CORRECTIVE EFFECTS OF THIAMIN ON CORTEX NEUROMARKERS DISTURBANCE OF RATS EXPOSED TO CHRONIC ETHANOL CONSUMPTION

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Aim. This study is designed to test whether degenerative changes in the cerebral cortex of rats subjected to long-term alcohol consumption are indeed due to the development of thiamine deficiency. If so, additional administration of vitamin B_1 should inhibit or slow down these changes.

Methods. White male albino rats (n = 12) were exposed to a 15 % (v/v) aqueous EtOH solution as an alternative-free drinking water source for 9 months. One week before the end of the experiment, 1/2 of the rats exposed to EtOH received thiamine (200 μg per 100 g body weight) daily. Thiamine status of the organism was checked by thiamine level in the liver and thiamindiphosphate (ThDP) level in the brain. The neurodegenerative processes were assessed by the changing in marker proteins level using Western blotting. Namely, the levels of phosphorylated and unphosphorylated rigid chain triplet neurofilament (NF-H), nuclear neuronal marker (NeuN), phosphorylated and unphosphorylated tau protein and astrocyte marker glial fibrillary acidic protein (GFAP) were assessed in cortical protein lysates.

Results. In the brain cortex of rats exposed to EtOH, we found signs of neurodegenerative changes, namely, there was an accumulation of phosphorylated and unphosphorylated forms of NF-H and tau protein, and the ratio of phosphorylated and unphosphorylated forms increased by 1.5 and 2.3 times, respectively. NeuN level were increased 2-fold, and GFAP level were sharply decreased compared to controls. Five-day administration of thiamine decreased the levels of NF-H, NeuN, and partially normalized the ph/non-ph ratio of the NF-H protein (but not tau protein) and increased the level of GFAP in the cortex. Although the level of ThDP in the brain was unchanged under these conditions, the activity of thiaminpyrophosphokinase (the enzyme responsible for ThDP synthesis) was significantly reduced, which may indicate disturbance in the rate of thiamine metabolism in the brain cells exposed to EtOH. In the liver thiamine level was significantly reduced, but normalized with a high dose thiamine administration.

Discussion. Thiamine ameliorated the consequence of chronic alcohol consumption, including neurofilaments protein hyperphosphorylation and accumulation, astroglia inhibition in cortex and thiamine deficiency in liver of rats. Beneficial effects of thiamine may be due to both its classic ability to improve aerobic metabolism, alleviate mitochondrial dysfunction, protect from oxidative stress, and its non-coenzymatic and neuroprotective function.

Conclusions. Impaired thiamine metabolism in brain cells of rats exposed to ethanol for a long time is the most likely cause of neurodegenerative changes. Thiamine administration can be used for effective correction of disorders associated with EtOH-induced brain damage, especially during alcohol abuse.