# Case Report

# Tramadol Dependence: A Case Series from India

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ABSTRACT

Tramadol is an atypical, centrally acting, synthetic analgesic, acting through opioid and non-opioid systems. We present a series of seven cases, all men, who sought treatment at our centre for tramadol-dependence. The majority were using other opioids at some point in their lives. Their tramadol use had begun with a prescription of tramadol for opioid detoxification, for headache and body pains, and as an alternative to injectable opioids. The doses of tramadol used varied from 50 to 1500 mg per day. All subjects reported an experience of euphoria with tramadol use. Four patients were put on naltrexone, but had poor compliance. This case series underscores the need for caution, while using tramadol in substance-dependent patients.

**Key words:** *Abuse, dependence, series, tramadol*

## INTRODUCTION

Tramadol is an atypical, centrally acting, synthetic, analgesic. Its antinociceptive effects are mediated by a combination of μ-opioid agonist effects, and norepinephrine and serotonin reuptake inhibition, and it can suppress opioid withdrawal.[1] The drug is easily available and widely prescribed for pain management.

First marketed in the 1970s, tramadol was said to have a low-abuse potential.[2-5] However, its abuse liability and diversion were soon recognized, with several reports on physical dependence.[6-12] The largest series of tramadol-dependence was reported from a study in Sweden,[13] comprising of 104 patients, where the majority were women. In another series 97% of the abusers had a history of abuse of other substances.[14] Association with seizures at therapeutic and toxic doses has been reported,[15] as has been the abuse among occupations like physicians[16] and air force personnel.[17]

In India, because of the laxity in drug regulation implementation, opioids are often available over-the-counter; increasing the risk of opioid misuse. However, we could trace only one case report of tramadol-dependence from India.[18] We present a series of seven cases seeking treatment at our centre for tramadol-dependence.

## CASE REPORTS

The seven cases with tramadol-dependence, diagnosed as per ICD-10,[19] sought treatment at the Drug De-addiction and Treatment Centre, Department of Psychiatry, PGIMER, Chandigarh [Table 1]. Their age ranged from 24 to 46 years. The dose of tramadol, taken on a regular basis, ranged 50 mg to 1500 mg per day. The reported reasons for initiation of tramadol included, as an alternate to other opioids, to counter opioid withdrawal, and being prescribed for headache and opioid detoxification. Six of the seven patients had been using other opioids at some point in their lives. Four subjects, treated as inpatients and started

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**Table 1: Case series**

| Demographic details | Substances details prior to tramadol | Reason for starting tramadol | Tramadol dose per day | Treatment and outcome |
|---|---|---|---|---|
| 30-year-old male, jeweler | Opium dependence for three years. Sought treatment and remained abstinent for three years till initiation of tramadol | Prescribed by physician for migraine; increased the dose to experience euphoria | 1000 mg in divided doses | Detoxified with clonidine, NSAIDS. Started on naltrexone 50 mg / day and later BPN 4 mg / day; relapsed in 2 months time, each time |
| 37-year-old male, unemployed | CCCS dependence for five years followed by DPP dependence for four years, intermittent heroin intake. Later dependence on sedative hypnotics and alcohol | Started for opioid detoxification from a de-addiction Center | Increased from 300 mg to 1500 mg | Admitted twice, started on naltrexone 50 mg / day, but relapsed after six months and dropped out of treatment |
| 25-year-old male, farmer | DPP dependence for four years | Started for opioid detoxification from a de-addiction Center | Increased from 200 mg to 500 mg | Detoxified with clonidine, NSAIDS. Abstinent and on follow-up for eight months |
| 36-year-old male, shop owner | Poppy husk dependence for nine years | Physician prescribed opioid detoxification | 50 – 100 mg | Detoxified with clonidine, NSAIDS. No follow-up |
| 33-year-old male, unemployed | Tobacco chewing since age seven, alcohol use since age 10, injection pentazocine at age 13, carisoprodol and DPP dependence subsequently. Also had substance use-independent manic episode | Started by self to alleviate body pains during withdrawals | 50 mg | Detoxified with clonidine, NSAIDS. Started on Naltrexone 50 mg / day. Abstinent and on follow-up for nine months, but with irregular compliance |
| 46-year-old male, unemployed | Alcohol use since age 14. Schizophrenia (fluctuating course) since age 18. Intravenous BPN since age 28. Substituted DPP or tramadol for BPN. Had diabetes and hypertension | Started as an alternative when injectable BPN not available. Later started tramadol regularly and stopped other opioids at 35 years | 250 mg | Admitted and psychotic symptoms controlled. Detoxified and then discharged. Abstained from opioids for two years |
| 24-year-old male, farmer | Tobacco chewing since age 17. Had provoked seizures with tramadol, also started self-medicating with alprazolam 2 mg/d | Started on friends advice to allay fatigue after working in the fields | Increased from 100 mg to 500 mg | Detoxified with clonidine, NSAIDS. Started on Naltrexone 50 mg / day. Abstinent and on follow-up for eight months |

DPP = Dextropropoxyphene, CCCS = Codeine containing cough syrup, BPN = Buprenorphine, NSAIDS = Non-steroidal anti-inflammatory drugs

on oral opioid antagonist naltrexone 50 mg / day, showed poor treatment compliance. One patient, who had earlier relapsed while taking oral naltrexone, was prescribed an oral buprenorphine–naloxone combination. Another patient reported generalized tonic–clonic seizures with therapeutic and toxic doses of oral tramadol. Four patients remained abstinent during the period of follow-up.

## DISCUSSION

As an opioid-type analgesic, which exerts its effects through multiple receptor systems, tramadol carries a dependence producing potential.[20] This needs to be taken into consideration when detoxifying the patient from other opioids. In three of our patients, initiation of tramadol use had begun with a prescription of tramadol for detoxification; they were not able to taper the doses of tramadol as per prescription. Experience of euphoria with tramadol was also reported. Thus, tramadol is used by opioids-dependent subjects as a substitute for the unavailable 'harder' drugs.

Detoxification of our patients was done largely with oral clonidine and non-steroidal anti-inflammatory drugs (NSAIDs), as reported by some,[18] but not others who used the buprenorphine–naloxone combination and methadone for tramadol-detoxification.[21,22]

Apart from those patients with medical disorders using tramadol;[8,17] the drug has the potential for abuse by opioids-dependent subjects. Given the easy availability of tramadol from pharmacies in India and some other countries, its abuse and diversion may become a bigger challenge in the future. There is a need to effectively regulate the distribution of this medication, and apply the appropriate safeguards, to prevent diversion.

This case series adds to the growing concern about tramadol-dependence. It emphasizes the need for caution before prescribing tramadol to patients, especially those who are opioids-dependent, and to apprise the drug regulatory authorities of such occurrences, for proper scheduling and issue of warnings.

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