

## Letter to Editor: Alarming Level of Tramadol Intoxication in Iran



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**T**he use of tramadol, as a medicine, has begun in Iran since 15 years ago and it is increasingly abused nowadays.

As clinical toxicologists in two distinctive referral hospitals in the northwest of Iran, we have been visiting many patients with tramadol overdose. The authors have also completed a clinical toxicology fellowship program in Mashhad (The northeast of Iran) for 1.5 years. Moreover, by obtaining information from other colleagues in different regions of Iran, we realized that a similar pattern of tramadol abuse and complications exist all around the country.

Observing patients with tramadol-induced seizures is a part of our daily practice. In the past, we had several patients with life-threatening complications following tramadol overdose. For example, a patient, who had tramadol overdose (20 grams), deceased following recurrent convulsions. Another patient, who had ingested 2g tramadol, had status epilepticus on admission resulting in hypoxic-ischemic encephalopathy and, finally, persistent vegetative state.

Other complications in our patients included the decreased levels of self-awareness and apnea (especially when tramadol was co-ingested with other sedative-hypnotics or alcohol), serotonin toxicity, rhabdomyolysis, electrolyte disturbances, renal failure, QT interval

prolongation, cardiac dysrhythmias, and various traumas (even life-threatening) during convulsive seizures such as skull fractures, intracranial hemorrhages, jaw dislocations, shoulder dislocations (unilateral or even bilateral), chest or abdominal injuries, and withdrawal syndrome because of the discontinuation or reduction of tramadol dose.

Several years ago, the importance of these complications was unclear for us. Therefore, we did not report the cases. Over time, by encountering the increasing number of patients with tramadol intoxication, the situation became more evident. By reviewing the literature, we found that only some of these side effects and complications of tramadol were implicitly mentioned in toxicology textbooks [1, 2]. Also, by reviewing the valid academic databases such as PubMed, Scopus, and Web of Science, we noticed a few reports about the complications of tramadol, such as convulsions, serotonin syndrome, or rhabdomyolysis in the literature. Besides, many of the published articles were either case reports or letters to the editor except 1 case series [3].

More recently, some interesting articles have been published by Journal of the American Medical Association (JAMA) and Lancet authoritative journals concerning “increased mortality in patients with tramadol use comparing other analgesics”, “increased tramadol intoxication and complications following excessive and inappropriate administration of tramadol”, or “an increasing

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trend in the prescription of tramadol for patients with osteoarthritis or postoperative pain” [4-7]. In these reports, the main reason for the increasing prescription of tramadol in the developed countries was the recommendations of pain control guidelines [4-7].

In Iran, several hypotheses may be considered for high rate of tramadol complications; they include 1. The abuse and misuse of the drug by Iranians; 2. The possibility of unauthorized access to tramadol through some pharmacies; 3. The falsification of tramadol available in the market and 4. Deceptive advertising about tramadol effects on sexual strength or treatment of obesity or body making.

Although tramadol was prescribed by doctors for pain control, it is easily accessible (in original or counterfeit forms) for people, who are seeking it. Domestic pharmaceutical manufacturers produce 50mg and 100mg oral forms of tramadol, but other forms (200mg, 225mg, 300mg, 400mg, and 500mg tablets) are produced either legally (by some pharmaceutical companies in other countries) or illegally (in clandestine laboratories inside or outside of Iran). Little information exists about the active ingredients and compounds of these illegally-presented drugs. There is also misleading advertising on the effects of tramadol on sexual strength, the treatment of impotency, or obesity. Therefore, the drug is more likely to be abused by adolescents and adult men. Nonetheless, in scientific resources, tramadol is recommended only for certain types of sexual dysfunction (premature ejaculation) [8]. Most women use tramadol for the treatment of obesity or suicidal attempts.

Although tramadol abuse and its complications in Iranian society have reached an alarming situation, the investigations in this field are not proper and adequate. Therefore, toxicologists, pharmacologists, and other clinicians are recommended to perform further studies concerning tramadol toxicity and its complications; meanwhile, determining the compounds presented in the counterfeit forms of tramadol supplied in Iran and their complications is essential.

## Ethical Considerations

### Compliance with ethical guidelines

There was no ethical considerations to be considered in this letter.

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### Author's contributions

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### Conflict of interest

The authors declared no conflict of interest.

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