CASE REPORT

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Fatal Verapamil Poisoning

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ABSTRACT: A case of fatal verapamil poisoning is reported. The pathologic and toxicologic findings are discussed.

KEYWORDS: toxicology, verapamil, poisons, overdose

Verapamil (Isoptin®, Calan®) is a synthetic papaverine derivative, first introduced in 1962 as an antianginal agent. It is a calcium channel blocker which has a profound effect on the cardiovascular system. It is commonly used in managing angina, cardiac arrhythmias, and hypertension. Only four published reports of fatal verapamil poisoning were found in a review of the English language literature [*1-4*]. As the use of verapamil is increasing, the number of patients at risk from accidental or deliberate poisoning is likely to increase. A fatal self-poisoning with verapamil is reported.

Case History

The decedent was a 70-year-old white female whose past medical history was remarkable for severe mental depression and hypertension. She had a history of two previous suicide attempts; one attempted drowning and one attempted drug overdose. Apparently she was in her usual state of health the evening antemortem when she retired early to her bedroom at 6 p.m. The next morning, at 7 a.m., her husband found her dead in bed. The local medical examiner was summoned. A search of the house revealed 40 medication containers, each labeled with the decedent's name. Fifteen different oral medications were found: Dalmane® (fourteen containers), Ludiomil®, Xanax®, Trilafon®, Fioricet®, Ascriptin®, Slow-K®, Darvocet-N 100®, phenergan®/promethazine, Trancopal®, Ornade®, Logan®, Quinamm®, Amphogel® antacid, and Titralac® antacid. No antihypertensive medications were found in the house. The local medical examiner assumed jurisdiction of the body and referred the case to the Office of the Chief Medical Examiner for an autopsy.

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Autopsy Results

The body was 159 cm (62.5 in.) long and weighed 68.1 kg (150 lbs). There was no evidence of recent trauma either externally or internally. There was no significant fluid accumulation or adhesions in the pleural, pericardial, or peritoneal cavities. The heart weighed 330 g. It was grossly and microscopically unremarkable. The coronary arteries had no significant atherosclerotic disease. The lungs weighed 980 g combined. They were grossly unremarkable and microscopic examination revealed only vascular congestion and mild pulmonary edema without significant inflammation. The liver weighed 1650 g. Microscopically, there was vascular congestion as well as mild portal fibrosis and chronic inflammation. There was a rare focal collection of acute inflammatory cells and necrotic hepatocytes. The pancreas, spleen, and adrenal glands were unremarkable. The kidneys contained mild to moderate arterionephrosclerosis. The brain weighed 1250 g. It was grossly and microscopically unremarkable. The stomach contained approximately one cup of dark-green liquid with small tan-brown flecks of solid material. The mucosa was intact. The remainder of the gastrointestinal tract was unremarkable.

Toxicological Findings

Postmortem blood was examined for ethanol and other volatiles, salicylates, phenytoin, and organic neutrals; none was detected. The blood contained 7 mg/L of verapamil, 2 mg/L of butalbital, and 0.2 mg/L of flurazepam. The verapamil, norverapamil, and flurazepam were identified using gas chromatography-mass spectrometry.

Upon investigation of the decedent's medical record, it was found that her antihypertensive medication was switched from Ser-Ap-Es to verapamil one month antemortem. She was given 100 80-mg tablets of verapamil and instructed to take one-half tablet three times a day (t.i.d.). Three weeks antemortem the dose was decreased to one-half tablet twice a day (b.i.d.) because of headaches.

Discussion

Verapamil causes an inhibition of the slow inward cell-membrane current of calcium ions. This block of slow calcium channels leads to a suppression of both spontaneous sinoatrial node activity and rhythmical discharge in the atrioventricular node, a slower conduction in specialized conducting tissues, a decrease in myocardial contractile force, and profound smooth-muscle relaxation. Therefore, the side effects among others consist of hypotension, sinus bradycardia, and atrioventricular conduction disturbances and can lead to fatal outcome in cases of intoxication [*5*].

A single 80-mg oral dose of verapamil produces a peak plasma concentration averaging 0.039 mg/L (range 0.030 to 0.125) occurring between 0.5 to 3 h after ingestion [*6*]. A single 120-mg oral dose results in a peak plasma concentration averaging 0.219 mg/L (range 0.142 to 0.262) occurring between 1.4 and 2.5 h after ingestion [*7*]. An intravenous infusion of 13 to 16 mg of verapamil given over 3.3 to 5.3 min results in plasma concentrations of 0.274 mg/L at 2 min after the infusion and 0.115 mg/L at 10 min [*8*]. In patients receiving long-term oral therapy with 480 mg of the drug daily, the average peak plasma concentration 1 h after a 160-mg dose is 0.355 mg/L [*9*]. The biologic half-life appears to be 3 to 7 h in adults [*7*]. About 70% of both oral and intravenous doses of verapamil are excreted by the kidneys and about 16% in the stool over a five-day period [*10*]. The urine contains only 3 to 4% of the dose as unchanged drug and about 6% as norverapamil [*11*].

There are a number of published reports of nonfatal verapamil poisoning. Patients usually exhibit nausea, weakness, dizziness, bradycardia, hypotension, and atrioventricular block. Only four published reports of fatal verapamil poisonings were found in a review of the En-

TABLE 1—*Tissue concentrations of verapamil in three of the deaths.*

Verapamil Concentration, mg/L			
Blood	Liver	Kidney	Gastric Contents
4.0	13	10	0
8.8	165	28	590 mg
5.9	55	20	3 mg

glish language literature [*1-4*]. The blood concentrations of verapamil in these four cases were 3.0, 4.0, 5.9, and 8.8 mg/L. The case with the 3.0-mg/L concentration was obtained from a blood sample obtained 12 h after admission [*3*]. Additional tissue concentrations were obtained in three of the deaths (see Table 1).

In our case, given the markedly elevated blood verapamil concentration (7.0 mg/L) and the absence of other significant postmortem findings, the cause of death was attributed to verapamil poisoning.

Conclusions

We herein report a case of fatal verapamil poisoning. This case illustrates two important points. First, it illustrates the potential fatal toxicity of verapamil. Verapamil is being increasingly used in managing angina, cardiac arrhythmias, and hypertension, and the number of patients at risk for deliberate or accidental poisoning is likely to increase. Second, this case illustrates the need for a complete toxicologic evaluation in all forensic science cases. No container of the fatal medication was found in a search of the decedent's house; it was only after receiving the toxicology report that a history of verapamil use for hypertension was obtained.

Addendum

After submission of this manuscript another case of fatal verapamil poisoning appeared in the literature. (Crouch, D. J., Crompton, C., Rollins, D. E., Peat, M. A., and Francom, P., "Toxicological Findings in a Fatal Overdose of Verapamil," *Journal of Forensic Sciences*, Vol. 31, No. 4, Oct. 1986, pp. 1505-1508.) In that case, the blood verapamil concentration was 9.3 mg/L and 180 mg of verapamil were found in the stomach.

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