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Case Report

Pediatric Case Report & Literature Review of Spurious Creatinine Elevation in the Setting of Nitromethane Exposure

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Abstract

Nitromethane along with methanol is a common component of model airplane fuel, rocket fuel and race car fuel. Reports of nitromethane exposure causing falsely elevated creatinine levels by its interference with Jaffe reaction analysis are noted in the adult literature, but pediatric reports are limited. We present a case report and literature review of nitromethane fuel toxicity in the pediatric population.

Introduction

Nitromethane is a common component of fuels including model airplane fuels, rocket fuels, and race car fuels. Reports of nitromethane exposure causing falsely elevated creatinine due to its interference with the Jaffe reaction have been reported in both the adult and pediatric literature, although the pediatric literature is limited. This case report describes the clinical course, with close attention to the renal workup, of a pediatric patient with intentional nitromethane exposure via race car fuel ingestion. A literature review on all pediatric cases reported thus far is included as well. Nitromethane exposure is an underrecognized etiology of false creatinine elevation and should be included in the differential of Acute Kidney Injury (AKI) secondary to fuel exposure, which in turn can help prevent unnecessary workup and treatment.

Case Report

A 12-year-old male with a past medical history of Attention-Deficit/Hyperactivity Disorder (ADHD), major depressive disorder complicated by prior suicidal ideation and attempts, and Medium-Chain Acyl-Coenzyme A Dehydrogenase (MCAD) deficiency presented an hour after intentionally ingesting a "mouth-full" of Torco Race fuel, ingredients of which include a methanol nitromethane mix. Patient initially presented to an outside hospital, where poison control was contacted and recommended treatment with fomepizole, as methanol is noted to be a key component of race fuel. This was not available at the outside facility, so he was transferred to our Pediatric Intensive Care Unit (PICU) and was immediately given one dose of 15 mg/kg fomepizole. He initially complained of headache and generalized abdominal pain, but review of systems was otherwise negative, with no nausea or vomiting endorsed. He was hemodynamically stable with initial vital signs notable for axillary temperature of 36.8°C, heart rate of 97/min, respiratory rate of 16 breaths/min, blood pressure of 126/52 mmHg, and oxygen saturation of 97% on room air. Physical exam was notable for a non-toxic appearing male with no increased work of breathing and clear breath sounds, bilaterally, regular rate and rhythm with no murmurs, and a soft, nondistended abdomen with mild tenderness to deep palpation in the left lower quadrant. He was awake, alert, answering questions appropriately, and following commands with no focal neurologic deficits.

Workup at an outside hospital was notable for an ethanol level <10 mg/mL with creatinine at 0.69 (0.4-1.0 mg/dL) one hour post ingestion, with no prior baseline creatinine levels available. A

methanol level was not obtained. Upon presentation to our hospital, a methanol level was drawn after fomepizole was administered, at approximately 6 hours after ingestion, and resulted undetectable at <10 mg/mL. Therefore, no further doses of fomepizole were given. The rest of the laboratory workup, obtained at approximately 4 hours post ingestion, is depicted in Table 1. Of note, creatinine had increased to 1.73 mg/dL (0.4-1.0 mg/dL) at that time.

As an initial treatment, the patient was started on Intravenous Fluid (IVF) with D10/0.9NS at 100 mL/hr. In light of the creatinine elevation, pediatric nephrology was consulted for recommendations for further evaluation and management of suspected AKI. The following morning, creatinine was down-trended to 1.58 mg/dL (0.5-1.0 mg/dL), and Cystatin C was obtained for further evaluation. There continued to be no electrolyte abnormalities, acidosis, or other notable abnormalities on the Complete Metabolic Panel (CMP). Further workup obtained by the pediatric nephrology team included a urine protein/creatinine ratio of <0.15 (<0.25), urine microalbumin/creatinine ratio of <11 (0-30 mg/g CRE), urine calcium/creatinine ratio of <0.12 (<0.20). Urinalysis showed a specific gravity of 1.012 (1.003-1.030) with no protein or blood. Renal ultrasound was notable for normal kidneys without signs of parenchymal insult, as well as no signs of obstruction. Finally, Cystatin C resulted at 0.68 mg/L, with resultant GFR of 137 mL/min/1.73m2 per the 2012 CKD-EPI Cystatin C equation. IVF were therefore discontinued, and creatinine continued to downtrend to 1.39 mg/dL (0.5-1.0 mg/dL) the following day. Other labs continued to be within normal limits (WNL) as well. The patient remained non-toxic and hemodynamically stable, as well as asymptomatic with regard to the renal standpoint; notably, blood pressure remained within normal limits for age, and he continued to make good urine output. Of note, the hospital laboratory technician was contacted, who confirmed that the methodology of measuring creatinine at our facility was the Jaffe assay.

Therefore, the unremarkable renal workup including normal Cystatin C level suggested that the patient's creatinine rise was in fact a false elevation due to nitromethane exposure. Patient was subsequently cleared for discharge from a renal standpoint with follow-up labs for continued monitoring. He was however lost to follow-up and the advised follow-up creatinine measurement was not obtained.

