

## Xylazine Intoxication, A Case report

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### Abstract

Xylazine is a colorless, bitter-tasted, crystalline substance, which is easily soluble in water. Xylazine is a strong alpha-2-adrenergic agonist, effective on alpha-2 receptors in central nervous system. It is a drug with relaxant, analgesic, and sedative properties. It reduces the release of noradrenaline and dopamine in the central nervous system; thus, it leads to sedation, muscular relaxation, and reduction of perception of painful stimuli. The use of xylazine in humans was investigated; however, it was not used due to significant hypotension. In this case report, we aimed to present a veterinary physician, who had attempted suicide by xylazine. Use of xylazine as a suicidal agent is a rare situation. There are few reports in which it was used for this purpose by veterinary physicians or people dealing with livestock. In recent years, it has started to be used as a narcotic substance. Since xylazine has started to be used as a narcotic substance, the probability of meeting with xylazine-related intoxication cases is increasing. With this case, we wanted to present xylazine in more detail, and to update, inform, and warn the emergency physicians on xylazine intoxication.

**Keywords:** Xylazine intoxication; Emergency medicine; Psychiatry

### Introduction

Xylazine is a colorless, bitter-tasted, crystalline substance, which is easily soluble in water. Its chemical structure is similar to phenothiazines, tricyclic anti-depressants, and clonidine. It is a non-narcotic drug and used as a sedative or in combination with other drugs for sedation, analgesia, or general anesthesia in animals [1]. It is approved for use in dogs, cats, horses, fallow deer (dama dama), mule deer (odocoileus hemionus), sika deer (cervus nippon), white-tailed deer (odocoileus virginianus), and elk (cervus canadensis) [2]. Xylazine is a strong alpha-2-adrenergic agonist, effective on alpha-2 receptors in central nervous system [3]. It is a drug with relaxant, analgesic, and sedative properties [4]. By the alpha-2 agonist effect, it has an inhibitory effect on brainstem vasomotor center [5]. In addition, it is suggested to have affinity for cholinergic, serotonergic, dopaminergic, alpha-1 adrenergic, histaminergic, or opiate receptors [3]. It reduces the release of noradrenaline and dopamine in the central nervous system; thus, it leads to sedation, muscular relaxation, and reduction of perception of painful stimuli [6]. Xylazine is metabolized in the kidney; 70% is excreted through the kidney, and 30% in the bile [3]. Only 8% of xylazine is excreted unchanged. Total excretion from the body occurs within 10-15 hours [5].

The basic use of xylazine is in veterinary medicine. The routes of administration in animals include intravenous, intramuscular and subcutaneous. Its dose is 0.5 mg/kg -5.0 mg/kg i.v or i.m and its therapeutic index is narrow. Twice or triple more amounts of the therapeutic dose may lead to mortality. The use of xylazine in humans was investigated; however, it was not used due to significant hypotension. Xylazine has initially a hypertensive effect; then, it leads to permanent hypotension, bradycardia, and reduction of cardiac output, with alpha-2 receptor blockage being dominant in the central nervous system [3]. Xylazine is not approved by the FDA for human use. It was investigated in humans as a sedative-hypnotic, analgesic and anesthetic drug, but it was rejected because of its frequent association with severe hypotension and central nervous system depression.

Use of xylazine as a suicidal agent is a rare situation. There are few reports in which it was used for this purpose by veterinary physicians or people dealing with livestock. In recent years, it has started to be used as a narcotic substance [6]. In subjects who use high-dose narcotics,

it should be questioned [6]. In this case report, we aimed to present a veterinary physician, who had attempted suicide by xylazine.

