

ANTIHYPERTENSIVE EFFICACY OF ADAPTATION TO INTERMITTENT HYPOXIA VS. BETA-BLOCKER AND NO DONOR THERAPY: ROLE OF NITRIC OXIDE

Eugenia B. Manukhina, Valery I. Buvaltsev, Dmitry A. Pokidyshev, Boris V. Smirin, Svetlana Yu. Mashina

Institute of General Pathology and Pathophysiology, Moscow, Russia

Adaptation to intermittent hypoxia (AIH) attracts a special attention as an antihypertensive means for its capacity of activating endothelial NO synthase (eNOS) and restricting free radical processes in the organism. The study objective was to compare drug and non-drug approaches to compensation for NO deficiency with respect of their antihypertensive potential in stroke-prone spontaneously hypertensive rats (SHRSP). AIH (40 daily 5-hour sessions at simulated altitude of 5000 above sea level) was used for non-drug stimulation of NO synthesis; the NO donor dinitrosyl iron complex (DINC, 170 µg/kg i.p., every 4th day for 40 days) was used for NO delivery to the organism; and the β-blocker nebivolol (1.25 mg/kg i.p. daily for 40 days) possessing an additional stimulatory effect on eNOS was used for pharmacological enhancement of NO production. It was shown that AIH and the NO donor DNIC decreased blood pressure (BP) in SHRSP to a similar extent. However DNIC did not improve the endothelium-dependent relaxation of isolated rat aorta. The eNOS stimulator nebivolol exerted both antihypertensive and vasoprotective effects, but these effects were less pronounced than in AIH. Therefore AIH appeared to be a more efficient antihypertensive and vasoprotective means than both the NO donor and the eNOS stimulator. We suggest that the advantage of AIH can be due to the following mechanisms: 1) AIH both stimulates eNOS activity and induces expression of eNOS gene; 2) AIH results in formation of NO stores in the vascular wall, which may serve as an additional source of free NO; 3) AIH activates antioxidant enzymes and thereby prevents detrimental effects of free radicals on eNOS; and 4) AIH possesses additional antihypertensive mechanisms such as stimulation of sodium and water excretion, decreasing vascular adrenoreactivity, etc.

The study was supported by Russian Foundation for Basic Research (grants 01-04-48699 and 03-04-06627)