Attempted Suicide by Ingestion of Methoxychlor

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Abstract

A rare case involving an attempt to commit suicide by ingestion of a commercially available product containing methoxychlor as the active ingredient is presented. Clinical symptoms exhibited by the patient included no response to stimuli, pale skin, and profuse sweating. A serum sample collected at the time of admission to the hospital was found to contain 0.67 μg/mL of methoxychlor. The determination of methoxychlor was performed using gas chromatography–mass spectrometry.

Introduction

Various different types of chlorinated hydrocarbon insecticides were used heavily during the 1960s and 1970s. Dichlorodiphenyltrichloroethane (DDT) is easily the best known of a group of organochlorine pesticides (OCPs) having the general form shown in Figure 1. Methoxychlor, 2,2-bis(4-methoxyphenyl)-1,1,1-trichloroethane, is a closely related OCP where $X = \text{OCH}_3$, $Y = \text{H}$, and $Z = \text{Cl}$. It is registered in Canada as an insecticide for use in the control of tent caterpillars in trees and ear wigs in plants. Methoxychlor acts as both a contact and stomach insecticide. It has also been used to control parasites on livestock.

Unlike other insecticides such as organophosphate and carbamate pesticides, the use of many OCPs has been highly restricted in North America. This restriction has limited the availability of these compounds, and therefore, reported cases of accidental or intentional poisoning by diphenyl alkyl OCPs are relatively rare. Although DDT has been banned for use since the early 1970s, methoxychlor continues to be used. It has been estimated that less than 10,000 kg are used annually in Canada (1). Despite its availability as a general use pesticide, there are limited data available regarding poisoning by accidental or intentional exposure to methoxychlor. One reported case involved a poisoning by exposure to the aerosol generated from the application of a chemical spray containing a mixture of methoxychlor and malathion (2). Although malathion and methoxychlor are generally considered to be only slightly toxic to humans, the victim suffered permanent neural sensory loss of hearing. The estimated lethal oral dose of methoxychlor is approximately 6400 mg/kg for humans (3).

Very recent exposure to methoxychlor can be demonstrated by measuring the amount of the unmetabolized pesticide in serum (4). It should, however, be noted that methoxychlor is rapidly metabolized and eliminated from the body. Therefore, any serum samples that are to be analyzed should be collected shortly after exposure (i.e., within 24 h).

Case History

A 62-year-old man (95 kg) from a rural area was seen sitting in a field with his head down. Regional police were notified of the situation, and upon investigation, they noted that the man appeared to be suffering from a self-inflicted poisoning. The man was subsequently taken to a local hospital by police. Upon admission to the hospital the man was not responsive to pain or verbal stimuli. His skin was pale, and he was diaphoretic. A strong chemical odor was pervasive. Initial diagnosis revealed that the man's blood pressure was 58/40 and his pulse rate was

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Table I. Parameters for GC–MS Analysis using SIM

<table>
<thead>
<tr>
<th>Compound</th>
<th>m/z Values monitored*</th>
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<tbody>
<tr>
<td>Methoxychlor</td>
<td>227 (100); 228 (16)</td>
</tr>
<tr>
<td>TCX</td>
<td>242 (81); 244 (100)</td>
</tr>
<tr>
<td>DBOFB</td>
<td>456</td>
</tr>
</tbody>
</table>

* Numbers in parentheses indicate relative intensity of ions normalized to most intense ion of each pair.

Table II. Recovery of Methoxychlor from Fortified Serum Samples

<table>
<thead>
<tr>
<th>Level of fortification (pg/mL)</th>
<th>Percent recovery ± SD*</th>
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</thead>
<tbody>
<tr>
<td>0.1</td>
<td>93 ± 6</td>
</tr>
<tr>
<td>1.0</td>
<td>99 ± 8</td>
</tr>
</tbody>
</table>

* SD = standard deviation (based on four replicate samples).

Figure 2. Reconstructed ion chromatogram for m/z 227 (A) and total ion chromatogram in GC–MS analysis of serum extract (B).

Experimental

Sample preparation

All serum samples including the patient’s serum and control samples plus a reagent blank were processed according to the following procedure. A 1-mL aliquot of serum was mixed with 1-mL of methanol containing 0.5 µg/mL of 2,3,5,6-tetrachloroxylene (TCX) and 5 mL of distilled water. The TCX was employed as an internal standard to monitor extraction efficiency for each serum sample and all quality controls. After mixing, the denatured and diluted serum samples were extracted with 3 × 5-mL portions of hexane. The hexane extracts were dried over anhydrous sodium sulfate and collected in a centrifuge tube. The sample extracts were evaporated down to 1 mL under a gentle stream of nitrogen gas. Prior to analysis, a 10-µL aliquot of a standard containing 40 µg/mL of 4,4’-dibromoocatfluorobiphenyl (DBOFB) was added to each extract. The DBOFB was used to permit quantitation by internal standardization.

Instrumentation

All analyses were performed using gas chromatography–mass spectrometry (GC–MS). The GC–MS system employed consisted of a Hewlett-Packard 5990 series II GC linked to a VG Trio 1000 quadrupole MS by a direct capillary interface. The GC was equipped with an HP7673 autosampler and a split/splitless injection port that was operated in the splitless mode. A 30-m, ICB-5, fused-silica capillary column with an inner diameter of 0.25 mm and a stationary phase film thickness of 0.25 µm (J&K Environmental Ltd., Sydney, NSW, Australia) was used for all analyses. The GC oven temperature profile consisted of an initial 88 beats per minute. Other clinical observations included that the man’s sinus rhythm and respiration were not labored.

