



COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF EMHPS AND ITS METABOLITE EMSP ON RESPIRATORY PARAMETERS, MOTOR ACTIVITY AND GENE EXPRESSION OF MITOCHONDRIAL COMPLEXES IN MICE UNDER CONDITIONS OF INTERMITTENT HYPOXIA

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Relevance: Intermittent hypoxia (IH) is a pathological factor that provokes oxidative stress, which can initiate a cascade of pathological conditions, mitochondrial dysfunction, inflammation, endothelial dysfunction and metabolic disorders. In this regard, the study of active antioxidants is relevant. In this work, we studied the antihypoxic properties of the metabolite of ethylmethylhydroxypyridine succinate (EMHPS) - ethylmethylsulfapyridine (EMSP) on the IH model in mice. In previous studies, EMSP exhibited antihypoxic and antioxidant properties [1-3].

The aim of the study: A comparative study of the effectiveness of EMSP with the native molecule in the IH model in mice.

Materials and methods: The study was conducted on 18 male white mice. The study was divided into 3 groups: Group 1 – control (n=6), IG + saline; Group 2 – (n=6), IG + EMSP at a dose of (85 mg/kg); Group 3 – (n=6), IG + EMHPS (100 mg/kg). The administration was performed intraperitoneally for 14 days in parallel with the modeling of IG, 30 minutes before IG. Modeling of IG was performed by placing the animals in a membrane hypoxicator. The following regime was set: oxygen content - 6%, duration of the hypoxic cycle - 6 hours. Duration - 14 days, daily. At the beginning and end of the study, the dynamic load was assessed (grip strength test), respiratory parameters were measured (in a plethysmograph), behavioral indicators (in the open field (OF) and elevated plus maze (EPM) tests, heart rate (HR) and saturation (SpO₂) were measured. After euthanasia, the expression of mitochondrial complex genes in the liver was determined in animals of all groups using the polymerase chain reaction (PCR) in real time. Были выбраны такие гены как: GAPDH – reference gene; NDUF51 – encodes the key subunit of the complex I (NADH-dehydrogenase); SDHA – catalytic subunit of the complex II (succinate dehydrogenase); UQCRC2 – structural component of the complex III (cytochrome bc1); COX1 – subunit of the complex IV (cytochrome c-oxidase).

Results: The results of the study showed that EMSP showed comparable effectiveness in terms of grip strength, plethysmograph, SpO₂ heart rate, and in the OF and EPM tests compared to EMHPS. According to the PCR results, a clear tendency towards expression of the UQCRC2 gene was noted in the EMSP and EMHPS groups. Moreover, in the EMSP group, the expression was more pronounced.

Conclusions: The studied compound EMSP showed protective properties against the background of IG comparable to EMHPS, and a more pronounced tendency for expression of the UQCRC2 gene.