CASE REPORT

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A Fatal Case of Chlorate Poisoning: Confirmation by Ion Chromatography of Body Fluids

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ABSTRACT: A 49-year-old male chemical industry worker was admitted to intensive care with a 24-hour history of respiratory failure, vomiting, headache, stupor, arterial hypotension, and cyanosed face and limbs. He had acute haemolysis (3.9 g/L plasma haemoglobin concentration) and 30% methaemoglobinaemia. Whereas the search for alcohol, barbiturates and opiates was negative, benzodiazepines and tricyclic antidepressants were present. The patient was in fact being treated with fluvoxamine, amitryptiline, and alprazolam. As the clinical and biological signs suggested chlorate poisoning, chlorate was looked for by using an aniline color reaction. It was found in gastric content and urine. Treatment consisted in mechanical ventilation, vasoactive amines, methylene blue, plasma exchange, exchange transfusion, and haemodialysis. Despite this, the patient had several cardiac arrests and refractory metabolic acidosis. He died 12 h after his admission. Specific ion chromatography was used afterhand to assay the chlorate in various body fluids. The technique was based on a separation on an ion exchange Dionex® AS 12A column coupled with conductivity detection. A quantitative estimation was carried out by using external calibration with a four-point calibration curve which was linear between 1 and 15 mg/L. The measured plasma levels of chlorate were 78 and 29 mg/L respectively before and after exchange transfusion. Gastric-lavage liquid contained 1300 mg/L of chlorate and urine 4300 mg/L. Ion chromatography, which is routinely used in environmental studies helped to confirm a massive oral intake of chlorate by measuring the corresponding blood and urine chlorate concentrations, data which had only rarely been reported previously.

KEYWORDS: forensic science, forensic toxicology, chlorate, ion chromatography, death, poisoning

Both sodium chlorate and potassium chlorate are white crystals which can be mistaken for sugar. Sodium chlorate is cheap and is used as a non selective herbicide. Potassium chlorate is an explosive and combustive agent used to make matches. Chlorate poisoning, which can be accidental or voluntary, is rather rare and potentially fatal. Chlorate salts may be absorbed either orally or by inhalation. Their metabolism is not well understood. Chlorate is probably reduced to chlorite and then to chloride, which is excreted in urine (1).

The mechanism of toxicity depends on a very strong oxidative effect which is responsible for acute intravascular haemolysis and autocatalytic methaemoglobinaemia production by oxidation of the ferrous iron of haemoglobin to ferric iron (2). Methaemoglobin is unable to fix oxygen. Lastly, chlorates have a direct oxidative effect on all cells and tissues, especially on liver and kidneys.

When chlorate poisoning is suspected, and the clinical picture combines haemolysis and methaemoglobinaemia, the laboratory will be asked to search for chlorate. This screening can be done on body fluids by using different color reactions (3,4). The quantitative determination can be done by a colorimetric (4) or a titrimetric method (5) but, these non-separative techniques lack of specificity and sensitivity (they are a hundred times less sensitive than the chromatographic method). In a forensic situation, it is necessary to be able to confirm the results of the screening with a more reliable technique which can measure the amounts of chlorate.

The authors propose a simple and rapid method for the assay of chlorate and chlorite ions which can be used on different body fluids like blood, urine and gastric content.

Case Report

A 49-year-old male, chemical industry worker, presented at his home respiratory distress, vomiting and headache. The on-call general practitioner examined him 24 h after the symptoms had started. The patient had deeply cyanosed face and limbs. His systolic arterial blood pressure was below 80 mm Hg, and he was in a stuporous state. He was therefore admitted to the intensive care unit for acute haemolysis and methaemoglobinaemia. The patient had port colored urine, before he became completely anuric.

Laboratory investigations revealed a metabolic acidosis, hyperkaliaemia, very low haematocrit and a severe coagulopathy (34% prothrombin, 27% factor V, 1.2 g/L fibrinogen, 47 G/L platelets, >50 μg/mL fibrin degradation products). The plasma color and the haemoglobin concentration (3.9 g/L confirmed the haemolysis. Bilirubin concentration was 199 μmol/L. Blood urea (15.5 mmol/L) and creatinine (341 μmol/L) concentrations were also increased.

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Treatment consisted of mechanical ventilation, vasoactive amines, methylene blue, plasma exchange (2 L), exchange transfusion (10 L), and haemodialysis. Despite this, the patient had several cardiac arrests and refractory metabolic acidosis. He died 12 h after his admission.

