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.[1,2] Understanding the ADR profile in the billion plus population of India may prevent ADR-related hospital admissions and mortality.[3] 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.[4] The PvPI has set up ADR Monitoring Centers (AMCs) across the country to fulfil 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.[5] 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

the tramadol-related ADRs. Patient demographics, reaction characteristics like system organ classification, and outcome were recorded as per the information provided by the health-care providers and medical records. Descriptive statistics were used to represent the data.

During the study period, 103 tramadol-related ADRs were recorded. The mean age of the sample was 36.69 ± 13.70 years, and all the patients were males. Various ADRs reported with tramadol are shown in Table 1.

The most common ADR reported was constipation, followed by decrease in appetite. Nearly, one-third of the ADRs (n = 32, 31.1%) were not labelled, suggesting that these were either hitherto unreported or so rare that they did not find mention in the package insert. Remaining (n = 71, 68.9%) were labelled ADRs.

According to the system organ classification, gastrointestinal (n = 43, 41.7%), skin and appendage (n = 22, 21.4%) and central nervous system (CNS) (n = 19, 18.4%), were the most common systems implicated, followed by psychiatric (n = 6, 5.8%), urinary (n = 5, 4.9%), metabolic (n = 4, 3.9%), musculoskeletal (n = 2, 1.9%), respiratory and ophthalmic (n = 1, 1% each) systems.

As per causality assessment, the ADRs were largely classified as 'possible' (n = 95, 92.2%). Six reports (5.8%) were considered causally 'probable.' One report (1.0%) was considered 'certain' in terms of causality, while another one was 'unlikely.' Four reports (3.9%) were considered serious (generalized seizures suggestive of tonic–clonic type and atonic type which required hospitalization), while the remaining were considered as nonserious.

The present report advances the knowledge about the ADRs related to tramadol. Constipation was the most frequent ADR reported. Though constipation is a natural effect of any opiate or opioid and is dose dependent in nature, it has the potential to impact on quality of life. Though a minor proportion of the ADRs was serious in nature, they merit attention as they escalate the health-care costs and pose a significant threat to the physical health of the individual. A fair proportion of the ADRs was unlabelled, indicating that new ADRs were discerned and hence continued surveillance is helpful.

The findings need to be interpreted in view of some constraints. It is likely that some ADRs were missed as the reporting was voluntary or they were transient or too mild in severity to be taken note of. Also, limited information can be gleaned from ADR reports. Yet, the present findings provide perspective with regards to the ADRS reported with tramadol. This would help practitioners in safer and more rational use of tramadol in the field of addiction psychiatry.

Table 1: Types of ADRs with tramadol

Variable	n (%)
Constipation	21 (20.4)
Appetite decreased	13 (12.6)
Seizures	8 (7.8)
Fullness of head	5 (4.9)
Itching	5 (4.9)
Pruritus and rash	5 (4.9)
Rash pruritic	5 (4.9)
Gastric irritation	3 (2.9)
Skin eruption	2 (1.9)
Skin exfoliation localized	2 (1.9)
Urinary hesitation	2 (1.9)
Weight decreased	2 (1.9)
Headache	2 (1.9)
Others*	28 (27.2)

*Others included 1 each of abdominal pain, acute gastritis, anxiety, bowel obstruction, breathing difficulty, bullous lesions, body aches, chills, eating disorder, insomnia, lacrimation increased, micturition pain, mouth dry, muscle spasticity, localized numbness, pica, polyuria, rash, rigors, sleep difficulty, tingling skin, tongue discoloration, oliguria, vertigo, vision difficulty, vomiting, and weight increase

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Conflicts of interest

There are no conflicts of interest.

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