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Case Report

Isopropyl alcohol poisoning in a female patient with history of post-partum depression

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- coma

Abstract

Severe isopropyl alcohol poisoning is usually manifested by central nervous system (CNS), respiratory depression and circulatory failure. Diagnosis is classically made based on the patient's history, clinical presentation and laboratory findings. Common findings include osmolal gap, ketonemia, and/or ketonuria with or without metabolic acidosis, accompanied by a fruity odour of the breath. Treatment predominantly consists of symptomatic supportive measures if the patient is not comatose and/or severely hypotensive; however haemodialysis increases the elimination of isopropanol and acetone substantially and should be considered in severely poisoned cases. Patients usually recover fully, on condition that they receive early proper supportive care, and were not complicated with coma or severe hypotension.

ABBREVIATIONS

CNS: Central Nervous System; ICU: Intensive Care Unit; ED: Emergency Department; GCS: Glasgow Coma Scale; FPIA: Fluorescence Polarization Immunoassay; TCA: Tricyclic Antidepressants; GC-HS: Gas Chromatography - Head Space; CT: Computed Tomography; BUN: Blood Urea Nitrogen

INTRODUCTION

Severe isopropyl alcohol poisoning is usually manifested by CNS, respiratory depression and circulatory failure. Diagnosis is classically made based on the patient's history, clinical presentation and laboratory findings. An Osmolal gap, ketonemia, and/or ketonuria with or without metabolic acidosis, accompanied by a fruity or sweet odour of the breath are common findings **[1].** Treatment predominantly consists of symptomatic supportive measures if the patient is not comatose and/or severely hypotensive; however haemodialysis increases the elimination of isopropanol and acetone substantially and should be well considered in severely poisoned cases. Patients usually recover fully, on condition that they receive early proper supportive care, and were not complicated with coma or severe hypotension **[2].**

CASE PRESENTATION

A 37-years old female presented to the emergency department (ED) with her husband stating a chief complaint of acutely deteriorating consciousness level, where she reached the hospital in a state of coma. The patient delivered a healthy full term baby boy three months back by spontaneous vaginal delivery. She didn't breast feed her baby as she started to show the manifestations of post-partum depression. Two weeks before presentation to ED, she was prescribed Amitriptyline in a dose of 100 mg once daily at bed time. The husband stated that the patient was on a non-pharmacological traditional herbal remedy for two days before hospitalization, as recommended by an Herbalist. The patient didn't experience postpartum haemorrhage, and had no previous history of any suicidal attempts, drug overdose, or substance abuse.

The husband also reported a history of progressive diffuse muscle pain where she became bed bound since approximately one month prior to her ED presentation. She had a history of recent limited food and fluid intake except for the previously mentioned herbal liquor. Her last menstrual period was 3 weeks before admission. Her previous medical history was unremarkable for any previous medical illness.

The patient arrested at arrival to ED, cardio-pulmonary resuscitation was initiated and she recovered. She was comatose since early presentation with GCS: 5 (Glasgow coma scale), blood pressure was 66/30, with widespread auscultatory ronchi and crepitations. Selected laboratory results are shown in Table 1.

The initial arterial blood gas results showed metabolic acidosis (pH: 7.1), with both wide Anion and Osmolal gaps.

Table 1: Laboratory Findings.

