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Evaluation and clinical application of ethyl glucuronide and ethyl sulphate as biomarkers for recent alcohol consumption

AKADEMISK AVHANDLING

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ABSTRACT

In recent years, there has been a growing interest in various biochemical markers for detecting acute and chronic alcohol consumption. Biochemical markers for acute and chronic drinking play important roles in detecting alcohol use, abuse and dependence in hospital settings, work place settings, traffic medicine and in forensic toxicology examinations. The alcohol biomarkers can be distinguished into two main classes: “short-term markers” and “long-term markers”. Short-term markers are sensitive enough to detect a single intake of alcohol e.g. ethanol, 5-hydroxytryptophol (5HTOL), ethyl glucuronide (EtG) and ethyl sulfate (EtS). Long-term markers detect chronic heavy drinking, or indicate body organ or tissue damage caused by long-term exposure to alcohol e.g. carbohydrate-deficient transferrin (CDT), phosphatidylethanol (PEth), γ -glutamyl transferase (GGT), aspartate and alanine aminotransferase (AST and ALT), and the mean corpuscular volume of erythrocytes (MCV).

Following alcohol consumption less than 5% of the ethanol is excreted unchanged via the urine, sweat and breath, while more than 95% instead becomes metabolized mainly in the liver in a two-stage oxidation process. A minor part undergoes non-oxidative metabolism to produce the phase II products EtG and EtS. The interest in EtG and EtS as biochemical markers for acute alcohol intake has primarily focused on the observation that the washout rates for these direct ethanol metabolites are much slower than for the parent compound, thereby allowing a longer detection time. A positive finding of EtG and/or EtS in urine or plasma thus provides a strong indication that the person recently drank alcohol, even if drinking is denied, since levels of EtG and EtS remain elevated for some time after ethanol itself is no longer detectable.

The purpose of this thesis was to evaluate the accuracy of urinary EtG and EtS measurement and the clinical application as biochemical markers for acute alcohol consumption. Urinary EtG and EtS were determined by liquid chromatography-mass spectrometry (LC-MS).

The current studies demonstrated that EtG is a direct metabolite of ethanol and represents a minor elimination pathway (<0.03%) in the human body and confirmed that EtG remains detectable in the urine for many hours after the ethanol has been eliminated. Drinking large amount of fluid prior to voiding was found to lower the urinary concentration of EtG, but this practice did not influence the concentration of the EtG/creatinine ratio, no significant accumulation of EtG or 5HTOL was observed upon multiple-dose administration of ethanol, and the detection time in urine for EtG was demonstrated to be longer than for 5HTOL. It was found that EtG but not EtS is sensitive to bacterial hydrolysis. To reduce the risk for obtaining false low or false-negative EtG results specimens should be stored refrigerated or frozen prior to analysis. Plasma EtG was found useful in the emergency department to detect recent drinking even when ethanol is negative to confirm alcohol abstinence. In 87% of the cases the information about recent drinking provided by self-report agreed with the EtG and EtS results in an outpatient treatment program for alcohol and drug dependence. EtG and EtS may also be objective outcome measures when evaluating new treatment strategies and pharmacotherapies.

In conclusion, the present results demonstrated that urinary EtG and EtS are very sensitive and specific biochemical markers for acute alcohol intake.