Oxcarbazepine Overdose in a Polysubstance Related Suicide

Melissa Beals
Children's Mercy Hospital, mabeals@cmh.edu

Robert J. Krumsick

C. Clinton Frazee III
Children's Mercy Hospital, ccfrazee@cmh.edu

Lindsey J. Haldiman

Uttam Garg
Children's Mercy Hospital, ugarg@cmh.edu

Follow this and additional works at: https://scholarlyexchange.childrensmercy.org/posters

Part of the Diagnosis Commons, Medical Biochemistry Commons, Pathology Commons, Pharmaceutical Preparations Commons, and the Psychiatric and Mental Health Commons

Recommended Citation
Beals, Melissa; Krumsick, Robert J.; Frazee, C. Clinton III; Haldiman, Lindsey J.; and Garg, Uttam, "Oxcarbazepine Overdose in a Polysubstance Related Suicide" (2018). Posters. 27.
https://scholarlyexchange.childrensmercy.org/posters/27

This is brought to you for free and open access by SHARE @ Children's Mercy. It has been accepted for inclusion in Posters by an authorized administrator of SHARE @ Children's Mercy. For more information, please contact library@cmh.edu.
Oxcarbazepine Overdose in a Polysubstance Related Suicide

Melissa Beals¹*, Robert J. Krumsick, DABFT ¹, C. Clinton Frazee III, MBA, NRCC-TC, CC, Lindsey J. Haldiman, D.O.², Uttam Garg, Ph.D., F-ABFT¹

¹Department of Pathology and Laboratory Medicine, Children’s Mercy Hospital, 2401 Gillham Rd., Kansas City, MO, 64108
²Office of the Jackson County Medical Examiner, 950 E 21st St., Kansas City, MO, 64108

Methods

Oxcarbazepine is a derivative of carbamazepine that is used primarily in the treatment of epilepsy, and experimentally as a mood-stabilizer in adjunctive therapy for the treatment of bipolar disorder. Oxcarbazepine is converted through oxidation to its pharmacologically active metabolite 10-OH-Carbazepine, which is thought to be responsible for most of the anticonvulsant action of the drug. Adverse effects of oxcarbazepine are generally dose-dependent and may include fatigue, somnolence, dizziness, diplopia, nystagmus, and ataxia. Additive sedative effects have been noted when oxcarbazepine is used in combination with other CNS depression-producing medications. Furthermore, oxcarbazepine and 10-OH-Carbazepine are powerful CYP2C19 inhibitors, potentially increasing the plasma concentration and pharmacological response of CYP2C19 substrates such as diazepam. The therapeutic range for oxcarbazepine is based on the metabolite and extends from 6-35 μg/mL. Toxicity has been reported with 10-OH-Carbazepine levels as low as 65 μg/mL, and one fatality has been documented with a 10-OH-Carbazepine concentration of 92 μg/mL.

Hydrocodone is a narcotic analgesic that undergoes demethylation and reduction to produce several pharmacologically active metabolites, including hydromorphone, norhydrocodone, and dihydrocodeine (6-β-hydrocodol), which contribute to its efficacy. Hydrocodeone toxicity may be characterized by respiratory depression, drowsiness, and coma. Therapeutic blood and plasma concentrations of hydrocodeone typically range from 10-50 ng/mL, while levels greater than 100 ng/mL are considered toxic, and concentrations exceeding 200 ng/mL can be potentially fatal.

Diazepam is a benzodiazepine known for its efficacy and rapid onset. Therapeutic ranges of diazepam and its metabolite nordiazepam in blood and plasma measure between 200-2500 ng/mL. Diazepam toxicity may result in drowsiness, weakness, ataxia, and coma; however, serious and fatal effects are uncommon with diazepam if used singularly. Most terminal adverse events associated with diazepam are the result of interaction or combination with other drugs, especially CNS depressants.

Results

<table>
<thead>
<tr>
<th>EIA (Heart Blood)</th>
<th>LC-MS/MS (Femoral Blood)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiates</td>
<td>10-Oxytocarbazepine: 180 μg/mL</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Hydrocodeine (free): 490 ng/mL</td>
</tr>
<tr>
<td></td>
<td>Hydromorphone (free): 6.1 ng/mL</td>
</tr>
<tr>
<td></td>
<td>Oxcarbazepine</td>
</tr>
<tr>
<td></td>
<td>Dihydrocodeine/1Hydrocodol (free): 47 ng/mL</td>
</tr>
<tr>
<td>Hydrocodeine</td>
<td>HPLC (Heart Blood)</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Diazepam: 465 ng/mL</td>
</tr>
<tr>
<td>Nordiazepam</td>
<td>Nordiazepam: 435 ng/mL</td>
</tr>
<tr>
<td>A颠amathophen</td>
<td>Diaz + Nordiaz Total: 900 ng/mL</td>
</tr>
</tbody>
</table>

Conclusion

The most significant finding in this case is the 10-OH-Carbazepine concentration of 180 μg/mL, which is greater than the highest known fatal level of 92 μg/mL.

The cause of death in this case was ruled oxcarbazepine and hydrocodeone intoxication with diazepam use, and the manner of death was suicide.

Case History

Presented in this case is a 67-year-old female with a history of depression, psychiatric hospitalization, and previous suicide attempts. The decedent was found lying supine in bed with a bottle of hydrocodeone in one hand and a can of soda in the other, next to a suicide note. Several other prescription medications, including oxcarbazepine, gabapentin, diazepam, quetiapine, tizanidine, and lorazepam were found at the scene.