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Blood glucose and lipid concentrations after overload are not associated with the risk of alcohol relapse

Jacek Budzyński[a,b,*], Marcin Ziółkowski[c], Maria Kłopocka[a], Damian Czarnecki[c]

[a] Department of Vascular and Internal Medicine, Faculty of Health Sciences, The Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus Universisty, Toruń, Poland
[b] Clinic of Vascular and Internal Diseases, Jan Biziel University Hospital No. 2, Bydgoszcz, Poland
[c] Department of Psychiatric Nursing, Faculty of Health Sciences, The Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Toruń, Poland

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ABSTRACT

Aims: There is evidence for the functioning of feedback between alcohol consumption and fat (positive) and carbohydrate (negative) intake. We tried to verify the hypothesis that blood glucose and lipid concentration in a fasting state and after loading may affect the risk of relapse in alcohol-dependent male patients during withdrawal therapy.
Methods: Blood glucose, total cholesterol (TC) and triglycerides (TG) were determined at the beginning of the study, and again after 4 weeks and 6 months of observation in 54 alcohol-dependent male patients treated against drinking relapse. Glucose concentration was checked after fasting and 2 h after loading with a 75 g water solution of glucose, and blood lipids were determined on an empty stomach and 5 h after butter loading (0.5 g of butter per kilogram of body mass).
Results: Patients who relapsed compared to subjects who remained abstinent during the 6-month observation did not differ significantly in relation to blood glucose, TC or TG blood concentrations, either in a fasting state or after loading. Patients with an initial above-median increase in TG blood concentration after butter loading (>38%) before the beginning of the study, and who smoked cigarettes with a greater content of nicotine and tar, preferred vodka and had lower values of aminotransferases.
Conclusion: Fasting and postprandial blood glucose, TC and TG concentrations had no relationship with the outcome of anti-relapse treatment. However, they presented some associations with the pathomechanism of addiction to nicotine.

1. Introduction

Plasma lipid concentration is widely recognized as a marker of cardiovascular risk, as well as a factor increasing the risk of acute pancreatitis, especially in patients who misuse alcohol (Budzyński et al., 2000, 2003; Perk et al., 2012; Ray et al., 2014). However, blood high-density lipoprotein (HDL) cholesterol concentration and hypertriglyceridemia have also been demonstrated to be markers of alcohol abuse (Budzyński et al., 2003). Moreover, recent data have also shown that a fat-rich diet and, secondary, an increase in blood lipid concentration, may be involved in the pathomechanism of alcohol overconsumption. Observation in animal models, mainly in rats, provides strong support for the existence of positive feedback loops that involve a close relation between fat and alcohol intake, the concentration of circulating lipids in the blood, and orexigenic gene expression, synthesis, and release of orexigenic peptides (e.g., galanin, enkephalin, dynorphin, and orexin) in the dorsal regions of the hypothalamus (Barson et al., 2009, 2011; Barson and Leibowitz, 2016; Leibowitz, 2007). Orexigenic peptides regulate food and alcohol intake and reward. They may produce alcohol craving, but they evoke a greater effect when their action is associated with a high-fat diet (Boutrel et al., 2013). In animal models, a high-fat diet stimulated hyperphagia and alcohol consumption when fat-rich meals were given in solid or liquid form, infused intragastrically, given in a sham-feeding paradigm or injected as fat emulsion (Carrillo et al., 2004; Krahn and Gosnell, 1991; Leibowitz, 2007; Pekkanen et al., 1978). In human studies, fat intake was increased in ethanol drinkers, and a fat-rich diet was associated with a higher prevalence of alcoholism, while drinkers who maintained a fat-rich diet compared to those on a

* Corresponding author at: Clinic for Vascular and Internal Diseases, Jan Biziel University Hospital No. 2 in Bydgoszcz, 75 Ujejskiego Street, 85-168 Bydgoszcz, Poland. Fax: +48 52 36 55 148.
E-mail address: budz@cps.pl (J. Budzyński).

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Table 1
Demographic and clinical data of alcohol-dependent males studied in relation to the maintenance of abstinence after 6 months of observation.

Feature	Abstinent (n = 23, 43%)	Relapsed (n = 31, 57%)	P
Age (years)	41.4 ± 8.1	40.5 ± 7.9	0.68
MAST (score)	28.6 ± 5.5	24.2 ± 8.7	0.038
SADD (score)	49.0 ± 25.1	41.3 ± 19.0	0.22
BDI (score)	16.7 ± 11.1	15.6 ± 10.5	0.72
TAS (score)	70.1 ± 10.1	70.4 ± 18.5	0.94
Age at the onset of alcohol dependence (years)	22.3 ± 7.4	22.1 ± 6.6	0.91
Length of alcohol dependence (years)	19.4 ± 7.5	16.7 ± 7.9	0.24
Number of drinking days during the 90 days before the start of the study (days)	47.3 ± 22.0	53.8 ± 27.6	0.37
Number of standard drinks consumed during the 90 days before the start of the study (drinks)	1013.6 ± 757.5	902.7 ± 607.3	0.57
Number of standard drinks consumed during the 30 days before the start of the study (drinks)	285.1 ± 183.5	242.1 ± 169.9	0.40
Smoking habit (n; %)	20 (87%)	25 (81%)	0.77
Length of smoking (years)	20.1 ± 11.4	18.5 ± 10.7	0.23
Number of cigarettes smoked per day	24.0 ± 12.6	19.8 ± 9.5	0.23
Average nicotine content per cigarette (mg)	1.01 ± 0.4	1.03 ± 0.4	0.91
Average daily nicotine dose (mg)	29.5 ± 17.5	23.3 ± 12.4	0.20
BMI (kg/m^2)	24.3 ± 2.8	25.5 ± 3.1	0.14
WHR	0.97 ± 0.05	0.97 ± 0.06	0.77

