Letter to the Editor

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How much Tramadol should be considered lethal in overdose?

Sayed Mahdi Marashi

Shiraz University of Medical Sciences, Shiraz, Iran

A 17-year-old female was admitted to our emergency room 30 min after suicidal ingestion of about 10 g Tramadol. The patient had several short-lived clonic seizures before admission. On arrival, she had an episode of tonic-clonic seizure, lasting for three minutes, which lead to cardiopulmonary arrest after administration of 10 mg diazepam intravenously. Endotracheal intubation and cardiopulmonary resuscitation were attempted. After 30 min, normal sinus rhythm with a palpable pulse was noted, and the patient was put on mechanical ventilation and transferred to the intensive care unit (ICU). Her vital signs were stable with vasopressor medication support (norepinephrine infusion at 10 μg min^{-1}). She had repeated short-lived tonic-clonic seizure-like movements, which responded well to midazolam. Her past medical and family history was negative for seizure, heart diseases, and hereditary disorders. Repeated neurological examination indicated that the patient had no motor response to pain and had fixed dilated pupils without corneal and vestibulo-ocular reflexes. About 48 h after admission to the ICU, she experienced asystole, which did not respond to resuscitation.

Tramadol HCl is a synthetic opioid drug that blocks reuptake of monoamine and inhibits NMDA glutamatergic activity, while it has low affinity for mu-opioid receptors (1). It has a low potential for abuse and is usually prescribed for control of moderate to severe pain (2). Tramadol is mainly metabolised by the hepatic cytochrome P450 2D6 (CYP2D6), and its active metabolites are responsible for complications, meaning that in a CYP2D6 rapid metaboliser patient excessive side effects may develop within a short time following its overdose (2, 3).

It has been reported that the LD50 value for Tramadol is about 300-350 mg kg^{-1} body weight in animal models (4). However, reviewing the literature, we found that it is generally considered to be non–life threatening in humans, hence, co-ingestion of Tramadol and other agents such as analgesics, muscle relaxants, and CNS depressants is occasionally reported from toxicological samples of postmortem human specimens (2, 5). In fact, there are only a few case reports of human fatality due to Tramadol overdose alone (2). It has been suggested that CYP2D6 ultra-rapid metaboliser patients may develop fatal complications (5). As its overstated toxic manifestations and accordingly its fatality are prospected during the first hours, which is related to its metabolism (5), this time is crucial in patient's care. Moreover, in the emergency situation, we have no idea about the activity of the cytochrome P450 2D6 in patients with Tramadol overdose, which can be induced by other drugs. Therefore, as cardiopulmonary arrest can be a fatal complication (5), we strongly suggest that all patients with exaggerated signs or symptoms of toxicity who consumed more than 150 mg kg^{-1} (the half dose of LD_{50} values in animal models) of Tramadol (4), should be intubated prophylactically and sedated with benzodiazepines, at least for the first nine hours, the reported half-life of Tramadol in human overdose (3). However, properly designed studies need to be conducted on this topic before any definite recommendation is made.

Correspondence to: Dr Sayed Mahdi Marashi, Trauma Research Center, Medical School, Emergency Room/Division of Medical Toxicology, Hazrat Ali-Asghar (p) Hospital, Shiraz University of Medical Sciences, Shiraz, Iran, E-mail: *marashi@sums.ac.ir*

Conflicts of interests

None declared.

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