

CASE REPORT

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Patient Survival After Acute Voluntary Poisoning With a Huge Dose of Oxcarbazepine and Olanzapine

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ABSTRACT

Introduction: Oxcarbazepine is a carbamazepine pre-drug with less drug interactions. Its adverse effects, including hyponatremia, somnolence and ataxia, are dose dependent. Olanzapine is an atypical antipsychotic drug most commonly used to manage psychoses and symptoms of irritability and aggressive behavior. Main side effects include extrapyramidal and anticholinergic symptoms, weight gain, and hyperglycemia. **Case Report:** In this manuscript a case of oxcarbazepine and olanzapine intoxication is discussed. A 45-year-old woman, previously diagnosed with bipolar disorder and chronic alcoholism, was presented two hours after ingestion of 30,000mg of oxcarbazepine and 140 mg of olanzapine, combined with alcohol. She was immediately treated with gastric lavage and administration of activated charcoal. During her hospitalization she was hemodynamically and respiratory stable with no neurological signs and symptoms except for somnolence. Another side effect was hyponatremia. She was discharged from our department in stable clinical condition after being evaluated by a psychiatrist. **Conclusion:** Early approach is crucial for the management of drug intoxication. Late symptoms can be avoided through close monitoring of vital signs, mental status and laboratory values. Psychiatric consultation is essential for a better long-term outcome.

Keywords: bipolar disease, intoxication, oxcarbazepine, olanzapine, poisoning, suicide attempt, voluntary.

1. INTRODUCTION

Oxcarbazepine was primarily used in the treatment of epilepsy (1, 2), but now it is prescribed for other indications, too, e.g. neuropathic pain (3). It can also be used as mood stabilizer in management of bipolar affective disorders (4, 5). Oxcarbazepine is a structural derivative of carbamazepine, with the advantage of being less myelotoxic and not being a CYP3A inducer, resulting in less drug interactions (6). Its active metabolite is 10-monohydroxy derivate (MHD) (1). Side effects are dose dependent. Most common are hyponatremia (1, 7), dizziness, somnolence, agitation, headache, ataxia, nausea, vomiting and difficulty in concentration. Rare adverse effects include anaphylaxis, angioedema, toxic epidermal necrolysis, Stevens-Johnson syndrome, photosensitivity and suicidality (1). Unlike other antiepileptic drugs, it does not seem to be proconvulsant in overdose (8).

Olanzapine is an antipsychotic drug, classified within the atypical antipsychotics. The psychiatrists use olanzapine to manage schizophrenia

(especially the negative symptoms) (9) and bipolar disorder (10). Side effects include extrapyramidal and anticholinergic symptoms (9, 11), weight gain, hypertriglyceridemia, hypercholesterolemia, hyperglycemia in patients with diabetes mellitus, galactorrhea, amenorrhea, gynecomastia, erectile dysfunction, neutropenia, seizure threshold lowering, personality changes and suicidality (10, 12). In case of overdose, patients may suffer from tachycardia, agitation, hyperpyrexia, leukocytosis, elevated creatine phosphokinase levels, paradoxical miosis mimicking opioid or α 2-agonist intoxication (13), dysarthria, low level of consciousness, dry mouth, ataxia and coma. Electrocardiographic (ECG) abnormalities may be present, including supraventricular tachycardias/arrhythmias and prolonged QTc interval, although it rarely led to torsades de pointes in a retrospective analysis, maybe due to the mild prolongation observed (mean QTc 453 +/- 48 ms) (14). Increased risk of death has been reported in elderly patients with dementia-related psy-

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chosis, mostly due to cardiovascular or infectious events (10).

