CASE REPORT

False acute kidney injury alert due to model car fuel ingestion

Darren Powell,¹ Louise Hassall,¹ David Scholes,² Mohammad Al-Jubouri¹¹Department of Clinical Biochemistry, St. Helens & Knowsley Teaching Hospitals NHS Trust, Prescot, UK²Department of Acute Medicine, St. Helens & Knowsley Teaching Hospitals NHS Trust, Prescot, UK**Correspondence to**Dr Mohammad Al-Jubouri,
mohammad.al-jubouri@sthk.nhs.uk

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SUMMARY

We report a case of accidental ingestion of model car fuel (Optifuel) resulting in an apparent elevation of serum creatinine of 274 $\mu\text{mol/L}$ (3.1 mg/dL) as measured by the Jaffe (alkaline picrate) reaction, which resulted in an acute kidney injury (AKI) stage 3 alert being reported. Optifuel contains nitromethane, which has been reported to interfere in the Jaffe reaction causing falsely high creatinine measurements. The laboratory staff were vigilant about this potential interfering substance so repeated the analysis of the creatinine using an enzymatic method that showed a markedly lower result of 47 $\mu\text{mol/L}$ (0.5 mg/dL). This report highlights the ability of nitromethane to potentially mimic AKI and the importance of being aware of the limitations of biochemical tests to avoid misinterpretation of results and instigating inappropriate treatment.

BACKGROUND

Non-intentional model car fuel ingestion is not commonly encountered in clinical practice and usually has no significant clinical consequences. Nitromethane (CH_3NO_2) is the main chemical component in such fuel along with methanol and synthetic oil. Therefore, ingestion of this material may result in methanol intoxication if an adequate amount is consumed.¹ It has been reported that nitromethane can cause a false elevation of serum creatinine when measured using the common Jaffe reaction method.²⁻³ We hereby report a case of model car fuel ingestion that resulted in false elevation of serum creatinine thus generating an acute kidney injury (AKI) stage 3 alert.

CASE PRESENTATION

A 61-year-old woman presented to the emergency department following an accidental ingestion of 1–2 mouthfuls of a model car and aviation fuel known as 'Optifuel'. The patient initially had a severe burning pain in her mouth and retching, which settled down, and clinical assessment was unremarkable. However, it was noted that the serum creatinine level was 274 $\mu\text{mol/L}$ (3.1 mg/dL) with an estimated glomerular filtration rate of 15 mL/min/1.73 m². This creatinine level represented a fivefold increase from her previous results (50 $\mu\text{mol/L}$, 0.63 mg/dL) thereby triggering an AKI stage 3 alert, despite normal urea (4.7 mmol/L = blood urea nitrogen 13.2 mg/dL) and electrolyte concentrations, all measured by a Siemens Advia 2400 chemistry analyser. The patient was admitted

to a medical ward for observation and management. The UK National Poisons Information Service was contacted, and it emerged that Optifuel contains nitromethane, synthetic oils and possibly methanol. Initially, the patient was given an ethanol infusion as a precaution against possible methanol intoxication. However, both the osmolar (4.3) and anion gap (11.2), together with serum bicarbonate (26.2 mmol/L), were within normal ranges, thus methanol toxicity was deemed unlikely, and the ethanol infusion was discontinued.

INVESTIGATIONS

A review of the literature indicated that ingestion of nitromethane may be the cause of the high serum creatinine.²⁻⁶ Measurement of the serum creatinine by an alternative enzymatic method (Roche Cobas C501 analyser) showed that the creatinine level was 45 $\mu\text{mol/L}$ (0.5 mg/dL). A subsequent creatinine level was measured as 228 $\mu\text{mol/L}$ (2.6 mg/dL) by the Jaffe method but was only 47 $\mu\text{mol/L}$ (0.5 mg/dL) by the enzymatic method. The patient remained in a stable condition and was discharged home after 2 days of hospitalisation.

OUTCOME AND FOLLOW-UP

The patient's initial elevated creatinine levels were determined to be falsely raised, thus allowing the AKI stage 3 alert to be discounted. The patient remained in a stable condition and was discharged home without any issues after 2 days of hospitalisation.

DISCUSSION

Creatinine is derived mainly from metabolism of skeletal muscle creatine phosphate. Creatinine is released into the blood at a constant rate resulting in minimum day-to-day variation in its serum concentration; therefore, it can be used as an indicator of glomerular filtration rate. The standard method of measurement of serum creatinine by most labs is a colorimetric Jaffe reaction where creatinine reacts with alkaline picrate to form a red coloured creatinine–picrate complex that is measured spectrophotometrically.²⁻⁴ The Jaffe reagent is known to non-specifically react to a lesser extent with other organic compounds, designated as pseudochromogens, and the Siemens ADVIA method is modified to include rate blanking and intercept correction to minimise interference from bilirubin and proteins. However, other pseudochromogens known to interfere in the assay include ketone bodies, ascorbic

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acid and cephalosporin antibiotics,^{7 8} and there are reports in the literature of exogenous substances, such as boldenone and 5-aminolaevulinic acid, causing falsely elevated creatinine levels that may be wrongly interpreted as renal failure.^{9 10}

Nitromethane is a nitroalkane compound that is a volatile and combustible colourless oily liquid, which interferes with the determination of creatinine by the Jaffe reaction. At the highly alkaline pH conditions of the Jaffe reaction, nitromethane exists in a form that includes an active methylene group. This group reacts with picrate to form a chromophore that is indistinguishable from that normally formed with creatinine. Therefore, the observed increased creatinine as measured by the Jaffe reaction likely reflects the concentration of the nitromethane.

