



## DOXYLAMINE SUCCINATE OVERDOSE PRESENTING WITH LATE RHABDOMYOLYSIS

### KEYWORDS

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### ABSTRACT

Doxylamine succinate is an antihistamine drug which also possess anti cholinergic side effects. Clinical symptoms of the drug overdose includes minor manifestations like sedation, tachycardia, mydriasis, urinary retention to life threatening manifestations like seizures, rhabdomyolysis leading on to acute kidney injury. The following case describes a patient with doxylamine toxicity presenting with seizures and acute kidney injury initially. Patient was managed symptomatically. Patient developed rhabdomyolysis after a week of admission which was treated with adequate hydration and alkaline diuresis. This case is atypical in terms of acute kidney injury presenting early without rhabdomyolysis during that episode and late onset rhabdomyolysis. Since doxylamine is an over the counter medication and is prone for misuse, knowledge about clinical manifestations and management of toxicity can be life saving.

### INTRODUCTION

The present report describes a case of doxylamine toxicity as a part of suicide attempt. Clinical manifestations of doxylamine toxicity are discussed. The most common life threatening complications are seizures, rhabdomyolysis leading to acute kidney injury.<sup>1</sup> This article is to enlighten that acute kidney injury can occur without rhabdomyolysis probably secondary to interstitial nephritis and late onset rhabdomyolysis. The intention is to remind clinicians about the toxicity of the drug which is available as over the counter medication.

### CASE PRESENTATION

A 29 year old male without any past medical history was brought to our emergency department on November 2014 with alleged history of consumption of unknown tablet and quantity with suicidal intention. Patient induced vomiting at home after an hour of consumption. Patient had 1 episode of generalised tonic clonic seizure lasting for 2 minutes.

On arrival to emergency, patient was conscious, disoriented. His blood pressure was 150/90mmHg with pulse rate of 116/min, respiration rate of 20 breaths/min, body temperature from axillary region was 37 °C and SPO<sub>2</sub> was 100% detected by pulse-oximeter. Patient had dry and flushed skin. Otherwise physical examination revealed normal systemic evaluation. In casualty, activated charcoal of 1gm/kg was administered for gastrointestinal decontamination.

Initially laboratory evaluation showed blood urea nitrogen of 10mg/dl (Normal-6-20mg/dl), serum creatinine of 1.2mg/dl (Normal-0.6-1.2 mg/dl), sodium of 136mEq/L (Normal -135-145 mEq/L), potassium of 3.9mEq/L (Normal -3.5-4.5mEq/L), creatinine phosphokinase of 427 U/L (Normal -26-160 U/L). His urine analysis, liver function test, serum amylase were within normal limits. The electrocardiogram showed sinus tachycardia. CT brain was done in view of seizures and was found to be normal.

On day 2, when his sensorium improved, he said that he had consumed 193 tablets of doxylamine succinate (25 tablet each) 4 hours prior admission. Patient had consumed 65mg/kg (4825mg). Patient developed acute kidney injury on day 3 without rhabdomyolysis since CPK value was not very high. Serum electrolytes and urine examination was normal during the kidney injury. It was probably attributed to interstitial nephritis. Later

patient had rise in CPK on day 8 of admission which was suggestive of late onset rhabdomyolysis.

Table 1 – Renal function and CPK monitoring

	Day 1	Day 3	Day 6	Day 8	Day 10	Day 12	Day 14
BUN	10	32	28	26	20	18	14
Serum creatinine	1.2	3.7	3.1	2.7	2.1	1.4	1.0
CPK	427	419	227	8876	4127	2276	390
Urine myoglobin	-ve			-ve		-ve	

In view of logistic reasons, estimation of the drug was not done. Patient was given adequate hydration. Alkaline diuresis with 75mEq of sodium bicarbonate in 500ml NS over 6 hours was given during rhabdomyolysis. Inj. fosphenytoin 150mg i.v TDS was given for seizures. Vital signs were monitored. Patient was discharged home after psychiatry consultation and stabilization with the duration of stay being 14 days.

### DISCUSSION

Doxylamine succinate is an anti histamine drug of first generation. CNS penetration of the drug is high. Its sedative effect is used for short term management of insomnia. It also has effect on morning sickness in combination with pyridoxine, reduces common cold symptoms in combination with anti tussives and decongestants.<sup>2</sup> Standard dose is 25mg od or bd dose. For induction of sleep dose of 6.25mg is sufficient.<sup>3</sup>

Half-life is approximately 6-10 hours. It is mostly excreted unchanged in urine. Remaining of the drug gets metabolised by the liver into N-demethyldoxylamine and N,N-didemethyldoxylamine. The lethal dose of the drug is 25-250mg/kg body weight.<sup>1</sup>

H1 receptor blocking effect causes side effects of sedation, tinnitus, fatigue, incoordination, tremors, decreased cognition and impaired psychomotor performance. Weak anti cholinergic side effect includes dry mouth, urinary retention, tachycardia, hypertension, delirious state, seizures and coma.<sup>4</sup> Other effects include rhabdomyolysis, acute kidney injury secondary to myoglobinuric effector anticholinergic effect which induce bladder outlet

obstruction. Rare side effect of acute pancreatitis also has been reported<sup>1</sup>. There is no correlation observed between doxylamine dose, plasma concentration and rhabdomyolysis.<sup>5</sup>

Rhabdomyolysis was said to be caused by direct toxic effect to sarcolemma which leads to leakage of intracellular contents and increase in sodium into the cell. This in turn activates sodium potassium ATPase pump thereby depleting ATP. Increase in intracellular sodium also activates intracellular calcium activating proteolytic enzymes.<sup>6</sup> Out of 109 patients studied and published in a toxicology article in 1987, 39% had no symptoms, 9 patients had rhabdomyolysis and AKI, 1 patient had pancreatitis and remaining with anti cholinergic side effect.<sup>7</sup>

Screening for doxylamine toxicity is usually performed on urine specimens using immunoassays. Confirmatory testing usually involves either gas chromatography or mass spectrometry<sup>8</sup>. There is evidence that doxylamine at toxic levels can lead to false positive methadone and phencyclidine results using immunoassay-based urine drug screen kits which may be due to the similarity between parent compounds.<sup>9</sup>

There is no antidote available for the poison. Since the drug is protein bound, it is not a dialyzable poison. Only supportive care is helpful. For seizures, benzodiazepines like diazepam are the first choice followed by phenytoin and Phenobarbital<sup>7</sup>. Treatment of rhabdomyolysis includes adequate hydration with or without alkaline diuresis<sup>6</sup>. Monitoring of serum electrolytes, renal function test atleast for 18- 24 hours is usually required in view of its half life. However, delayed presentation of rhabdomyolysis as in our case requires monitoring for atleast 72 hours to prevent mortality. Delayed rhabdomyolysis can be explained by the protein bound fraction of the drug which prolongs the half life. Doxylamine overdose might also present as a direct nephrotoxic drug like our case though the exact mechanism is not known. Possible explanation in our case can be due to interstitial nephritis though biopsy might be helpful.

Since doxylamine is available over-the-counter and widely misused for suicidal attempt, proper knowledge of the clinical presentation and management is mandatory for the treating physician.

## CONCLUSION

- Doxylamine is over the counter anti histamine which causes anticholinergic side effects, seizures, rhabdomyolysis and acute kidney injury during toxicity.
- Rhabdomyolysis may occur as a late presentation due to prolonged half life as it is protein bound. So monitoring for creatinine kinase is required atleast for 72 hours of consumption.
- Acute kidney injury can rarely occur independent of rhabdomyolysis probably secondary to interstitial nephritis.

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