2. CASE REPORT

A 45-year-old female (weight 77 Kg and height 1,70 m) with known chronic alcoholism and bipolar disorder (at least 20 years) was admitted to the intensive care unit (ICU) 2 hours after an overdose of 50 tablets (immediate release) of 600mg oxcarbazepine and 28 tablets (immediate release) of 5mg olanzapine combined with alcohol. She denied ingestion of other substances. On admission the patient was conscious with the following vital signs: Blood pressure 120/80 mmHg, heart beats 113/min, temperature 35,3 °C, saturation O₂ 98% and capillary glucose 76 mg/dl. With the exception of mild dysarthria, neurologically no abnormalities were found. The patient had normal tendon and pupillary reflexes, with neither signs of nystagmus, ataxia nor Babinski's sign. Glasgow coma scale (GCS): 15 /15. Normal ECG with sinus rhythm, QRS: 90 ms, QTc: 465 ms. Treatment was immediate, according to the instructions of Poison Control Center: gastric lavage followed by administration of activated charcoal (1g/kg). During her hospitalization she remained hemodynamically and respiratory stable. Somnolence was presented only within the first 20 hours. Laboratory findings, including liver and kidney function, remained normal. Hyponatremia presented on the second day, with serum sodium declining from 137 mEq/L at time of admission, to 129 mEq/L and 127 mEq/L, without nausea, headache or neurological signs. Treatment was based on one course of intravenous infusion of 3% hypertonic saline (150ml) and fluid restriction (800ml/day) and sodium levels gradually returned to normal values. ECG monitor did not show any arrhythmias. The patient was examined by a psychiatrist to manage the acute event and the underlying disease. Three days after admission to the ICU she was discharged.

3. DISCUSSION

A large amount of olanzapine and an even larger amount of oxcarbazepine voluntary consumption is reported, compared to usual daily therapeutic dose of each drug.

The maximum therapeutic dose is approximately 30 mg/d and 2400 mg/d, respectively. The peak serum time of oxcarbazepine is 1-3 hours, its half-life 1-5 hours (15). On the other hand, olanzapine has a peak serum time of 6 hours and a half-life of 21-54 hours (10). Activated charcoal administration appears essential to manage poisoning from both drugs. It may decrease olanzapine's oral bioavailability by 50%–60%. As for oxcarbazepine, it has a very good effect both for inhibiting absorption and accelerating drug elimination. Second dose of activated charcoal seems beneficial (16).

The patient ingested a total of 30000 mg of oxcarbazepine and 140 mg of olanzapine (x12.5 and x4.6 of the maximum daily dose respectively). It could have been troublesome if the patient had been presented to ER later. However, mild adverse effects were arisen, including hyponatremia and somnolence.

To our knowledge, there are no cases in the literature with oxcarbazepine and olanzapine coadministration in toxic doses, with or without ethanol consumption. No pharmacokinetic interactions were noticed when these two drugs were given together in therapeutic doses (1, 10, 17). However, alcohol enhances respiratory depression caused by sedative drugs, and along with olanzapine, may cause orthostatic hypotension (10). It is worth mentioning that both drugs have been used to alcohol dependence and alcohol withdrawal management, although randomized evidence and cost-effectiveness data favoring their use for this indication are lacking, except if the patient has other indication of taking them, too (18, 19, 20, 21).

Mortality from olanzapine overdose alone seems to be low from previous case series, but a significant proportion of these cases may need short-term intubation, predominantly due to agitation or coma (13, 22, 23). Low mortality has also been observed from oxcarbazepine poisoning for doses even bigger than our patient's, with only 5 deaths from US Poison Centers in 18867 cases of oxcarbazepine exposure (8, 24).

4. CONCLUSION

In this case report we emphasize on the early approach of management of drug intoxication with oxcarbazepine and olanzapine. Gastric lavage and activated charcoal administration as soon as possible after ingestion, are the key to prevent severe adverse effects. Close monitoring of vital signs, mental status and laboratory values are also needed to stabilize the patient and prevent or manage late symptoms. Last but not least, a psychiatric consultation is necessary in order to control underlying disease and prevent future suicidal events.

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REFERENCES

1. DailyMed – OXCARBAZEPINE–oxcarbazepine tablet [Internet]. Dailymed.nlm.nih.gov. 2018 [cited 24 May 2018]. Available from: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=17325a80-fb9c-4a83-b4b4-98e0b999d852>.
2. Glauser T. Oxcarbazepine in the Treatment of Epilepsy. *Pharmacotherapy*. 2001; 21(8): 904-919.
3. Zhou M, Chen N, He L, Yang M, Zhu C, Wu F. Oxcarbazepine for neuropathic pain. *Cochrane Database Syst Rev*. 2017; (12): CD007963.
4. Ghaemi S, Berv D, Klugman J, Rosenquist K, Hsu D. Oxcarbazepine Treatment of Bipolar Disorder. *J Clin Psychiatry*. 2003; 64(8): 943-945.
5. Hirschfeld R, Kasper S. A review of the evidence for carbamazepine and oxcarbazepine in the treatment of bipolar disorder.

