

Fatal combination of moclobemide overdose and whisky

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ABSTRACT

The antidepressant moclobemide (Aurorix) is a reversible inhibitor of monoamine oxidase-A. Pure moclobemide overdose is considered to be relatively safe. Mixed drug overdoses including moclobemide are potentially lethal, especially when serotonergic drugs are involved. So far, only one fatality due to moclobemide mono-overdose has been reported. We report here on a fatality following the ingestion of a moclobemide overdose in combination with half a bottle of whisky. Although dietary restrictions during moclobemide therapy are not considered necessary, the combination of large quantities of moclobemide and tyramine-containing products seems to be lethal, probably because monoamine oxidase-A selectivity is overwhelmed after massive overdoses. Since there is no specific antidote and treatment is only symptomatic, the severity of an overdose with moclobemide must not be underestimated.

INTRODUCTION

The antidepressant moclobemide (Aurorix) is a specific reversible inhibitor of monoamine oxidase-A (MAO-A), which is responsible for the metabolic degradation of monoamines such as noradrenaline and serotonin in nerve terminals. The MAO-B of the gut and liver remains active for the metabolic degradation of tyramine absorbed from food.¹ The recommended dosage range is 300 to 600 mg a day.² Moclobemide does not appear to be associated with many of the adverse effects produced by the older MAO inhibitors. Most commonly reported adverse effects

are headache, nausea, dry mouth, insomnia, dizziness and epigastric discomfort. Serotonin syndrome may occur.³ Moclobemide potentiates the effects of orally administered tyramine approximately three to fourfold, which is considered not to be clinically significant. Dietary restrictions are therefore not thought to be necessary during moclobemide therapy.² Previous reports suggest that moclobemide is a safe drug even when taken in large quantities.^{4,5} The few reported fatalities have all been ascribed to serotonin syndrome, due to an interaction between moclobemide and other serotonergic agents.³ However, one case report has been published, where death was attributed to the toxic effects of moclobemide alone.⁶ We report here on a fatality due to the ingestion of a moclobemide overdose in combination with half a bottle of whisky.

CASE REPORT

A 38-year-old man was admitted at 8.30 am after ingesting approximately 12 tablets of moclobemide (150 and 300 mg) the night before. Apart from the ingestion of moclobemide he had drunk over half a bottle of whisky (>350 ml). His wife had found him in the morning in a confused and agitated state and brought him to hospital. Within minutes of entering the hospital, the patient suddenly collapsed. He was tachypnoeic, tachycardic and suffered from spontaneous muscle spasms. His Glasgow Coma Score was E2M4V1 and body temperature was 37°C. The electrocardiogram showed a supraventricular tachycardia of 174 beats/min and a right bundle branch block. He received 40 mg diazepam in

three injections intramuscularly within 35 minutes, which was followed by a decrease in his heart rate to 80 beats/min. Because of absent pupillary light responses he then received a total of 5 mg flumazenil, which was followed by cardiac arrest. Resuscitation was unsuccessful and our patient died at 9.50 am. Laboratory tests of blood drawn on admission showed leucocytes $22.3 \times 10^9 / l$ (N $4.0-10.0 \times 10^9$), creatinine $212 \mu\text{mol}/l$ (N $60-100 \mu\text{mol}/l$), urea $10.8 \text{ mmol}/l$ (N $2.5-7.5 \text{ mmol}/l$), sodium $149 \text{ mmol}/l$ (N $135-146 \text{ mmol}/l$), potassium $5.4 \text{ mmol}/l$ (N $3.5-5.0 \text{ mmol}/l$), and creatinine kinase 284 (N <105). There was a slight metabolic acidosis (pH 7.34 , pCO_2 34.3 mmHg , bicarbonate $18.2 \text{ mmol}/l$, pO_2 65 mmHg). Serum moclobemide was $55 \text{ mg}/l$ (N $1.5-2.5 \text{ mg}/l$). Ethanol and cocaine, assessed five months after his death, were not detectable in the serum. No urine was available for analysis. A post-mortem was not conducted. The patient had complained of suffering from depression during the last few weeks. Because of a past history of abuse and overdose of sedatives, however, his general practitioner did not prescribe any antidepressants. Being an irregular user of cocaine he had managed to obtain Aurorix tablets on the illegal circuit. He had never used moclobemide before. It is unclear if our patient had used cocaine the night before admission. He had no history of cardiac or neurological diseases.

DISCUSSION

This patient died as a result of cardiovascular collapse due to moclobemide intoxication. He had no history of cardiovascular disease and had not used any other drugs in the days before admission to the emergency room. Although we can not exclude that the administration of flumazenil contributed to the patient's death,⁷ it is unlikely that this explained the clinical course in this patient. Although he was known to use cocaine irregularly it is unclear if he had used cocaine the night before his death. The fact that cocaine was not detectable in his serum cannot completely rule out the possibility of cocaine abuse, but there were no indications for this in the night before admission. Although ethanol was not detectable in the patient's serum, his wife had said that he had drunk over half a bottle of whisky together with the ingestion of moclobemide. This could have potentiated the sympathicomimetic overactivity due to moclobemide overdose, because of the potential presence of tyramine in whisky.⁸ The fact that ethanol is lost from fluoride-free specimens with prolonged storage may explain why no ethanol was found in the serum.⁹ Unfortunately, due to the sudden collapse of the patient and the rapid deterioration despite resuscitation, his blood pressure was not recorded. Reported symptoms of moclobemide overdose range from no symptoms or mild gastrointestinal symptoms at doses

up to 2 g, to fatigue, agitation, tachycardia, increased blood pressure and dilated, slowly-reacting pupils at doses of 7 to 8 g. The MAO-A selectivity seems to be overwhelmed after massive overdoses of moclobemide.¹⁰ Intoxication with non-selective MAO inhibitors can be divided into four phases. First there is a period with no symptoms, followed by a hypermetabolic phase with agitation, neuromuscular excitation, hypertension and tachycardia. Then there is a phase of cardiovascular collapse, probably as a result of a decrease in catecholaminergic activity followed by the last phase with multiorgan failure with pulmonary oedema and renal insufficiency. There is no specific antidote. Treatment is symptomatic and aimed at maintaining vital functions.¹¹

Pure moclobemide overdose is considered to be relatively safe. At doses as high as 20.55 g and plasma concentrations as high as $84 \text{ mg}/l$,¹ no fatalities have been reported. Mixed drug overdoses including moclobemide are considered to be potentially lethal, especially when serotonergic drugs are involved. So far, only one fatality due to moclobemide mono-overdose has been reported. A 48-year-old woman was found dead at home. Her plasma concentration of moclobemide was $137 \text{ mg}/l$.⁶ As our patient died with a relatively low plasma concentration of $55 \text{ mg}/l$, we hypothesise that the potential combination with tyramine in the whisky may have aggravated the clinical picture. In conclusion, moclobemide (mono-)overdose is potentially fatal. Although dietary restrictions during moclobemide therapy are not considered necessary, the combination of large quantities of moclobemide and tyramine-containing products seems to be lethal, probably because MAO-A selectivity is overruled after massive overdoses. Since there is no specific antidote and treatment is only symptomatic, the severity of an overdose with moclobemide must not be underestimated.

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