CASE REPORT

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Body Distribution of Ethchlorvynol

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ABSTRACT: Ethchlorvynol (Placidyl®) is a nonbarbiturate sedative hypnotic. Two fatal cases of ethchlorvynol overdose are reported. Toxicological analyses of body fluids and tissues were performed by gas chromatography using a flame-ionization detector. The quantitative method was sensitive and reproducible. Body distribution of ethchlorvynol in blood and other tissues is presented. Biological samples analyzed included blood, urine, bile, liver, kidney, eye fluid, and gastric contents. Results presented add to the pharmacokinetic data needed to study the disposition of drugs in different tissues. Findings in present two cases are compared with published toxicological data.

KEYWORDS: toxicology, ethchlorvynol, chromatographic analysis, body fluids, tissues, dodecane, internal standard, gas chromatography

Abuse of ethchlorvynol (Placidyl®) may lead to tolerance and dependence [*1*]. Two case reports are presented in which ethchlorvynol abuse resulted in two fatalities, one intentional and the second accidental.

Case Reports

Case 1

A 28-year-old white male was found face down in a creek. The deceased was last seen on the day of his demise taking 10 to 15 Placidyl® capsules and drinking vodka and beer. An empty unlabeled prescription container and a half full bottle of beer were found next to the body. The deceased had a history of prior suicide attempts, depression, and drug abuse. He was scheduled to be admitted to a rehabilitation center for treatment of substance abuse the next day. Autopsy findings were unremarkable except for congestion and edema of lungs and congestion of the viscera. Trauma of the head and face was observed. Biological samples were collected for toxicological analyses (Table 1).

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TABLE 1—*Ethchlorvynol distribution in present and published cases (mg/L or mg/kg).*[a]

	Blood	Urine	Bile	Eye Fluid	Liver	Kidney	Stomach Contents (total)	Brain	Adipose Tissue
Present cases:									
Case 1	198.2	261.8	361.8	10.0	620.0	...	130 000	...	...
Case 2	29.0	10.6	22.7	...	21.3	17.3	533 (219 mg)	...	...
Published data:									
Average Concentrations	74	76	198	...	316	222	283	114	414
Range	13-213	36-160	125-240	...	18-1600	18-860	10-940	13-285	60-1040

[a]References *2-4* and footnotes 4 and 5.

Case 2

This 31-year-old white male was found unresponsive by the custodian of his apartment building. Resuscitation attempts by paramedics were unsuccessful. Many prescription containers were found at the scene. The deceased had a history of drug abuse.

Autopsy findings were unremarkable. Biological samples were collected for toxicological analyses (Table 1).

Methodology

Gas Liquid Chromatography

A Perkin-Elmer (PE) Sigma-1 gas chromatograph (GC) equipped with a flame-ionization detector (FID) attached to a Sigma-1 integrator (PE) was used. The column used was a 6-ft (2-m) glass column packed with 3% OV-17 on 100-200 chromasorb WHP (PE). The GC operating parameters used were: injector temperature, 180°C; column temperature, 80°C; detector temperature, 105°C; and helium (carrier gas) flow rate, 52 mL/minute.

Quantitative Analysis of Ethchlorvynol in Body Fluids and Tissues

The method of analysis of ethchlorvynol content in biological samples was a modified procedure of the one described by Evenson and Poguette [*5*]. This modified procedure was shown to be reliable and reproducible [*6*].

Results

Table 1 shows the body distribution of ethchlorvynol. Ethchlorvynol concentrations in all biological samples of Case 1 were considerably higher than in Case 2. In Case 1 there was poor distribution of the drug to the vitreous humor (10 mg/L). The liver showed the highest concentration (620 mg/kg) among all samples examined, approximately three times the level of the blood.

Other toxicological findings in the blood of Case 1 were ethanol (0.03%), diazepam, and nordiazepam (0.25 and 0.17 mg/L, respectively). Diazepam, nordiazepam, and hydrocodone (0.2, 2.1, and 0.06 mg/L, respectively) were also detected in the blood of Case 2.

Table 1 also lists a comparative distribution of ethchlorvynol in different biological com-

partments. It was observed that the blood and liver concentrations of the drug in Case 1 were higher than the mean level among the reported cases [2-4].[4,5] In only 5 out of the 24 reported cases the bile was analyzed for ethchlorvynol concentration while adipose tissue ethchlorvynol concentrations were determined in only 3 cases.

Discussion

Two fatal ethchlorvynol cases are reported. The subject in Case 1 had threatened suicide. There was no evidence of drowning as the cause of death in this case. In Case 2 there was little information. However, the history of drug abuse and the results of toxicological analyses led to the conclusion that the cause of death was accidental. Table 1 lists a comparison of ethchlorvynol distribution in the present two cases to published cases. There is a wide variation in reported ethchlorvynol levels [2-4].[4,5] This may be due to the amount ingested and the time interval between ingestion and death, or more precisely, between ingestion and toxicological analysis [2]. It has been demonstrated that there is a loss of ethchlorvynol from biological samples even when stored at temperatures between 0 and 6°C [2,3]. The time lapse between death and collection of blood samples in the two cases presented is not exactly known. There was at least a 24-h period between the collection of the samples and the quantitative analysis. During this period of time all body fluids were refrigerated (4°C) while tissues were kept frozen (−20°C).

The availability of body distribution data (Table 1) becomes valuable in cases where one tissue is present while a proper blood sample is not available. The more data available, the better the chance of relating blood to tissue concentrations. Among the 24 reported cases only 5 bile samples were analyzed and reported and 2 of these were the current cases. Recently we encountered a case [8] in which in an embalmed body it was only possible to quantitate ethchlorvynol in the bile. By referring to past studies where both blood and bile ethchlorvynol were determined, it was possible to estimate, within a range, the concentration of ethchlorvynol in the blood. Unfortunately, bile is largely ignored by forensic toxicologists as a valuable biological sample for toxicological analyses.

The ethchlorvynol concentration in the kidney was variable, possibly reflecting the rate of excretion of the drug in a particular case [3]. Cravey and Baselt [3] concluded that adipose tissue would be a useful tissue for detection and quantitation of ethchlorvynol. On the other hand, vitreous humor is not the tissue of choice because of the poor water solubility of ethchlorvynol and its preferential affinity to adipose tissue [3,6].

In Cases 1 and 2 it was decided that each of the deceased died of combined drug overdose. It is therefore concluded that ethchlorvynol abuse may result in a fatality, sometimes accidental (Case 2). Published fatality cases (Table 1) as a result of ethchlorvynol overdose list a range of liver concentrations from 18 to 1600 mg/kg and the present cases were 21.3 and 620. Even in the absence of blood levels, one could assume that liver concentrations are sufficiently high to prove fatal. Ethchlorvynol concentrations in other fluids and tissues collected from Cases 1 and 2 fall within the ranges listed in Table 1 and those listed in other references as well [7].

More drug disposition data are needed to provide the forensic toxicologist with enough data to help in interpretation of his/her results, especially in the absence of a suitable blood sample [8]. Such data can be helpful in comparing tissue concentrations with fatal cases at hand.

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