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Ethanol and ethyl glucuronide urine concentrations after ethanol-based hand antisepsis with and without permitted alcohol consumption

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Background: During hand antisepsis, health care workers (HCWs) are exposed to alcohol by dermal contact and by inhalation. Concerns have been raised that high alcohol absorptions may adversely affect HCWs, particularly certain vulnerable individuals such as pregnant women or individuals with genetic deficiencies of aldehyde dehydrogenase.

Methods: We investigated the kinetics of HCWs' urinary concentrations of ethanol and its metabolite ethyl glucuronide (EtG) during clinical work with and without previous consumption of alcoholic beverages by HCWs.

Results: The median ethanol concentration was 0.7 mg/L (interquartile range [IQR], 0.5-1.9 mg/L; maximum, 9.2 mg/L) during abstinence and 12.2 mg/L (IQR, 1.5-139.6 mg/L; maximum, 1,020.1 mg/L) during alcohol consumption. During abstinence, EtG reached concentrations of up to 958 ng/mL. When alcohol consumption was permitted, the median EtG concentration of all samples was 2,593 ng/mL (IQR, 890.8-3,576 ng/mL; maximum, 5,043 ng/mL). Although alcohol consumption was strongly correlated with both EtG and ethanol in urine, no significant correlation for the frequency of alcoholic hand antisepsis was observed in the linear mixed models.

Conclusions: The use of ethanol-based handrub induces measurable ethanol and EtG concentrations in urine. Compared with consumption of alcoholic beverages or use of consumer products containing ethanol, the amount of ethanol absorption resulting from handrub applications is negligible. In practice, there is no evidence of any harmful effect of using ethanol-based handrubs as much as it is clinically necessary.

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During hand antisepsis, health care workers are exposed to the applied alcohols by dermal contact, but also by inhalation.¹⁻⁶ Concerns have been raised that high alcohol absorptions may adversely affect health care workers, and particularly certain vulnerable individuals such as pregnant women³ or individuals with genetic deficiencies of aldehyde dehydrogenase.⁷ During past years a small number of studies have been published that concluded that alcohol absorption even after excessive use of alcohol-based handrubs is minute and below any toxic levels for humans.² However, most data

on alcohol absorption after hand antisepsis were obtained from standardized experimental studies under controlled conditions. So far, real exposure during regular work, which includes application of alcohol-based handrubs by individuals having had previous intake of alcoholic beverages, had not been investigated.

Therefore, the aim of this study was to measure the ethanol absorption from an ethanol-based handrub (EBHR) during regular 8-hour working shifts under strict abstinence from alcohol compared with ethanol absorption after use of EBHRs with the permission to consume alcoholic beverages and to use food or cosmetic products containing alcohol during leisure time. Additionally, ethyl glucuronide (EtG), a direct metabolite of ethanol and marker of ethanol consumption⁸⁻¹⁰ was measured in urine as a forensic parameter to monitor participants during the alcohol abstinence phase of the study.

MATERIAL AND METHODS

In total, 34 healthy, voluntarily participating clinical staff members were recruited. With the exception of 1 participant (participant #7) all participants completed both study phases. Therefore, a total of 33 participants (male, $n = 16$; female, $n = 17$) yielded results for further analysis. Participants #1-#6 and #8-#10 worked at surgical wards of the Department of Surgery ($n = 9$), participants #11-#34 were laboratory staff members working at the Institute of Hygiene of the University Medicine Greifswald and of Hygiene Nord GmbH ($n = 24$). The Ethics Committee of the University Medicine Greifswald approved the study (approval no. BB 110/12). All participants gave written consent and had the right to withdraw at any time from the study without giving any further reasons. To ensure anonymity, each participant received an individual number (ie, an anonymous identifier between #1 and #34). For further analysis, only the workplace of the participants was identifiable.

The study was divided into 2 phases consisting of a single 8-hour working shift each. During the first phase, participants were instructed to refrain from any ethanol intake or use 48 hours before the study day and during the next 24 hours after repeatedly using EBHR during a single 8-hour working shift. Prohibition of alcohol intake included consumption of beer, wine, spirits, grape juice, apple juice, malt beer, or alcohol-free beer, alcohol-containing food such as jams, chocolate pralines, Worcester sauce, sauerkraut, kefir, and ripe bananas, and the use of alcohol-containing cosmetics such as cough syrup, mouthwash, or aftershave.

