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The acute effects of alcohol on cerebral hemodynamic changes induced by the head-up tilt test in healthy subjects☆

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ABSTRACT

Background: Alcohol is a known triggering factor for orthostatic dysfunction, increasing the risk of neurally-mediated syncope. Since orthostatic tolerance may be affected by both systemic and cerebral hemodynamic changes, our aim was to investigate the acute effects of alcohol on cerebral vasoreactivity measured during the head-up tilt (HUT) test in 20 healthy subjects.

Methods: Mean arterial blood pressure (mBP), heart rate, and flow parameters in both middle cerebral arteries (MCAs) were continuously recorded in the supine and during a 10-minute HUT positions before and after alcohol intake.

Results: The HUT test resulted in a more prominent decline of adjusted mBP at the level of MCAs (mBP_{MCA}) and a significantly larger decrease of MCA mean flow velocities (MFV_{MCA}) in the post-alcohol period than before alcohol intake. During the HUT phase, the relative decrease in MFV_{MCA} was significantly smaller than the reduction in mBP_{MCA} before drinking alcohol, while these changes were similar after alcohol ingestion. The cerebrovascular resistance index (CVRi) decreased during the HUT phase in the control period, however, it increased after alcohol intake.

Conclusion: The similar decrease in mBP_{MCA} and MFV_{MCA} during orthostatic stress after alcohol ingestion together with the increased CVRi indicated the impairment of the compensatory vasodilation of cerebral resistance vessels, i.e. impaired cerebral autoregulation. These findings suggest that alcohol may contribute to impaired orthostatic tolerance not only by a hypotensive response but also by the alteration of cerebral blood flow regulation.

1. Introduction

In healthy subjects, arterial blood pressure is restored within a few seconds after standing up, resulting in similar mean arterial blood pressure values in the standing and recumbent positions. Since venous return is decreased in the standing position and results in a decreased stroke volume, the maintenance of normal arterial blood pressure requires adjustments in the cardiovascular system to compensate for these changes and later to sustain arterial blood pressure within normal limits. This compensation is mainly induced by the rapid activation of the baroreceptor reflex leading to increased sympathetic activity, which induces tachycardia and increases the sympathetic vasomotor tone and thus systemic vascular resistance [1–3]. If these compensatory mechanisms are not effectively regulated, patients may display orthostatic hypotension, and consequently, decreased cerebral perfusion. A number of conditions are known to disturb the finely adjusted physiological reflex mechanisms being responsible for maintaining normal systemic blood pressure in the upright position. Drinking alcohol is one of the known triggering factors for orthostatic dysfunction, leading to neurally-mediated syncope [4–7]. Japanese researchers [5,6] showed that the HUT test alone did not provoke syncope, however, it was positive after alcohol intake in 44–75% of patients being prone to unexplained post-alcohol ingestion syncope.

This effect of acute alcohol consumption might be attributed to the attenuated response of muscle sympathetic nerve activity [7], the impairment of systemic vasoconstriction [4], as well as the decreased level of vasoconstrictor eicosanoids developing shortly after alcohol intake [8]. All of these alcohol-related changes induced either by decreased sympathetic activity or the decreased level of vasoconstrictors may contribute to hypotension or the attenuation of blood pressure increase during orthostatic challenge in otherwise healthy subjects. Although orthostatic tolerance may not only be affected by systemic but also cerebral hemodynamic changes, none of the studies aimed to specifically investigate the acute influence of ethanol on cerebral vasoreactivity induced by the HUT test in healthy subjects. In addition,

☆ The study was performed at the Department of Neurology, University of Debrecen.

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acute alcohol ingestion has recently been reported to increase the stroke risk already 1 h after alcohol intake [9]. Therefore, investigation of the acute effects of alcohol on cerebral hemodynamics is challenging because it may give insight into the potential pathomechanisms of ethanol not only in orthostatic dysfunctions but also in cerebrovascular disorders.

Our specific aim was to investigate the acute effects of alcohol on systemic and cerebral hemodynamic changes induced by the HUT test in healthy volunteers. In addition to the blood pressure and heart rate measurements, flow velocities in the middle cerebral arteries and cerebrovascular resistance calculated from blood pressure and MCA flow velocity values were also recorded in the recumbent and vertical positions before and after alcohol intake.

2. Subjects and methods

Twenty healthy, young students (11 males, 9 females, mean age: 23 ± 2 years, body mass index: 23.3 ± 3.5 kg/m^2) were included in the study that was approved by the Regional and Institutional Ethics Committee, Clinical Center, University of Debrecen, Hungary. Subjects were informed about the experimental procedures and possible risks involved in the study, and each volunteer gave a written, informed consent. All subjects were social drinkers only and had abstained from alcohol for at least 24 h before the study. None of the volunteers had any history of syncope or respiratory disease. The participants were screened for cerebrovascular risk factors including smoking habits, arterial hypertension, obesity (body mass index), diabetes mellitus (fasting glucose levels), hyperlipidemia (levels of total cholesterol, LDL, HDL), and coronary or peripheral artery disease, and subjects with risk factors were excluded. The included subjects did not take any medicine regularly. The study protocol included a complete neurological examination, carotid artery and vertebral artery duplex, transcranial Doppler, and routine clinical laboratory tests (serum ions, blood urea nitrogen, creatinine, fasting glucose, hepatic enzymes, creatine-kinase, hemostasis screening test, serum lipids and inflammatory markers, capillary blood gases and pH). Blood was drawn after overnight fasting between 8 and 10 a.m. on the day of the experiment. Subjects were instructed to abstain from exercise and caffeine 12 h before, and from food 6 h before experimental testing. The room temperature was 22–23 °C.