Parameter studied	Result	Reference Interval
Arterial blood gases		
pH	7.156	7.35 –7.45
PCO2 in mmHg	29.4	35 – 45
PO2 in mmHg	48.3	80 –100
Calculated bicarbonate in mmol/l	17.8	24 – 31
Base deficit in mmol/l	19.2	0.0 – 2.0
Lactate in mg/dl	34	3.6 – 9.0
Anion gap in mmol/l	21	3 – 11
Electrolytes		
Sodium in mmol/l	137	136 – 145
Potassium in mmol/l	5.1	3.7 – 5.2
Chloride in mmol/l	105	98 – 108
Bleeding/Coagulation profile		
PTT in seconds	47.8	26 - 36
PT in seconds	16.1	10.4 – 12.6
INR	1.4	0.9 – 1.2
Renal Profile		
Blood Urea Nitrogen (BUN) in mg/dl	13	15 - 50
Creatinine mg/dl	5.2	0.2 – 1.1
Liver Profile		
Albumin in g/dl	1.4	3.5 – 5.2
Total protein in g/dl	5.9	6.4 – 8.2
ALT in IU/l	42	0 – 65
AST in IU/l	70	0 – 37
Total Bilirubin in mg/dl	0.3	0.2 – 1.2
Cardiac Panel		
LDH in IU/l	590	98 – 192
CK in IU/l	1057	38 – 397
Bone Panel		
Calcium in mg/dl	7.3	8.6 – 10.2
Phosphorus in mg/dl	8.5	2.7 – 4.5
Alkaline Phosphatase in IU/l	69	50 – 130
Serum		
Glucose in mg/dl	136	75 – 105
Iron in mcg/dl	38	50 – 175
Total iron binding capacity in mcg/dl	172	250 – 450
Measured Osmolality in mOsm/kg	326	280 – 300
*Calculated Osmolality in mOsm/kg	275.2	10 – 15
**Osmolal gap in mOsm/kg	50.8	(-10) – 10
β-Hydroxybutyrate in mg/dl	125.4	0 – 2.8
Blood and urine Gas Chromatography head space findings		
Blood ethanol level in mg/dl	< 10 mg %	Negative
Urine ethanol level in mg/dl	< 10 mg %	Negative
Blood methanol level in mg/dl	Negative	Negative
Urine methanol level in mg/dl	Negative	Negative
Serum acetone level in mg/dl	48	0 – 1.9
Urine acetone level in mg/dl	74	3 – 15
Blood isopropyl alcohol level in mg/dl	316	0 – 1.9
Urine isopropyl alcohol level in mg/dl	250	0 – 1.9
Serum and urine drug screen enzymatic immunoassay		
Tricyclic antidepressants level in ng/ml	246	Machine Cut-off
Drugs of abuse (Amphetamine, Barbiturates, Benzodiazepines, Cannabis, Cocaine, & opiates)	Negative	Machine Cut-off
Radiological & ECG findings		
Chest X-ray	left lower zone haziness suggestive with aspiration pneumonitis	
CT brain	Normal	
ECG after restoration of heart beat	Wide-complex tachycardia and ST segment elevation.	

***Osmolal Gap:** Measured Osmolality - Calculated Osmolality.
****Calculated Osmolality:** (1.86 X [Sodium]) + ([Glucose]/18) + ([Urea Nitrogen]/2.8) + 9, where the sodium concentration is expressed in milli-equivalents per liter and the glucose and urea nitrogen concentrations are expressed in milligrams per decilitre.

Low levels of albumin and urea nitrogen might be indicative of malnutrition. The observed hypocalcaemia of 7.3 mg/dl could be clarified partly as being a result of low albumin concentration, because calcium is bound to albumin **[3].** The patient's plasma was mildly hyperglycaemic, although no history of diabetes was given by the husband, as acetone conversion to glucose and other products of intermediary metabolism is to be expected **[2].**

Urine samples of the patient were screened for drugs of abuse (Amphetamine, barbiturates, benzodiazepine, cannabis, cocaine, and opiates) and were negative for all screened drugs, using fluorescence polarization immunoassay (FPIA) principle on ARCHITECT system c4000, model i1000 SR by Abbott laboratories.

TCAs serum level was found to be 246 ng /ml. The positive result for this analyte could be due to Amitriptyline prescription.

