CASE REPORT

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High Haloperidol Concentrations in a Traffic Suicide

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ABSTRACT: High concentrations of haloperidol are seen in a psychiatric patient who ran from a health care facility into traffic. Haloperidol concentrations were found to be 1.2 mg/L in heart blood, 2.7 mg/L in brain, and 10.8 mg/L in liver. No other drugs were detected.

KEYWORDS: toxicology, psychiatry, haloperidol, suicide

Haloperidol (Haldol®) is a butyrophenone derivative that was synthesized in 1958 and first marketed in the United States in 1967. It is an effective antipsychotic agent often used interchangeably with the phenothiazines. It is administered orally or by intramuscular injection as lactate in single doses of 0.5 to 5 mg and daily doses of 100 mg and more [*1*].

This is an unusual case involving an individual with extraordinarily high tissue concentrations of haloperidol who died of other causes.

Case History

The subject of this report was a patient at a psychiatric hospital for 5 weeks. His admission diagnosis was major depression. After psychiatric examination, he was classified as schizophrenic. He was a 29-year-old male weighing 207 lbs (94 kg). He was treated during hospitalization with haloperidol, 2 mg four times a day. He also received trihexyphenidyl, 2 mg twice a day and hydroxyzine, 25 mg as needed.

Upon discharge, the patient was prescribed haloperidol, 10 mg twice a day, oxazepam, and trihexyphenidyl. His discharge summary indicated that he feared losing control and consequently harming himself and others. He reportedly had recurring impulsive suicidal thoughts.

The patient voluntarily entered a county operated mental health facility six weeks after discharge from the hospital at the suggestion of his social worker. He had reportedly threatened to take the life of the social worker and himself.

At the county facility, the patient was given three doses of haloperidol: 5 mg at 1420 h, 10 mg at 1700 h, and 5 mg at 1850 h.

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At 1930 h, the chart noted "PRN Haldol not effective." Until then it appears from the chart that he had been sitting quietly, although he had again mentioned suicide.

One hour after the last dose of haloperidol, the patient ran from the facility into the path of a truck. The truck was able to avoid the patient, who struck the side of the pickup with his fists before returning to the curb. Moments later, he jumped to his death in front of a tractor-trailer.

Autopsy findings were consistent with the injuries from the incident and no other significant findings were noted.

Toxicology

Samples of heart blood, liver, and gastric contents were screened for drugs by ultraviolet spectroscopy and thin-layer chromatography. Haloperidol was detected by thin-layer chromatography. No other drugs were detected.

Tissue samples were analyzed for haloperidol by gas chromatography employing a nitrogen/phosphorous detector. Concentrations of haloperidol are shown in Table 1.

Method

One millilitre of blood or one gram equivalent of homogenized tissue is added to a sixteen-by one hundred-millimetre silanized glass screw cap culture tube along with one millilitre of saturated sodium borate and the internal marker (alfentanyl). Add 5 mL of *N*-butyl chloride and shake 1 min. Centrifuge and transfer the organic layer to another silanized culture tube containing 3 mL of 0.5*N* sulfuric acid (H_2SO_4) and shake for 1 min. Centrifuge and aspirate the organic layer. At this point, for postmortem or "dirty" samples, wash with an aliquot of *N*-butyl chloride, centrifuge, and aspirate the organic layer. Make the aqueous basic with a few drops of saturated sodium hydroxide (NaOH) and extract with 5 mL of *N*-butyl chloride. Centrifuge and transfer the organic layer to a rinsed, silanized conical tube and evaporate just to dryness. Reconstitute with 25 μL of ethanol and inject 8 to 10 μL into the gas chromatograph.

The instrument used was a Shimadzu GC-7A equipped with a nitrogen/phosphorous detector and a Quadrex 25-m (0.25-mm inside diameter) methyl silicone bonded phase capillary column. The oven temperature was 260°C. The injection split ratio was approximately 30:1.

Results and Discussion

Analytical results are presented in Table 1. The blood, brain, and liver concentrations are the result of two separate determinations.

A single 10-mg oral dose resulted in a peak serum concentration of 0.003 mg/L at 5 h [*2*]. In patients receiving an average daily dose of 5.7 mg (range 1 to 90) of haloperidol, the mean steadystate serum concentration was 0.006 mg/L (range 0.0005 to 0.121). The half-life of the drug was observed to range from 14 to 41 h [*3*].

It has been established that a wide variability exists in the absorption and metabolism of haloperidol. Patients given the same dosage (mg/kg) may achieve a broad range of plasma or serum concentrations at steadystate. One report [*4*] found that patients with plasma haloperidol concentrations between 5 and 14 ng/mL (0.005 and 0.014 mg/L) showed greater improvement after 14 days of haloperidol therapy than those outside that range. Mavroidis et al. [*5*], using a similarly designed study, suggested a therapeutic window for plasma haloperidol of 4.2 to 11 ng/mL (0.004 to 0.011 mg/L) by the end of a 14-day treatment. This study also showed greater response in patients within this suggested therapeutic range than below or above that range. Accepting those steadystate concentrations, the blood concentra-

TABLE 1—*Concentrations of haloperidol in postmortem tissue.*

Blood	1.2 mg/L
Brain	2.7 mg/L
Liver	10.8 mg/L
Gastric (as submitted)	2 mg total

tion in this case would be considered at least 80 times therapeutic and not representative of the dosage given at the county facility shortly before death. The total dosage taken is not known, however, since the patient was self-medicated on an outpatient basis and had partially filled prescription bottles in his possession at the time of admission. This case emphasizes the importance of the case history and circumstances of death when attempting to interpret analytical findings in forensic toxicology.

References

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