

## Summary

Alcohol use disorder and their secondary somatic diseases are a major social and economic problem. Changes occurring in the body, as a result of chronic intoxication, arise not only from the harmful effects of ethanol metabolites, but also from induced oxidative stress. The dominance of redox reactions and the weakening of the antioxidant abilities seem to intensify during the alcohol withdrawal. The accompanying anxiety, the sympathetic nervous system excitation, apathy and insomnia remind the symptoms of anxiety or depression syndrome. The theory of oxidative stress, which underlies affective disorders, has turned the author towards the exploration for a relationship between the severity of oxidative stress and the reactive oxygen species produced in its course, with the affective and anxiety components that are accompanying the cessation of alcohol.

The aim of the study was to demonstrate the relationship between selected parameters of oxidative stress and the severity of depressive and anxiety symptoms associated with the end of alcohol withdrawal. The effects of seven-day abstinence on the studied parameters have been also checked. The specific objectives of the study were to determine the differences between the study group and control in total protein (TP), caspase-3 (CAS-3) and NADPH oxidase (NOX), nitric oxide (NO), advanced glycation end products (AGE), advanced protein oxidation products (AOPP), dityrosine, kinurenine, tryptophan, N-formyl-kinurenine, and the severity of anxiety and depression symptoms. A correlation between oxidative stress markers and psychometric test results was also searched. The relationship between the parameters of the mental state and the duration of alcohol addiction, the length of alcohol consumption, the amount of previous detoxifications, the sum of ethanol consumed per day, age and BMI were also analyzed.

The study involved 33 men fulfilling the addiction criteria, whose last alcohol consumption did not exceed 48 hours. They didn't have any other chronic or acute conditions. The average age in the group of respondents was  $\pm 44.55$  years, and the addiction duration  $\pm 16$  years. The alcohol course of the studied cases has been lasted on average  $\pm 9.5$  weeks. The subjects consumed an average of  $\pm 347.3$  g of ethanol per day. 23 somatic and mental healthy men (control), with an average age of  $\pm 41.13$  years, has also participated the study. Subjects blood was received from the peripheral vein in a volume of 2.7 ml. The spined blood serum was frozen at  $-80^{\circ}\text{C}$  until laboratory tests. The tests were made using colorimetric or fluorescent methods. Psychometric assessment of the depression was performed with the help of the Hospital

Depression and Anxiety Scale - Depression subscale (HADS-D). The dimensions of anxiety were measured using the State-Trait Anxiety Inventory (STAI) and the HAD-D anxiety subscale (HADS-L).

The following conclusions were obtained, as a result of the research:

1. Oxidative stress, in the course of alcohol withdrawal, increases protein catabolism. It should be taken into account in the simultaneous determination of the other compounds status.
2. Oxidative enzymes activity (CAS-3, NOX), concentrations of oxidatively damaged protein and amino acid products (AGE, AOPP, dityrosine), and concentrations of the kinurenine pathway elements (tryptophan unrelated to albumin, N-formyl-kinurenine) remain elevated compared to control, both at the beginning and after a week's abstinence period.
3. One week after cessation of chronic alcohol consumption, NOX activity, NO, AOPP and kinurenine increase. Nitric oxide and kinurenine concentrations increase significantly relative to control after a week of abstinence. This indicates an increase in the severity of oxidative stress and stimulation of the kinurenine pathway in the course of withdrawal.
4. Nitric oxide appears to be neutralizing ROS and anxiety reducing agent. The relationship between NO and anxiety symptoms appears to be bidirectional.
5. The severity of depressive symptoms after alcohol withdrawal is associated with the length of addiction and current alcohol intake as well as with the enzymatic indicator of apoptosis / damage caused by oxidative stress - CAS-3.
6. The greater the severity of anxiety preceding withdrawal, the lower the level of dityrosine and kinurenine at its onset, and the increase in AGE and N-formyl-kinurenine after one week of abstinence. This suggests that anxiety is associated with the severity of oxidative reactions in alcohol withdrawal.
7. The period of alcohol dependence and the current concentration of AGE (not other markers of oxidative stress) are the predictors of the severity state of anxiety after a week of abstinence. This suggests that anxiety in the course of alcohol withdrawal is an interim condition that decreases as the oxidation reaction decreases.
8. The use of antioxidants among addicts and at an early stage of alcohol withdrawal could potentially reduce not only the ongoing oxidative stress, but also reduce the level of anxiety. This requires further research.