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Tapentadol Withdrawal, A Newer Trend in Opioid Overuse in Nepal: A Case Report

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ABSTRACT

Tapentadol, a dual-acting mu-opioid receptor agonist and noradrenaline reuptake inhibitor, is increasingly used because of its availability and low cost, with seizures rarely complicating withdrawal. Here, we present a case of tapentadol withdrawal complicated by seizures in a patient with a history of polysubstance abuse. The patient received symptomatic management in the intensive care unit and was subsequently started on anti-craving medications and antidepressants. Clinicians should be vigilant about the dependence potential of tapentadol and the occurrence of withdrawal-related seizures using safer prescribing practices to counter its emergence as a prescription opioid of abuse.

Keywords: Analgesics; opioids; tapentadol; withdrawal.

INTRODUCTION

Tapentadol hydrochloride is a centrally acting analgesic that inhibits norepinephrine reuptake and exhibits strong mu (μ)-opioid receptor agonism. It has been used to treat both acute nociceptive and chronic neuropathic pain. [1] Although it has been reported to have a lower divergence rate and abuse potential than other potent opioids, abuse is still possible owing to its μ-opioid receptor agonistic effects. [2,3] There is a paucity of literature regarding cases of tapentadol withdrawal and its management. We describe a case of tapentadol abuse with withdrawal symptoms complicated by seizures and its management at a peripheral hospital in Nepal.

CASE REPORT

A 36-year-old man presented to the emergency department (ED) complaining of abnormal jerky body movements for the previous hour, which were generalized and associated with up-rolling eyes, involuntary micturition, and postictal confusion. A detailed history revealed polysubstance abuse, the most recent of which was tapentadol tablets. He had consumed 15-20 pills of 50 mg tapentadol daily for the last ten months. His last intake was one day prior, but he had significantly reduced its use the previous week due to financial issues. The patient had a history of impulsive behavior, anxiety, excessive sweating, and increased indulgence in daily chores (washing, cleaning, and consuming tea). He also reported chest pain and increased awareness of his heartbeat. However, there was no history of head injury, seizure disorder, high fever, or altered sensorium in the past. Additionally, there was no personal or family history suggestive of any psychiatric or neurological illness.

He started smoking cigarettes at 16 years of age and gradually experimented with and abused multiple substances, including cannabis, brown sugar, alcohol, amphetamines, prescription drugs, and tapentadol. However, more recently, he had been using only tapentadol, with occasional marijuana and alcohol consumption (his last alcohol intake was two weeks ago, as corroborated by family members). In Figure 1, we provide a chronological chart showing the medications the patient abused and the effects and withdrawal experienced.

On physical examination, his Glasgow Coma Scale (GCS) was E4V4M6 (14/15). He was agitated and afebrile, had a pulse of 140 beats per minute, a BP of 140/90 mmHg, a respiratory rate of 16 breaths per minute, and maintained saturation in room air. His lungs were clear,

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with equal bilateral breath sounds. He was aware of the time, place, and person and had no focal neurological deficits. Other systemic examination results were unremarkable.

His laboratory workup showed anemia (Hb 12 g%), a total leukocyte count of 1.9 × 109/L, and a neutrophil count of 70%. Serological tests for infectious diseases were non-reactive, and renal and liver function test results were within normal limits. The urine toxicological screen was positive for opiates and cannabis; however, a specific tapentadol assay was unavailable in our setting.

The patient was admitted to the intensive care unit (ICU) and treated with intravenous levetiracetam, lorazepam, tapentadol, propranolol, haloperidol, promethazine, fluids, and oral naproxen. He remained disoriented until day 5 in the intensive care unit and continued to be agitated and delirious, with loss of bowel and bladder function. Given the ongoing agitation, physical restraints were added to the abovementioned chemical restraints. His delirium was slow to improve, and he was discharged on the 8th day of admission to follow up in the outpatient department (OPD) for further rehabilitation and management of potential opioid dependence.

He developed craving and depressive symptoms during the first follow-up seven days after admission. He was subsequently started on 20 mg fluoxetine and 50 mg naltrexone, with plans to escalate the therapy to achieve the desired results.

