

# Falsely elevated plasma creatinine levels as a marker of nitromethane poisoning

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**To the Editor:** We report 6 cases of accidental nitromethane poisoning, of which there are only 4 reported cases in the world literature. The significance of this poisoning is that nitromethane interacts with the widely used Jaffe reaction method of determining plasma creatinine values. The enzymatic creatinine assay method and cystatin C determinations are not yet widely available in South African laboratories. The resulting, falsely elevated plasma creatinine values, which can be very high, can be misinterpreted by clinicians as a marker of severe renal failure and could lead to inappropriate management. We also report the first known death following nitromethane ingestion-induced status epilepticus.

## Case report

Six homeless people presented at a regional hospital in the Western Cape. They had all ingested unknown quantities of the liquid contents of a discarded wine bottle.

The index patient was a 34-year-old man who presented to the emergency department having suffered three generalised tonic-clonic seizures. He had a Glasgow Coma Score of 9/15, blood pressure 110/70 mmHg, pulse rate 62/min, respiratory rate 24/min, finger-prick glucose test 13 mmol/l and oxygen

saturation 94% on room air. He was markedly agitated and initially displayed paranoid delusions. He had status epilepticus and was treated with intravenous diazepam (a total of 40 mg in 12 hours), phenytoin 1 500 mg and later phenobarbitone 1 000 mg. Failing to respond to treatment, he was transferred to the intensive care unit (ICU) of the central hospital for ventilation. Co-amoxiclav was prescribed for possible aspiration pneumonia, and he was maintained on a diazepam infusion for the convulsions. Later he required inotropic support for haemodynamic instability and a thiopentone infusion for control of seizures. A lumbar puncture and contrasted computed tomography (CT) scan showed no abnormalities. His urine output remained more than 1 ml/kg/h during admission. He deteriorated progressively, developed diabetes insipidus, and was declared brain-dead 11 days later.

Initial arterial blood gas analysis revealed methaemoglobinaemia (blood methaemoglobin level 2.6 g/dl) with arterial saturation of 95% on FiO<sub>2</sub> 40%; blood results were plasma Na 137 mmol/l, plasma K 4.4 mmol/l, plasma urea 8.6 mmol/l, and plasma creatinine 10 122 µmol/l. The spontaneous decrease in plasma creatinine levels of the index patient is shown in Fig. 1.

The 5 other intoxicated patients all suffered severe visual hallucinations and paranoid delusions upon admission but their clinical examinations and vital signs were all normal. Each patient received saline infusions of 100 ml/h to maintain an adequate urine output of more than 1 ml/kg/h. They also received haloperidol 10 mg and clonazepam 2 mg with minimal effect on their mental status. Three of these patients had a single tonic-clonic seizure each, responding well to intravenous diazepam. All the patients received a loading dose of phenytoin of 1 500 mg. The psychotic symptoms dissipated by day 3. These patients' presenting creatinine values were 6 377 µmol/l, 3 531 µmol/l, 2 971 µmol/l, 3 212 µmol/l, and

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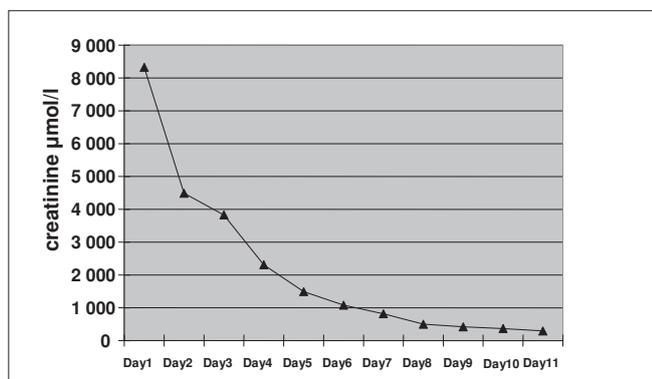


Fig. 1. Index patient's sequential plasma creatinine values measured by the Jaffe reaction at the tertiary institution.

2 232 µmol/l. Despite these elevated creatinine levels, no other signs of renal dysfunction were demonstrated. They had normal urea levels and maintained good urine output. They were discharged on day 9 with no residual effects, and normal plasma creatinine values.

## Discussion

Creatinine is an invaluable biochemical marker of renal function. Although it is freely filtered by the glomerulus, a small percentage is actively secreted by the proximal tubules. When measured in the serum, this is balanced by the slightly higher value of creatinine due to nonspecific chromophores, which react with the colorimetric Jaffe reaction assay.<sup>1</sup> The Jaffe reaction is the determination of creatinine by measuring the spectral absorbance of the chemical structure of the reaction between creatinine and alkaline picrate. Other false chromophores produced by binding to alkaline picrate cause small non-significant variations in the measured creatinine value, including bilirubin, acetoacetate, pyruvate and cephalosporins. Nitromethane also reacts with alkaline picrate and the product of this reaction is comparable in spectral structure to that of creatinine/picrate with similar absorbance changes across 250 - 550 nm.<sup>2</sup> When plasma-based nitromethane mixtures were analysed using the Jaffe reaction, the resulting spectral absorbance increased linearly with increasing nitromethane concentrations. The following relationship was demonstrated (concentrations in mmol/l): apparent creatinine = 0.99 (nitromethane)+0.21 (±0.013).<sup>2</sup>

Nitromethane (CH<sub>3</sub>NO<sub>2</sub>), also known as nitrocarbol, has a molecular weight of 61.04 and is a highly flammable,

colourless liquid. It is commonly used in motor racing fuel and in different proportions with methanol as a model aircraft fuel. Animal studies reveal an LD50 of 940 - 950 mg/kg if given orally. It is metabolised to acetone and nitrate in the presence of NADPH and oxygen. It can be absorbed through intact skin and is reported to cause dermatitis in humans. Other adverse effects in humans include the formation of methaemoglobinaemia, which can cause cyanosis in sufficient quantities.<sup>3</sup> Four cases of nitromethane intoxication have been described previously;<sup>2,4-6</sup> all had markedly elevated plasma creatinine values out of keeping with the clinical situation. The plasma creatinine values were all measured by the Jaffe reaction, some of which were proven to be falsely high using the enzymatic method. No deaths, seizures or psychosis have previously been reported following the ingestion of nitromethane. In all 6 cases, nitromethane was identified as the agent responsible for the abnormal Jaffe reaction. Our findings regarding nitromethane intoxication differed, especially in the clinical presentations. Four of the 6 patients had seizures, and 1 developed status epilepticus, complicated by fatal hypoxic ischaemic encephalopathy. All the patients suffered from visual hallucinations and paranoid delusions, which subsided with supportive management. Most of them had a mild metabolic acidosis, most probably attributable to mild muscle damage from convulsions or concomitant alcohol ingestion. None of the patients developed renal failure.

Nitromethane remains a dangerous substance when ingested. The most helpful indication of this type of poisoning is the disproportionately high creatinine values. Clinical clues include psychotic symptoms, agitation and seizures. The emphasis of treatment should be on supportive management, including adequate fluid intake.

## References

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