



### K27 A Fatality Due to Lorazepam and Morphine Intoxication During Long Term Therapy

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The objective of this presentation is to report the concentration and distribution of both lorazepam and morphine in various specimens collected from a single fatality after documented chronic high dose treatment with both drugs for 17 days.

Content: A 48-year-old male was brought to the emergency room complaining of chest pain/discomfort due to an alleged assault he had sustained. Hospital records failed to document evidence of the assault, a CT scan of the chest showed a "spot" on the lower lobe of the left lung that was described as a small pulmonary contusion. He was subsequently admitted to hospital, intubated and dosed IV with morphine, lorazepam and propofol to sedation with plans to biopsy the lung for possible pathogens. The patient had a history of active HIV with a low CD<sub>4</sub> count. The hospital also documented pneumonia. The patient was on HIV medications and arrived at the hospital alert and talking. Multiple biopsies, tissue cultures and other studies with special stains failed to yield the pathogens usually seen in AIDS such as pneumocystis carinii and cytomegalovirus. Antibiotics were administered for the pneumonia and the patient remained on a ventilator for the entire course of his hospital stay. The original doses of morphine and lorazepam began at 2 mg per hour for both drugs and increased over the term of his hospital stay (37days) until they reached 20 mg IV per hour where they remained for his last 17 days of life. The orders regarding the increase of both drugs were to "titrate to sedation" or "to any signs of discomfort." The family had agreed to sign a do not resuscitate order, and on the last hospital day the patient was extubated and died approximately 5 hours later. Prior to extubation the dose of both lorazepam and morphine was not discontinued nor was it decreased. At autopsy the deceased was cachectic at 126 pounds and 6 feet in height. Autopsy findings were unremarkable as no cause of death could be determined, and no evidence of recent or remote blunt trauma was observed. Specimens obtained at autopsy were evaluated for the presence of drugs and alcohol. Positive toxicology results are listed in

**Table 1.**

	<b>Femoral Blood</b>	<b>Bile</b>	<b>Kidney</b>	<b>Spleen</b>	<b>Vitreous Humor</b>
Lorazepam	5.8 mcg/mL	44 mcg/mL	39 mcg/g	12 mcg/g	1.0 mcg/mL
Morphine	1.6 mcg/mL	6.6 mcg/mL	1.3 mcg/g	0.5 mcg/mL	
Metoclopramide	QNS	Positive	TNP	TNP	TNP
Trimethoprim	QNS	Positive	TNP	TNP	TNP

QNS – Specimen quantity not sufficient for analysis

TNP – Test not performed

The toxicology findings were remarkable for the presence of free lorazepam and free morphine at markedly elevated concentrations. The cause of death in this case was acute lorazepam and morphine intoxication and the manner of death is undetermined. Free lorazepam was quantitated using solid phase extraction with subsequent derivatization with MTBSTFA with 1% t-BDMCS and EI-GC/MS analysis in SIM mode. The LOD for lorazepam is 12.5 ng/mL with a linear range up to 400 ng/mL and a %CV of less than 10. The free morphine was quantitated by liquid:liquid extraction with subsequent derivatization with MSTFA and EI-GC/MS analysis in SIM mode. The LOD for morphine is 12 ng/mL with a linear range up to 1000 ng/mL. This case raises serious ethical concerns about the practice of comfort care for those patients who are not immediately terminal.

#### Lorazepam, Morphine, Fatality