A Sertraline-Intoxicated Driver

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Abstract

Sertraline is a selective serotonin reuptake inhibitor (SSRI) that is chemically unrelated to other SSRIs, tricyclic antidepressants, and other currently available antidepressant medications. This report documents a case of driving under the influence of sertraline. The subject was involved in a motor vehicle accident. Upon contact by law enforcement, the subject was confused and could neither stand nor walk. The officer noted mumbled speech, droopy eyes, and that the subject seemed sleepy. No alcohol was present in the vehicle, and no odor of alcohol was detected on the subject's breath. The subject was determined to be under the influence of some intoxicating substance. Toxicological analysis revealed only the presence of sertraline. Sertraline was extracted from the blood sample utilizing solid-phase extraction and identified and quantitated by gas chromatography-mass spectrometry. The blood sertraline concentration was determined to be 1285 μg/L.

Introduction

Sertraline hydrochloride (Zoloft®) is a selective serotonin reuptake inhibitor (SSRI) used in the treatment of symptoms of depression. (1) Sertraline has a novel chemical structure, the chemical name (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine hydrochloride, and is chemically unrelated to tricyclic antidepressants or other commonly available antidepressant medications. It is available for oral administration in scored tablets containing 25, 50, or 100 mg of sertraline. The normal dosage of sertraline is 50–200 mg a day, with the initial dose at 50 mg once daily and a maximum dose up to 200 mg once daily. (2) In controlled studies (3,4), sertraline doses up to 200 mg did not appear to cause significant sedation and did not interfere with psychomotor function. However, subjective tests indicated an increase in perceived sedation at doses of 100 mg or more. Reports of drowsiness appeared to occur ~2 times as frequently after sertraline doses at 25, 50, and 75 mg and 3 times as frequently after a 100-mg dose than after placebo. (5) Single-dose studies of 50, 100, and 200 mg resulted in mean plasma (Cp,max) concentrations of 9.5, 16, and 56 μg/L, respectively, at times (Tmax) of 6–8 h. Patients on chronic daily doses of 100, 200, or 300 mg achieved steady-state plasma sertraline concentrations averaging 32 (range 20–48), 91 (range 40–187), and 206 (range 99–309) μg/L, respectively. (6)

In a previous study (3), single doses of sertraline in volunteers caused changes in the quantitative pharmaco-electroencephalogram, suggesting antidepressant and anxiolytic actions with sedative potential evident only at doses of 200 mg or more. Sertraline did not impair psychomotor performance, including simulated car driving, and overall seems neither stimulating nor sedating. A later study (4), done in 1995, also supports these findings with results that suggest sertraline does not adversely affect psychomotor performance and may even enhance it in mild to moderately depressed patients. Although psychomotor performance was not affected, subjective tests indicate an increase in reports of perceived sedation and drowsiness at doses of 100 mg or more (3,5), whereas sertraline at 200- and 400-mg doses caused dissociative changes suggesting a sedative effect compared with placebo (3).

Our investigation of literature identified only one reference (7) of a sertraline driving under the influence charge, and it was in the form of a letter to the editor. An individual was arrested for DUI after being stopped for speeding and the officer saw an unopened bottle of sertraline on the passenger seat. The charges were dropped after his physician submitted a letter stating that sertraline was not an intoxicant. Concern was expressed that the misinformation of law enforcement is a serious problem causing undue harm and emotional distress to people on this medication. The letter to the editor did not indicate that any toxicological studies were performed.

Case History

Law enforcement was notified of a motor vehicle accident. The responding officer arrived on the scene of the accident at 1359 hours. The vehicle was westbound and rear-ended a vehicle that was stopped at a red light. The female subject reported it...
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was very bright, she was upset about being involved in a wreck, and that her husband was leaving her. The officer asked if she had been drinking, and the subject stated she had consumed 1 beer (time of ingestion unknown) and had also taken 8–10 tablets of unknown strength of sertraline, for which she had a prescription. She communicated that she knew the normal dose was not 8–10 tablets, but she “just wanted to be happy”. Upon further investigation, the husband reported that the subject could possibly have taken anywhere from 30 to 50 tablets at the residence. The subject was reported by law enforcement to be confused, unaware of her location, and unable to walk. Her eyes were droopy, and her speech was mumbled. She reported that she gets this way when she has a single beer and mixes it with her medication. The subject was then transported to a hospital where she gave consent to a blood draw for toxicological analysis. The blood was collected at 1541 hours, and the medical staff decided to admit the subject for observation and treatment because of the amount of drug residue that was present in her stomach.