From a toxicological point of view, the first step consisted in the routine search for the more usual poisons as in all cases of coma of unknown origin. The first investigations were carried out using an immunochemical technique (fluorescence polarization immuno assay, Abbott®). These did not reveal any alcohol, salicylates, barbiturates in blood or opiates in urine. There was no phenothiazine in urine.

Amongst the common psychotropic drugs were found some urinary benzodiazepines and antidepressants, which were in fact due to the patient's treatment. Only tricyclic antidepressants were found in the patient's blood. The blood concentrations were consistent with therapeutic treatment levels. It was later learned that the patient was indeed being treated with fluvoxamine, amitryptiline and alprazolam. However, even a very high intake of these drugs could not explain the clinical picture.

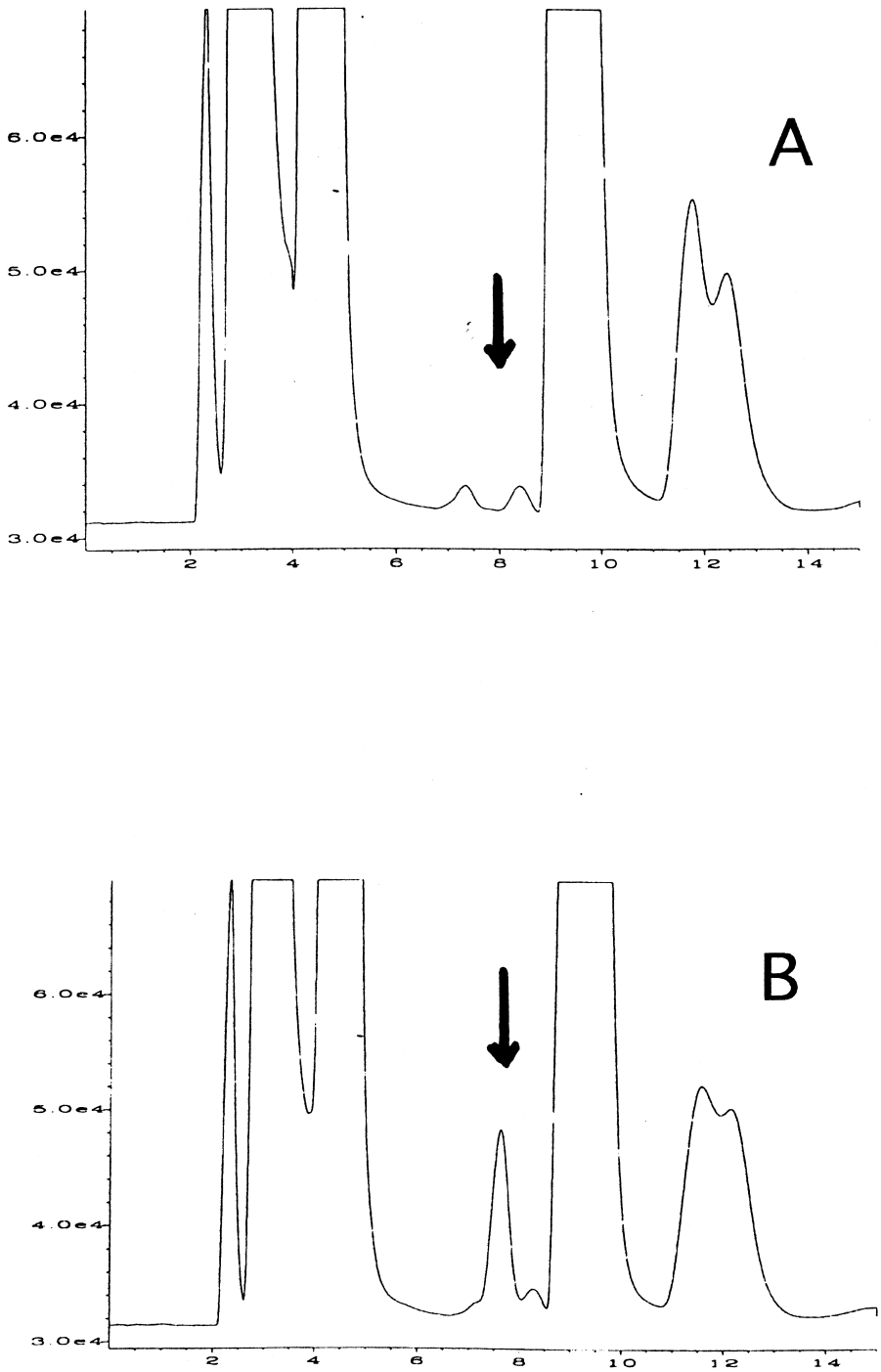

FIG. 1—*Ion chromatogram from a blank postmortem whole blood (A) and the same sample spiked with 50 mg/L of chlorate (B). 20 μL of sample were injected into a Dionex® 4500 I ion chromatograph equipped with suppressed conductivity detection.*

As the blood had an unusual chocolate brown color, the methaemoglobin could not be assayed by the usual automatic technique. Kaplan's method was therefore used. It is based on the study of the absorption spectrum of intraerythrocytic haemoglobin between 450 and 650 nm (6). The methaemoglobin level was 30%. This is not very high for such a rapidly fatal case. However, the assay was carried out 48 h after sampling. It is well known that methaemoglobin does not keep well (7).