### The Case

The 24-year-old man weighing 110 kg (242 lb) veterinarian physician, was found at home by emergency team lying on the bathroom floor. He has called his girlfriend and said he would commit suicide. His clinical history unremarkable. Only we known that he was smoker and social alcohol user. He was admitted in our emergency department unconscious state by ambulance. According to the information obtained from his friend, and he might have injected himself one vial of xylazine (500 mg) intravenously, with suicidal purpose. Additionally, it was learned that he had several suicidal attempts by various drugs, previously. There was the sign of injection on his arm. His physical examination revealed that he was unconscious, GCS = 3, and blood pressure could not be measured and the pulse could not be felt. The patient was monitored; there was regular pulseless electrical activity with a rate of 122/min on the monitor, and SpO<sub>2</sub> was 80%. Since he was considered to be in the state of cardiopulmonary arrest due to pulseless electrical activity, CPR was initiated. In the early period of resuscitation, the patient went into ventricular fibrillation, and he was defibrillated. During resuscitation, the rhythm changed to asystole. The patient was considered as dead ninety minutes later, not responding to continuing resuscitation.

### Discussion

Due to xylazine intake, central system findings such as areflexia, asthenia, blurred vision, orientation disorder, dizziness, numbness, dysarthria, dysmetria, fainting, hyporeflexia, speech disorder, coma,

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respiratory irregularities extending from apnea to agonal respiration, cardiac effects such as hypotension, bradycardia, tachycardia, ventricular premature contractions and hypoglycemia may be observed in patients. Additionally, hypotonia, xerostomia, and enuresis were observed [6].

When the intake of xylazine was mixed with ketamine and heroin or when xylazine was used together with alcohol, it was shown that its toxic effects and the fatality increased. It is suggested that similar pharmacological effects of xylazine and heroin increase the toxicity by synergic effect [6]. In our case, ethanol was 124 promile; we considered that its coexistence might have increased the mortality risk for the patient. In recent years, xylazine has started to be used as a narcotic substance. In one study, the xylazine intoxication-related hospital admissions between 1966 and 2014 were screened; 43 cases were identified, in 22 cases the prognosis was recorded as fatal, and in 21 cases as non-fatal. Of 22 fatal cases, 18 cases used xylazine as a narcotic substance, 2 used for the suicidal attempt, and 2 used for murder attempt. Of 21 non-fatal cases, 9 cases used xylazine accidentally, 3 for the suicidal attempt, and 3 for relaxation. Uses of xylazine for sleep disorder and pain control were also reported. In non-fatal patients in whom blood xylazine measurement could be made (n = 10), the blood or plasma concentration was between 0.03-4.6 mg/l. Measurements made in fatal patients (n = 22) revealed that the blood xylazine concentration varied within the range from trace amount to 16 mg/l. Therefore, a distinct range was not possible to be determined in terms of safe, toxic, and fatal doses. The intake dose of xylazine, which is known to cause fatal and toxic effects in humans, varies between 40 mg and 2400 mg. In other words, while toxicity may develop in low doses, recovery may be observed with supportive treatment in high doses [7,8]. In our case, the blood xylazine concentration was not measured; however, it was considered that he had received 500 mg intravenously.

To our knowledge, there are five cases of xylazine intoxication with the suicidal purpose in the medical literature. The outcome was fatal in two of them. Ours was the third fatal case. The common characteristics of the cases who attempted suicide was dealing with veterinary medicine or livestock; while one of the fatal cases was a salesperson for veterinary products, the other was a veterinary technician. Our patient was the first veterinary physician who had used xylazine with the suicidal purpose.

No antidote is present for using in humans. Alpha-adrenergic antagonists such as phentolamine, yohimbine, and tolazoline were suggested as antidotes for xylazine; however, they were not tested in humans [9]. In subjects who had performed intramuscular xylazine self-injections, due to being an alkaloid substance, it was found to be present in significant amounts within the gastric juice; therefore, gastric lavage is important in this patient group [3]. In the treatment of xylazine overdose, supportive care is much more important. Supportive care should include oxygenation, endotracheal intubation when required, intravenous fluid infusion, gastric lavage, active charcoal, urinary catheterization, electrocardiography (ECG) and hyperglycemia monitorization. Hemodialysis is ineffective for treatment [10].

Since xylazine has started to be used as a narcotic substance, the probability of meeting with xylazine-related intoxication cases is increasing. With this case, we wanted to present xylazine in more detail, and to update, inform, and warn the emergency physicians on xylazine intoxication.

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