Using Gas Chromatography - Head space GC ultra-model K0C33B730000000, Milano, Italy, acetone, and isopropyl alcohol were detected in both blood and urine samples as shown in Table 1. High acetone level might be attributed to malnutrition or as a metabolite of isopropyl alcohol. Methanol, ethanol were not detected. Chest X-ray showed left lower zone haziness suggestive of aspiration pneumonitis. CT brain showed normal findings. The first ECG after restoration of heart beat showed wide-complex tachycardia, and ST segment elevation.

The patient was prepared for haemodialysis, and then referred to the intensive care unit (ICU) for further management. The analysis of the liquid remedy using Gas Chromatography Mass spectrometer GC-MS–QP2010, Shimadzu revealed presence of isopropyl alcohol, a mixture of zingerone demethoxycurcumin, myricitin, and muercetine.

METHODOLOGY

Solid-phase micro extraction (SPME)

The 85-m polyacrylate fibers (Supelco no. 57318) with a manual SPME fiber holder (Supelco 57330-U) were used with a 15 min sorption time at room temperature and a 2.0 min desorption time at 280°C. The high inlet temperature was chosen to ensure the recovery of heavier volatile and semi-volatile compounds, to complement the scanning MS detection system for the detection of a wide range of analytes **[4].**

GC–MS

We used an Agilent 6890 Series GC System with an Agilent 5973 Network Mass Selective Detector, and an RXI-624Sil MS 20 m x 0.18 mm x 1.0 µm (Restek Corporation). Helium was the carrier at 27 cm/s average velocity, the temperature program began with a 2 min hold at 40°C, ramping to 110°C at 8°C/min and holding 2 min, then ramping at 20°C/min to 180°C and holding an additional 5 min, for total run time 21.25 min **[5].**

Internal Standards

Gas standards were prepared by dilution with UHP nitrogen in 2.0 L, 9 in. × 9 in. Tedlar bags (Alltech no. 41049, Deerfield, IL) using an initial standard from nor lab (Boise, ID) containing 100 ppm (v/v) isopropyl alcohol with the balance nitrogen.

DISCUSSION

Isopropanol is a flammable, colourless and clear liquid with a sweet odour and a mild bitter taste, which is miscible in water, ethanol, chloroform, and ether **[3]**. It is available at homes as rubbing alcohol, it is also found in numerous household and commercial products including pharmaceuticals, cosmetics, cleaners, disinfectants, antifreezes, solvents, and inks. **[6]**

There are nearly about 27 published cases of isopropyl alcohol intoxications. Four of these reported cases were children; whose ages ranged from 6 months to 2 years. Apart from one adult who committed suicide after isopropyl alcohol ingestion, the remaining cases were in alcoholics. Most reported cases were for males (17 of 27 cases). A dose of 20 mL can produce signs and symptoms of intoxication, whereas 150 to 250 mL can be lethal owing to central nervous system and myocardial depression, leading to hypotension and shock. Of the 27 reported cases, 5 cases only, had fatal ending. **[7]**.

Isopropanol is rapidly absorbed following oral intake, and peak plasma concentrations might be seen within 30 min. Isopropanol is mainly metabolized in the liver by alcohol dehydrogenase enzyme to form acetone **[8]**. Acetone is additionally metabolized by a range of enzymes to acetol and methylglyoxal, propylene glycol, and acetate. According to subjective hormonal status and metabolic demands, conversion of these metabolites to glucose and other by-products is to be expected. Acetone, the primary metabolite of isopropanol, has been reported to peak in plasma at 7.5 to 30 hours post exposure. **[9]** Elimination of isopropanol is predominantly renal, though some pulmonary excretion of unchanged isopropanol and acetone also occurs **[8]**. The exact mechanism of toxicity due to isopropanol exposure has not been fully clarified; however brain stem depression and myocardial depression, leading to decreased respiratory drive hypotension and shock are of importance **[11].**

