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**Postmortem forensic toxicology of selective serotonin reuptake inhibitors: a review of pharmacology and report of 168 cases.**

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This paper reviews the complex pharmacology of the new class of antidepressant medications exhibiting selective inhibition of serotonin reuptake. The four selective serotonin reuptake inhibitors (SSRIs) considered--fluoxetine, fluvoxamine, sertraline and paroxetine--can result in toxicity and death through contributing to serotonergic excess resulting in serotonin syndrome, inhibiting the metabolism of other centrally acting drugs, leading to accumulation of toxic concentrations, and exerting complex vasoactive effects on the vascular smooth muscle. This latter feature is of particular concern in patients with preexisting heart disease. An analytical method involving isolation of the drugs by liquid/liquid extraction at alkaline pH into n-butyl chloride, and analysis by gas chromatography/mass spectrometry (GC/MS) is described, together with some of its limitations. Toxicologic and cause and manner of death data were examined in 60 deaths involving fluoxetine, 5 involving fluvoxamine, 75 involving sertraline, and 28 involving paroxetine. Deaths

involving drug toxicity were generally a result of ingestion of multiple drugs, and in only a small number of the cases was death attributed principally to the SSRI involved. The potential for drug interactions between members of this class of drugs is discussed as well as their metabolites and a variety of other therapeutic and abused drugs which can contribute to their toxicity. In the absence of other risk factors, the lowest concentrations determined to have resulted in death were 0.63 mg/L for fluoxetine, 0.4 mg/L for paroxetine, and 1.5 mg/L for sertraline. We had insufficient data to make even this crude assessment for fluvoxamine. Drug-induced elevation of serotonin concentrations may be a significant risk factor for patients with atherosclerotic cardiovascular disease (ASCVD). Other factors including preexisting disease and the presence of other drugs and their pharmacology need to be carefully considered before determining the appropriate cause and manner of death in these cases.

Publication Types:

- Review
- Review of Reported Cases

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