K20 Death Attributed to Quetiapine Overdose

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This is a case report where the cause of death was attributed to quetiapine overdose. There is little literature regarding minimum lethal concentrations of this drug, and presentation of this case may help with compiling such data.

Quetiapine (Seroquel) is an antipsychotic drug belonging to a new chemical class, the benzothiazepine derivatives. We present the first case of quetiapine overdose causing death reported in the Province of British Columbia.

A 56-year-old Caucasian female was found unresponsive on the bedroom floor. The deceased's medical history included bipolar disorder and severe obsessive-compulsive disorder. A full autopsy was performed approximately 32 hours after death. Significant findings included evidence of localizing interstitial pneumonitis. There was no evidence of underlying chronic lung disease or of an aspiration event. Specimens were collected for toxicological analysis.

The blood specimen was initially subjected to a thorough qualitative analysis. Basic drugs were screened for by liquid-liquid extraction followed by GC-NPD and GC-MS electron impact detection. Acidic and neutral drugs were screened for by liquid-liquid extraction followed by HPLC-DAD. Volatiles were assayed by GC-FID. Qualitative analysis identified acetaminophen, carbamazepine, lorazepam, clonazepam, diphenhydramine and quetiapine. The concentration of acetaminophen was less than 10 mg/L, carbamazepine was 8.5 mg/L (36 umol/L), lorazepam was 0.05 mg/L (0.16 umol/L), and clonazepam was 0.027 mg/L (0.086 umol/L). With the exception of acetaminophen, which is less than therapeutic, these concentrations are consistent with levels achieved therapeutically. The concentration of diphenhydramine was 3.7 mg/L (14 umol/L); although this is greater than the therapeutic range (0.010 – 0.10 mg/L) it is less than the commonly accepted minimum lethal level of 8 mg/L.

Quetiapine was assayed in biological specimens as follows: briefly, to each tube add 1 mL of appropriate fluid, 50 uL of Internal Standard (Hydroxytriazolam 0.01 mg/mL), 1 mL of saturated sodium carbonate solution was added, and extracted into 6 mL n-butyl chloride. The extract was concentrated under nitrogen, reconstituted and derivatized with 50 uL of MTBSTFA, heated at 60^{o}C for 30min, and 1 uL was injected into an Agilent model 5890 gas chromatograph coupled to a NP Detector using a 12 m Ultra-1 (0.33um film thickness) capillary column (Agilent). The initial temperature was 260 ^{o}C and increased 10 ^{o}C/min for one min then 50 ^{o}C/min until 300 ^{o}C, then held for 2 min. The concentration was measured by comparison of peak height ratios of quetiapine to that of hydroxytriazolam against a standard curve. Linearity was observed up to 2.0 mg/L. Samples with concentrations exceeding the linearity were diluted.

Elevated concentrations of quetiapine were found in blood 7.20 mg/L (19 umol/L) and in vitreous fluid 0.93 mg/L (2.4 umol/L). Quetiapine is well absorbed from the gastrointestinal tract and reaches peak plasma levels 1.5 hours after oral administration. The drug's halflife ranges from 2.7-9.3 hours. The volume of distribution of quetiapine is 10 L/kg and it is 83% bound to plasma proteins. The specimen in this case were approximately 7 fold greater than the reported therapeutic range (0.1 – 1.0 mg/L), assuming the red cell serum distribution ratio is 1:1, and is comparable to that reported in the literature to be associated with serious/potentially fatal toxicity. The cause of death was ascribed to solely quetiapine overdose.

Quetiapine, Overdose, Fatal

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