K5 A Quetiapine-Linked Fatality

Patricia C. Studts, BS, Henry C. Nipper, PhD, and Richard Baltaro, MD, PhD, Creighton University Medical Center, Forensic Toxicology Laboratory, 601 North 30th Street, Omaha, NE 68131*

The goal of this presentation is to present a case of quetiapine overdose which resulted in a fatality and review the pharmacokinetics and adverse reactions to this drug, which has been assumed to be relatively non-toxic.

Few case reports of fatalities involving this drug have been published. This report will impact the forensic community and/or humanity by adding to the literature, and may assist forensic toxicologists and others in interpreting similar findings.

A 37-year-old white male with a history of depression was found dead at home. His current medications were listed as quetiapine, buspirone, and sertraline. Investigators estimated that approximately 96 quetiapine tablets were not accounted for, including one new bottle of 30 (300 mg) tablets. The older bottles contained 200 mg tablets. The Forensic Toxicology Laboratory received urine, blood, and vitreous humor. Cocaine and its metabolites, quetiapine metabolite, and nicotine were detected in the urine by GC-FID/NPD and by ion-trap GC-MS. Ethanol was also found in the urine by an ADH enzymatic assay. Blood ethanol was 0.029 g/dL. In the heart blood, quetiapine was 32,100 ng/mL, cocaine was 53 ng/mL, and benzoylecgonine was 819 ng/mL. The quetiapine and cocaine quantitations were performed at MedTox Laboratories.

Quetiapine (Seroquel) is classified as an "atypical" antipsychotic drug. Baselt (1) describes it as "a dibenzothiazepine derivative developed in 1993 for use as a neuroleptic agent." Its defined daily dose is 400 mg/d, has a half-life of 5-8 hours and is typically found in blood in the range of 195-632 ng/mL when used therapeutically (1).

The metabolite found in the decedent's urine is only one of approximately 20 metabolites of the parent drug. Metabolic pathways include sulfoxidation, carboxylic acid formation on the ethoxyethyl side chain, as well as hydroxylation in the 7 position. The 7-hydroxy metabolite does not apparently have significant pharmacologic activity.

According to the PDR (2), the clinical trial databases reported 6 overdoses with ingestions ranging from 1200–9600 mg with no fatalities. The 9600 mg overdose was associated with hypokalemia and first-degree heart block. Mortality cited for overdose of hospitalized patients is cited as 0.5% for the neuroleptic class of drugs (3). Overdose of these drugs is cited as similar to TCA overdose, but less toxic. So-called 'atypical' agents cause ECG abnormalities, but other case reports allege that quetiapine was less toxic than other atypical antipsychotic drugs. One series reports seizures, hypotension, QTc prolongation, and sedation to the point of requiring mechanical ventilation, similar to those effects seen with clozapine and olanzapine overdose (4).

Plasma concentrations, unhelpful in clinical management, may be useful in postmortem considerations. Dart (3) cites typical therapeutic concentrations of quetiapine of 190-630 ng/mL overlapping considerably with lethal blood concentrations of 240-4000 ng/mL. Postmortem redistribution, if any, remains unreported at this time for quetiapine.

References:

1) Baselt, R.C., Disposition of Toxic Drugs and Chemicals in Man, 6th edition, Foster City, CA; Chemical Toxicology Institute, 2002.
2) Physicians' Desk Reference, 53rd edition, Montvale, NJ, Medical Economics Co., 1999.
3) Dart, Richard C., editor, Medical Toxicology, 3rd edition, Philadelphia, PA, Lippincott, Williams & Wilkins, 2004.
4) Trenton, A, Currier, G, Zwemer, F., Fatalities Associated with therapeutic use and overdose of atypical antipsychotics, CNS Drugs, 2003; 17(5): 307-324.

Quetiapine, Fatality, Overdose

Copyright 2005 by the AAFS. Unless stated otherwise, noncommercial *photocopying* of editorial published in this periodical is permitted by AAFS. Permission to reprint, publish, or otherwise reproduce such material in any form other than photocopying must be obtained by AAFS. ** Presenting Author*