Mini Review

Comparison of the diagnostic performance of phosphatidylethanol and carbohydrate-deficient transferrin as biomarkers of alcohol dependence in women

Abstract

Aims: To compare the performance of phosphatidylethanol (PEth) and carbohydrate-deficient transferrin (CDT) for detecting alcohol dependence in women.

Methods: The concentrations of PEth and CDT in blood of 25 alcohol-dependent women **admitted to 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 PEth was 385 ng/mL. At this cut-off, the model demonstrated strong performance with sensitivity 100%, specificity 98%, PPV 86% and NPV 100%. For CDT a cut-off of 371 ng/mL yielded sensitivity 95%, specificity 100%, positive predictive value 100%, and negative predictive value 95%. **Conclusions:** The main findings of this study are that PEth and CDT are reliable indicators of alcohol dependence in women. The results also suggest a higher sensitivity for PEth compared with CDT.

Keywords: phosphatidylethanol, carbohydrate deficient-transferrin, performance, alcohol dependence, women

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Introduction

Alcohol abuse is a leading cause of premature mortality in many countries.[1] The problems in identifying early persons with harmful drinking hamper preventive measures. The limited diagnostic efficiency of self-reports and conventional liver enzymes have led to an intensive search for more sensitive and specific biochemical markers for detecting harmful drinking.[2] In the last decades several reliable biomarkers, such as phosphatidylethanol (PEth) and carbohydrate-deficient transferrin (CDT) have been developed.[3,4] PEth has been gaining popularity as a direct biochemical marker to identify chronic alcohol abuse.[5] PEth is a group of abnormal phospholipids which are formed on the membranes of the red blood cells from phosphatidylcholine only in the presence of ethanol.[3] PEth has been validated as a reliable biomarker for harmful drinking in a variety of settings.[4] However, evaluation of PEth as a biomarker of alcohol dependence is lacking, and space data are available regarding alcohol-related women. Carbohydrate-deficient transferring (CDT) is considered among the most specific serum biomarker used clinically for detecting heavy drinking.[2] In contract to the high specificity, sensitivity of CDT for detection of harmful alcohol consumption is rather low.[6] Previous studies have identified several variables that affect diagnostic sensitivity of CDT including gender, insulin resistance and dyslipidemia.[7] Despite extensive researches, little is known regarding diagnostic performance and optimal cut-off values of PEth and CDT for detecting alcohol dependence in women. The present study was undertaken to compare the diagnostic performance of PEth and CDT as biomarkers of alcohol dependence in women.

Methods

The study involved 25 alcohol-dependent white women admitted to Grodno (Belarus) regional clinical center 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 concentration of PEth (homologue 16:0/18:1) in blood was determined by high-performance liquid chromatography - tandem mass spectrometry (HPLC - MS).[8] The concentration of CDT in serum was determined by an turbidimetrics immunoassay.[6] 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 PEth 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 PEth and CDT values above the upper cut-off for harmful alcohol consumption. The mean and median values of the PEth concentration in blood of alcohol-dependent women were significantly higher than in blood of moderate drinkers. The mean and median values of the CDT concentration in blood of alcohol-dependent women were significantly higher than in blood of moderate drinkers (Table 1). The optimal cut-off value for PEth was 385 ng/mL. At this cut-off, the model demonstrated strong performance with sensitivity 100%, specificity 98%, PPV 86% and NPV 100%. The AUROC was 0.99, indicating a very 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 very good predictive value of the model (Table 2).

Table 1 Values of PEth concentration in the blood (ng/mL)

Biomarker	Control		Alcohol dependence	
	mean	median	mean	median
PEth	50.7 ± 7.69	23.6 (CI:16.9-42.1)	1887 ± 192*	1768 (CI:1298-2501)*
CDT	301.4 ±28.6	301.3 (CI:236-350)	1444.7 ±722*	1462 (CI:313-2660) *

* – p< 0.05 in comparison to control

Table 2 Results of ROC analysis

Parameter	PEth	CDT
AUROC [95% CI]	0.99 [0.99-1.0]	0.98 [0.95-1.0]
cut-off value	385 ng/mL	371 ng/mL
Sensitivity	100%	95%
Specificity	98%	100%
PPV	86%	100%
NPV	100%	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.[9] Several studies on the gender dimension of laboratory diagnosis of alcohol abuse show lower diagnostic effectiveness of biochemical markers in women.[6,7] 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.[6] 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.[4] The outcomes clearly demonstrate that CDT is highly effective in diagnosing alcohol dependence in women. Available data show the advantage of direct biochemical markers in diagnosing alcohol dependence compared to indirect markers.[9]

In a study conducted in Germany comparing the effectiveness of different biochemical markers in diagnosing alcohol dependence, sensitivity and specificity of PEth were 95% and 100%, respectively, whereas the sensitivity and specificity of CDT were 77% and 88%, respectively.[3] According to the results of present study PEth and CDT yield a similar diagnostic performance in detecting alcohol dependence. It should be noted, however, that the analysis suggests a higher sensitivity for PEth compared with CDT. 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 FEth and CDT values were not controlled. In conclusion, the analysis of blood PEth and CDT provides an efficient diagnostic tool to detect alcohol dependence in women.[10] Combined use of PEth 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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None.

Conflicts of interest

The author declares there is no conflicto of interest.

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