

# Doxylamine Succinate Overdose: Case Report and Literature Review

## Doksilamin Süksinat Aşırı Alımı: Olgü Sunumu ve Literatür Taraması

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#### Abstract

Doxylamine succinate is an antihistamine of the ethanolamine class and commonly used as a nighttime sleep aid in the short-term management of insomnia. It is also used in combination with antitussive and decongestant agents for the temporary relief of common cold symptoms. There are few issues related with doxylamine succinate monointoxication in the literature and they are mostly associated with rhabdomyolysis. In this case report, we aim to overview a doxylamine succinate monointoxication case which seen rarely in the literature and make a review related with doxylamine succinate overdose.

Key words: **Intoxication; Doxylamine; Overdose.**

#### Özet

Doksilamin süksinat, etanolamin grubundan sedatif ve antikolinergik etkileri olan bir antihistaminiktir. Genellikle uyku bozukluğu tedavisinde kullanılan kısa etkili bir ilaçtır. Tek başına kullanılabildiği gibi soğuk algınlığı için kullanılan ilaçlarla da kombine halde bulunabilmektedir. Literatürde tek başına doksilamin süksinat intoksikasyonu ile ilgili az sayıda yayın bulunmakta ve bunların çoğunluğunu da rabdomiyoliz meydana gelen olgular oluşturmaktadır. Bizim amacımız literatürde az sayıda olan ancak ölüm ve ciddi komplikasyonlar ile karşımıza çıkabilen doksilamin süksinat aşırı alımı olan bir olguyu incelemek ve doksilamin süksinat intoksikasyonu ile ilgili olarak literatürü gözden geçirmektir.

Anahtar Kelimeler: **Aşırı Alım; Doksilamin; İntoksikasyon.**

## Introduction

Doxylamine succinate is an antihistamine that maintains short-term sleep aid. Its combination with other drugs provides nighttime cold and allergy relief, and the combination with vitamin B6 (pyridoxine) prevents morning sickness in pregnant women.

The dosage required to induce sleep can be as low as 6.25 mg, but is usually effective in dosages of up to 25 mg. Doxylamine succinate half-life is approximately 6 hours and reaches peak plasma concentration of 0.1 µg/ml in 2 to 3 hours after oral administration of a standard dose of 25 mg. The majority of the dose (60%) is excreted unchanged in the urine and the remainder is metabolized through various metabolic pathways (1). The lethal dosage of doxylamine in humans is 25–250 mg/kg body weight (2).

The main clinical features of peripheral anticholinergic effects include hypertension, warm and dry skin, dilated pupils, diminished bowel sounds, flushing, urinary retention, and tachycardia. Central anticholinergic activity is characterized by delirium, seizures, and coma (3). Beside these general anticholinergic manifestations it has also rare side effects like acute pancreatitis (4), diffuse toxic myopathy (5) and rhabdomyolysis (6-12).

Herewith, we reported a doxylamine succinate monointoxication without deleterious side effects and reviewed the literature.

## Case Report

A 37-year-old previously healthy woman without any past medical history was admitted to our emergency department. She ingested 26 *Hoggar Night*<sup>®</sup> 25 mg tablets, including 11.6 mg/kg doxylamine succinate two hours before her admission and was found to be mildly confused. Her blood pressure was 190/85 mmHg with a pulse rate of 130/min, respiration rate was 20 breaths/min, body temperature from axillary region was 37 °C and SPO<sub>2</sub> was 98% detected by pulse-oximeter. She was in sleepy appearance and could be awake by verbal stimulation. Physical examination revealed unremarkable findings except dry and flushed skin. Initial laboratory results were as follows: blood urea nitrogen 6 mg/dl (6-20 mg/dl), serum creatinine 0.66 mg/dl (0.5-1.10 mg/dl), sodium 137 mEq/L (133-145 mEq/L), potassium 4.23 mEq/L (3.30-5.10 mEq/L), creatine phosphokinase 135 U/L (26-140 U/L), amylase 65 U/L (28-100 U/L). Her urinalysis was in normal limits. The electrocardiogram was normal except sinus tachycardia.

The patient's vital signs were monitored and observed for the development of anticholinergic symptoms. Activated - charcoal in dose of 1g/kg was administered for gastrointestinal decontamination.

The patient was admitted to the Internal Medicine Unit for observation against possible complications. The patient had no any change in vital signs such as blood pressure and heart rate. After 24 hours follow up the patient had no laboratory abnormalities and was discharged after psychiatry consultation.

## Discussion

According to Bockholdt and co-workers (13), in 6570 autopsies carried out in the Institute of Legal Medicine at Free University Berlin from 1987–1997, in two cases (0.30%) doxylamine alone was found. In that study doxylamine blood concentration values was less than 165 mg/l (13). It was reported that lethal dosage of doxylamine was less than 1 g (14, 15). The lethal dosage of doxylamine in humans is 25–250 mg/kg body weight (2). Our case took 650 mg orally, 11.6-mg/kg doses in total. This dose was not lethal for this patient but anticholinergic symptoms such as tachycardia and hypertension were occurred.

The most common manifestations of doxylamine succinate overdose are related to their anticholinergic effects. There is no correlation between plasma doxylamine succinate level and clinical manifestations according to Poison Control Center data that were collected by phone calls mostly (1). Moreover, there were no symptoms in 39% of 109 patients. In this case we observed anticholinergic symptoms such as hypertension and tachycardia.

Although it is not shown between central and peripheral side effects occurred in antihistamine overdoses, in the literature there are nine rhabdomyolysis cases and one acute pancreatitis case (4, 6-12). The cause of rhabdomyolysis is not known precisely but it is thought to be due to the direct effect of the drug to the muscle. There was no correlation found between doxylamine succinate dose, plasma concentration and rhabdomyolysis level. Other possible explanations of rhabdomyolysis are prolonged seizures, muscle ischemia, trauma and infections (9). In our case which are the indicator of rhabdomyolysis diagnosis, increased levels of blood creatinine and myoglobinuria is not occurred.

According to drugs and toxins, as a subgroup of diffuse toxic myopathies, necrotizing myopathy can occur. As a result of direct effects of drugs to the muscles, weakness at proximal muscle groups and myalgias, increased blood creatinine level and myoglobinuria in serious cases may occur. Ipecac syrup that used in drug overdose is one of these drugs (5). For this reason use of Ipecac syrup must be avoided in patients with doxylamine succinate overdose that can cause toxic myopathy.

The therapy for doxylamine succinate poisoning is symptomatic and supportive. It consists of removal of the ingested drug by gastric lavage in conscious patients in the early stage and by administration of activated-charcoal. Patients should be monitored and treated for airway compromise, central nervous system depression, seizure activity, arrhythmias, cardiovascular collapse, and hyperthermia. If the patient has resistant hypotension against fluid therapy or both central and peripheral effects of antihistamine overdose or supraventricular or ventricular dysrhythmies on the electrocardiography, physostigmine must be given. (3). The presented case was hypertensive in spite of hypotension during the 18 hours follow up of mean arterial blood pressure.

Antihistamines are available worldwide, and many do not require a prescription. They often are used for symptomatic relief of allergy symptoms and are included in many combination cold preparations. They also are found in nonprescription sleeping aids. Antihistamines are frequently ingested in suicide attempts, probably because of their ready availability. Patients treated with activated-charcoal, continuous assessment, supportive care, management of abnormal vital signs, electrocardiography, cardiac monitoring, and mental status have an excellent outcome with little risk of adverse sequelae. Familiarity with the more severe complications of antihistamine and decongestant overdoses results in early and appropriate interventions to reduce both morbidity and mortality from these exposures.

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