

## Case Report

# Tramadol abuse potential and resultant withdrawal seizures

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### ABSTRACT

Tramadol is a centrally acting atypical opioid analgesic with additional serotonin-norepinephrine reuptake-inhibiting effects used to treat moderate to moderately severe pain with propensity for abuse potential. The case of tramadol dependence discussed in this case report developed severe dependence with high doses of tramadol, used as a drug for treating his migraine. The individual learned to self-medicate with the medication. The author further emphasize on the regulation of tramadol prescription.

**Keywords:** Central opioid, Abuse potential, Analgesic, Dependence, Tramadol

### INTRODUCTION

Tramadol has antinociceptive effects which makes it useful in providing analgesia. Its antinociceptive effects are mediated by a combination of  $\mu$ -opioid agonist effects and norepinephrine and serotonin reuptake inhibition, and it can suppress opioid withdrawal.<sup>1</sup> It is an atypical, centrally acting synthetic analgesic used to treat moderate to severe pain. However, various controlled studies have reported a small number of patients developing tramadol abuse/dependence; with the incidence rate of 6.9/1000 persons per year.<sup>2</sup> A majority of tramadol abusers (97%) had a history of other substance abuse.<sup>3</sup> Tramadol has also been reported to cause seizures at therapeutic and toxic doses.<sup>4</sup>

In one study, tramadol dependence due to frequent and excessive intake were commonly seen in a young female who was taking it for migraine attacks which was also associated with withdrawal seizures.<sup>5</sup> In this case report, the young female presenting with tramadol dependence developed it by self-medicating herself with the drug when initially being prescribed for treating her migraine attacks.

### CASE REPORT

A 30 year old female was sent by the neurophysician who was managing her for chronic migraine to the psychiatric centre with history of daily intake of tab. tramadol (50 mg) upto 25 tablets per day leading to a dependence pattern.

Detailed history revealed that the female first sought treatment for her recurrent migraine attacks that would interfere in her workplace and day to day functioning. She first sought medical consultation with her family physician who after initial evaluation suggested that she seek neurophysician referral as she had started to develop retro orbital pain. The neurophysician did routine hematological parameter investigations and neuroimaging with MRI Brain which did not reveal any pathology. Detailed diet history also did not reveal any precipitants nor did a further history probing reveal any relieving factor.

She was prescribed tab. nortriptyline 25 mg HS with an ergotamine preparation to abort an attack. At subsequent follow up, when she was not getting adequate relief from

her symptoms, she was prescribed tab. sumatriptan 50 mg on SOS basis and as per advised instruction.

After one year of regular follow up the lady continued to get migranous attacks with hemicranial headaches with retro ocular pain and diplopia. Various drug titrations with increased dosages of prescribed medicines did not provide relief. The physician then prescribed the patient Tab Tramadol 50 mg on a strict SOS basis. As patient found the medicine to bring substantial relief in her symptoms, she started to gradually increase the intake of the drug from initial dose of 1 tab. to about 2-3 tablets in a day. Over the next 3 months the patient realized that she required increased dose to get the pain relief that she always required. She started to take 4-5 tablets in a day. By the end of almost 06 months her intake of tab. tramadol had increased to 10-12 tablets in a day (500 mg to 600 mg). At this point in time the patient realized that when she would miss her dose of tramadol she would experience nausea, giddiness with sweating and a strange tingling sensation all over her body. She developed diarrhea which was very disturbing. These symptoms would subside after she would medicate herself with tab. tramadol within few hours much to her relief. She increased her intake of tab. tramadol to about 30 tablets in a day (1500 mg/day). On days when she could not maintain the dose schedule she would get anxiety attacks with intense nervousness, irritability, crying spells with dryness of mouth, malaise with coordination disturbance, insomnia, with abdominal discomfort.

At her place of work she developed two episodes of generalized tonic clonic convulsions with frothing from mouth. She was taken to the emergency room in a hospital where her seizures were attended and managed. Detailed history taken at a later time revealed that she had missed her daily dose of tab. tramadol the day before and had to rush to her place of work as she had become late. As she was unable to medicate herself that morning and previous day she probably developed withdrawal seizures. This was later confirmed by the physician who did her comprehensive work up.

Subsequent management was done by inpatient admission as risk of subsequent seizures occurring was high. Patient was started on incremental doses of tab. clonidine 0.1 mg BD and later increased to thrice a day. Resultant bodyaches was managed by use of painkillers. On the 5<sup>th</sup> day tab. naltrexone 50 mg OD was started and continued. She was given motivational counseling, individual psychotherapy. After 2 weeks admission the patient was discharged and advised regular follow up on alternate days and then weekly. The history given by her would be corroborated by the accompanying spouse. Till the first month after discharge there was no report of any consumption of the said drug. But in the following review i.e. two months following hers discharge, patient accepted taking 2 tablets of tab. tramadol on three separate days. She was then subjected to counseling sessions with emphasis on cue management and coping

skills and individual psychotherapy. She showed adequate motivation to abstain from the drug. She was on regular medication for her migraine with low dose tricyclic agent and Triptans.

Patient has been in regular follow up thereafter and after one year of therapy she was weaned of the maintenance drug regime and she has remained non dependant on tab. tramadol.

## DISCUSSION

As seen in the index case and discussed above, tramadol seems to have abuse potential that is now being recognized. This action is probably due to its action at the  $\mu$ -opioid receptor.<sup>5</sup> This is further borne out by the fact that in the patient, the pattern of use was similar to that seen with other opioids. Its use as an antimigraine therapy is also in keeping with the supposition that it is recognized and used as an opioid analogue by experienced users. The withdrawal symptoms described and observed were non-specific, but this could be more a function of the potency of the drug at the opioid receptor and modulation of symptoms by the complex neuropharmacology of the drug.<sup>6,7</sup>

## CONCLUSION

The case discussed here had dependence with Tramadol in higher dose, which she was using for migraine attack relief and at a later stage started self-medicating herself for its abuse potential. The probable euphoric effects of the opioid present in the drug molecule associated with the pain relief provided to the subject led to its high abuse potential.<sup>8</sup> We would like to use this case report as a call to practitioners to be aware of the abuse and seizure potential of Tramadol, and to call for strict regulation on the sale of the same.

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