The Diagnosis and Treatment of Ethylene Glycol Poisoning

Amanda Jenkins,[1,2] Richard Amato,[1] and Yiqin Xiong[2]
[1]Quest Diagnostics, Marlborough, MA, USA; [2]UMass Memorial Medical Center, Worcester, MA, USA

IATDMCT 2020 Virtual Congress
September 14-16, 2020

Correspondence: Amanda Jenkins
Amanda.L.Jenkins@QuestDiagnostics.com

Introduction

Ethylene glycol (EG, 1,2-ethanediol, $C_2H_6O_2$) is a colorless, hygroscopic, sweet-tasting liquid of relatively low volatility. EG has many uses: as a component of automotive antifreeze solutions and hydraulic brake fluids, as a solvent in the plastic and paint industries, in the formulation of inks, and in the manufacture of explosives, synthetic fibers and waxes.[1]

EG is metabolized in the liver to glycoaldehyde by the enzyme alcohol dehydrogenase, then to glycolic acid by aldehyde dehydrogenase. It is then metabolized to glyoxylic acid, followed by the formation of oxalic acid (HOOCCOOH) and formic acid (HCOOH). These metabolites result in toxicity, including a metabolic acidosis with multisystem organ effects if therapy is not administered. The lethal oral dose of pure EG in adult humans is approximately 1.4 mg/kg body weight, or 100 mL/70 kg.[2]

EG poisoning is a medical emergency requiring timely diagnosis so that treatment can be initiated as soon as possible. Treatment may include supportive care, correction of the metabolic acidosis, inhibition of metabolism, and enhanced elimination of EG and metabolites. Early diagnosis and treatment reduces morbidity and mortality from EG poisoning.[3]

Many hospital laboratories do not have the capability to directly measure EG. Determination of an osmolal gap is a potentially useful test for making a presumptive diagnosis of EG poisoning.[4] However, clinicians should be aware of the limitations of this test since the absence of a gap does not rule out EG, and other substances (eg, methanol) and conditions (eg, diabetic ketoacidosis, shock) can also cause an osmolal gap.

Here we describe a gas chromatographic mass spectrometric (GC/MS) assay for the quantitative detection of ethylene glycol in human serum and its application to a clinical case.

Methods

GC/MS Assay Procedure

Serum specimens (200 µL) were subject to protein precipitation with the addition of 200 µL acetonitrile containing a 2,3-butanediol internal standard (IS, 500 mg/L). Specimens were mixed then centrifuged at 14,000 rpm for 10 minutes.

Methods (continued)

A portion of the supernatant (200 µL) was transferred to GC autosampler vials with inserts, secured with crimp caps, and placed on an Agilent 7890 GC and 5975 MS (Agilent Technologies, Santa Clara, CA) operated in selected ion monitoring mode.

Chromatographic separation was achieved with a Zebron ZB-WAXplus 30 m x 0.25 mm, 0.25 µm film thickness capillary column (Phenomenex, Torrance, CA) with helium carrier gas (1.0 mL/min flow). The temperature gradient program started at 80 ºC for 1.2 minutes with a ramp of 15 ºC/minute for a final temperature of 170 ºC, which was held for 1 minute, resulting in a total run time of 8.2 minutes.

The assay was calibrated daily with an EG standard (Fisher Scientific, Waltham, MA) at 200 mg/L.

The following serum quality control materials were run: drug-free bovine serum albumin and 400 and 800 mg/L EG (UTAK Laboratories, Valencia, CA).

Assay Validation

Precision was evaluated by assaying quality control material at 3 concentrations (200, 400, and 800 mg/L) with 5 replicates for 5 days.

Linearity was determined by assaying a 6-point calibration curve from 100 to 10,000 mg/L on 5 separate days.

Carryover was measured by assaying drug-free serum followed by 2 runs of 10,000 mg/L EG, followed by 3 more runs of drug-free serum.

Interference was assessed using 30 substances, including metabolites of EG.

Results

Assay Validation

- IS and EG demonstrated good chromatography with a relative retention time of 1.06 (example, **Figure 1**).
- The within-run precision of the assay at the 3 concentrations tested was <6.1%; between-run precision was <7.6%.