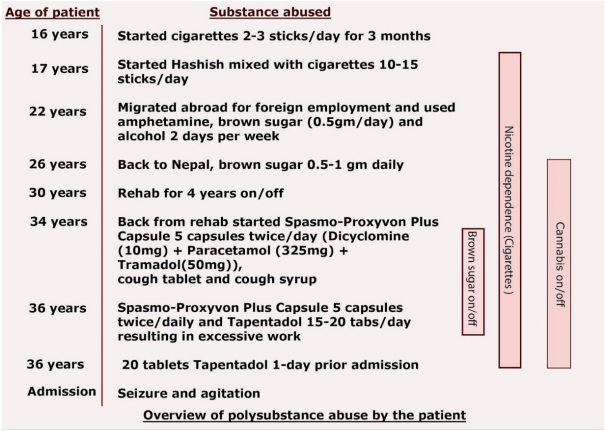

Figure1. Chronological overview of substances abused by the patient.

DISCUSSION

Tapentadol is a centrally acting opioid with a complementary mechanism of action, that is, μ-opioid agonism and norepinephrine (NE) reuptake inhibition. [4] The synergistic action of these mechanisms enhances the overall analgesic effectiveness for various pain conditions, including nociceptive and neuropathic pain. Additionally, a reduction in the frequency of opioid-related gastrointestinal side effects also contributes to improving patient compliance. [4,5]

Tapentadol has a 50-fold lower affinity for μ-opioid receptors than morphine. [6] Since the activation of the μ receptor is responsible for mood alteration and euphoria associated with morphine, the risk of abuse associated with tapentadol may be expected to be lower than that associated with other strong opioids. [2]

A literature review revealed five deaths attributed to tapentadol use, either alone or in combination with other drugs, with respiratory depression and cardiac arrest as the primary causes. Therefore, caution is advised in patients with cardiovascular diseases, respiratory disorders, CNS depression, and those receiving other sympathomimetic drugs. [1,7]

Withdrawal symptoms may be present when a person is physiologically dependent on opioids or after the abrupt discontinuation of tapentadol following long-term use.[8] Common symptoms such as irritability, hyperactivity, seizures, abnormal sleep patterns, loss of appetite, diarrhea, sweating, flu-like symptoms, and hallucinations are usually observed.[5,8] However, some studies have shown that tapentadol withdrawal is less severe than that of other opioids.[2]

Convulsions and prolonged delirium following opioid withdrawal are uncommon and suggest a complex neuropsychiatric response. Although the literature on this is scarce, there are some reported cases of prolonged delirium and convulsions after opioid withdrawal, but no such cases specifically involve tapentadol.[9] Tapentadol, with its dual mechanism of mu-opioid receptor agonism and norepinephrine reuptake inhibition, may contribute to the atypical withdrawal syndrome.[4] Although he denied any benzodiazepine use in recent years, given his history of prescription drug abuse, benzodiazepine withdrawal could not be entirely ruled out despite a negative urine toxicology screen.

The diagnosis of tapentadol withdrawal requires a detailed history of substance use, including prescription drug exposure, dosage, concurrent substances, abuse duration, prior withdrawal episodes, and any other adverse effects, in addition to medical examinations and laboratory tests. [2,7]

The physical examination must include a primary survey, head-to-toe examination, and the Glasgow Coma Scale (GCS) assessment. This should be followed by a secondary survey, looking for signs of trauma and conducting a detailed systemic examination focusing on the chest and neurological evaluation to check for seizures or coma. Electrocardiography (ECG) should be performed. [5,10]

Laboratory tests should include routine biochemical tests and urine toxicology screening. Chest radiography should be performed when hypoxia is not corrected, even after addressing hypoventilation. If available, a toxicological test should be performed to check for drug levels and the presence of other prescription drugs and substances of abuse. [4,6]

Management includes initial stabilization with continuous monitoring of vital signs and ECG. Hypoglycemia must be ruled out, and resuscitation with adequate fluid is necessary to prevent acute kidney injury (AKI).[10] The most effective treatment for opioid dependence includes opioid agonist treatment, such as buprenorphine and methadone in tapering doses, along with motivational interviewing to identify barriers, cognitive behavior therapy to address opioid-related thoughts and feelings, symptomatic treatment of somatic symptoms, and peer support programs. Treatment also involves strengthening the network of family and friends, offering support and addressing all factors, including biological, psychological, and social aspects.[3,10]

CONCLUSIONS

Tapentadol has the potential to become a common opioid of abuse in Nepal, considering its poor regulation and porous border with neighboring India, where it is seen as a newer prescription drug of abuse. Our case serves as a reminder to clinicians to be aware of the dependence potential of tapentadol and to adopt safer prescription practices to prevent its abuse as a prescription opioid.

CONFLICTS OF INTEREST

All authors declare no conflict of interest.

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