Discussion

Nitromethane is commonly found as an additive to fuels for race cars, power boats, cars, and planes, among others. It is also used as a solvent, propellant, rocket fuel, as well as an explosive. It is a colorless, oily liquid, which can be irritating to the skin and eyes through external contact and irritating to the nose, throat, and lungs through inhalation. It can also cause nausea, vomiting, diarrhea, especially when ingested, as well as headache, weakness, and loss of coordination. When high levels accumulate in the blood, methemoglobinemia can occur. There are reports that it may even damage the kidneys and liver and may also be regarded as a carcinogen, all of which are extrapolated with data from animal studies [1]. As noted above, it is a common fuel additive and was in fact an ingredient of the fuel that our patient ingested.

Interestingly, it has been reported in the literature that nitromethane exposure can cause false elevation of creatinine when creatinine measurement is obtained via the Jaffe assay [2-7]. This assay is commonly used to obtain creatinine in many laboratories. As noted, our hospital also utilizes the Jaffe reaction to measure serum creatinine. The mechanism is based on the Jaffe reaction or otherwise known as the Jaffe colorimetric method, in which alkaline sodium picrate reacts with creatinine to form an orange-red color. The rate of absorbance is directly proportional to the creatinine concentration in the serum [5, 8]. Nitromethane has been found to interfere with this reaction, and it forms a complex of similar absorbance to that of the creatinine-picrate complex [5], which can resultantly cause a spurious rise in creatinine. Of note, other substances including acetoacetate, cephalosporins, bilirubin, and ascorbic acid, have been found to interfere with this reaction as well [2, 5].

Several cases in the literature demonstrated the above by comparing creatinine measured with Jaffe reaction with that measured by an enzymatic assay, which is another method of measuring creatinine which does not interfere with nitromethane [3, 6-8]. Our hospital laboratory did not have the enzymatic assay available, but we were able to show that our patient had normal renal function as demonstrated by Cystatin C measurement when compared to that measured by the Jaffe reaction.

Although nitromethane exposure causing a false elevation of creatinine has been reported in both the adult and pediatric population, reports in the pediatric population are limited. (Table 2) presents a PubMed search of all reported case reports of nitromethane exposure in the pediatric age group and their varied clinical presentation and biochemical profiles. Of note, articles were gathered by searching through PubMed between April-June 2023 using key words that included "nitromethane," "nitromethane pediatric", "falsely creatinine nitromethane", "fuel nitromethane," "race car fuel," "car fuel pediatric." Therefore, this case serves to support the finding that creatinine rise caused by Torco Fuel ingestion is spurious rather than secondary to true renal injury, due to the interaction of nitromethane with the Jaffe reaction. This was evidenced by simultaneous Cystatin C comparison as well as a thorough renal evaluation which revealed no signs of renal dysfunction. This is important to recognize as it can lead to unnecessary workup and interventions which can have their own consequences. However, in patients with concern for combined methanol/nitromethane exposure, treatment of methanol toxicity should take precedence. In patients with toxic ingestion and an unknown etiology of elevated creatinine levels, nitromethane ingestion should be included in the differential.

Table 1: Laboratory Workup Obtained at our Facility approximately 4 Hours after Ingestion.

Lab	Obtained Value	Reference
Sodium	138 mmol/L	136-145 mmol/L
Potassium	3.9 mmol/L	3.5-5.1 mmol/L
Chloride	109 mmol/L	98-107 mmol/L
Bicarbonate	22 mmol/L	22-30 mmol/L
Anion gap	7 mmol/L	<18 mmol/L
BUN	15 mg/dL	9-21 mg/dL
Creatinine	1.73 mg/dL	0.4-1.0 mg/dL
Total bilirubin	0.2 mg/dL	0.2-1.2 mg/dL
AST	18 U/L	5-34 U/L
ALT	19 U/L	0-55 U/L
ALP	260 U/L	<750 U/L
Serum Osmolality	290 mOsm/kg	275-295 mOsm/kg
Lactate	1.4 mmol/L	0.7-2.0 mmol/L
CK	102 U/L	30-200 U/L
Methemoglobin level	undetectable	undetectable
Salicylate level	undetectable	undetectable
Ethylene glycol	undetectable	undetectable

Table 2: Literature Review of Pediatric Cases of False Creatinine Elevation in setting of Nitromethane Exposure.

