INTRODUCTION:

- Nitromethane is the simplest nitroalkane (CH₃NO₂).
- Has minimal acute toxicity requiring mostly supportive management.
- Ingestion of a fuel containing nitromethane and methanol can produce significant toxicity from the methanol component:
  - Retinal and optic nerve injury
  - Basal ganglia hemorrhage
- Nitromethane interferes with plasma creatinine measured via the Jaffé reaction by mimicking the spectrographic properties of creatinine: alkaline picrate complex.
- The interference presents diagnostic and management challenges.
- Point-of-care (POC) testing with the Stix® Chem 5+ measures creatinine by an enzymatic methodology which is not known to be interfered with by nitromethane.

HYPOTHESES:

1. Nitromethane will increase measured creatinine using the Jaffé reaction more than using the enzymatic reaction.
2. The difference between the measured creatinine using the Jaffé reaction and the enzymatic reaction can estimate nitromethane concentration.
3. Nitromethane will cause no change in the measured uric acid or uromol gap using the two different laboratory panels.
4. Plasma nitromethane concentrations will remain stable under standard laboratory conditions after 1 week.

METHODS:

- The study was approved by the IRB prior to enrollment of participants.
- The study used whole blood samples from 4 healthy volunteers with predicted normal baseline renal function.
- Nitromethane was added to whole blood to achieve 5 concentrations (0.25, 0.5, 1, and 2 mM/L).
- Basic metabolic panel (BMP) with Jaffé reaction, POC Chem 5+, plasma uromol, and gas chromatography (GC) were performed at each concentration.
- Remaining blood samples were refrigerated at 2–8°C and analyzed by GC after 7 days for nitromethane.
- Uric acid and uromol gaps were calculated for each patient sample at each concentration.
- Data collected for Jaffé creatine, POC creatinine, urinary gap, plasma uromol, and nitromethane recovery were analyzed using single-factor ANOVA (p < 0.05).
- Linear regression was used to determine the magnitude of nitromethane interference on apparent creatinine.
- GC data was used to verify nitromethane in each patient sample and to estimate degradation of nitromethane under standard storage conditions.

RESULTS:

- Two male and two female participant blood samples were used for analysis.
- Creatinine:
  - All participants had creatinine within the normal range for analysis method with mean of 0.95 mg/dL by POC analysis and 0.76 mg/dL by Jaffé reaction.
  - The mean measured creatinine was a linear function of the nitromethane concentration using the Jaffé reaction R² = 0.998.
- (Measured creatinine in mg/dL) = 7.1 x (Nitromethane in mM/L) + 0.79
  - No significant difference was detected for POC creatinine across nitro-methane concentrations (p = 0.09).
- Anion and Uromol Gaps:
  - No significant difference was detected across nitromethane concentrations for anion gap using POC (p = 0.3), anion gap using BMP (p = 0.11), esterase gap using POC (p = 0.12), and eserine gap using BMP (p = 0.36).
- Nitromethane Recovery by Gas Chromatography:
  - Nitromethane peaks were detected at all concentrations on day 0.
  - Detection of nitromethane at the 0.25 mM/L concentration was inconsistent on day 7.
  - Nitromethane degradation over 7 days was most pronounced at the 2 mM/L, concentrations with a mean 91% recovery.

CONCLUSIONS:

- Nitromethane significantly alters the apparent creatinine as measured by the Jaffé reaction in a linear fashion.
  - The difference between Jaffé and POC creatinine may be used to estimate the concentration of nitromethane in blood.
- No alteration in the anion or uromol gap by nitromethane.
- BMP measured anion and uromol gaps can be used as clinical adjuncts in co-exposures that involve toxic alcohols.
- Nitromethane at concentrations between 0.5 to 2 mM/L, remain stable under standard storage conditions and retrospective analysis may be feasible within the first 1 week.

LIMITATIONS:

- Ex vivo model with no known data on nitromethane pharmacokinetics or pharmacodynamics.
- Nitromethane is volatile, and small fractions may have been lost during preparation steps.

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