Ethanol-Based Hand Sanitizing Gel Vapor Causes Positive Alcohol Marker, Ethylglucuronide, and Positive Breathalyzer

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Context: Ethylglucuronide (EtG), a minor metabolite of alcohol, is an important new marker that can detect alcohol use for several days or more after alcohol itself leaves the body. The test has rapidly gained widespread use where alcohol abstinence is desirable (eg, in health professional monitoring programs, alcohol treatment programs, high schools, criminal justice settings, liver transplant clinics). As with any new test, it is important to understand its limitations, especially, it turns out, regarding nonbeverage sources of alcohol that can affect EtG levels. We describe a case and follow-up studies in which ethanol-based hand sanitizing gel (EthGel) caused elevated EtG levels for a pharmacist who disputed disciplinary actions by her licensing board.

Objective: To document that EthGel causes elevated EtG levels and to identify the route of absorption.

Design, Setting, and Participants: After discovery of the index case in 2004, 24 subjects were tested for EtG before and 30 minutes and 6 hours after exposure to EthGel in 4 groups: controls, skin exposure only, vapor exposure only, and both skin and vapor exposure. Breathalyzer was used to measure breath alcohol levels.

Results: Primarily EthGel caused elevated EtG and breathalyzer from alcohol vapor. For "skin only," "vapor only," and "both" groups the mean EtG levels at 30 minutes were 42 (range 0 to 102) ng/mL, 106 (18 to 328) ng/mL, and 176 (0 to 348) ng/mL, respectively. Breathalyzer levels of 0.01 to 0.02 g% persisted for up to 40 to 60 minutes in subjects who had high-EtG levels.

Conclusions: EthGel exposure, particularly inhalation of fumes, caused positive EtG levels. Subjects being monitored with EtG testing should be warned to avoid products containing alcohol, including fumes from EthGel and similar compounds. Further studies should be conducted to better quantitate the amount of ethanol absorbed from EthGel to determine if frequent use, particularly in poorly ventilated areas, might cause toxicity, especially for fetuses, where zero tolerance to alcohol is desirable.

Key Words: ●●●

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Ethylglucuronide (EtG) is a nonoxidative metabolite of ethyl alcohol that has recently gained widespread use in monitoring alcohol abstinence. Depending on the amount of alcohol consumed, EtG can detect alcohol use for several days or more after alcohol leaves the body. It has rapidly gained widespread use in professional monitoring programs, alcohol treatment programs, schools, criminal justice settings, liver transplant clinics, and other situations where alcohol abstinence is desirable. Shortly after the test became commercially available in the United States in 2003, concerns arose regarding "false positive" tests due to incidental exposure to nonbeverage alcohol. The situation is similar to that of poppy seeds that can cause positive tests for morphine. As with any new test, it is important to understand its limitations and identify nonbeverage sources of alcohol (eg, mouthwash, foods, over-the-counter cough and cold meds) that might cause positive EtG levels.

In 2004, 2 of the authors (G.E.S. and M.L.) were contacted by health professionals who claimed that they tested positive in the absence of alcohol consumption, suspecting that their positive EtG tests had resulted from frequent use of ethanol-based hand sanitizing gel (EthGel) at work. One of the health professionals, a pharmacist, was willing to undergo testing and was admitted to an addiction treatment center for a trial exposure to EthGel.

EthGels have become ubiquitous in hospitals, homes, schools, prisons, nursing homes, daycare centers, and even gas stations or grocery stores. The frequent use of EthGel is strongly encouraged by agencies such as the US Center for Disease Control to prevent the spread of infections.[1] A search in the internet showed 14 name brand EthGel products containing 60% or higher content of ethanol. Surprisingly, little has been reported about potential absorption, abuse, or possible toxicity from these products.

Acceptance of the use of EthGels has been remarkable. One hospital report describes a 4% to 29% increase in the use of EthGel for hand cleansing between 2001 and 2004.[2] According to another report, 440,000 uses of the gel were counted in the first year of its introduction alone.[3] Some nurses, particularly those in neonatal intensive care units, reported using EthGels up to 50 or more times per shift.[4] Numerous studies demonstrate the popularity[5,6] of EthGel use. It is well tolerated[7] and leads to lower infection rates in hospitals,[8] extended care facilities,[9] and acute care facilities,[10] and it has been correlated with decreased transmission of illness in homes,[11] less absenteeism in elementary schools,[12] and fewer upper respiratory illness and absenteeism in university residence halls.[13] The only hazard mentioned in the literature from regulatory agencies regarding these prod-

ucts relate to their flammability and fire hazard (Joint Commission and Center for Disease Control).[14,15] A recent study designed to assess possible human toxicity from EthGels concluded that such an occurrence was highly unlikely.[16] Unfortunately, they neglected to test for alcohol markers and did not specifically examine skin versus inhalation exposure.

Because of the growing use of EtG testing and concerns regarding "false accusations of drinking" the Substance Abuse and Mental Health Services Administration published an advisory in 2006 warning against over-reliance on positive tests as proof of drinking, especially if disciplinary or punitive action is being considered.[17]

It is known that ethanol is not readily absorbed through adult skin[18]; however, there is a case report of a 1-month old Italian infant who became lethargic and was found to have a blood alcohol of 0.362 g/dL after application of an umbilical cord stump dressing soaked in methylated alcohol (95% ethanol/5% methanol).[19] There is a single report of a subject who had a slightly elevated EtG after the use of EthGel.[20] Another study showed no significant blood alcohol levels after use of EthGel.[21] One study reported examining the effect of heavy exposure to EthGel (30 times/hr) and detected alcohol on the breath of 6 of 20 subjects (0.001% to 0.0025%) at 1 to 2 minutes postexposure and in the serum of 2 subjects at 5 to 7 minutes postexposure. Another study demonstrated EtG levels as high as 713 ng/mL after 8 uses of EthGel over an 8-hour period.[22] However, none of these studies controlled for skin versus vapor exposure.[23]

Even minimal ethanol absorption, especially if recurrent, could present a concern for certain individuals. The Surgeon General's Advisory on Alcohol Use in Pregnancy states "No amount of alcohol can be considered safe during pregnancy."[24] However, no warnings have been issued for pregnant women to avoid use or exposure to EthGel.

METHOD

Testing Methods

Determination of EtG was performed by liquid chromatography-tandem mass spectrometry (LC-ESI-tandem MS) method by NW Toxicology. The breathalyzer was an Intoximeter Breathalyzer with lower level of detection at 0.001 g%.

Index Case

The index case, a pharmacist, was admitted to a secure residential alcohol treatment program where her possessions were searched and all potential items containing alcohol (hairspray, etc) were removed. On the first day, she was instructed to apply 2 squirts of 62% EthGel to her hands and forearms every hour for 8 hours and on the following day every half an hour for 8 hours. Urine for EtG was obtained before beginning testing and at 7 PM and 7 AM for both days of exposure. Neither blood alcohol nor breathalyzer was tested.

Exposure Study

A study was subsequently carried out, after Institutional Review Board approval, on 24 volunteer subjects (inclusion/exclusion criteria are age >21 years, body mass index <25, not pregnant or lactating, had not consumed alcoholic beverages in the last 5 days, no skin lesions on hands, not sensitive to alcohol, and no history of alcoholism or drug addiction). Subjects were divided into 4 groups of 6 each including controls (unexposed to EthGel), skin only exposure (EthGel on hands but inside a plexiglass box), vapor only exposure (subjects stood in bathroom with "both vapor and skin" exposure, but did not touch EthGel themselves), and "both vapor/skin" exposure (EthGel on skin with no recommendation regarding location of hands relative to face, in a 6 × 10 × 8, 540 ft^3 bathroom, a relatively closed space where vapor would be inhaled). All subjects using EthGel applied 2 squirts on their hands every 4 minutes for 1 hour. Blood alcohol concentrations were measured by an Intoximeter Breathalyzer at baseline, 20, 40, and 60 and at 90 minutes after completion of exposure. Urine samples for EtG were collected at baseline, 30 minutes, and 6 hours postexposure. All EtG results were from urine and were corrected to U100Creatinine standard to minimize the effect of variations in hydration (U100Creatinine EtG = 100/urine creatinine × urine EtG). All urine samples were tested for urine alcohol using an enzymatic test.

RESULTS

Index Case

The pre-exposure EtG at admission to the treatment program was negative (100 ng/mL cutoff). Postexposure EtG levels were positive: day 1, 7 PM = 225 ng/mL, and day 2, 7 AM = 441 ng/mL and 7 PM = 770 ng/mL.

Exposure Study

For this study, the EtG levels obtained from the laboratory were at the lower limit of detection. All urine alcohol tests were negative. The control group had negligible EtG levels throughout. All handgel-exposed groups showed significant intersubject variability. EtG levels in both and vapor-only groups were significantly higher than controls at 30 minutes ($P = 0.0044$) and at 6 hours ($P = 0.0049$) postexposure (See Charts 1–4 for details).