Age	Sex	Ingested Material, Quantity - Contents	Creatinine Trend via Jaffe Reaction (time obtained) [reference range]	Comparison Creatinine Trend (time obtained) [reference range]	Method of Creatinine Comparison	Renal Workup	Treatment	Reference
5 yr	M	model car fuel	7.13 mg/dL (15min) [0.3-0.7 mg/dL] > 4.86 mg/dL (15h)	0.32 mg/dL (15 min)	direct enzymatic measurement	renal ultrasound, CMP, serum osmolality, urine studies, serum gas chromatography all within normal limits (WNL)	no treatment; poison control was contacted and noted racing car fuel can contains nitromethane which can interfere with measurement of serum creatinine	6
2 yr	F	model car fuel - nitromethane only	274 µmol/L (4h) [35–62 µmol/L] > 234 µmol/L (12h) > 84 µmol/L (48h) > 46 µmol/L (10d)	1. 31 µmol/L (4h) [adult normal 35–62 µmol/L] > 30 µmol/L (12h) > 29 µmol/L (48h)	1. enzymatic assay	CMP, serum osmolality WNL	no treatment; monitored creatinine again at 10d, which was normal	12
				2. 35 µmol/L (4h) [adult normal 35–62 µmol/L] > 45 µmol/L (12h) > 34 µmol/L (48h)	2. creatinine mass spectrometry			
21 mo	F	radio controlled toy fuel, - methanol, nitromethane (20%), other lubricants	0.23 mg/mL (10h) [0.2 - 0.5 mg/dL] > 2.63 mg/dL (19.5h) > 0.82 mg/dL (60h)	measurements at 10h, 19.5h, 60h WNL	enzymatic assay	BMP, venous pH, serum osmolality, methemoglobin WNL	treated with fomepizole and folic acid due to methanol content of fuel, transfer to PICU to university hospital, toxicology consult	3
				(exact values not specified)				

4 yr	F	"Blue Thunder" model engine fuel - mixture of methanol and nitromethane	0.4 mg/dL (3h) [normal 0.3 - 0.7 mg/dL] > 4 mg/dL (9h) > 3.9 mg/dL (13h) > 3.0 mg/dL (21h) > 2.5 mg/dL (25h) > 0.7 mg/dL (28h)	measurements at 3h, 9h, 13h, 21h, 25h, 28h WNL (exact values not specified)	enzymatic assay	BMP, serum osmolality, osmolar gap WNL	transferred to tertiary care hospital PICU, treated with fomepizole which was stopped once patient remained asymptomatic with normal osmolar gap and no acidosis, observed for 24h	10
2 yr 4 mo	M	"Dynamite Blue Thunder", < 5mL - mixture methanol and nitromethane	926 µmol/L (1h) [adult normal 60-100 µmol/L] > 817 µmol/L (4h) > 712 µmol/L (9h) > 178 µmol/L (48h)	29 µmol/L (1h) [adult normal 60-100 µmol/L] > 27 µmol/L (4h) > 28 µmol/L (9h)	enzymatic assay	BMP WNL with AG 14, serum osmolality WNL, UA unremarkable, methanol level 4.2 mmol/L > 2.2 mmol/L, ethanol, isopropanol, acetone, methyl ethyl ketone undetectable, lactate, creatinine kinase, LDH WNL	bolus of 300 mL NS over 1 hour followed by D5/0.45NS at 60 mL/hr, observed for 24 hours in ED with peds nephro follow up in 48 hours with repeat CMP, phosphorous, CBC WNL	9
2 yr 9 mo	M	model aviation fuel	0.53 mmol/L (time of presentation) [0.02-0.05 mmol/L]	WNL at time of presentation (exact value not specified)	enzymatic assay	not specified in abstract	not specified in abstract	11
2 yr	not specified	model racing fuel, 30-40mL - methanol, nitromethane	8.6 mg/dL (1h) [0.2 - 0.5 mg/dL] > 5.8 mg/dL (4h)	None reported	N/A	1 hr CBC, BMP, serum osmolality WNL, 4h BMP WNL other than bicarb of 20 mg/dL, 9h methanol level 17 mg/dl, 9h serum acetone, ethanol, and isopropanol levels undetectable, 9h Venous blood gas pH 7.33, pCO^2 50, pO^2 < 30, HCO_3 20	poison control contacted, treated with fomepizole x1 prior to transfer, transfer to tertiary pediatric hospital PICU	15, 16
2 yr	M	model car fuel, "mouthful"	173 µmol/L (6h) [53-115 µmol/L] > 311 µmol/L (12h) > 273 µmol/L (17h) > 30 µmol/L (4d)	None reported - acute renal failure deemed unlikely considering all other biochemical markers were normal	N/A	BMP, urea, blood gas values WNL	no treatment; repeat check at 4d which was 30 µmol/L (WNL)	13
1 yr	M	Blue Thunder RC racing fuel-nitromethane 20% and unspecified amount of methanol	3.5 mg/dL (1.5 hr) [0.2 - 0.5 mg/dL]	None reported	N/A	BMP WNL, 1.5 hr methanol 10 mg/dL [normal < 15 mg/dL]	no treatment; observation	14
2 yr	M	As above	3.8 mg/dL (1.5 hr) [0.2 - 0.5 mg/dL]	None reported	N/A	BMP WNL, 1.5 hr methanol 12 mg/dL [normal < 15 mg/dL]	no treatment; observation	14

Conclusion

Spurious elevation of creatinine secondary to nitromethane exposure is an underrecognized issue that can lead to unnecessary therapeutic interventions. We present a pediatric case report as well as a pediatric literature review of nitromethane ingestion and its varied clinical presentations.

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