



Invited critical review

Biomarkers in alcoholism

Onni Niemelä *

Department of Laboratory Medicine and Medical Research Unit, Seinäjoki Central Hospital and University of Tampere, FIN-60220 Seinäjoki, Finland

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Abstract

Alcoholism ranks as one of the main current threats to the health and safety of people in most Western countries. Therefore, a high priority should be given to aims at reducing its prevalence through more effective diagnosis and early intervention. The need for objective methods for revealing alcohol abuse in its early phase has also been widely acknowledged. It is postulated here that the diagnosis of alcohol use disorders could be markedly improved by a more systematic use of specific questionnaires and laboratory tests, including blood ethanol, serum γ -glutamyltransferase (GGT), carbohydrate-deficient transferrin (CDT), and mean corpuscular volume of erythrocytes (MCV). Recent research has provided new insights into the relationships between ethanol intake, biomarkers, and factors affecting their diagnostic validation, including gender, age, and the effects of moderate drinking and obesity. It appears that the concept of reference intervals for several ethanol-sensitive parameters in laboratory medicine needs to be revisited. CDT is currently the most specific marker of alcohol abuse, and when combined with GGT using a mathematically formulated equation a high sensitivity is reached without loss of assay specificity. Possible new biomarkers include minor ethanol metabolites (protein–acetaldehyde condensates and associated autoimmune responses, ethylglucuronide, and phosphatidylethanolamine), 5-hydroxytryptophol, and genetic markers although so far their routine applications have been limited.

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* Tel.: +358 6 415 4719; fax: +358 6 415 4924.

E-mail address: onni.niemela@epshp.fi.

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1. Introduction

Health problems created by excessive ethanol consumption have been rapidly growing in most Western countries [1,2]. Current statistics indicate that 20–30% of all hospital admissions and health care costs may be attributable to alcohol abuse. There has also been a rapid increase in total per capita ethanol consumption, which may even be expected to lead to a lower life-expectancy especially in countries with the highest incidences of heavy alcohol intake [3,4].

In order to develop more effective policies for reducing alcohol consumption both at individual and population level, it is important to gain further insight on the pathogenic mechanisms of alcohol-related disorders and to develop more effective diagnostic modalities for early detection of hazardous drinking. However, physicians far too often fail to detect alcohol use disorders despite of the fact that a wide variety of specifically designed questionnaires and laboratory tests have already been made available [5–11]. Since questionnaires (such as CAGE, MAST, or AUDIT) depend on self-reports they have often been avoided in routine use due to prevailing attitudes towards drinking both among patients and health care personnel. Objective laboratory evidence of heavy drinking is clearly needed to help the clinicians to raise the possible issue of alcohol use as the real cause for symptoms. Biomarkers have also proven practical in the follow-up use improving both compliance and treatment outcome [5,8,9]. However, to date the diagnostic validation of the biomarkers has been incomplete and the information on the sensitivities and specificities of even the most commonly used tests have remained controversial.

This article will focus on recent progress in the clinical use and interpretation of current biomarkers for alcohol abuse. It appears that the clinical value of the laboratory tests could be markedly improved if biological variation induced by factors, such as moderate drinking, obesity, increasing age, gender and liver disease, could be more efficiently controlled in their diagnostic validation.

2. Alcohol consumption and health problems

Information on the actual amounts of ethanol consumption by patients is important since it determines the risk for subsequent medical problems [1]. At the population level, alcohol use is followed as mean per capita consumption, whereas at the individual level it is based on self-reports, which is known to account for only about half of the alcohol sold.

Although most individuals who drink alcohol are able to limit their intake to amounts that produce no apparent health problems, it should be noted that the percentage of individuals who drink no alcohol and can be categorized as abstainers or teetotallers is continuously decreasing in most Western countries. For example, the national statistics from Finland have indicated that over the past two decades the proportion of abstainers in population has decreased to less than 10% in both genders, the changes having been especially rapid among women (Fig. 1). The individuals who are able to control their drinking and consume amounts that are so small that no adverse consequences are to be expected can be categorized as moderate drinkers [12,13]. Population studies have suggested that the rate of mortality in such individuals (consuming one to three drinks daily or 10–30 g ethanol/day) may be even smaller than that in teetotallers [14–16]. However, at higher levels the risk for adverse health effects rapidly increases [1,2,8,14–16].

Heavy drinkers drink large amounts on any single occasion or frequently consume moderate amounts. Although there is no clear threshold for heavy drinking, epidemiological data has indicated that exceeding the level of approximately 300 g (men) or 200 g (women) per week creates a significant health risk. This type of consumption is also referred to as at-risk or hazardous drinking or harmful use of ethanol. Quantities exceeding 5–7 drinks (men), or 3–5 drinks (women) on any single occasion are also harmful. Clinically, hazardous drinking should be differentiated from alcohol abuse, which refers to problem drinking that has resulted in adverse health consequences, social problems or both. In such individuals, there are either mental or physical complications, although the criteria for alcohol dependence or alcoholism may not be fulfilled. Alcoholism is the most severe stage of problems involving

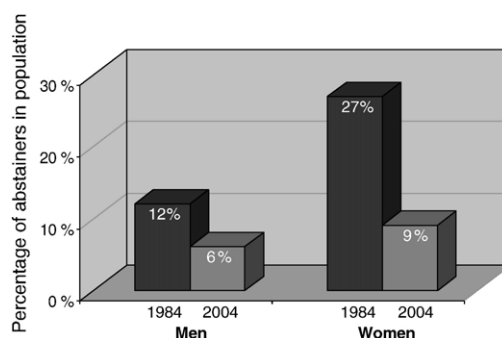


Fig. 1. Percentages of abstainers in adult population in Finland in years 1984 and 2004. Although a clear decrease is noted in both genders, the change has been especially striking among women. Source: National Statistics, Stakes.

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