Sir,

Opioids have been abused by humans since ages to obtain pleasure. Repeated use of this group of substances leads to a loss of control and a compulsive pattern of use, which ultimately leads to the development of dependence. The reduction in the usual dose or abstinence from opioids can result in a varying range of withdrawal symptoms, including rhinorrhoea, lacrimation, salivation, body aches, anhedonia, tremors, restlessness, mydriasis, diarrhoea, etc. Dystonia is a movement disorder characterized by sustained or intermittent muscular contraction resulting in either abnormal posturing, movements, or both. They are mainly known to occur as a side-effect to a certain group of medications (antipsychotics, antiemetics, etc.) and are also seen in some neurological conditions. Very few reports of opioid withdrawal-related dystonia are available in the existing literature. We report a case of opioid dependence who presented with acute dystonia during the acute opioid withdrawal phase and discuss the possible neurobiological mechanism to explain the presentation.

A 24-year-old educated, employed, unmarried male was brought to the emergency unit by his mother, with complaints of an involuntary movement of his neck to the right side, along with head tilting, which was associated with a pain in the nape of the neck for the last half an hour. A call was given to the psychiatry department because the history revealed a recent use of brown sugar. The patient could well sense the motor symptom and also reported difficulty in swallowing. A diagnosis of acute dystonia was made, and he was given intramuscular injection of promethazine 1 ampoule (50 mg) that resulted in a dramatic recovery of the motor problem.

A detailed interview revealed daily intake of brown sugar (street heroin or diamorphine), an opioid, for the last 3 years. He was introduced to it by one of his close friends, and he started to chase it as a means to experiment with the substance. He used to buy around 1 g of brown sugar from a drug peddler and would consume it in 2 days. He developed tolerance to its effects, and although he tried to stop chasing, he failed because of withdrawal symptoms like lacrimation, runny nose, low back pain, tremulousness of the whole body, insomnia, anhedonia, and diarrhoea. He last consumed brown sugar 15 h before experiencing the current motor symptom. There was no history of taking any antipsychotic, antiemetic, or any over-the-counter medications prior to this motor problem. He had neither history of any past neurological condition nor any family history of such problems and also no history of taking other substances of abuse. Such symptom never occurred to him in the past. He responded well to promethazine.

On physical examination, he showed signs and symptoms of opioid withdrawal and no focal neurological deficits. Clinical Opiate Withdrawal Scale (COWS) revealed a score of 22, suggestive of
moderate opioid withdrawal. He was admitted to the psychiatry department with plans for acute withdrawal management and maintenance therapy. His routine blood investigations (complete hemogram; liver, renal, and thyroid function tests; serum sodium, potassium, calcium, and phosphate) were all found to be within normal ranges. A computed tomography (CT) scan of the brain revealed no abnormality.

The patient was taking brown sugar for a long period of time in a dependence pattern. The temporal relation between sudden discontinuation of brown sugar and the emergence of acute dystonia possibly suggests this movement disorder to be a withdrawal effect. The absence of intake of any antipsychotic or other dopamine blockers/depleters and a negative history of any neurological disorder, both in the patient and his family, rules out other possible causes for the presentation. He also experienced other symptoms of opioid withdrawal, as objectively revealed by COWS.

A literature search revealed a single report that depicted dystonia which occurred as a withdrawal effect to injection pentazocine, morphine, and pethidine (also opioids), which the patient was taking in a dependence pattern for 3 years. While the patient in our case presented with acute dystonia that responded well to anticholinergic medication, the previously reported case had persistent dystonia for 2 years, which was nearly refractory to available treatment modalities.

Dystonia is an extrapyramidal symptom that occurs due to dopamine depletion in the basal ganglia. It can be caused by both inherited and acquired conditions of the nervous system. In psychiatry, it is mostly seen as a side-effect of antipsychotics, though a host of other pharmacological agents can also lead to this symptom. What caused acute dystonia in opioid withdrawal is not clear. However, a plausible causative mechanism between the two can be postulated in light of underlying neurobiological underpinnings of these two conditions.

Opioid receptors have been found on the GABAergic interneurons in the ventral tegmental area (VTA). Here, they facilitate dopaminergic transmission to the nucleus accumbens (NA) by inhibiting the inhibitory gamma-aminobutyric acid-A (GABA-A) interneurons, which mechanism explains the addictive potentiality of opioids. This inhibition of GABAergic interneurons is thought to be because of activation of potassium conductance. Hence, during an opioid abstinent state, opioid receptors will not be activated, resulting in a lack of inhibition of the inhibitory GABAergic interneurons in the VTA, ultimately leading to decreased dopamine neurotransmission to the NA, creating a dopamine depletion state, which in turn causes dystonia.

There are evidences to this proposed mechanism. Morphine withdrawal has been shown to dramatically alter medium spiny neurone density of the shell portion of NA, thereby impoverishing dopamine transmission. In addition, kappa receptor activation by agonists have been found to have antidystonic property. These might be the postulated biological mechanisms that can explain dystonia in opioid withdrawal state.

However, there are some limitations of the current report. First, temporal relation between discontinuation of the opioid and the occurrence of dystonia has been considered to be the possible proof for causality here, though this cannot be taken as a full proof for such causality. Second, street heroin may contain many chemical impurities whose discontinuation can possibly cause dystonia. We did not conduct a test to unravel the chemical nature of these impurities, which stays a limitation of our report.

Nevertheless, in conclusion, it may be pointed out that clinicians should be observant about the occurrence of motor symptoms like dystonia in opioid withdrawal state to guide early recognition of the problem, thus facilitating a targeted management protocol.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Santanu Nath, Biswa R. Mishra, Shree Mishra, Jigyansa I. Pattnaik

Department of Psychiatry, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India
Tramadol-Related Adverse Drug Reactions at an Addiction Psychiatry Setting: A Cross-Sectional Analysis

Sir,

Continued reporting of adverse drug reactions (ADRs) is important for the promotion of safe use of medications and to encourage well-informed prescribing practices among health care providers. Understanding the ADR profile in the billion plus population of India may prevent ADR-related hospital admissions and mortality. The Pharmacovigilance Programme of India (PvPI) has been launched to collect, synthesize, classify, and disseminate information about ADRs on a national scale and contributes to global data generation and synthesis. The PvPI has set up ADR Monitoring Centers (AMCs) across the country to fulfill its objective, and the National Drug Dependence Treatment Centre (NDDTC), Ghaziabad has been serving as an AMC and providing key insights into ADRs related to medications used for the treatment of substance use disorders. Tramadol is a synthetic opioid and serotonin reuptake inhibitor drug utilized in opioid detoxification. Sometimes, the detoxification may be prolonged, reaching almost the status of maintenance treatment. However, several adverse events with tramadol have been reported. We present the ADRs encountered with tramadol in a specialized treatment facility for substance use disorders.

This cross-sectional, descriptive analysis of data was done at the NDDTC, Ghaziabad. The Center is a specialized treatment facility which caters to patients with substance use disorders. The center has both inpatient and outpatient facilities, and patients with opioid and alcohol use disorders primarily comprise the clientele. Tramadol is commonly used for detoxification in patients with opioid dependence. All spontaneously reported ADRs with tramadol over a period of 12 months from March 2017 to February 2018 were analyzed. Both inpatient- and outpatient-based reports were included. The nature and type of ADRs due to tramadol were analyzed along with patient-related factors. The World Health Organization Uppsala Monitoring Center’s terminology was used to report...