Several groups have attempted to quantify the degree of interference, and through a series of experiments, spiking whole blood with nitromethane *ex vivo* demonstrated a marked positive interference in the Jaffe reaction that increased linearly with nitromethane concentration. In contrast, these spiking experiments exhibited no effect on the creatinine measurements made using a point of care testing enzymatic-based method.^{2 11 12} These observations are in line with our own findings that nitromethane exhibited no obvious effect on the Roche enzymatic creatinine method employed to double check our own patient's results. In fact, the difference between the Jaffe-based and enzymatic-derived creatinine results could potentially be exploited as a surrogate for measuring the nitromethane level and thus may be used to monitor its excretion indirectly. This may have important clinical utility since the direct measurement of nitromethane requires complex gas chromatographic analysis that is not routinely available in most clinical laboratories. Additionally, the mechanism and time scale of nitromethane metabolism is uncertain and has yet to be elucidated. Animal studies so far have focused on assessing the carcinogenic properties of the compound, while *in vitro* studies examining its metabolism in isolated rat hepatocytes observed only the formation of trace amounts of formaldehyde.¹³

The lack of obvious lasting harm in our patient and in other cases of nitromethane poisoning^{1–3 6} together suggests that ingestion of small amounts of the compound itself may pose only a limited risk to health, with the main issues being local irritation and nausea. However, it is important not to underestimate the potential impact of methanol intoxication in cases of nitromethane-containing fuel ingestion. The Optifuel range of products contain between 5% and 30% of nitromethane complemented with varying proportions of synthetic oil plus methanol as a secondary combustible, while other brands and enthusiast home-made blends can contain up to 60% methanol. Therefore, ingestion of this material may result in methanol intoxication if an adequate amount is consumed.

Following ingestion, methanol is converted first to formaldehyde by the hepatic enzyme alcohol dehydrogenase and then to formic acid. Although formaldehyde is more toxic than formic acid, a short half-life of 1–2 minutes⁸ limits its impact. Formic acid, however, accumulates leading to the clinical indications of toxicity including, nausea, dizziness, blurred vision and a raised anion gap with metabolic acidosis. It is important to note that although the osmolar and anion gap are useful in the diagnosis of methanol toxicity,¹⁴ the absence of an increased anion or osmolar gap does not necessarily exclude methanol toxicity especially if patients have low or negative baseline values that can mask an increase.¹⁵ The presence of an osmolar and anion gap also depends on the methanol concentration in the blood, the time after exposure and whether there has been coingestion of ethanol.

In our patient, the osmolar and anion gap, as well as serum bicarbonate, remained within normal ranges; thus, methanol intoxication was deemed to be unlikely, and due to the lack of a locally available HPLC/GC assay for timely methanol estimation, nor a point of care test method for assessing formic acid or toxic alcohols, this avenue was not pursued any further. Interestingly, as nitromethane was not shown to affect the osmolar or anion gap in our case or in others,^{2 12} then it is unlikely to directly interfere with the investigation of toxic alcohol exposure, which may be concomitant in a severe case of fuel ingestion.

This case report highlights the importance of being aware of the interference of nitromethane with the Jaffe alkaline picrate creatinine assay. This interference is not well recognised by the clinicians, and there is a risk that the creatinine result may be misinterpreted to indicate renal failure. In this case, we have documented the real serum creatinine concentration by applying a specific enzymatic creatinine method using the Roche analyser. Clinicians and laboratory professionals should be aware of the potential interfering substances with the colorimetric creatinine method whenever there is a discrepancy between serum urea and creatinine results as this case highlighted. Rapid recognition of such scenario would obviate the misdiagnosis of AKI and unnecessary hospitalisation and management.

Learning points

- ▶ Be vigilant about potential interference of nitromethane, a chemical present in many model car and aviation fuels, with the Jaffe creatinine assay.
- ▶ Discrepancy between normal urea and high creatinine should prompt consultation with the laboratory about performing specific enzymatic creatinine assay.
- ▶ Rapid recognition of such case obviates the misdiagnosis of acute kidney injury and unnecessary management and hospitalisation.
- ▶ Be mindful about the possibility of methanol poisoning in cases of nitromethane fuel ingestion.

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Competing interests None declared.

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