Abuse of Tramadol in a Binge Pattern in a Young Woman

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Tramadol [(±)-trans-2-(dimethylaminomethyl)-l-(3-methoxyphenyl)-cyclohexanol HCl] is a central analgesic, widely used in the treatment of acute and chronic painful conditions of moderate and severe intensity. In comparison to opioid analgesics such as morphine, tramadol is considered to have a low potential to cause abuse and dependence (Raffa 2008). We described a case of abuse of tramadol in a binge pattern in a 32-year-old young woman who had initially received the prescription of tramadol as an analgesic as needed. She had no history of drug or alcohol abuse, but suffered from depression. Over time, despite having no more pain, she had increased the doses up to 30 ml of tramadol 100 mg/ml oral solution a week. She took the drug in consecutive "pinches", up to 48 (600 mg of tramadol) from afternoon to evening, until she fell asleep. Tramadol improved her mood, gave her euphoria and detachment, but also caused constipation and urinary retention. She reported intense fatigue, loss of appetite, insomnia, and tachycardia. Her physical health screen, neurological examination, lab tests, ECG, and a cardiology consult did not reveal any abnormalities. The total raw score of Zung Self-Rating Anxiety Scale was 49 and the Zung Self-Rating Depression Scale scored 68. Tramadol and M1 metabolite blood levels, determined by liquid chromatography/electrospray tandem mass spectrometry [LC/ESI-MS/MS (Agilent technology, Palo Alto, CA, USA)], were respectively 532 ng/ml and 318 ng/ml. Detoxification was carried out by a partial replacement with tramadol 100 mg extend release and a gradual reduction of the number of pinches. However, the patient found it hard to follow the program for the appearance of withdrawal symptoms of opioid type, and especially for the worsening of depression. After 40 days, when she was taking tramadol 150 mg/day, the patient left the treatment.
A binge pattern of administration is typical of stimulant drugs such as cocaine and amphetamines, but it is unusual for an analgesic. However, tramadol has a unique pharmacological profile, as it is both a weak opioid agonist and an inhibitor of the reuptake of serotonin and norepinephrine. The expression of the opioid component is due primarily to the conversion in the M1 metabolite, also consisting of 2 enantiomers, that has a significant affinity for the opioid receptors. Instead, not metabolized tramadol has very low affinity for the opioid receptors and is an inhibitor of the reuptake of norepinephrine and serotonin (Gillen et al., 2000). It is likely that taking tramadol in a binge pattern the monoaminergic action could increase and the patient had obtained an intense effect of mood improvement, antidepressant-like. This hypothesis is supported by literature. In a study that characterized tramadol in a discrimination procedure in 8 subjects with active opioid and stimulant use, trained to discriminate among placebo, 8 mg hydromorphone, and 60 mg methylphenidate, an oral dose of tramadol 400 mg had stimulant-like effects and increased ratings on the stimulant scale (Duke et al., 2011). The action of tramadol on monoaminergic system is considered the basis of its antidepressant activity, observed in experimental animal models and reported as helpful in the treatment of pain patients. However, this antidepressant, stimulant-like effect also imply the risk of complicating the condition of the patients. Besides the opioid dependence, a strong link with the drug could indeed develop, maintained by the worsening of depression when trying to stop taking tramadol. In conclusion, tramadol can be abused to enhance mood in a binge pattern as if it were a stimulant agent. An extreme caution and a careful management of the therapy are therefore needed when tramadol is prescribed to patients with pain and depression.

Duke et al. (2011). *J Pharmacol Exp Ther.* 338, 255-262.
Gillen et al. (2000). *Arch Pharmacol.* 362,116-121.
Raffa (2008). *J Clin Pharm Ther.* 33, 101-108.