Results

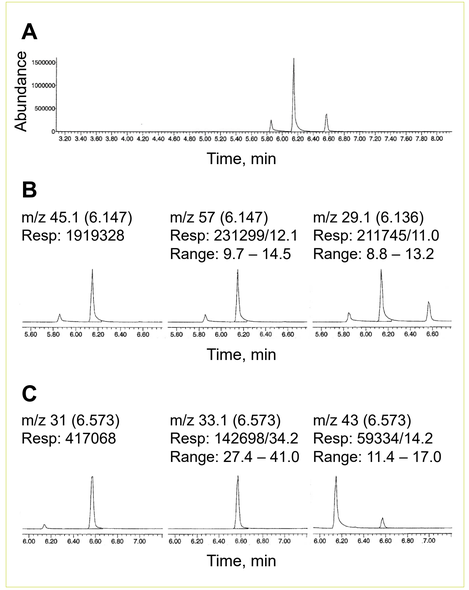

Figure 1. Total ion chromatogram (A) and selected ion chromatagrams of (B) the internal standard 2,3-butanediol (500 mg/L) and (C) ethylene glycol (200 mg/L calibrator), with ion m/z (retention time, min), response (Resp) indicated, as well as response ratios and their acceptable ranges for qualifier ions.

- The assay was linear from 100 to 10,000 mg/L, with r^2 >0.99. The recoveries at each concentration ranged from 93% to 108%, with CVs ranging between 5.9% and 8.2%.
- Carryover above the lower reporting limit (limit of quantitation, 100 mg/L) was observed in the first drug-free run following the 2 runs of 10,000 mg/L of EG. As a result, solvent blanks were run between all samples (calibrators, QC, and patient specimens).
- No interference was observed from propylene glycol, 1,4-butanediol, diethylene glycol, 1,3-propanediol, formic acid, glycolic acid, glyoxylic acid, oxalic acid, or from any of the other 22 substances tested.

Case Report

- A 54-year-old female patient was brought to the emergency department of a local hospital by emergency medical services. According to paramedics, while at home, the patient had made suicidal threats.
- The patient's medical history included T-cell leukemia, autoimmune neutropenia, migraine headaches, anxiety, and depression.
- At the home, a 3.75 L bottle of antifreeze was found with approximately 3 L remaining.
- At the local hospital, a bicarbonate drip was started (150 mL/h) and fomepizole was administered.
- The patient was intubated and transferred to UMass Memorial Medical Center, a Level I Trauma Center and regional medical facility located in central Massachusetts, USA.
- The patient's serum pH, osmolality, and EG concentration (using this GC/MS assay) were monitored over the course of her stay (**Table 1**).
- Testing at admission demonstrated metabolic acidosis, elevated osmolality, and an EG concentration of 8501 mg/L (**Table 1**).
- Hemodialysis was initiated. The patient received a total of 3 hemodialysis treatments. On day 5, her serum EG concentration was <100 mg/L (**Table 1**).

Table 1. Laboratory Findings in the Reported Case of Ethylene Glycol Poisoning

Day	1	2		3	4	5
Time	20:01	07:57	14:45	21:00	04:10	01:59
pH	7.18	7.36	not done	not done	7.46	not done
Osmolality, mOsm/kg	465	343	304	297	302	296
Ethylene glycol, mg/L	8501	2560	987	152	109	<100

Hemodialysis treatments

Conclusions

- This GC/MS assay performed well in validation studies and had no interference from a wide panel of substances, including EG metabolites.
- This GC/MS assay for EG is available 24 hours/day, 7 days/week, to support regional medical facilities. It is available on a STAT basis with a 4-hour posted turnaround time.
- In the case of EG poisoning presented, the measurement of EG concentrations in a critical patient was a useful tool for clinicians to monitor the effectiveness of treatment, which contributed to a successful outcome.

References

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Acknowledgments

The authors thank Allison TerBush and the Quest Diagnostics Global Scientific Publications department for their assistance preparing the poster.