Tramadol Dependence: A Case Report

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Introduction

Tramadol is a synthetic analgesic and appears to have a dual mechanism of action; a weak μ -opioid receptor agonism and a reuptake inhibition of serotonin and noradrenaline [1]. These actions are believed to primarily contribute to tramadol's antinociceptive effect. Its major active metabolite, *o*-desmethyltramadol (M1 metabolite) also has an agonistic effect at the μ -opioid receptor, but with a higher affinity than tramadol [2]. Studies into the dependence liability of tramadol show that patients are no more likely to abuse the drug than non steroidal anti inflammatory drugs (NSAIDs) [3]. Although there is extensive preclinical, clinical, post-marketing and epidemiological data indicating relatively low, but not zero abuse/dependence, questions continue to arise about its abuse potential and appropriate regulatory classification [4]. Unlike most other opioids, tramadol is not considered a controlled substance in many countries and is available off the shelf [2]. The authors present a singular case of tramadol dependence syndrome, which was reported in this hospital. The case has its salience in novelty.

Case Report

This 37 year old male was referred for abnormal behaviour in looking dazed with restlessness, sleep disturbance and deterioration in socio-occupational performance. History revealed that around five years ago, following a sprain injury in his leg, he took some pain killers from a chemist shop. Initially he was given ibuprofen, which did not help him much, subsequently piroxicam and finally tramadol. He got significant relief in his pain, and also found the medicine to have some euphoric effect. Having become comfortable with the medicine he started taking it on his own after any injury, however trivial. Gradually he increased it in frequency and amount over next five years to the present level of eight tablets of 50 mg each three times daily. He would consume these tablets in stereotyped manner and whenever there was delay in consumption he would start having headache, sneezing, extreme fatigue, bodyache and disturbed sleep. He

would often wake up at night and have the strong urge to consume that medicine and would eventually do so, to feel better. He would consume those tablets surreptitiously and would appear dazed during working hours. Gradually his performance in socio-occupation front deteriorated. There was no past or family history of any psychiatric illness or stressors. He was in the athletics team for over a decade and the physical stress of the same was part of his daily routine. He consumed alcohol in moderation on social occasions. Positive findings on physical examination were digital tremors and sweating. He had consumed eight tablets six hours prior to examination. Mental status examination revealed rationalisation and minimization of his drug intake habit. Psychomotor activity was decreased. Mood was euthymic with anxious affect. There was no psychotic feature. Apart from mild distractibility there was no impairment of cognition. Sensorium was clear but biodrives were reduced. Relevant haematological and biochemical parameters were within normal limits. Initial ward observation revealed withdrawal features as shown in Table 1. He was managed as inpatient with forced abstinence, short course of benzodiazepines, tab clonidine (tapered up to the total of 300 microgram/day), antacids, NSAIDs for analgesia, vitamin supplements,

Table 1

Nature of complaints and their duration during inpatient observation

Complaints	Started on (Inpatient days)	Duration of complaints
Tremor	On admission	7 day
Sweating	On admission	4 day
Sleep disturbance	On admission	3 day
Headache	1 st day	4 day
Malaise	1 st day	4 day
Anxiety	1 st day	3 day
Yawning	1 st day	3 day
Rhinorrhea	1 st day	2 day
Nausea	1 st day	1 day
Increased lacrimation	2 nd day	2 day
Loose motion	2 nd day	2 day
Excess Fatigue	2 nd day	2 day
Stiffness lower limbs	2 nd day	2 day

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psychotherapy and other supportive measures. There were no clear-cut signs of serotonergic withdrawal. After a week he was placed on Tab Naltrexone 50 mg/day to reduce craving. After five weeks of inpatient management he was discharged as a case of opioid dependence syndrome, on anticraving medication. During periodic follow up he was found compliant and abstinent.

Discussion

This 37-year-old person presented with behaviour problems in the background of prolonged consumption of tramadol tablets. Longitudinal history and clinical presentation was typical of substance dependence syndrome. Withdrawal features as given historically by the patient and as observed by us were typical of an opioid, though milder and lasting at most for one week. The overall profile, rapid escalation of number of tablets consumed and continued consumption was suggestive of definitive dependence potential. This might be attributed to tramadol and the M1 metabolite of tramadol, which though having weaker affinity for opioid receptors than other opioid, is adequate enough to cause the desired effect to promote dependence without causing strong withdrawal features on abstinence [2]. Standard protocol of sudden cessation and forced abstinence of the substance was practiced. There was no exaggerated or atypical serotonergic withdrawal seen during abstinence or withdrawal period. His withdrawal period was shorter and return to normalcy was much faster than any typical opioid dependent individual seen so far by us in our clinical set-up or endorsed in the available literature [5]. He was managed with clonidine to which he responded well. Few researchers have reported the same in the past [6]. Based on the clinical profile of the patient and chemical profile of the drug he was diagnosed as a case of opioid dependence syndrome. However, the drug is being commonly used without being given the appropriate label of schedule of drugs. This alarms us to the possibility of increased chances of tramadol dependence due to easy accessibility over the counter and no restriction from the medico-legal side. Because of

rampant use of tramadol in medical practice, iatrogenic dependence and abuse in medical professionals is also a possibility [7].

To conclude, tramadol has potential for dependence, howsoever weak, due to its action on opioid receptors. We, as medical practitioners, should be open to the possibility of tramadol dependence and should resort to optimal and judicious use of such a substance. A hospital based analysis of all patients using tramadol should be done to explore frequency of dependence and nature of morbidity. Being the prescribing arm of the medicine, we are ethically bound to understand the nature of side effects caused by the drugs being manufactured by the pharmaceutical industry and apprise drug regulatory authorities of such occurrences for proper scheduling and issue of warnings.

Conflicts of Interest

None identified

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