CASE REPORT

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A Fatality Due to Moclobemide

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ABSTRACT: A fatality due to ingestion of the antidepressant drug moclobemide is reported. Moclobemide is a selective and reversible inhibitor of monoamine oxidase type A. Previous reports have suggested that it is a safe drug even when taken in large quantities. The few reported fatalities have all been ascribed to serotonin syndrome, due to an interaction between moclobemide and other serotonergic agents.

A 48-year-old woman with a history of depression and suicide attempts was found deceased at home. Autopsy revealed no evidence of significant natural disease or injury. Toxicologic analysis was performed and drug levels measured by capillary gas chromatography. The blood concentration of moclobemide was 137 mg/L and the liver concentration was 432 mg/kg. Low levels of diazepam, nordiazepam, and trifluoperazine were also detected. Death was considered to be due to acute poisoning by moclobemide. This case report is the first, to our knowledge, where death has been attributed to the toxic effects of moclobemide alone.

KEYWORDS: forensic science, forensic pathology, forensic toxicology, moclobemide, monoamine oxidase inhibitor, antidepressant, overdose, poisoning, death

Moclobemide is an antidepressant drug which acts via reversible inhibition of monoamine oxidase (MAO). It is relatively selective for type A MAO (1). The metabolism of noradrenaline and serotonin is decreased by MAO inhibition, resulting in increased concentrations of these neurotransmitters and relief of symptoms of depression.

After oral administration, moclobemide is completely absorbed from the gastrointestinal tract into the portal blood. It has an extensive volume of distribution and is rapidly eliminated from plasma by metabolic conversion in the liver. Its half life is 1 to 2 h. It is almost completely metabolized before elimination.

Moclobemide can be identified and quantified by capillary gas chromatography or high performance liquid chromatography. To date, the majority of reported cases of moclobemide poisoning have been non-fatal and have followed a benign course (2–6). Authors have concluded that moclobemide is safe to prescribe to the depressed patient.

Limited cases of fatalities ascribed to poisoning by moclobemide have been reported. All have been attributed to a combination of moclobemide with other antidepressants or benzodiazepines (7,8).

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Case Report

A 48-year-old woman was found apparently dead in bed at her home. Partly empty bottles of trifluoperazine and benztropine were found by the bed. No moclobemide or diazepam bottles were found. She had suffered from depression for many years and had attempted suicide on nine previous occasions. She had recently separated from her husband. Cardiopulmonary resuscitation was attempted by ambulance personnel.

Autopsy revealed a 61 kg, 153 cm tall woman. There was a large volume (236 g) of tablet residue in the stomach. Pulmonary oedema was present and there was a mild lymphocytic thyroiditis. No evidence of cardiac, neurological, or other significant natural disease was seen. No needle marks or signs of violence were observed. Specimens of blood and liver were submitted for toxicological analysis. No urine was available for analysis.

Methods

Toxicological analyses of blood and liver were carried out by the Division of Analytical Laboratories, Lidcombe, New South Wales, Australia. In accordance with laboratory policy, gastric contents were not analyzed. Specimens were extracted using 1-chlorobutane with the addition of ammonia. After centrifugation, the solvent was quantitatively recovered and evaporated and the residue was reconstituted in methanol.

Quantitation was performed on a Hewlett-Packard 5890 gas chromatograph equipped with a nitrogen-phosphorus detector. An external standard supplied by Roche Products Pty Ltd was used at 5 ppm. Both the standard and samples were run through a temperature program on a Hewlett-Packard Ultra 2 column (25 m $\times$ 0.32 mm internal diameter $\times$ 0.17 μm film thickness). Confirmatory testing was performed by gas chromatography/mass spectroscopy. Recovery in blood with an external standard was 60%.

Results

Comprehensive drug screening detected very high levels of moclobemide in both blood and liver. Diazepam was present within the therapeutic range. Nordiazepam, a metabolite of diazepam, and trifluoperazine were detected at subtherapeutic concentrations. Flumazenil was also detected (Table 1).

TABLE 1—*Results of toxicological analysis.*

	Blood Level, mg/L	(Therapeutic Range)	Liver Level, mg/kg
Moclobemide	137	(0.36–3.00)(7,9)	432
Flumazenil	7.7		—
Trifluoperazine	0.08	(1.00–2.00)(11)	1.5
Diazepam	0.14	(0.05–2.00)(11)	0.66
Nordiazepam	0.08	(0.63–1.84)(12)	0.32

Discussion

Reported therapeutic blood concentrations of moclobemide range from 0.36–3.00 mg/L (7,9). Toxic levels of moclobemide in blood and liver have not been defined. The blood level of moclobemide in this patient was 137 mg/L and the liver level was 432 mg/kg. The total amount of the drug ingested was unknown.

Non-fatal moclobemide overdose has been described in 35 patients (3–6,10). Symptoms have included drowsiness, disorientation, central nervous system depression, agitation, hyporeflexia, nausea, tachycardia, and hypertension (4–6,8). The amount ingested ranged between 0.30 and 20.55 g (3–6). Blood levels of moclobemide were not given for these patients.

Previous reports of fatalities involving moclobemide have been poly-drug reactions, the result of interactions between moclobemide and other serotonergic agents, principally clomipramine and citalopram (7,8). These latter agents were present at levels above the reported therapeutic ranges and their interaction with moclobemide produced a central serotonin syndrome. Moclobemide was detected at blood levels of 3.2–90 mg/L (7,8). The serotonin syndrome has also been reported in non-fatal poly-drug poisoning involving moclobemide (10).

In the present case, the diazepam level is towards the lower end of the therapeutic range and the nordiazepam and trifluoperazine levels are both well below the therapeutic ranges. This excludes any significant synergistic effect with moclobemide (8,12).

Flumazenil, an antidote to benzodiazepine poisoning, was administered by ambulance staff during attempted resuscitation. Death in this case was attributed to acute moclobemide poisoning alone.

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