Breathalyzer registered zero in controls and 0.01 in one subject in the skin only group at 20 minutes, otherwise the skin-only group registered zero throughout. All but one subject in the vapor-only group registered 0.01 persisting for 40 minutes postexposure and then returned to zero. One subject in the both group registered 0.02 and the other 5

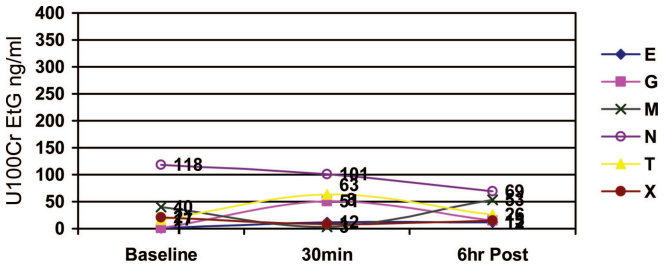

CHART 1. Effect of handgel on EtG—Skin-only group.

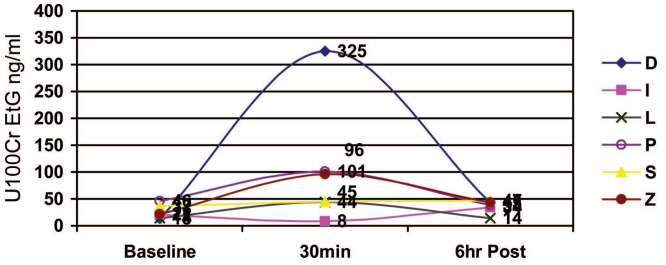

CHART 2. Effect of handgel on EtG—Vapor-only group.

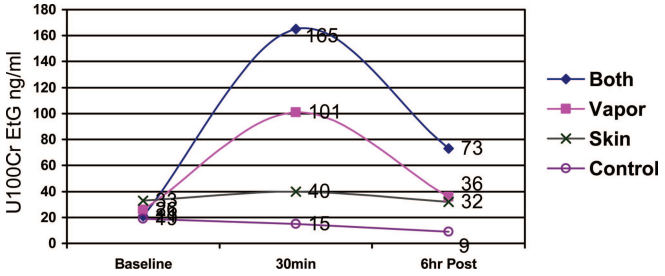

CHART 4. Grouped mead data—Effect of handgel on EtG.

registered 0.01 that persisted for 40 minutes, otherwise all 6 subjects in the both group registered 0.01 persisting for 60 minutes before returning to zero by 90 minutes.

DISCUSSION

In 2004, when the index case was discovered, EtG testing was new, used only by a few professional monitoring programs in the United Sates. As concerns over possible false-positive results were raised, it became increasingly important to understand the effect of different sources of alcohol exposure. This became especially important because laboratories had asserted, in marketing materials, indisputable reliability of a positive EtG as a proof of drinking.

After documentation of findings in the index case, we proceeded to verify this phenomenon in other subjects to determine whether absorption was from inhalation of vapor or through skin. It is known that vapor of alcohol can cause elevated ethanol levels. In many animal studies, use of alcohol vapor has been the preferred route of administration, because of the difficulty of orally administering alcohol to animals. In addition, a device for aerosolizing alcohol has been recently marketed for use in bars.[25] What has not been known is that use of EthGel, according to recommendations, produces enough ambient vapor to trigger positive tests for EtG.

This study demonstrated that the breathing EthGel vapor caused positive EtG tests and elevation of breathalyzer levels for up to 60 minutes. The significantly elevated alcohol markers in urine after exposure to EthGel vapor are of particular concern to individuals in monitoring programs where positive readings could result in sanctions such as loss or suspension of professional license, loss of child custody, return to jail, or uninsurability.[26]

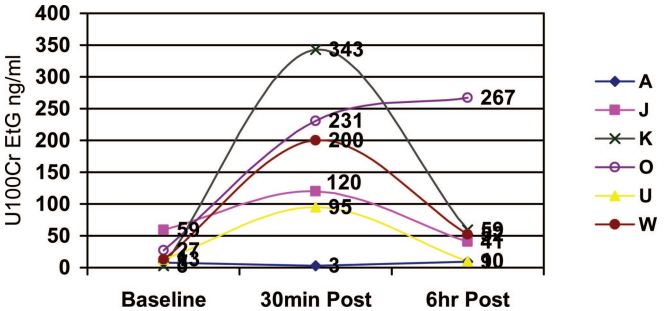

CHART 3. Effect of handgel on EtG—Both skin and vapor group.

