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Short Communication

Ethyl Glucuronide: A biomarker for Acute Alcohol Ingestion

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Abstract

Ethyl glucuronide (EtG) along with ethyl sulfate (EtS) test validity are commented on. Sensitivity, specificity and reference threshold levels for urine screen are outlined. The accidental ingestion and absorption of ethanol from household products are also discussed. Ethyl glucuronide, a biochemical marker for ethanol, is a useful screen after acute alcohol ingestion, whether intentional or accidental.

Keywords: Ethyl Glucuronide, Biomarkers, Ethanol, Alcohol ingestion

1. Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) as Biomarkers for Acute Alcohol Ingestion

After consuming alcoholic beverages, a small portion (<5%) of the ethanol is excreted unchanged in the urine, sweat and breath. The majority (>95%) is metabolized mainly in the liver in a two stage oxidative process, first to aldehyde by alcohol dehydrogenase and further to acetate by aldehyde dehydrogenase. Another small part undergoes non-oxidative metabolism to produce ethyl glucuronide (EtG) and ethyl sulfate (EtS). There is interest in these products as biochemical markers for acute alcohol intake due to their slow wash out period (compared to parent compound), allowing for longer detection time. EtG has been detected in blood up to 14 hrs after consumption, and in urine, up to 35 hrs, and even 80 hrs. EtS may be detectable in the urine for 24 hours or more. Ethanol in the urine, on the other hand, is only detected up to 9 hrs after drinking. Therefore, a positive finding of EtG (and EtS) in urine or serum provides an indication that a person was recently drinking alcohol, even if drinking is denied and after ethanol is no longer detectable (Wurst et al., 1999).

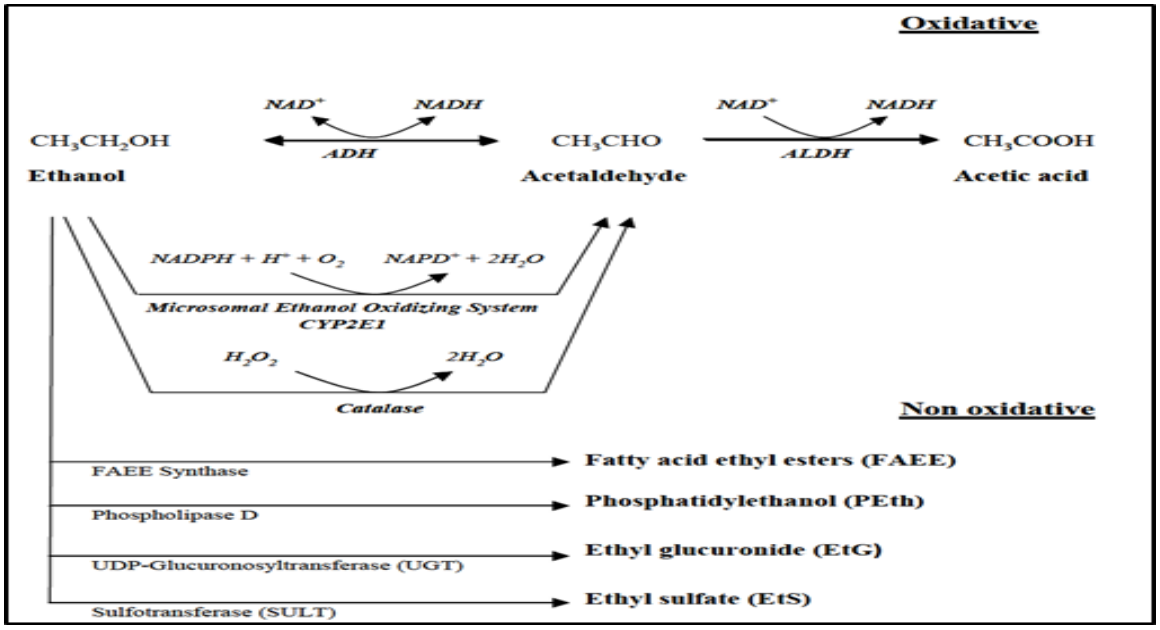

Figure 1: The major oxidative and minor non-oxidative pathways for ethanol elimination in the human body (Dahl, 2006).

2. Detection time and Sensitivity

Helander and colleagues determined the detection times for EtG and EtS in alcoholic patients undergoing alcohol detoxification. They found that the detection time for urinary EtG was weakly correlated with the initial alcohol concentration, and that for EtG, the time range until return to below the <500 ng/mL cut-off limit was 40–130 hrs (median 78 hrs) with a similar time course observed for EtS. For EtG, the detection times after an estimated zero ethanol concentration (i.e. after no ethanol was detected) were ~ 30–110 h (median 66 h) and ~30–70 hrs (median 56 hrs) after correction for urine dilution (Helander et al., 2009).

