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Iatrogenic tramadol addiction

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ABSTRACT

Tramadol, either alone or in combination with paracetamol, is a commonly prescribed opioid analgesic in routine clinical practice. It has reportedly low abuse potential. There are, however, a few reports of tramadol misuse among health care professionals and persons with a family history of addiction. We describe the clinical profile of three women developing addiction to tramadol. In all these cases tramadol was initially prescribed for pain by the physician. Physicians should not only prescribe tramadol cautiously and for a limited time period but also be trained in identifying misuse (self-use, over the counter procuring, using for mind altering properties) and dependence (craving, withdrawal symptoms etc.).

Key words: *Addiction, opioid, tramadol*

INTRODUCTION

Tramadol is a synthetic codeine analogue having a weak μreceptor agonist action (1/6000th that of morphine). Part of its analgesic effect is also due to inhibition of uptake of norepinephrine and serotonin.[1] It has 68% oral bioavailability, 100% through intramuscular route, and has a half-life of 6-7.5 h.[1] Tramadol alone or in combination with paracetamol has been widely used for relief of mild to moderate pain. Unlike other opioids, the abuse potential with tramadol is not clear. Tramadol abuse or addiction is mainly reported among physicians, who have easy access or people with previous history of drug abuse.[2,3] Here, we report three cases of tramadol addiction among women following prescription for pain relief.

CASE REPORTS

Case 1

A 20-year-old woman, with nil significant past history or family history presented with restlessness, aches and pains in body parts, abdominal cramps, feeling of cold and lacrimation for the last 3-4 h. On enquiry, she reported injecting (intra muscular) tramadol about 6 h ago. Further history revealed that she had been taking tramadol injection regularly for the last 1 year following a hysterectomy procedure. Initially, the treating gynecologist gave her 100 mg twice a day for 2 weeks to relieve post-surgical pain. After stopping the injection, she had restlessness, body pain, a cold feeling, abdominal cramps, and loose motions, which got relieved completely by injection tramadol. Thereafter, she continued to inject herself with tramadol twice daily to get rid of withdrawal symptoms. She also started to feel very happy, relaxed, and more energetic for half an hour to 1 h following the injection. Over the next 2-3 months, she developed tolerance and the amount increased to 5-6 injections per day. In spite of multiple abscesses and swellings in the injected site, she continued to use the drug. She would procure the tramadol injection from different chemists without any prescription. She also reported a strong desire to inject and would have opioid withdrawal symptoms whenever she stopped injecting. Before coming to us, she had visited different doctors for this problem without any benefit. Patient's clinical opioid withdrawal scale[4] rating during presentation was 13. There was no history of needle sharing, high-risk sexual behavior, engagement in criminal activity, or use of any other drugs. Urine toxicological analysis was negative for any other substance. She tested negative for HIV and hepatitis B. There were inter-personal problems with her husband and poor socio-economic support. She reported a low mood often in relation to the family context. However, there was no independent diagnosis of either a depressive or any other psychiatric disorder.

She was initiated on buprenorphine-assisted treatment. She was stabilized on 4 mg of buprenorphine sublingual tablets. The withdrawal symptoms as well as craving improved significantly. At the end of 3 months, she is doing fine with buprenorphine substitution treatment. It is planned to slowly taper down buprenorphine over the next 4-6 months.

Case 2

Mrs. A, a 28-year-old female presented with a history of use of oral tramadol tablets (tramadol 37.5 mg and acetaminophen 325 mg) for the past 5 years. She was prescribed these medications by gynecologist for pain following her third cesarean delivery. She continued to use the tablets once a day for few months. She had increased it to 3-4 tablets/day since the past 2 years. Her husband would get these tablets from the chemist without any prescription. She would always keep a stock of tramadol tablets in her purse. She increased her use to 6-7 tablets per day in spite of having no pain. She would have body ache, restlessness, mild lacrimation, rhinorrhea, and abdominal cramps if she did not take the tablets. She would constantly worry that her tablets might get exhausted. Her physical examination revealed opioid withdrawal symptoms. A urine drug screen was positive for opioids. Patient was started on tapering doses of tramadol. She was educated about the abuse potential of tramadol and the withdrawal symptoms. She dropped out of the treatment. After 6 months, she was using but had reduced use to two tablets per day.

