. In this paper, we have reviewed the Alprazolam indications, pharmacological property, misuse liability, special warnings and precautions for use, and steps to avoid misuse.

**Keywords:** alprazolam, benzodiazepines, kutta goli, misuse liability.

### INTRODUCTION

Alprazolam, a highly potent benzodiazepine, has been extensively misused, particularly in France and the United States, as highlighted by various studies.<sup>1,2</sup> The misuse of alprazolam is associated with intensifying therapeutic effects, euphoria, and managing substance withdrawal, with an increasing trend in combining it with opioids, leading to a higher risk of dependence and misuse compared to other benzodiazepines.<sup>1</sup> Despite being widely prescribed for anxiety disorders, alprazolam's addictive nature and misuse liability have raised concerns among addiction specialists, especially due to its unique psychodynamic properties that limit its clinical utility.<sup>2</sup> Additionally, inhalation of alprazolam has been reported among adolescents, leading to severe complications like endonasal necrosis, emphasizing the need for further research and interventions to address this concerning trend.<sup>3</sup> Understanding the motivational factors behind benzodiazepine-related aggression, including alprazolam use, is crucial for effective intervention strategies and rehabilitation programs.<sup>4</sup> One study suggests that regulatory changes in Australia may not have effectively curbed alprazolam misuse, and instead, there may be an

increase in illicit use. This underscores the need for targeted public health interventions to address the rising trend of alprazolam use among individuals who inject drugs.<sup>5,6</sup>

One of the modern day's biggest issues is the problem of substance abuse among the youth. Another dubious drug to have hit Malegaon, Maharashtra's streets is Alprazolam, whose code name is 'kutta goli' which damages the brain cells. These tablets are in circulation and many school-going kids and college students are hooked on them. The sale of this 'kutta goli' in Malegaon and Nashik is illegal but still rampant which may increase the crime rate.

The Food and Drug Administration Department has been trying to curb this menace for the past few years. This pill is being taken in the garb of a 'medicine' and it is not only the case of Malegaon but the entire Nashik district has been reeling under this menace. In this case, the police, along with the Food and Drug Administration Department have arrested many suspects, and thousands of pills have been seized from them, according to a report by Maharashtra Times.

### Pharmacodynamic properties and Misuse liability

Alprazolam, like other benzodiazepines, has a high affinity for the benzodiazepine binding site in the brain. It facilitates the inhibitory neurotransmitter action of gamma-aminobutyric acid, which mediates both pre-and post-synaptic inhibition in the central nervous system (CNS). 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. Administration of alprazolam, and not lorazepam, has been found to elicit a significant increase in extracellular dopamine concentrations in the striatum and a marked trend towards increased levels of serotonin, which induced behavioral stimulatory effects on animals. The striatum is a heterogeneous structure connected to dopaminergic reward circuitry, receiving input from the prefrontal cortex and ventral tegmental area to guide behavioral output, including motor planning, decision-making, motivation, and reward. Most drugs involved in misuse or addiction consistently lead to dopamine release in the striatum.<sup>7-12</sup>

Alprazolam's misuse potential stems from its unique pharmacokinetic properties of rapid absorption, low lipophilicity, and short half-life ( $t_{1/2}$ ), and pharmacodynamic properties of high potency and more severe withdrawal symptoms occurring after a shorter period of use.<sup>13</sup>

### Indications of Alprazolam

Alprazolam is indicated for short-term symptomatic treatment of anxiety and panic disorder in adults. It is only indicated when the disorder is severe, disabling, or subjecting the individual to extreme distress.<sup>2,14</sup>

### Duration of treatment

Alprazolam should be used in the lowest possible effective dose, for the shortest possible time, and for a maximum of 2-4 weeks. The need for continued treatment should be reassessed frequently. Long-term treatment is not recommended. The risk of dependence may increase with the dose and duration of treatment.<sup>14,15</sup>

### Anxiety

250 micrograms (0.25 mg) to 500 micrograms (0.5 mg) three times daily, increasing if required to a total of 3 mg daily.<sup>14,15</sup>

### The elderly or in the presence of debilitating disease

250 micrograms (0.25 mg) two to three times daily to be gradually increased if needed and tolerated.