Stewart and colleagues evaluated the performance of urine ethyl glucuronide (EtG) and ethyl sulfate (EtS) in detecting alcohol use in the days preceding a clinical encounter (Stewart et al., 2013). They found urine EtG (sensitivity 76%, specificity 93%) and urine EtS (sensitivity 82%, specificity86%) to perform well in identifying recent drinking, and that liver disease severity does not affect biomarker performance (see table)

Urine Ethyl Glucuronide and Ethyl Sulfate in the Detection of Recent Alcohol Use[a]

	Ethyl glucuronide, %	Ethyl sulfate, %
Past 3-day drinking		
Sensitivity	76 (62–91)	82 (70–95)
Specificity	93 (88–98)	86 (78–93)
Positive predictive value	81 (68–95)	70 (56–84)
Negative predictive value	91 (85–97)	93 (87–98)
Past 7-day drinking		
Sensitivity	70 (57–84)	73 (60–86)
Specificity	99 (96–100)	89 (83–96)
Positive predictive value	97 (91–100)	80 (67–92)
Negative predictive value	85 (78–93)	85 (77–93)

[a]95% confidence intervals shown in parentheses.

3. Ethyl Glucuronide with Confirmation Urine test

One should test both EtG and EtS levels. At the Maine VA Healthcare System, this test is sent out to a reference laboratory, Quest Diagnostics, and must be received by the laboratory within 3-5 days of specimen collection. Specimens are stable up to 7 days at room temperature. The reference thresholds are:

Ethyl Glucuronide	*<500 ng/mL*
Ethyl Sulfate	*<100 ng/mL*

In order to be reported positive for EtG, Quest Diagnostics' reporting criteria require that EtS be present in a specimen at a minimum concentration of 50 ng/mL whenever EtG is present at a concentration greater than or equal to 500 ng/mL. As with EtG, the presence of EtS does not establish the source of the ethanol containing product & the possibility of "incidental exposure" and post-collection specimen changes needs to be considered when interpreting results.

3. Challenges with EtG Testing

Urine Concentration: EtG and EtS are subject to dilution affects of the urine, and can be artificially lowered by consuming fluids in excess. With the same logic, elevated concentration of urine artificially increases EtG and EtS levels.

Sample stability- microbial activity: EtG (but not EtS) can be degraded in urine due to certain bacteria. Furthermore, in the presence of alcohol, EtG can be synthesized by bacteria within the urine sample. The inclusion of the EtS biomarker, in conjunction with EtG, may eliminate the potential for a false positive or negative result.

Variation in amount of EtG produced for a given exposure to alcohol: There appears to be significant intra-subject variation in the amount of EtG produced from a given exposure to alcohol; exact limits of this variation are not known.

Establishing appropriate cut-off levels: The cutoff for possible incidental exposure vs intentional use has not been accurately established. However, it is logical to assume that higher levels are more likely to be from drinking but this is not definitive. Presently, EtG levels > 500 ng/mL and/or EtS levels >100 ng/mL are popularly accepted threshold values.

False Positives: The EtG test is sensitive to the presence of any alcohol, even low-levels, and can detect alcohol in the urine several days after consumption. It is so sensitive, that it can even produce a positive test for ethyl glucoronide from the mere exposure to alcohol that is present in many daily use products. According to the Substance Abuse and Mental Health Services Administration's (SAMHSA) research (Palmer, 2009), positive EtG tests can result from the use of:

- Hand sanitizers (alcohol-based)
- Hygiene products
- Laundry detergents
- Medications
- Cosmetics
- Foods

(a) Mouthwash: There were two studies that evaluated the effect of alcohol containing mouthwash on the appearance of ethyl glucuronide (EtG) in urine. In the first study, 9 volunteers were given a 4-oz bottle of mouthwash, which contained 12% ethanol. They gargled all 4 oz. of the mouthwash at intervals over a 15-min period, and urine samples were collected over the next 24 hrs. Of 39 provided urine samples, there were 20 results > 50 ng/mL, 12 results > 100 ng/mL, 5 results > 200 ng/mL, 3 results > 250 ng/mL, and 1 results > 300 ng/mL. The peak concentrations were all within 12 hrs after mouthwash exposure. In the second study, 11 participants gargled mouthwash 3 times daily for 5 days, and the first morning void was collected. 16 of the 55 submitted samples contained EtG concentrations > 50 ng/mL, and all of them were < 120 ng/mL. These studies show that incidental exposure to mouthwash containing 12% ethanol, when gargling according to the manufacturer's instructions, can result in urinary EtG values greater than 50 ng/mL (Costantino et al., 2006).

(b) Hand sanitizer: Eleven volunteers applied Purell™ hand sanitizer (62% ethanol) every 5 min for 10 hrs on three consecutive days, and urine specimens were obtained at the beginning and end of each day of the study. The maximum EtG and EtS concentrations over the course of the study were 2001 and 84 ng/mL, respectively, and nearly all EtG- and EtS-positive urine specimens were collected at the end of the individual study days. Only two specimens had detectable EtG at the beginning of any study day (96 and 139 ng/mL). The author's concluded that currently accepted EtG cutoffs do not distinguish between ethanol consumption and incidental exposures, particularly urine specimens taken shortly after sustained use of ethanol containing hand sanitizer (Reisfield et al., 2011).

4. Where It Stands Now

The Ethyl Glucuronide w/ Confirmation Urine test, which looks at both EtG and EtS levels, is a reliable test to determine alcohol consumption within the last 7 days. However, there is not a clear line between the distinction of incidental exposure and positive results from alcohol consumption. Always consider the possibility of incidental exposure and post-collection specimen changes when interpreting results.

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