Experimental

Materials

ZSDAU020 Clean Screen extraction columns were purchased from United Chemical Technologies, Inc. (Bristol, PA). Sodium acetate (trihydrate), glacial acetic acid, methanol, hexane, methylene chloride, isopropanol, and ammonium hydroxide were all analytical grade and obtained from Fisher Scientific. Alphaprodine and sertraline standards were obtained from Alltech.

Sample preparation

A calibration curve was prepared by adding the appropriate amounts of internal standard (alphaprodine) and working stock sertraline solutions to labeled tubes and adding 1 mL of drug-free human blood. To 1-mL case samples, the internal standard was added. To each tube, 3 mL of 0.1M acetate buffer (pH 4.5) and 3 mL DI water were added; the tubes were then mixed/vortex mixed and left to stand for 5 min. The samples were then centrifuged for ~10 min at ~2000 rpm. The supernatant was decanted to a clean tube.

Extraction

The extraction was carried out using a Visiprep vacuum manifold. The extraction columns were prepped with 3 mL methanol, 3 mL DI water, and 3 mL 1M acetic acid. The columns were not allowed to dry and the vacuum adjusted to allow the sample to drip through at a rate of ~1 mL/min. After all the sample had passed through, the vacuum was increased and the columns washed with 3 mL 1M acetic acid, 3 mL DI water, 3 mL hexane, and 3 mL methanol, then dried for ~5 min at full vacuum. The sertraline was eluted from the column by gravity into clean, labeled test tubes. The eluate was then dried under a gentle stream of nitrogen at ~40°C. The tubes were allowed to cool to room temperature and reconstituted in 150 µL of ethyl acetate and injected into the gas chromatograph–mass spectrometer (GC–MS).

Instrumentation

The GC–MS system consisted of an Agilent 6890 GC and 5973N MS. The GC was equipped with a Restek Rtx-1 MS 15-m x 250-µm x 0.25-µm column. Helium was used as the carrier gas. The injection port was kept at 250°C, and 2 mL of sample was injected under splitless conditions. The initial temperature of the GC oven was 80°C for 1.0 min, ramped to 300°C at 30°C/min with the final temperature held for 0.67 min with a total run time of 9 min. The MS was operated in the selected ion monitoring mode, and the ions collected were *274, 159, 262 for sertraline and *172 and 187 for alphaprodine (*quantitation ions).

Results and Discussion

The submitted blood sample was analyzed for the presence of ethyl alcohol and common acidic, neutral, and basic drugs. The results of the examination revealed only the presence of sertraline and its metabolite, N-desmethylsertraline. The concentration of sertraline was determined to be 1285 µg/L. The N-desmethylsertraline was not quantitated because of the unavailability of a standard. However, the apparent parent to metabolite ratio, based upon peak height, was 10:1.

Although no ethyl alcohol was identified upon toxicological analysis, the time difference between the accident to the time of the blood draw, 1359 and 1541 h, respectively, could explain the absence of ethyl alcohol in the blood due to metabolism. The subject stated she only consumed one beer.

The subject also claimed that the sun was bright. Pupil size may increase in a dose-dependent fashion, as is expected from administration of higher doses of antidepressants (8). Studies have shown that this pupillary effect may be exacerbated by the use of sertraline. It was found that although there was a slight trend toward a reduction on pupillary diameter with placebo, highly significant pupil dilation was noted at all sertraline dosage levels (100, 200, and 400 mg) (9). Whereas 100 mg sertraline tended to improve overall psychometric performance, 200 and 400 mg sertraline produced deterioration. Higher doses of sertraline (200 and 400 mg) produced deterioration in psychophysiological memory changes as reflected by attention, concentration, and complex reaction tests. In a study of 31 overdosed patients averaging 31 years of age with an average acute dosing of 1109 mg, plasma sertraline concentrations averaged 245 pg/L (median concentration: 89 µg/L, SD ± 324) at a mean time of 4.8 h postingestion (10). All patients survived the event, after manifesting symptoms that included vomiting, lethargy, and ataxia.

The measured sertraline concentration in this case was ~6 times greater than that normally found in chronic high-dose therapy. Although previous studies showed therapeutic doses of sertraline had no psychomotor impairment, this case demon-
strated that at high concentrations, psychomotor impairment would occur.

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References


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