Abbreviations: MAST: Michigan Alcoholism Screening Test; SADD: Short Alcohol Dependence Scale; BDI: Beck's Depression Inventory; TAS: Toronto Alexithymia Scale; BMI: body mass index; WHR: waist-to-hip ratio.

carbohydrate-rich diet abstained from alcohol for a shorter period (Forsander, 1998; Hasunen et al., 1977; Herbeth et al., 1988; Kesse et al., 2001; Leibowitz, 2007; Yung et al., 1983). Moreover, blood circulating triglycerides (TG) and fatty acids stimulate synthesis of orexigenic peptides and the intake of fat and alcohol (Barson et al., 2009, 2011; Barson and Leibowitz, 2016; Leibowitz, 2007). It is also known that drinking alcohol is a risk factor for hypertriglyceridemia (Barson et al., 2009; Klop et al., 2013; Shen et al., 2014; Slagter et al., 2014). On the other hand, carbohydrate intake has been shown to be inversely related to ethanol consumption (Barson et al., 2009; Forsander, 1998; Gruchow et al., 1985).

The above-mentioned data show that there is positive feedback between dietary fat supply and plasma lipid concentration, as well as between fat and alcohol consumption. These data also suggest the presence of a negative relationship between carbohydrate and alcohol intake. On this basis, we assumed that postprandial glycemia and lipemia might be one of the factors regulating alcohol consumption in alcohol-dependent patients. According to this hypothesis, a higher blood glucose level after loading could act to decrease alcohol craving, and greater lipemia ought to result in an increase in alcohol drinking. Blood glucose concentration after loading, e.g., during an oral glucose tolerance test (OGTT), may depend on glucose intestinal absorption and blood glucose clearance and be related to insulin secretion, sensitivity to insulin, liver function, diabetogenic hormone activity, etc. On the other hand, the degree of postprandial triglyceridemia may depend on the following: the quantity of fat in the diet, body mass and blood volume, taking exercise before the ingestion of a fat-rich meal, which may affect either lipid intestinal absorption (due to intestinal barrier injury, gall and pancreatic juice excretion, intestinal perfusion), may change lipid turnover (e.g., due to changes in pituitary–thyroid and pituitary–suprarenal axes function) and may alter metabolism regulating blood lipid clearance (e.g., due to changes in lipoprotein lipase [LPL], hepatic lipase [HL] and lecithin-cholesterol acyltransferase [LCAT] activities, and energy expenditure; Budzyński et al., 2003; Hyson et al., 2003; Maraki and Sidossis, 2015; Pownall, 1994). Drinking alcohol may affect all of these mechanisms (Torres do Rego et al., 2013). It was reported that drinking approximately 60 g of vodka (the equivalent of 24 g of pure ethanol) or 370 ml of white wine (the equivalent of 44.4 g of pure ethanol) when eating leads to a significant increase in postprandial triglyceride level, independently of a history of abstinence maintenance or regular alcohol drinking (Pownall, 1994; Superko, 1992). In this way, in those who are predisposed, e.g. due to an individual's higher orexigenic peptide synthesis in response to the plasma lipid level, such an effect of ethanol might potentially start a vicious circle of alcohol drinking stimulated by a fat-rich diet. Alcohol abstinence and a low-fat diet should lead to a decrease in postprandial lipemia and, according to the above-mentioned hypothesis, should reduce alcohol craving. A hypolypemic diet would also have anti- atherogenic effect.

This work was initiated to verify the relationship between the risk of alcohol relapse during a 6-month observation period and blood glucose and lipid concentrations after loading. In other words, to answer the question of whether lower glucose blood concentration in OGTT and greater lipids blood concentration in butter loading tests can predict an alcohol relapse.

2. Methods

The investigation was performed during 2000 and 2001 with 54 alcohol-dependent male patients (Budzyński et al., 2003). The criteria for inclusion were: male sex, age between 30–50 years, International Classification of Diseases, 10th Revision [ICD-10] criteria for alcohol dependence performance, the motivation to remain abstinent, and with no history of alcohol abuse in the 14 days prior to the start of the study. The criteria for exclusion were: the concomitant presence of diseases that could have an influence on lipid metabolism (e.g., liver failure and nephrotic syndrome), psychotic or dementia disorders, addiction to substances other than alcohol (except for cigarette smoking), and the taking of any medication. The demographic and clinical data for the alcohol-dependent patients who took part in the study are presented in Table 1.

Blood samples for biochemical determinations were taken from all the patients after 14 h of fasting at the start of the study, after 4 weeks and again after 6 months of observation. In addition to fasting blood glucose (FBG), total cholesterol (TC) and TG, we measured: peripheral blood morphology, thyroid stimulating hormone (TSH), creatinine and biochemical markers of alcohol abuse levels, such as the activity of γ-glutamyl transpeptidase (GTP), aspartate aminotransferase (AST) and alanine transferase (ALT), and mean corpuscular volume (MCV). The triglycerides-glucose (TyG) index was calculated as a logarithm of the product of the levels of TG and fasting blood glucose (ln[fasting triglycerides (mg/dl) × FBG (mg/dl)/2]) (Lee et al., 2014), as it is recognized as a reliable marker of insulin resistance. After undergoing blood sampling, all the subjects drank a water solution containing 75 g of glucose as preparation for performing the OGTT. After 2 h, following blood collection from the fingertip for capillary blood glucose determination, each patient received the same breakfast, which comprised two slices of