There was no history of any other addiction or any emotional problem except that she had a family history of alcohol dependence.

Case 3

Mrs. C, 28-year-old female presented with history of using injection tramadol regularly since past 3 years. Three years back, a

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general practitioner prescribed her injection tramadol and injection diclofenac for her shoulder pain. The pain was relieved immediately but used to recur off and on. The doctor would advise her to take injection whenever there was shoulder pain, i.e., 2-3 days once for initial 6-7 months. After 6 months, she started injecting by herself and more frequently, i.e., almost daily. She would take both the injections (tramadol and diclofenac), one ml. (50 mg/1 ml tramadol) each in the deltoid and gluteal region. Slowly, she started having a sense of relaxation with the tramadol injection and increased the frequency to 300 mg per day. She had suffered abscesses over the gluteal region several times. During the last year, she had no shoulder pain but would have intense desire to take tramadol injection. She would have withdrawal symptoms in the form of severe body ache, lack of interest to do any work, tremors of hand, easy fatiguability, and insomnia when she would try to stop. Around a week back, following the injections, she became unresponsive for 10-15 min, had cold and clammy skin. Her breathing also decreased substantially, suggestive of tramadol overdose. She was managed conservatively in local hospital and later referred to us for her addiction. There was no mental illness except sinus ulcers over both gluteal regions. There was no personal, past, or family history of substance abuse. In view of severity of opioid dependence, she was initiated with buprenorphine maintenance treatment. At the end of 5 months follow-up, she is abstinent from tramadol injections.

DISCUSSION

In view of their lower abuse potential and relatively better safety profile, the newer opioids such as tramadol and dextropropoxyphene are extensively used by doctors for amelioration of moderate to severe pain. There are reports that tramadol has no abuse potential because of weak affinity toward opioid receptors, unlike drugs like morphine. However, case surveillance reports are increasingly pointing toward its abuse potential and associated withdrawal symptoms.[5] In a review of health record of physicians, tramadol abuse was noted as the third most commonly abused opioid following hydrocodone and meperidine. Of the 33 physicians who mentioned tramadol use, 32 had a diagnosis of drug dependence.[3] One-fourth of them had primary tramadol abuse.[3] Tramadol abuse is commonly associated with history of previous drug addiction or substituting tramadol when the primary drug of abuse was not available. A study among 219 opioid addicts who had a history of tramadol abuse had reported significant withdrawal symptoms, euphoric effects, sedation, and craving for tramadol.[6]

The risk of potential abuse liability is high among persons with current or past history of addiction, chronic pain, and healthcare professionals.[5] Also tramadol dependence has been reported in a lady without any history of substance abuse, similar to the cases presented here.[7] The management of tramadol dependence is mostly directed to control opioid withdrawal symptoms with non-steroidal analgesic drugs or slow tapering of tramadol under supervision, treatment of comorbid conditions, and counseling.[2,7] Like in the first case, buprenorphine-assisted withdrawal treatment has been reported.[2] Relapses are probably common as illustrated in the second case.[7] Even though tramadol might cause physical dependence, a few people can develop psychological dependence due to its μ-opioid action. Both our patients had withdrawal symptoms similar to μ agonist opioids.

These three cases illustrate the possibility of abuse of tramadol even in the absence of high-risk factors, i.e., history of addiction, if it is continued for a longer time. Tramadol and preparations containing tramadol and paracetamol combination are not scheduled medications unlike other opioid medications and can be easily procured. In our country, the risk further increases in view of poorly monitored dispensing practices in medical shops and dispensing without prescription.[8,9] Apart from abuse liability, there is also risk of overdose leading to seizure as well as respiratory depression which can be fatal as in the case of other opioids. The combination of paracetamol with tramadol (case 2), raises the concern of hepatic toxicity with overdose.

These three reports highlight the fact that an effective painkiller can be misused and the physician should be aware of the abuse potential of tramadol. It is important to check for past or family history of substance addiction, associated concomitant disorders, limited duration of prescription along with good follow-up, and educating the person regarding the risk of abuse all of which will help to minimize the problem.

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