K24 Demographic and Toxicological Profiles of 127 Decedents Testing Positive for Ephedrine Alkaloids

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Attendants will learn the basic profile of ephedrine-related deaths, as well as the relationship between blood ephedrine, blood norephedrine concentrations, and possible episodes of ephedrine toxicity.

This presentation will impact the forensic community by providing the substantial toxicological and pathological data needed to make informed diagnostic decisions about cause of death when ephedrine is detected by postmortem toxicological screening.

The relative safety of ephedra-containing dietary supplements is disputed, and the toxicology of ephedra-supplements remains poorly understood. Two theories have been advanced to account for purported episodes of ephedrine toxicity; (1) It has been suggested that humans may metabolize ephedrine to form norephedrine (phenylpropanolamine) which, in turn, may cause dangerous elevations of pulse and blood pressure; (2) It has been suggested that, when ephedrine-related toxicity occurs, it "results from accidental overdose often prompted by exaggerated off-label claims and a belief that 'natural' medicinal agents are inherently safe. " According to this theory ephedrine toxicity results from inadvertent overdosage, occurring when consumers ingested poorly produced supplements containing unpredictable amounts of ephedrine. Both theories are plausible, but evidence is lacking. Accordingly, a review of all autopsies performed in our Medical Examiner's jurisdiction was undertaken, from 1994 through 2000, where ephedrine or ephedrine-related compounds (E+) were detected in blood or urine drug screening. Methods: When available, urine samples were initially screened with the polyclonal EMIT test. When no urine was available, blood was screened using GC/MS. Following alkaline extraction, ephedrine, pseudoephedrine, and norephedrine were identified by gas chromatography with nitrogen-phosphorus detection. Samples were subsequently confirmed using full scan electron impact mass spectrometry. Other drugs were identified following a similar protocol. Drug concentration values in E+ cases, where trauma was the cause of death, were compared with values in E+ cases dying of all other causes. Results: A total of 127 cases were identified. The mean postmortem interval was 17.4 hours in the trauma group, and 18.4 hours in the non-trauma groups (not significantly different). The mean age for the 127 cases was 44.9 ± 1.2 years. Fifty-nine percent were Caucasian, 22.8% black, 10.2% Asian, and 3.9% Hispanic. Decedents were mostly male (80.3%). Thirty-three (25.9%) died of trauma. Mean blood ephedrine concentrations in trauma vs. non-trauma were not significantly different (1.27 mg/L, SD = 2.49 for trauma cases vs. 1.61 mg/L, SD = 2.47 for nontrauma cases, $p = 0.603$). Blood ephedrine concentrations were < 0.49 mg/L in 50% of the cases, and ranged from 0.07 to 11.73 mg/L in trauma victims and from 0.02 to 12.35 mg/L in non-trauma cases. Norephedrine (NE) was present in the blood of 22.8% (29/127) of all cases (mean of 1.81 mg/L, SD = 3.14 and in the urine of 36.2.% (mean of 15.6 mg/L, SD = 41.12). Pseudoephedrine (PE) was present in the blood of 6.3% (8/127). More than 88% (113/127) of all cases tested positive for drugs in addition to ephedrine alkaloids, the most common being cocaine or its metabolites, and morphine, each detected in the blood of 21.3% (27/127). Blood concentrations in E+ cases, where only ephedrine alkaloids were present, and E+ cases where cocaine and/or methamphetamine were present were not significantly different ($p = 0.231$). In only eight of the 127 cases (6%) was ephedrine the only drug detected in the blood. Conclusions: (1) Blood concentrations of E+ in trauma deaths completely overlap concentrations in non-trauma deaths and cannot, in isolation be used to identify the occurrence of ephedrine toxicity. This is exactly the same situation previously observed with cocaine and methamphetamine-related deaths. (2) Based on the high blood concentrations observed in this group of decedents, especially in those dying of trauma, it seems unlikely that variations in production and quality control could have much of an impact on toxicity, since the average doses contained in supplements are too low to account for the blood levels seen in this group of decedents. (3) Norephedrine was detected in the blood in only a quarter of all E+ cases, suggesting that demethylation of ephedrine does not occur to any great degree in humans, (4) blood concentrations in cases where ephedrine and illicit stimulants were both present were not significantly different, suggesting that actions of ephedrine and other stimulants are not synergistic.

Ephedrine, Norephedrine, Polydrug Abuse

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