## CASE REPORT

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# Timely Antemortem and Postmortem Concentrations in a Fatal Carbamazepine Overdose

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**ABSTRACT:** There are no published reports that include both timely antemortem and postmortem carbamazepine concentrations after massive overdose. We report a fatal overdose of carbamazepine with both timely antemortem and postmortem carbamazepine concentrations. Carbamazepine concentrations were 47.7 mcg/mL 2 h antemortem and 53 mcg/mL at 9 h postmortem. The slight rise in drug concentration may reflect continued absorption of the drug in the last 2 h before death. Postmortem carbamazepine concentrations drawn from a peripheral vessel in this patient appeared to reflect drug concentrations at the time of death.

**KEYWORDS:** forensic science, postmortem, carbamazepine, overdose, drug concentrations

There is limited literature on interpretation of postmortem carbamazepine concentrations and no reports evaluating such concentrations in the situation of a massive overdose (1). The value of having both timely antemortem and postmortem carbamazepine concentrations is to evaluate if any significant changes in blood concentrations occur postmortem. We report a fatal overdose of carbamazepine with both timely antemortem and postmortem carbamazepine concentrations.

### Case Report

A distraught 19-year-old female arrived in the emergency department claiming to have taken an overdose of carbamazepine and phenytoin 1 h prior to arrival. Her medical history included a seizure disorder for which she was prescribed carbamazepine 400 mg once a day, phenytoin 100 mg three times a day, and valproic acid 250 mg three times daily. Drug concentrations shortly after arrival (10 h antemortem) were carbamazepine 14.5 mcg/mL, phenytoin 5.5 mcg/mL, and valproic acid less than 4 mcg/mL. Blood for these drug concentrations was drawn from a peripheral vein in the left arm. The patient was lavaged and given 50 g of activated charcoal. She rapidly lost consciousness and was intubated, and mechanical ventilation was initiated. There was no evidence of aspiration and the lungs were clear. Approximately 6 h post-arrival the patient began to have discrete generalized tonic-clonic convulsions that ceased on their own without intervention. These seizures continued to increase in frequency to the point where there were seizures lasting 2 to 3 min. A sodium amobarbital infusion was begun. The patient's condition continued to worsen and at 9 h post-ingestion (2 h antemortem) a second set of drug concentrations was drawn. These revealed a carbamazepine concentration of 47.7 mcg/mL, phenytoin concentration of 4.6 mcg/mL, and valproic acid concentration of 76 mcg/mL. The patient's condition deteriorated with status epilepticus despite an increase in the amobarbital infusion. There was evidence of a metabolic acidosis and an EKG suggestion of a myocardial infarction. Between 10.5 and 11 h post-ingestion the patient suffered a brief period of bradycardia and then asystole. Resuscitation efforts were not successful, and all efforts at life support were stopped. Nine hours after death the body was prepared in the operating room for organ harvesting (i.e., cornea, cardiac valves, and tibia and fibula). Prior to organ harvesting a blood sample for postmortem evaluation was drawn from the left subclavian vien. The postmortem blood concentrations were Carbamazepine 53 mcg/mL, Phenytoin 3.2 mcg/mL, and amobarbital 1.5 mcg/mL. Autopsy revealed 24 softened tablets in the stomach. These were identified, as several remained recognizable, as 400 mg carbamazepine tablets by size, shape, and tablet imprint code. The stomach also contained approximately 1 quart of a liquid-activated charcoal solution.

### Laboratory Methods

Antemortem serum drug measurements were performed on an Ortho Clinical Diagnostics Vitros Chemistry Analyzer and were assayed within approximately 30 min of being drawn from the patient. This assay is based on an enzymatic heterogeneous competitive immunoassay format. The postmortem blood concentrations were measured on an Abbot Laboratories Diagnostics division TDX FLX analyzer and were assayed within one week of being removed from the patient. This assay utilizes a fluorescence Polarization Immunoassay.