The clinical picture with a combination of haemolysis and methaemoglobinaemia was strongly suggestive of chlorate poisoning. A qualitative assay was therefore carried out using a color reaction to aniline in acid (4). This was highly positive, but, not being very specific, the result was confirmed with ion chromatography. A supplementary search for chloralose and cyanide was negative.

A forensic autopsy was performed on the instruction of the legal authorities. The external examination was normal. Internal examination reveals a moderate haemothorax without other organ abnormality. Histological analysis of organs allows to eliminate lesional pulmonary oedema and corrosive lesion of trachea. On the other hand, an acute tubular necrosis and numerous microthrombosis in hepatic sinusoïd were identified. All these observations were initially reported in chlorate poisoning (8).

Methods

Sodium chlorate and sodium chlorite were purchased from Sigma (Saint Quentin Fallavier, France). All other chemicals and reagents, purchased from Prolabo and Merck (Paris, France), were of analytical grade. Deionized water was used to minimize background noise during the chromatography. Chlorate and chlorite quantitation was carried out according to a method widely used in the paper industry (9). The analysis was based on a separation by ion chromatography coupled with conductivity detection.

Prior to analysis, biological samples were subjected to an adjusted dilution with eluant and to a simple 0.45 μm filtration. 20 μL of this sample were injected isocratically into a Dionex (4500 I) ion chromatograph equipped with suppressed conductivity detection. The flow rate of the mobile phase (2.7 mM sodium carbonate/0.3 mM sodium bicarbonate) was 2 mL/min. The suppressor consisted in an Anion Micro Membrane Suppressor (AMMS II®) with a 36 mN H_2SO_4 regenerant solution at 1 mL/min flow rate. A Dionex Ion Pac® AS 12A column, 4 mm in diameter and 200 mm long, was preceded by its associated guard column, the Ion Pac® AG12A (4 × 50 mm). Quantitation was obtained with external standardization from a linear calibration curve of chlorate (1 to 15 mg/L) and chlorite (1 to 10 mg/L).

Results

The treatment of the biological samples was really easy and rapid. It needs a simple dilution and filtration. The color and the consistency of the samples were not modified and were not a limitation for the chromatographic analysis. In our case, only plasma samples were interesting for the toxicological diagnosis and were tested but the method can be used with postmortem whole blood. Typical ion chromatograms from a blank and a spiked post mortem whole blood are shown in Fig. 1.

The concentrations of chlorate and chlorite found in various body fluids are given in Table 1. These results are in fact minimum values which presumably underestimate the levels actually reached in the patient. Chlorates are unstable, as they are rapidly reduced in the body, as is confirmed by the presence of chlorites in urine. Levels of chlorate in urine and gastric contents were very high and confirm the oral route of intake. Moreover, the plasma level of chlorates fell after the exchange transfusion. There are virtually no published reports which could indicate a possible interpretation for these levels (10–12), which, in any case, were very high. Steffen (13) reported the only published non fatal serious case of suicidal intake of 150 to 200 g of herbicide by a young female. No chlorate was found in plasma. On the other hand, there were 7181 mg/L of chlorate in urine in the first hours following the poisoning, this level then decreasing progressively.

TABLE 1—*Chlorate and chlorite quantitative estimation in different biological fluids.*

	Biological Fluids	ClO_3^- (mg/L)	ClO_2^- (mg/L)
Deceased Patient	First plasma	54	nd
	Plasma after plasma exchange	78	nd
	Plasma after exchange transfusion	29	nd
	Gastric content	1300	13
	Urine	4300	1500
Control Patient	gastric content	4	nd
	urine	2	nd

nd: not detected.

Conclusion

In this fatal case of poisoning with forensic implications, the use of ion chromatography helped to confirm the involvement of chlorate with good specificity, and to confirm the oral route of intake. Provided the laboratory has ion chromatography equipment, which is quite specific, the assay can be simply and easily carried out. The blood and urine concentrations measured in this fatal case are worthy of note, as there is so little published data on this subject.

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