A bottle from a commercial formulation containing methoxychlor had been found by the police. The man was suspected of ingesting between 100 to 150 mL of a product that contained 120 mg/L of methoxychlor as the active ingredient. Treatment at the hospital included two IV bags of Ringer’s Lactate 02. Once the patient responded to treatment, his blood pressure was found to be 110/70. Neurological activity included hypertonic lower extremities.

A serum sample collected at the time of admission was sent to the Provincial Laboratory for analysis of methoxychlor.
temperature of 120°C maintained for 1 min and subsequently increased to 300°C at 10°C/min. The final oven temperature was held for 5 min.

The MS was operated in the electron impact (EI) ionization mode using an electron energy of 70 eV. Selected ion monitoring (SIM) was used for screening the serum samples while full scan (60 to 500 amu) MS analysis was used for confirmation of analyte identity. The SIM parameters are summarized in Table I.

Results and Discussion

Most of the methods that have been developed to test for OCPs in clinical samples such as blood or adipose tissue were not validated for methoxychlor since it is eliminated rapidly from the body. The United States Environmental Protection Agency (U.S. EPA) method for determining OCPs in human serum reported minimum reporting limits as low as 0.001 µg/mL (5). The U.S. EPA method recommends the extraction of serum with hexane and subsequent analysis of the concentrated extract by gas chromatography with electron capture detection (GC-ECD). Other reported methods have denatured the serum with methanol (6), acetic acid (7), or formic acid (8) prior to extraction of the sample. One reported method used for the determination of OCPs in serum samples employed liquid–liquid partitioning of the sample extract with sulfuric acid as a cleanup step (7). The treatment of the extracts with concentrated sulfuric acid was reported to degrade methoxychlor as well as dieldrin and chlordane. This treatment step was found to reduce the background contamination present when the final analysis was performed by GC–ECD.

A pooled serum sample was obtained by mixing several serum samples from unexposed individuals. Two sets of four replicate samples of 1 mL of serum were fortified with 0.1 and 1.0 µg/mL equivalents of methoxychlor. These samples were processed in the same manner as all other samples and were used to determine the accuracy and precision of the analytical method. The results of the replicate analyses are summarized in Table II. Each of the replicate serum samples was also spiked with 0.5 µg/mL of TCX. Based on the eight replicate samples that were analyzed, the average recovery of TCX was calculated to be 90 ± 2%.

The serum sample from the patient who had ingested the pesticide was analyzed by GC–MS with SIM and found to contain 0.67 µg/mL of methoxychlor. In order to confirm the identity of the analyte as methoxychlor, a 0.3-mL aliquot of the extract was concentrated down to 0.1 mL and analyzed under full scan conditions. Figure 2 shows the total ion chromatogram and reconstructed ion chromatogram for m/z 227, the base peak in the EI mass spectrum of methoxychlor. The mass spectra of the analyte peak that eluted at 14.35 min and the resulting match of the computerized library search are given in Figure 3. Clearly the analyte spectrum was found to match very well with the library spectrum. The GC retention time was also found to match that obtained when a solution of methoxychlor standard material was analyzed under identical conditions.

The recovery of the internal standard (TCX) added to the patient’s serum sample prior to extraction was determined to be 103%. Therefore it was assumed that the recovery of methoxychlor was also acceptable (i.e., little analyte would have been lost in the sample preparation procedure).

Figure 3. Mass spectra of analyte eluting at 14.35 min (A) and methoxychlor from data system reference library (B).
It should be noted that most of the analytical methods reported in the literature for the determination of OCPs in human serum were intended for use in determining residual concentrations in samples collected from the general population. The concentrations of OCPs present in serum samples of unexposed individuals are typically below 0.010 µg/mL. In fact, the method utilized by the Centers for Disease Control was optimized for determining OCPs ranging from approximately 0.0002 to 0.04 µg/mL with method detection limits ranging from 0.0001 to 0.0007 µg/mL (8). The method used for the determination of methoxychlor was found to be applicable for samples with concentrations ranging from 0.1 to 1.0 µg/mL. Clearly these concentrations are much higher than those of other OCPs found in the serum of unexposed individuals. In order to apply this method to low concentrations of methoxychlor, further experimentation would be required to determine the accuracy and precision at these concentrations.

Unlike DDT and many other organochlorine pesticides, methoxychlor does not accumulate to any appreciable extent in fatty tissues of humans. Although there have been numerous studies examining residual OCPs in human adipose tissue, most of these did not include methoxychlor amongst the analytes. In one such study of OCP residues including methoxychlor in adipose tissue, samples were collected from residents of British Columbia (9). The maximum concentration found in 41 samples tested was 4.05 ng/g lipid. Most samples, however, did not have detectable concentrations of methoxychlor. An earlier study conducted on autopsied adipose tissue samples from Ontario residents did not find methoxychlor in any of the 175 samples tested (10). The quantitation limit in the Ontario study was 10 ng/g and thus was higher than the highest concentration found in the British Columbia study.

Because methoxychlor does not bioaccumulate in humans and the patient appeared to have fully recovered by the time he was discharged from the hospital, it was expected that there would be no permanent or long-term impact on his health.

References


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