Isopropanol might lead to mucosal irritation and, gastrointestinal effects classically include nausea, vomiting, and abdominal pain. Haemorrhagic gastritis, hematemesis, anaemia, and accompanying decreased haematocrit level may sporadically be detected. The most common observed feature is CNS depression with symptoms ranging from lethargy or drowsiness to stupor and finally coma **[12].**

Initial general laboratory tests should include serum electrolytes, serum BUN or creatinine, blood glucose, and creatine kinase activity. Care should be taken interpreting serum creatinine concentrations as falsely elevated concentrations have been reported due to interference by acetone with the assay for creatinine **[13]**. The most common metabolic effects are increased Osmolal gap, **[14]** ketonemia, **[15]** and ketonuria. **[16]** A fruity or sweet odour of the breath may occur **[12]**. Some case reports have described mild hyperglycaemia. **[17].** The measurement of serum isopropanol level is the most decisive means of diagnosing the poisoning. Serum levels are usually measured using gas chromatography paired with flame ionization, or mass spectrometry **[18]**. In summary, diagnosis is typically made on the basis of the patient's history and clinical presentation with cardiac and, CNS depression. Increased Osmolal gap, ketonemia, and/or ketonuria with/or without metabolic acidosis, along with the presence of acetone in the breath (fruity odor) and urine, in the absence of glycosuria or hyperglycemia, may be invaluable clues to the diagnosis of isopropanol poisoning. Evaluation involves recognition that poisoning has occurred, distinguishing isopropanol intoxication from other alcohols (Table 2), and assessing its severity.

Close monitoring for respiratory or cardiovascular functions is mandatory. Stabilization entails proper airway management (including intubation and ventilation in obtund patients), securing intravenous lines and administration of intravenous fluids, and cardiac monitoring, are mandatory in all patients. Hypotension will commonly respond well to intravenous fluids such as crystalloids, but in more severe cases, vasopressors and/or inotropes may be needed, preferably administered in a critical care unit with central hemodynamic monitoring. The onset of shock is regarded as a poor prognostic factor **[19]**. Comatose patients are at risk of rhabdomyolysis, and should have their creatine kinase activity measured; serum or urine myoglobin concentrations can also be useful in making the diagnosis **[20]**.

Owing to low molecular weights of isopropanol and acetone, their relatively low volumes of distribution, and minimal serum protein binding, they are hence responsive to removal by extracorporeal techniques such as haemodialysis and hemodialfiltration, whose beneficial effects had been, reported

Table 2: Biochemical Differences of Alcohol Intoxications.

	Methanol	Ethanol	Isopropanol	Ethylene Glycol
Characteristic odor	Yes	Yes	Yes	No
Metabolic acidosis	Severe	Mild	No	Severe
Ketones	Ketobutyric	Acetoacetic	Hydroxybutyrate	Acetone
Anion gap	Large	Moderate	Slight	Large
Osmolar gap	Yes	Yes	Yes	Yes
Elevation of serum Creatinine	No	Yes	Yes	No
Hypoglycemia	No	Yes	Yes	No
Metabolites	Formic acid	Hydroxybutyric	Acetone	Glycolic acid, oxalic acid
Other findings	Blindness	Acetoacetic acids	Gastritis, hematemesis	Crystalluria

[15]. Ethanol or fomepizole (Alcohol dehydrogenase inhibitors), are not recommended as they will inhibit the metabolism of isopropanol to acetone **[21]**. As the toxicity of isopropanol is principally due to the parent alcohol, thus inhibiting the metabolism of isopropanol would only result in prolonged CNS, and respiratory depression, in addition to hypotension **[22].**

FOLLOW UP

While in the ICU, the patient was mechanically ventilated and was placed on inotrope infusion. She subsequently developed myoclonus requiring Valproic acid (Depakine) for control. She remained in metabolic acidosis which required treatment with sodium bicarbonate. Forty eight hours post ICU admission and haemodialysis, she suddenly developed ventricular fibrillation which was refractory to treatment and she finally died.

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