The highest EtG value noted from EthGel exposure in our study was 770 ng/mL in the index case, achieved after EthGel use every 30 minutes for 8 hours. EtG levels seem to vary widely between subjects with similar exposure even when controlled for dilution, suggesting that some individuals either absorb more ethanol or produce more EtG. It is not known whether actively avoiding inhalation of vapor from EthGel (ie, holding hands away from the face) can prevent positive tests. This might be the case since most absorption seems to be from inhalation rather than skin absorption.

CONCLUSIONS

Use of EthGel, in accordance with product literature causes positive urine EtG levels, primarily from inhalation of vapor. Further investigation is warranted to assess the potential public health hazard of frequent or prolonged use of EthGels, as occurs in some professions (eg, nurses in neonatal intensive care units), especially if exposure involves pregnant women, where repeated small exposures could threaten fetal health and development.

Although the maximum achievable levels of EtG from EthGel exposure is unknown, the highest recorded level was 770 ng/mL in this study. It will likely prove difficult to establish a clear cutoff that distinguishes between drinking and incidental exposure to alcohol due to the plethora of products containing alcohol and the multiple and highly varied exposures they could produce.

In consideration of the above, it is recommended that EtG can be primarily used as a screening tool for recent drinking. When used properly the test remains useful and fair. In our experience, up to half of all positive EtG tests are associated with the patient's admission of drinking. However, if the patient denies drinking when confronted, one or more of the following can be considered: (1) continue observation and close monitoring; (2) obtain further intensive evaluation from an addiction medicine provider (potentially involving in-depth history and the questioning of collateral sources of information about the patient's drinking); (3) corroborate further drinking episodes by adding an additional "confirmatory" method of alcohol use detection, such as wearing a transcutaneous alcohol sensing device, recently shown to be accurate[27]; and/or (4) in safety sensitive situations consider administering disulfiram for enhanced prevention of drinking behavior.

Although all laboratory tests have potential for false-positives and many drug tests the potential for "incidental exposure" (ie, poppy seeds, hemp oil, coca tea) the presence

of ethyl alcohol in so many products presents a dilemma. Patients being monitored using EtG should be warned to avoid incidental alcohol exposure and should be provided a list of products to avoid.[28] Because of the multitude of products containing alcohol, it is unrealistic, however, to expect monitoring program participants to completely avoid all incidental exposure to alcohol.

Although EtG testing remains a valuable tool for early detection and deterrence of drinking, it is important to be cautious by acknowledging its limitations, especially in forensic settings where a positive test can have serious consequences. Further naturalistic studies in larger populations are needed to better understand the reliability of EtG and similar tests and produce better guidelines for their proper use.

COUNCIL OF MEDICAL SPECIALTY SOCIETIES

CMSS TASK FORCE ON PROFESSIONALISM AND CONFLICT OF INTEREST IN MEDICINE
RECOMMENDATIONS
NOVEMBER 15, 2008

Recommendation (1) *– it is recommended that the following core principles be considered by specialty societies for incorporation into conflict of interest policies:*

a. Definitions of conflict of interest, including financial and fiduciary, whether considered "real" or "perceived";

b. Clarification of who is addressed in the society's policy, including elected leaders, volunteers, representatives, members, staff, and the society itself;

c. Delineation of activities addressed in the policy, including governance; undergraduate, graduate and continuing medical education; research; and clinical practice guideline development;

d. Examples of conflicts of interest addressed in the policy;

e. Disclosures of relationships addressed in the policy, including criteria for disclosure, and manner of disclosure (written, verbal, web, other);

f. Consequences for failure to disclose relationships with a "real" or "perceived" conflict of interest;

g. Management and resolution strategies for disclosed conflicts of interest;

h. Clarification of circumstances requiring recusal, removal from participation or from the disclosed relationship;

i. Adherence to external standards and guidelines, such as the ACCME Standards for Commercial Support of CME, the AMA Ethical Opinion on Gifts to Physicians from Industry, and potentially others.

Recommendation (2) *– it is recommended that specialty societies consider publically disclosing on their websites the following information:*
a. Society Conflict of Interest Policies;
b. Financial support received by the society from commercial interests;
c. Society endorsements of external policies related to Conflict of Interest (such as the ACCME Standards for Commercial Support of CME, the AMA Ethical Opinion on Gifts to Physicians from Industry, and potentially others).

Recommendation (3) *– it is recommended that CMSS consider developing standardized model templates of conflict of interest policies, disclosure forms, and potentially management and resolution strategies, for use by specialty societies.*

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