Comparison of the Urinary Alcohol Markers EtG, EtS and GTOL/5-HIAA in a Controlled Drinking Experiment

G. Høiseth¹, J. P. Bernard¹, N. Stephanson², P. T. Normann*,¹ A. S. Christophersen¹, J. Mørland¹, and A. Helander²
¹Norwegian Institute of Public Health, Division of Forensic Toxicology and Drug Abuse, Oslo, Norway
²Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden

AIMS: Urinary ethyl glucuronide (EtG), ethyl sulphate (EtS) and the ratio between 5-hydroxytryptophol-glucuronide and 5-hydroxyindoleacetic acid (GTOL/5-HIAA) are used as biomarkers for alcohol relapse with longer detection times compared with measurement of ethanol itself. This controlled study determined the sensitivities and detection times of EtG, EtS and GTOL/5-HIAA in urine samples collected after a single ingestion of ethanol.

METHODS: Ten healthy male volunteers ingested 0.5 g ethanol/Kg body weight after an overnight fast. Urine collections were made before start of drinking, then at every voiding until 45 - 50 h after the start of drinking. This corresponded to approximately once every 2 h for the first 8 h after intake, thereafter at variable intervals. The total volume of each urine collection was determined.

Ethanol was measured by headspace gas chromatography equipped with a flame ionization detector. EtG, EtS and the ratio GTOL/5-HIAA were determined using a liquid chromatography-mass spectrometry (LC-MS) method. The limit of detection (LOD) was for ethanol 0.005 g/L and for EtG and EtS 0.1 mg/L. All values above these levels were reported as positive results. For the ratio GTOL/5-HIAA, an administrative cut-off (15 nmol/µmol) was used and values above this level were reported as positive.

RESULTS: During the first 8 h after drinking, urinary EtG, EtS and GTOL/5-HIAA showed 100% sensitivity as alcohol markers. The median maximum concentration (Cmax) for ethanol was 0.6 g/L (range 0.4 - 0.7), and for GTOL/5-HIAA 275 nmol/µmol (range 199 - 622). The Cmax for EtG (median 60 mg/L, range 47 - 88) was higher than for EtS (median 21 mg/L, range 14 - 29) in all subjects. Compared with ethanol testing, the detection times for GTOL/5-HIAA were ~5 h longer and for EtG and EtS ~25 h longer. A higher fraction of the ethanol dose was excreted as EtG (median, 0.019%) compared to EtS (median, 0.011%).

CONCLUSIONS: Measurement of EtG, EtS and GTOL/5-HIAA in urine was confirmed useful as biomarkers to detect recent drinking. Positive results were obtained for some time after the ethanol has been eliminated with the longest detection times for EtG and EtS. The GTOL/5-HIAA ratio was equally sensitive in the short run, but showed a much shorter window of detection. In cases where surveillance of alcohol relapse is needed, EtG and EtS in urine are excellent alternatives to ethanol measurement.

Keywords: Alcohol, Relapse markers, Urine kinetics