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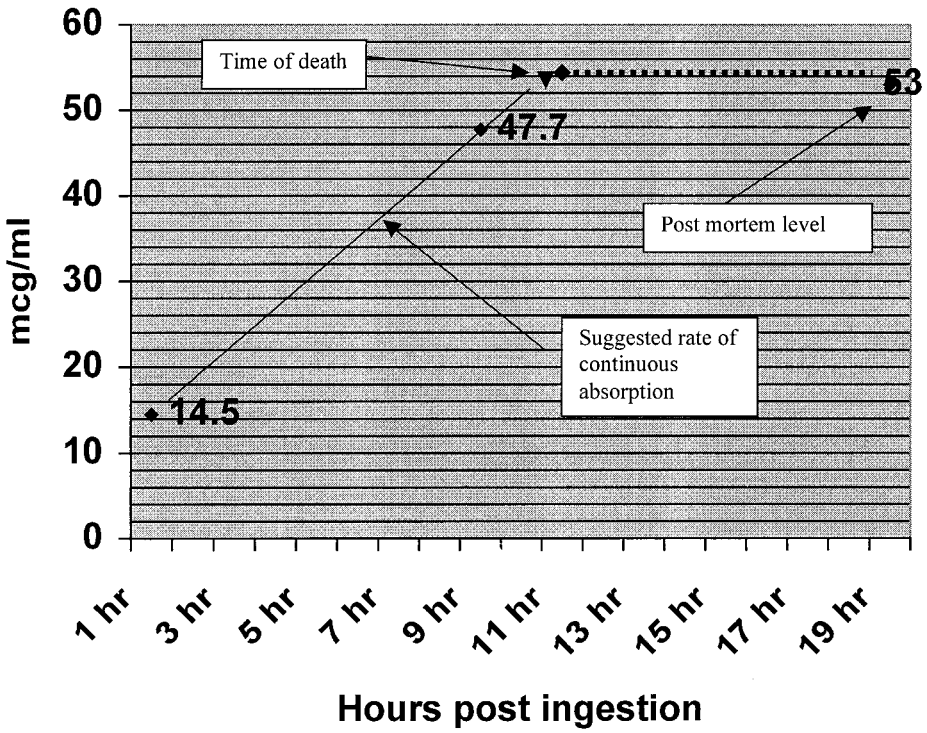


FIG. 1—*The slight rise in the postmortem carbamazepine concentration—the continued absorption of the drug in the last 2 h of life.*

## Discussion

There are very limited data available to help with interpretation of postmortem carbamazepine concentrations (1–3). An animal model of postmortem drug redistribution presented by Hilberg et al. suggested that drugs with apparent volumes of distribution of less than 3 L/kg did not display significant changes due to redistribution (3). In the model presented by Hilberg et al., postmortem carbamazepine concentrations displayed little or no change from antemortem concentrations (3). Phenytoin was not evaluated in this animal model but has an apparent volume of distribution of less than 1 L/kg. A case-series report following epileptic patients with therapeutic serum concentrations also suggested that there is limited or no postmortem redistribution of carbamazepine (1). However, there are several questions that remain. In the nine patients with carbamazepine concentrations presented by May et al., the mean antemortem sampling time was 32 h (1). This period of time allows for the development of confounding factors such as noncompliance by the patient with their medication and continued elimination of the carbamazepine prior to death. Additionally there were no patients in this group with massive ingestions typical of the overdose patient. There are no data to indicate if the large concentrations encountered in the fatal overdose might alter the interpretation of postmortem carbamazepine concentrations. Our patient, after a massive ingestion, showed no apparent fall in carbamazepine concentrations as would be suggested by May et al. The slight rise in the postmortem carbamazepine concentration may be explained by the continued absorption of the drug in the last 2 h of life (see Fig. 1). The rate of rise in carbamazepine concentration from 1 h post-ingestion to 9 h post-ingestion appears to be similar to the rate of rise between the 9-h post-ingestion concentration and the postmortem concentration, suggesting this may have been the concentration at the time of death. Alternatively, the slight difference in carbamazepine concentrations (antemortem and postmortem) may reflect variations seen when concentrations were measured with different methods in two separate laboratories.

Tomson et al. has investigated the potential differences in antemortem serum carbamazepine concentrations and postmortem whole blood carbamazepine concentrations in an animal model and found no significant difference (4). There did, however, appear to be a significant difference in antemortem serum phenytoin concentrations and postmortem whole blood phenytoin concentrations (4).

Redistribution of carbamazepine from a large depot in the stomach is unlikely because the postmortem sample was drawn from a peripheral vein (subclavian). In one study of postmortem redistribution by Pounder et al., the lowest levels were found in the femoral and subclavian vessels, suggesting these would represent the least change from antemortem levels (5). The decrease in phenytoin concentrations from the first measurement (5.5 mcg/mL) to second measurement (4.6 mcg/mL) that was 2 h antemortem is also seen in the postmortem concentration (3.2 mcg/mL) and may reflect a continued process just before death. In summary, this is the first report with both timely antemortem and postmortem carbamazepine and phenytoin concentrations after a massive overdose. Postmortem drug concentrations of carbamazepine and phenytoin drawn from a peripheral vessel appear to change very little from antemortem concentrations and may reflect drug concentrations at the time of death.

## References

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