- Int J Neuropsychopharmacol. 2004; 7(4): 507-522.
6. Buggy Y, Layton D, Fogg C, Shakir S. Safety profile of oxcarbazepine: Results from a prescription-event monitoring study. *Epilepsia*. 2010; 51(5): 818-829.
 7. Berghuis B, van der Palen J, de Haan G, Lindhout D, Koeleman B, Sander J. Carbamazepine- and oxcarbazepine-induced hyponatremia in people with epilepsy. *Epilepsia*. 2017; 58(7): 1227-1233.
 8. Spiller H, Strauch J, Essing-Spiller S, Burns G. Thirteen years of oxcarbazepine exposures reported to US poison centers. *Hum Exp Toxicol*. 2016; 35(10):1055-1059.
 9. Shrestha G, Keyal N, Pradhan S, Maharjan R, Acharya S, Marhatta M. Olanzapine overdose presenting with acute muscle toxicity. *Int J Crit Illn Inj Sci*. 2017; 7(1): 69.
 10. DailyMed – OLANZAPINE–olanzapine tablet, film coated [Internet]. *Dailymed.nlm.nih.gov*. 2018 [cited 24 May 2018]. Available from: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=676ace4e-7706-742d-cab0-430dd1f83408>.
 11. Rummel-Kluge C, Komossa K, Schwarz S, Hunger H, Schmid F, Kissling W et al. Second-Generation Antipsychotic Drugs and Extrapyramidal Side Effects: A Systematic Review and Meta-analysis of Head-to-Head Comparisons. *Schizophr Bull*. 2010; 38(1): 167-177.
 12. Albaugh V, Singareddy R, Mauger D, Lynch C. A Double Blind, Placebo-Controlled, Randomized Crossover Study of the Acute Metabolic Effects of Olanzapine in Healthy Volunteers. *PLoS ONE*. 2011; 6(8): e22662.
 13. Chue P, Singer P. A review of olanzapine-associated toxicity and fatality in overdose. *J Psychiatry Neurosci*. 2003; 28(4): 253-261.
 14. Ciszowski K, Sein Anand J. [Electrocardiographic abnormalities in acute olanzapine poisonings]. *Przegl Lek*. 2011; 68(8): 422-425.
 15. May T, Korn-Merker E, Rambeck B. Clinical Pharmacokinetics of Oxcarbazepine. *Clin Pharmacokinet*. 2003; 42(12):1023-1042.
 16. Keränen T, Sorri A, Moilanen E, Ylitalo P. Effects of charcoal on the absorption and elimination of the antiepileptic drugs lamotrigine and oxcarbazepine. *Arzneimittelforschung*. 2011; 60(07): 421-426.
 17. Rosaria Muscatello M, Pacetti M, Cacciola M, La Torre D, Zoccali R, Arrigo C et al. Plasma Concentrations of Risperidone and Olanzapine during Coadministration with Oxcarbazepine. *Epilepsia*. 2005; 46(5): 771-774.
 18. Littlewood R, Claus E, Arenella P, Bogenschutz M, Karoly H, Ewing S et al. Dose specific effects of olanzapine in the treatment of alcohol dependence. *Psychopharmacology (Berl)*. 2014; 232(7): 1261-1268.
 19. Barrons R, Roberts N. The role of carbamazepine and oxcarbazepine in alcohol withdrawal syndrome. *J Clin Pharm Ther*. 2009; 35(2): 153-167.
 20. Pani P, Trogu E, Pacini M, Maremmani I. Anticonvulsants for alcohol dependence. *Cochrane Database Syst Rev*. 2014; (2): CD008544.
 21. Hutchison K, Wooden A, Swift R, Smolen A, McGeary J, Adler L et al. Olanzapine Reduces Craving for Alcohol: A DRD4 VNTR Polymorphism by Pharmacotherapy Interaction. *Neuropsychopharmacology*. 2003; 28(10): 1882-1888.
 22. Ciszowski K, Sein Anand J, Wilimowska J, Jawień W. [The clinical picture of acute olanzapine poisonings]. *Przegl Lek*. 2011; 68(8): 426-433.
 23. Palenzona S, Meier P, Kupferschmidt H, Rauber-Luethy C. The Clinical Picture of Olanzapine Poisoning with Special Reference to Fluctuating Mental Status. *J Toxicol Clin Toxicol*. 2004; 42(1): 27-32.
 24. Wills B, Reynolds P, Chu E, Murphy C, Cumpston K, Stromberg P et al. Clinical Outcomes in Newer Anticonvulsant Overdose: A Poison Center Observational Study. *J Med Toxicol*. 2014; 10(3): 254-260.