K39 Postmortem Concentrations in a Suspected Nikethamide Death

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After attending this presentation, attendees will learn about nikethamide, its use and potential toxicity, as well as postmortem concentrations found in blood, urine, liver tissue, and brain tissue in a suspected nikethamide death case.

This presentation will impact the forensic community and/or humanity by primarily providing the forensic toxicology/pathology community with postmortem concentrations in various bodily fluids and tissues from a suspected death case for which no readily apparent levels have been previously reported.

The decedent in this case was a sailor on a transport ship traveling from South America to the United States. Shortly after leaving a South American port, the individual in this case was discovered dead in the ship's engine room. A search of the decedent's cabin did not reveal any evidence of drug use; however, an investigation of the crew disclosed that the decedent, along with a couple of friends, went ashore and returned to the ship shortly before it set sail. As part of the postmortem examination, bodily fluids and tissues were submitted for toxicological testing. These tests included assays for carbon monoxide, alcohols, common substances of abuse and therapeutic drugs. The findings of the screen tests on cardiac blood detected and identified nikethamide by gas chromatography/mass spectrometry (GC/MS). Further quantitative testing for nikethamide by gas chromatography with nitrogen- phosphorus detection found 32 mcg/mL in cardiac blood, 3.6 mcg/mL in urine, 22 mcg/g in liver and 2.6 mcg/g in brain tissue. Other than an incidental finding of caffeine no other findings of toxicological significance were detected.

Nikethamide is a central nervous system (CNS) stimulant that causes an increase in the respiratory rate through its direct action on the brain or by indirect action on the carotid chemoreceptor. Although it has no direct affect on the heart or the blood vessels, it can cause an increase in the heart rate and blood pressure. It has been used to treat respiratory and/or circulatory depression caused by central nervous system agents such as barbiturates, alcohol, opiates, etc., as well as cholinesterase inhibitors and carbon monoxide. Nikethamide has also been used in patients in shock, respiratory failure secondary to chronic obstructive respiratory disease, and cardiac decompensation and coronary occlusion. It is available as a powder and as a solution for oral and parenteral injection. The usual dose is 0.5 to 1 gram intravenously, intramuscularly or subcutaneously. It is well absorbed and metabolized partly to niacinamide then further metabolized to N- methylniacinamide.

Nikethamide has a narrow margin of safety. The CNS stimulant effects produced by nikethamide for respiratory therapy may lead to generalized seizures and potentially death. As a result, the use of nikethamide as well as other similar types of drugs termed analeptics is strongly discouraged. Not only is nikethamide discouraged from clinical use, it is banned by the World Anti- Doping Agency. Nikethamide is on the NCAA Banned Drugs list forbidding its use. It also appears on several lists of banned substances in horse racing.

With no available information on blood or serum concentrations associated with nikethamide therapy or toxicity, or information regarding a lethal dose, the determined values were compared to reported levels of similarly acting analeptic drugs such as doxapram and pentylenetetrazol. Average peak plasma concentrations following a therapeutic infusion of doxapram ranged from 2.6 to 4.1 mcg/mL, with signs of toxicity expected at levels exceeding 9 mcg/mL of doxapram plus its metabolite, 2-ketodoxapram. Peak plasma concentrations of pentylenetetrazol following therapeutic dosages were reported to range from 1.5 to 3.1 mcg/mL.

Nikethamide, Postmortem, Toxicology

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