Institutionen för Laboratoriemedicin, Klinisk Kemi

Studies on the reliability of biomarkers for alcohol use and abuse

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av

Naama Kenan Modén

Huvudhandledare:
Adj. Professor Anders Helander
Karolinska Institutet
Institutionen för Laboratoriemedicin

Bihandledare:
Adj. Professor Olof Beck
Karolinska Institutet
Institutionen för Medicin, Solna

Professor Jonas Bergquist
Uppsala Universitet
Institutionen för kemi
Avdelningen för analytisk kemi

Fakultetsopponent:
Docent Mikael Hedeland
Uppsala Universitet
Institutionen för läkemedelskemi

Betygsnämnd:
Professor Åsa Emmer
Kungliga Tekniska Högskolan
Skolan för kemivetenskap
Tillämpad fysikalisk kemi

Professor Erik Eliasson
Karolinska Institutet
Institutionen för Laboratoriemedicin

Docent Tom Palmstierna
Karolinska Institutet
Institutionen för klinisk neurovetenskap

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ABSTRACT

Alcohol is consumed by the vast majority of the population, but prolonged excessive drinking is associated with various negative health and social consequences. It is therefore important to identify individuals with at-risk alcohol consumption, before it turns into abuse or dependence. Early detection of alcohol use and abuse can be done by the use of biomarkers such as ethyl glucuronide (EtG), carbohydrate-deficient transferrin (CDT), and phosphatidylethanol (PEth) that provide objective information about current consumption. However, since misleading test results can have devastating consequences, the use of reliable biomarkers is substantial. The aim of this thesis was to evaluate several factors, both clinical and analytical, that could generate erroneous test results when testing for alcohol use by these biomarkers.

Measurement of urinary EtG levels was done in 482 samples using different liquid chromatography-mass spectrometry procedures. Accurate determination of EtG concentrations was done according to specific criteria suggested by international guidelines. The sensitivity and specificity were calculated for each of four methods by comparing EtG results obtained with a fifth reference method that demonstrated the highest selectivity. These results showed that meeting the guideline criteria does not always guarantee correct identification, and the likelihood of different analytical methods to provide reliable analytical results depends on the reporting limit applied.

Evaluation of the analytical performance of CDT testing was done by comparing two different methods in routine use, capillary electrophoresis (CE) and high-performance liquid chromatography (HPLC). Most of the problems encountered by CE could be solved by using the HPLC method, and it was therefore advised to have access to a confirmatory HPLC analysis, when a high throughput method like CE is employed.

Evaluation of the clinical performance of CDT in pregnancy was done by measuring serum transferrin glycoforms in 171 samples collected from 24 healthy women during and after pregnancy. A gradual increase in the CDT (%disialotransferrin) level was observed during pregnancy, and in many subjects the level approached the upper limit of the reference interval. For use in pregnant women, the cutoff value for CDT used to detect risky drinking therefore needs to be raised slightly to minimize the risk for false-positive results.

The possible interference by transferrin glycation on CDT testing was also evaluated. Samples subjected to in vitro glycation and samples collected from diabetic patients were tested for CDT by HPLC. No interferences were observed in samples from diabetics, which contrasted to the effect seen in vitro by transferrin glycation. The results indicated that CDT, and also PEth, are reliable markers to identify risky drinking in diabetic patients.

Taken together, the results of the present studies have identified and suggested ways to overcome a number of analytical and clinical interferences with these alcohol biomarkers, and thus helped to improve their routine use.