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Research Article

Diagnostic Performance of Ethyl Glucuronide and Carbohydrate-Deficient Transferring as Biomarkers of Alcohol Dependence in Women

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Abstract

Aims: To compare the performance of ethyl glucuronide (EtG) and carbohydrate-deficient transferring (CDT) for detecting alcohol dependence in women.

Methods: The concentrations of EtG in hair and CDT in the blood of 25 alcohol-dependent women **admitted to the hospital for detoxification were determined.** To assess diagnostic performance (sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)), as well as to determine the optimal cut-off values of biochemical markers, receiver operating characteristic (ROC) analysis was performed.

Results: The optimal cut-off value for EtG was 38 ng/mL. At this cut-off, the model demonstrated strong performance with a sensitivity 93%, a specificity 92%, a PPV 83%, and an NPV 67%. For CDT, a cut-off of 371 ng/mL yielded a sensitivity 95%, specificity 100%, positive predictive value 100%, and negative predictive value 95%.

Conclusions: The results suggest that EtG and CDT are reliable indicators of alcohol dependence in women. CDT performed better in identifying alcohol dependence in women.

Introduction

Alcohol dependence is a globally prevalent disorder [1]. Recent evidence suggests that gender differences in alcohol use disorders are decreasing in many countries [2]. Some authors hypothesized that stress among women due to pursuing a career leads to increased alcohol drinking [2]. In relation to this, early diagnosis of alcohol use disorders in women using biochemical markers is an important prevention strategy.

A minor non-oxidative metabolite of ethanol, Ethyl glucuronide (EtG) in hair, has emerged as a useful direct long-term biomarker for the objective detection of chronic alcohol abuse [3]. EtG demonstrated a strong potential to identify heavy alcohol consumption in comparison to the traditional biomarkers [4]. The diagnostic power of EtG was not significantly influenced by confounders, including age, gender, prevalent beverage, and hair color [5,6].

Carbohydrate-deficient transferring (CDT) is considered among the most specific serum biomarkers of heavy drinking [7]. At the same time, CDT has limited sensitivity as a biomarker of harmful alcohol consumption [8]. Previous studies have identified several variables that affect the diagnostic sensitivity of CDT, including gender, liver cirrhosis, insulin resistance, and dyslipidemia [9,10].

EtG and CDT are formed by different mechanisms and are detected by different analytical techniques [7,11]. The combined use of both markers may increase the accuracy of the diagnosis and avoid incorrect results caused by biological variables and by analytical errors. Despite extensive research, sparse data are available regarding diagnostic performance and optimal cut-off values of EtG and CDT for detecting alcohol dependence in women.

This study aimed to compare the performance of EtG and CDT for detecting alcohol dependence in women.

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Methods

The study involved 25 alcohol-dependent women admitted to the hospital for detoxification. The control group consisted of 25 moderately drinking women randomly recruited from the general population. The study was approved by the clinic's Ethics Committee, and written informed consent was obtained from all participants. Venous blood was samples upon patient admission, prior to the initiation of any medical or detoxification procedures. Whole blood samples collected in Vacutainer were kept at room temperature in sampling room and during transport. The EtG level was assessed in the proximal 3-cm segment of scalp hair as per SoHT guidelines for alcohol marker detection. EtG concentration was determined by high-performance liquid chromatography – tandem mass spectrometry (HPLC-MS) [12]. The concentration of CDT in serum was determined by an immunoenzyme analysis (IFA).

Statistical data analysis was performed using Statistica, version 10.0 (StatSoft Inc., Tulsa, OK, USA). The Shapiro-Wilk criterion was used to test statistical hypotheses about the type of distribution. Since EtG and CDT values were non-normally distributed, Mann-Whitney test was used for calculations. Receiver Operating Characteristic (ROC) analysis was performed to assess diagnostic accuracy (sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV)). ROC curve were plotted in order to assess the ability of biomarkers to discriminate between moderate drinking and alcohol dependence and to identify optimal cut-offs. The most commonly index of accuracy is the area under the ROC curve (AUROC). The values close to 1 indicate a high diagnostic performance. The 95% confidence interval of the AUROC was calculated according to DeLong. The difference in areas under the ROC curves was tested for significance calculating the P-value for a two-tailed test. The Youden index was used to determine the threshold level.

Results

The median age of alcohol-dependent women was 35.6 years (IQR: 32.8 - 37.7). The median age of moderate drinkers was 35.9 years (IQR: 33.1 - 40.1). There was no statistical significant difference in age between two groups (p = 0.152). All patients have the EtG and CDT values above the upper cut-off for harmful alcohol consumption. The median value of the EtG concentration in hair of alcohol-dependent women was significantly higher than in hair of moderate drinkers. The median value of the CDT concentration in blood of alcohol-dependent women was significantly higher than in blood of moderate drinkers (Table 1). The optimal cut-off value for EtG was 38 ng/mL. At this cut-off, the model demonstrated strong performance with sensitivity 93%, specificity 92%, PPV 83% and NPV 67%. The AUROC was 0.98, indicating a good predictive value of the model. For CDT a cut-off of 371 ng/mL yielded sensitivity 95%, specificity 100%, positive predictive value 100%, and negative predictive value 95%. The AUROC was 0.98, indicating a good predictive value of the model (Table 2).

Table 1: Values of EtG concentration in hair (pg/mg) and PEth concentration in the blood (ng/mL).

Parameter	Control	Alcohol dependence
EtG	9.8 (CI:8.9 – 35.1)	59.4 (CI:20.2 – 400)*
CDT	301.3 (CI:236 - 350)	1462(CI:313 - 2660) *

* – $p < 0.05$ in comparison to control.

Table 2: Results of ROC analysis.

Parameter	EtG	CDT
AUROC [95% CI]	0.98 [0.95 - 1.0]	0.98 [0.95 - 1.0]
cut-off value	38 ng/mg	371 ng/mL
Sensitivity	93%	95%
Specificity	92%	100%
PPV	83%	100%
NPV	67%	95%

Discussion

Due to physiological characteristics, the rate of alcohol metabolism differs between men and women, which may affect the diagnostic performance of biochemical markers [11]. Several studies on the gender dimension of laboratory diagnosis of alcohol abuse show lower diagnostic effectiveness of biochemical markers in women [3,11]. In particular, there is evidence that women produce less CDT in response to alcohol consumption, making this marker less sensitive to diagnosis of alcohol abuse in women [9].

The findings from present study contradict the results of previous studies, which suggest that CDT has limited sensitivity as an objective biomarker of prolonged heavy alcohol consumption [9,10]. The outcomes clearly demonstrate that CDT is highly effective in diagnosing alcohol dependence in women. Furthermore, the results of analysis suggest that CDT outperforms the diagnostic value of EtG.

Before concluding, several limitations of this study should be discussed. In particular, the sample size is relatively small, which may limit the robustness and generalizability of the findings. Further, potential confounding factors affecting EtG and CDT values were not controlled.

In conclusion, the analysis of EtG in hair and CDT in blood provides efficient diagnostic tools to detect alcohol dependence in women. Combined use of EtG and CDT decreases a risk of false interpretation and improves the accuracy of the detection of alcohol dependence. Further studies with larger number of patients are needed to fully understand the diagnostic potential of these biomarkers.

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