The volunteers underwent HUT testing in a fasting state in a quiet room at the same period of the day (between 4:00 and 7:00 p.m.). During the experiment, non-invasive, continuous monitoring of hemodynamic parameters including heart rate (HR), systolic (sBP), diastolic (dBP) and mean (mBP) arterial blood pressure values was performed using Task-Force Monitor (CN Systems Medizintechnik GmbH, Graz, Austria) which incorporates electrocardiography and devices for oscillometric and continuous blood pressure measurements. Bilateral continuous recordings of mean flow velocity (MFV) in both middle cerebral arteries (MCAs) were also obtained with transcranial Doppler ultrasound (Multidop T2, DWL, Überlingen, Germany) that was attached to the Task Force Monitor. To detect the flow parameters in the MCAs, two 2-MHz TCD probes were mounted by an individually fitted headband. The MCAs were insonated through the temporal cranial window on both sides at a depth of 50 mm. The procedure of finding and identifying the vessels followed the description of Fujioka and Donville for the transtemporal approach [10]. An index of cerebrovascular resistance (CVRi) was also calculated as the quotient of mBP adjusted for the MCA level (mBP_{MCA}) and MCA MFV (MFV_{MCA}), i.e. $CVRi = mBP_{MCA}/MFV_{MCA}$ [11–14]. A correction of mBP was necessary during the HUT phase, because the mBP at the level of MCA insonation was decreased due to the hydrostatic reduction of pressure values in the upright position [2]. (During the calculation, pressure changes caused by the decrease of hydrostatic pressure were converted to millimeters of mercury. The calculation took into account the vertical distance between the levels of the heart and the MCA after raising the subjects to an inclination of 70°, and based on the following equation: $\varrho_{blood} \cdot g \cdot h_1 \cdot \sin 70° = \varrho_{Hg} \cdot g \cdot h_2$, where ϱ_{blood} and ϱ_{Hg} are the densities of blood and mercury, respectively, g is the gravitational constant, h_1 is the distance between the heart and the TCD probe, and h_2 is the height of a mercury column that counteracts with the '$h_1 \cdot \sin 70°$' height of the blood column.)

2.1. Experimental protocol

First, each volunteer was positioned in the supine position on an electrically-driven tilt table equipped with a footboard. After proper positioning, the instruments (3-lead ECG, blood pressure recorder, TCD probes) were placed on the volunteers. The experimental protocol (Fig. 1A) included a 30-minute supine rest and a 10-minute HUT phase both during the control period before, and during the test period after alcohol intake. After a 30-minute supine rest, the HUT test was performed by raising the subjects to an inclination of 70° for a period of 10 min. After the control measurements, alcohol (vodka, 37.5% alcohol content) was administered orally over a 10-minute period. Volunteers were allowed to dilute the alcoholic beverage with sugar-, and caffeine-free non-carbonated soft drinks up to a total volume of 200 mL. The overall fluid intake was 200 mL in each subject. Our aim was to investigate the effects of mild-to-moderate drunkenness on hemodynamic parameters, therefore the target blood alcohol level was chosen to be 100 mg/dL (1 g/L = 0.1 g/dL, i.e. 1.0‰). In order to reach this concentration with low variance, we used the following formula for calculating the required amount of alcohol in grams: BAC·BW·WF, where BAC means the target blood alcohol concentration expressed in ‰ or g/L, BW is the body weight in kg, and WF is the Widmark factor that is 0.68 in males and 0.55 in females [15].

During the 10-minute drinking period and for an additional 30 min the subjects were sitting. Subsequently, they were positioned again on the tilt table in the supine position, and the same protocol was performed as before alcohol ingestion. Briefly, after 30 min of supine rest, the HUT test was performed again for a period of 10 min. It means that 1 h passed between the end of alcohol intake and the start of tilting to the upright position under the effect of alcohol. At the end of the 10-minute HUT test during the post-alcohol test period, blood was drawn for the measurement of blood alcohol concentration and blood gas values. Alcohol produced only a mild level of intoxication; all volunteers were able to walk after completion of the study, although incoordination could be detected with detailed examination. None of the subjects complained of pre-syncope signs (nausea, sweatiness, blurred or tunnel vision, limb or generalized weakness) during the HUT phases before or after alcohol intake.

Heart rate, blood pressure values, and MFVs in both MCAs were continuously recorded, and beat-to-beat data were averaged separately in the last 5 min of the resting phase in the supine position (baseline) and over the last 9 min of the 10-minute HUT phase both in the control period before and in the test period after alcohol intake. Data from the first minute of the HUT phase were not used for analysis because physiological variables were unstable at the beginning of this phase and steady state was reached within 30–60 s after tilting the subjects to the upright position. Fig. 1B shows the representative time courses of the changes in heart rate, systemic mean arterial blood pressure (mBP), and left MCA mean flow velocity (MFV_{MCA}) during head-up tilt test in the same volunteer before and after alcohol intake.

2.2. Statistical analysis

Values were expressed as median and ranges. Since variables were not normally distributed, the non-parametric Wilcoxon signed-rank test was used for the comparison of paired data in the supine and HUT positions before and after alcohol intake. The relative changes of hemodynamic parameters induced by orthostatic stress (HUT test) were expressed in the percentage of the baseline value, which was calculated using the following formula: