



K4 Prevalence of Desmethylsertraline in Postmortem Tissue Samples

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After attending this presentation, attendees will better understand the distribution of desmethylsertraline in postmortem tissue samples and its relationship to the study of postmortem toxicology.

This presentation will impact the forensic science community and analysts/pathologists involved in postmortem undertaking toxicology investigations by making them more aware of the levels of this drug that may be found in tissue samples.

Aims: The aim of this poster presentation is to inform the forensic toxicology community about levels of the primary metabolite, desmethylsertraline, of the selective serotonin re-uptake inhibitor (SSRI) sertraline found in postmortem tissue samples. Levels of this particular metabolite are referenced to parent drug/ metabolite in blood and tissue postmortem samples.

Methods: In 2006, over 890 cases were submitted to the Forensic Toxicology Laboratory, Center for Forensic Sciences in Syracuse, NY (CFS) by the Medical Examiner's Office. In each of the cases, analyses of blood/vitreous humor, tissue (liver), and urine were performed for volatiles (GC-FID), drugs of abuse (ELISA), and weak acid neutral/ bases (GC-MS). Tissue samples were analyzed as 1: 4 homogenates of the original sample. Where sertraline was confirmed by GC-MS amongst other confirmed drugs (some 23 cases) in blood and tissue samples, quantitative analysis of setraline/ desmethylsetraline was performed employing a liquid-liquid sample extraction (n-butyl chloride/ ammonium hydroxide/ 0.1 M sulfuric acid) using certified reference standards for calibrators and controls. Chromatographic analysis was performed by GC-MS/ GC-NPD (internal standard: Mepivacaine). This was carried out according to the standard operating procedure currently in use at CFS.¹ Data from the analysis of setraline/desmethylsetraline in blood/tissue samples were collected and assessed. This information (along with other quantified drugs) was used to offer an interpretation to the office of the Chief Medical Examiner for Onondaga County to assist with the determination of cause and manner of death in forensic investigations.

Results: In this presentation, data from the sertraline/ desmethylsetra- line analysis of the postmortem samples are presented. The range of desmethylsertraline in postmortem tissue samples was 0.78 mg/kg to 402 mg/kg. The corresponding range of the parent was 0.04 mg/kg to 188mg/kg. Blood levels were reported as 0.05 mg/ L to 1.51 mg/ L desmethylsertraline and 0.03 mg/L to 0.45 mg/L sertraline, respectively. In several cases i.e. # 5, 10, 14, 16, 19, and 21, respectively the levels of the primary metabolite reported in tissue samples reached 402, 51, 50, 70, 34, and 242 mg/kg, respectively. In cases like these drugs such as bupropion/ metabolite, fluoxetine/ metabolite, and tricyclic antidepressants were also present with and without the presence of ethyl alcohol.

Conclusions: Sertraline is metabolized in the liver by CYP2D6 to the primary metabolite desmethylsetraline. This hepatic isoenzyme (2D6) of the cytochrome P450 group is also involved in the oxidative metabolism of other drugs. It has been reported that desmethylsetraline may accumulate in plasma due to its slow elimination ($t_{1/2}$ 62-104 hrs).² In the cases presented this may be a similar effect occurring (i.e., accumulation) in the liver tissue giving rise to excessive figures. It has been reported that desmethylsetraline has only 10-20% of the pharmacological activity of the parent drug,² at these levels it is pertinent to ask what effect this compound on the toxicity and cause of death and its impact on postmortem drug re-distribution.

Based on data presented, toxicologists involved in the analysis of sertraline/desmethylsertraline in postmortem cases (especially tissue samples) should review all the relevant information pertaining to these cases before offering advice/ interpretation. High levels as seen in the presented cases may skew the interpretation as to a possible overdose in the assessment of cause and manner of death.

References:

- ¹ Forensic Toxicology Laboratory Standard Operating Procedures Manual, Center For Forensic Sciences, Syracuse NY (2006).
- ² R.C. Baselt, Disposition of Toxic Drugs and Chemicals in Man 5th Ed (2000).

Desmethylsertraline, Chromatography, Toxicology