If side effects occur, the dose should be lowered. It is advisable to review treatment regularly and to discontinue use as soon as possible. Should longer-term treatment be necessary, then intermittent treatment may be considered to minimize the risk of dependence.<sup>14,15</sup>

### **Pediatric population**

The safety and efficacy of alprazolam in children and adolescents below the age of 18 years have not been established.<sup>14,15</sup>

### **Special warning and precautions for use**

The use of benzodiazepines may lead to the development of physical and psychic dependence upon these products. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a history of alcohol and drug abuse. Pharmacodependency may occur at therapeutic doses and/or in patients with no individualized risk factor. There is an increased risk of pharmacodependency with the combined use of several benzodiazepines regardless of the anxiolytic or hypnotic indication. Cases of abuse have also been reported. Alprazolam may be subject to diversion. There have been reports of overdose-related deaths when alprazolam is abused with other central nervous system (CNS) depressants including opioids, other benzodiazepines, and alcohol. These risks should be considered when prescribing or dispensing alprazolam. To reduce these risks the smallest appropriate quantity should be used and patients should be advised on the proper storage and disposal of unused drugs.<sup>16,17</sup>

### **Withdrawal symptoms**

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion, irritability, and insomnia. In severe cases, the following symptoms may occur derealisation, depersonalization, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations, or epileptic seizures. The dose must be gradually reduced to avoid withdrawal symptoms.<sup>2,18</sup>

### **Rebound insomnia and anxiety**

A transient syndrome whereby the symptoms that led to treatment with a benzodiazepine recur in an enhanced form may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances, and restlessness. Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, the dose must be gradually reduced to avoid withdrawal symptoms.<sup>19</sup>

### **Amnesia**

Benzodiazepines may induce anterograde amnesia. The condition occurs most often several hours after ingesting the product and therefore to reduce the risk patients should ensure that they will be able to have uninterrupted sleep of 7-8 hours.<sup>20</sup>

### **Psychiatric and paradoxical reactions**

Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behavior, and other adverse behavioral effects are known to occur when using benzodiazepines. They are more likely to occur in children and the elderly.<sup>21</sup>

### **Tolerance**

Some loss of efficacy to the hypnotic effects of benzodiazepines may develop after repeated use for a few weeks.<sup>22</sup>

Episodes of hypomania and mania have been reported in association with the use of alprazolam in patients with depression. Benzodiazepines are not recommended for the primary treatment of psychotic illness.<sup>23</sup>

## DISCUSSION

### Steps to avoid misusing alprazolam

To avoid misusing alprazolam and mitigate its potential consequences, several crucial steps can be taken based on the research findings. Firstly, it is essential to raise awareness about the risks associated with alprazolam, especially regarding its abuse potential. Monitoring and analyzing adverse event reports related to alprazolam can provide valuable insights into its safety profile and help identify potential risks. Additionally, healthcare providers should adhere to appropriate prescribing practices, considering factors such as dosage, duration of treatment, and patient characteristics to minimize the likelihood of misuse. Furthermore, implementing specialized preventive plans, regulatory measures, and public health programs can help address the growing concern of alprazolam misuse and addiction, particularly in vulnerable populations like the elderly. By combining these strategies, it is possible to reduce the incidence of alprazolam misuse and its associated adverse outcomes.<sup>24,25</sup>

The subtherapeutic dose of Atropine is added to diphenoxylate to discourage misuse, as diphenoxylate can lead to dependence. Atropine also helps in reducing the potential abuse of diphenoxylate.<sup>26</sup> Pharmaceutical companies may use a similar pharmacodynamic property to avoid the misuse of Alprazolam.

## CONCLUSION

Alprazolam is the most widely prescribed and misused benzodiazepine in France and the United States and now in India. It can be used safely and effectively when prescribed appropriately, after thoroughly evaluating the risks and benefits of treatment. The respective country and region policymakers and healthcare professionals should work coordinately to avoid the excess burden on healthcare and crimes arising after alprazolam misuse.

### Conflict of Interest

The authors declare no conflicts of interest relevant to this article.

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