K45 Fatal Intoxication Due to Trihexyphenidyl - A Case Report

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After attending this presentation, attendees will learn about trihexyphenidyl pharmacological effects, metabolism and poisoning, method of analytical detection, and autopsy findings.

This presentation will impact the forensic science community by noting that fatal poisoning with trihexyphenidyl is very rare, based on the literature data, especially when no other central nervous system depressants and/or significant pathological changes are taken into account.

Trihexyphenidyl (THP) is an anticholinergic agent with forensic toxicological interest due its frequent abuse and reported overdose, while fatal poisoning is rare. It is a potent anticholinergic drug used in the treatment of Parkinsonism and in the control of drug-induced extrapyramidal side effects. Its mode of action is preventing the effects of acetylcholine by blocking its binding to muscarinic cholinergic receptors at neuroeffector sites on smooth muscle, cardiac muscle, and gland cells, in peripheral ganglia, and in the central nervous system. Side-effects of THP include disturbance of recent memory, tachycardia, bradycardia, and can precipitate glaucoma in predisposed patients. THP- hydrochloride is well absorbed from the gastrointestinal tract producing average peak plasma levels at 1.3 h after single oral dose of 2 and 15 mg and reaching Cmax of 0.01 and 0.05 mg/l, respectively. The half-life time varies from 3.6 h up to 33 h, following multi-compartmental kinetics. THP undergoes extensive metabolism and hydroxy-THP was reported as the major metabolite present in plasma and urine. Ethanol and other central nervous system (CNS) depressants, such as anxiolytics, sedatives, and hypnotics, can increase the sedative effects of THP.

This report presents a case of a 59-year-old female with a history of paranoid disorder being treated in an outpatient program and who was found dead in the house where she lived alone. External examination of the body yielded no evidence of external injuries or violence. Autopsy findings revealed no marked pathological changes. Femoral venous blood, urine, bile, and gastric content were collected for toxicological analyses. Toxicological analysis based on gas chromatography-mass spectrometry (GC-MS) analysis revealed THP and its major metabolite (hydroxy – THP) in blood and urine. Ethanol was analyzed in femoral venous blood and urine by head-space gas-chromatography with a flame ionization detector (GC/FID).

Qualitative GC/MS analysis confirmed the presence of THP in blood and urine, hydroxy-THP in blood, urine and bile. The presence of these substances and other xenobiotics wasn't confirmed in gastric content. GC/MS quantitative analysis revealed THP concentration of 0.053 mg/L in femoral venous blood and 0.560 mg/L in urine. The blood and urine ethanol concentrations were 0.096 g/L and 0.100 g/L, respectively.

Based on these results and literature data the cause of death was determined to be THP poisoning. It is suggested that rare case of death associated with THP overdosage should be taken in conjunction with central nervous system depressants (benzodiazepines, ethanol) and/or with other pathological disorders. Thus, this case could not be supportive for this allegation. The circumstances of the case exclude homicide; however, these data are not sufficient to determine neither suicide nor accident as a manner of death.

Trihexyphenidyl, Fatal, Poisoning

 ** Presenting Author*