During the second phase, participants were permitted to drink alcoholic beverages during their leisure time and to eat alcohol-containing food or use cosmetics as usual. After 48 hours of regular alcohol intake or use, participants performed routine hand antisepsis using the EBHR during another 8-hour working shift. On the study day and 48 hours before, participants documented their own alcohol consumption.

Handrubs and their application

In both study phases the same EBHR with an alcohol content of 79.9 g ethanol 96% w/w (AHD 2000; Lysoform Dr. Hans Rosemann GmbH, Berlin, Germany) was used. Per hand antisepsis, a volume of 3-4 mL EBHR was used. This was provided either by wall-mounted dispensers or pocket bottles. To ascertain correct use, the performance of hand antisepsis was observed and documented during the 2 8-hour working shift phases.

Sample processing and chemical analysis

To measure systemic ethanol absorption, ethanol and its metabolite EtG were measured in participants' midstream urine

obtained immediately at the start of each study phase until the following 24 hours. To determine the concentration of urine, creatinine was measured in each sample of urine.¹¹ Participants collected their urine samples themselves and noted the time of passing urine. To exclude subsequent enzyme activity,^{12,13} samples were protected from sunlight by collecting them in polystyrene boxes and stored at 4°C up to a maximum of 24 hours.

Quantification of ethanol in urine was performed by gas chromatography following a modification of Roemhild et al,¹⁴ which uses a headspace injection (CombiPal-Autosampler; CTC Analytics AG, Zwingen, Switzerland) and a flame-ionization detection (Gas Chromatograph 5890 Series II; Hewlett Packard, Wilmington, DE). The detection limit for ethanol was 0.14 mg/L (working range, 0.14-500 mg/L) with a quantification limit of 0.34 mg/L.

EtG and creatinine were analyzed by immunoassay (MGC-240; Thermo Fisher Scientific GmbH, Passau, Germany). The quantitative analysis of EtG was done by liquid chromatography-mass spectrometry/mass spectrometry (QTrap 3200; AB Sciex GmbH, Darmstadt, Germany). The liquid chromatography-mass spectrometry/mass spectrometry was validated for EtG with a detection limit of 5 ng/mL (working range, 5-500 ng/mL) and a quantification limit of 16 ng/mL.

Statistical methods

The relationships among the frequency of hand antisepsis, self-rated alcohol consumption, and the respective maximum EtG and ethanol concentrations in urine were statistically analyzed using the software IBM SPSS Statistics (version 22) (IBM-SPSS Inc, Armonk, NY). Descriptive analyses included calculation of (Pearson) correlation coefficients and graphical visualization of data. Data were described as mean \pm standard deviation, median, and 25%-75% interquartile range (IQR). In addition, a linear mixed model was applied to account for dependencies among paired data. For each dependent variable (ie, EtG and ethanol), a random intercept model, which included study period, alcohol consumption, and frequency of hand hygiene as fixed effects were modeled. A P value $< .01$ was considered statistically significant.

RESULTS

During both phases, participants performed an average of 32 hand antisepsis procedures during the 8-hour working shift (Table 1).

Phase 1

During phase 1, 2 participants (participants #21 and #29) were not compliant to strict alcohol abstinence and were excluded from further analysis. Participants started with a median ethanol baseline of 0.4 mg/L. Starting from the second hour after baseline, the ethanol level increased until the 10th hour after beginning the monitoring to a median concentration of 0.4 mg/L. After 14 hours, the median concentration decreased to 0.3 mg/L and stabilized until the next morning at a median of 0.3 mg/L (Fig 1). The median of the maximum concentration was 0.7 mg/L (IQR, 0.5-1.9 mg/L) ethanol with the maximum measured value of 9.2 mg/L ethanol (Table 1).

For EtG, the overall median of the maximum concentration was 230 ng/mL (IQR, 141-372 ng/mL) with a maximum of 958 ng/mL (Table 1). In 22 of 32 participants, EtG was detected at the beginning of the working shift (range, 0-121 ng/mL). Only 1 participant (participant #8) exceeded 100 ng/mL total urinary EtG (121 ng/mL). The highest median EtG concentration was observed at the end of the working shift at 12 hours with 141 ng/mL (Fig 2). Thereafter, the median EtG concentration decreased to 37.5 ng/mL the next morning (Fig 2). Three participants exceeded 100 ng/mL EtG

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