

## Tramadol as a Misusing or Addiction Agent

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### Dear Editor,

In the emergency ward of the hospital, I work in, which is Sina Medical Research and Training Hospital, seeing cases of tramadol poisoning is not an unusual thing. Moreover, it is a common trend throughout other hospitals in our country, Iran.

Tramadol is a synthetic codeine analog, and has central analgesic properties, acting on specific opioid receptors, causing it to have effects like morphine and codeine. Tramadol also has a weak inhibitory effect on norepinephrine and serotonin reuptake (1,2). It is usually prescribed for moderate to moderately severe chronic pain (3).

Tramadol has an oral bioavailability value of 75%, reaching a peak plasma concentration around 2 hours (4,5). It has a half-life of  $6.3 \pm 1.4$  hours (4), and reaches steady state after 2 days, after being administered in constant dosing of 4 times a day (3).

The most common adverse effects of tramadol therapy are nausea, somnolence, constipation, dizziness, vomiting, and headache (3). There is also a risk of seizures in patients receiving tramadol, and even though it occurs mostly in doses above the therapeutic range, it may also occur within the recommended dosing range. Its occurrence increases in patients using tricyclic compounds (e.g., tricyclic antidepressants), selective serotonin reuptake inhibitors, Monoamine oxidase inhibitors, neuroleptics, and other drugs that reduce the seizure threshold (3). It also increases in patients with epilepsy, those with a history of seizures, or in patients with a recognized risk for seizure, such as head trauma, metabolic disorders, alcohol, and drug withdrawal, and central nervous system infections (3). Treating tramadol overdose with naloxone may also increase the risk of seizures (3).

Also, tramadol has a low potential for abuse (6). Abuse cases are not infrequent, due to its effects, and also the fact that it is used off-label for erectile dysfunction. Tramadol, which is used in Iran, is either manufactured inside the country or is imported. Those manufactured in Iran are tablets in 100 mg and 200 mg doses. The imported ones are mostly as 200 and 220 mg tablets. Also, it seems that adverse effects, esp. seizures are most prominent in those who use imported forms. There are a few cases worthy of mentioning of tramadol misuse and abuse, which are as follows:

In a case of misuse, the patient a 25-year old male who suffered from premature ejaculation, consumed tramadol solely based on the suggestion of his friends to help with his problem. About an hour after consuming the drug (first time-a single dose tablet of 100 mg) the patient was admitted to the hospital with seizures. Patient was completely unaware of the abuse potential of tramadol and assumed it was a treatment for sexual dysfunction and premature ejaculation. In another case, patient was a 37-year old male which following occupational trauma, presented with sever pains that were unresponsive to routine analgesic drugs, and his physician prescribed for him tramadol 100 mg every 12 hours. This patient was admitted to the hospital in the post ictal phase, after having a seizure following consumption of 7 or 8 100 mg tablets. After an inquiry we found that the patient's tramadol was of those manufactured in Iran.

Finally, the last case was a male patient around the age of 30, which subsequent to ingestion of 60 100 mg tablets, had seizures which lead to a head trauma causing intracranial hemorrhage. Due to the severity of the patient's condition and the state in which the patient was brought to the emergency room, unfortunately he was expired.



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Unfortunately, there is not enough evidence, because almost all of the hospital admissions are abuse cases and patients are not willing to participate in studies due to its consequences. Also, there are not enough regulations to control the import and use of these forms. Adding fuel to the fire, tramadol can be obtained with much ease much like over the counter medications, despite the guidelines and regulations of the ministry of health.

In conclusion, we need more studies related to this issue and an immediate revision on guidelines and regulations related to this matter.

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