The effects of interval hypoxia have attracted considerable interest for many years. In the 1970s, a hypoxic stimulus and an intermittent hypoxic effect were reported to activate vital functions and cause a complex of changes in the organism’s adaptation [1–3]. Interval hypoxic training (IHT) is this widely used at present to increase the nonspecific resistance of the organism [4–6]. However, the biochemical aspects of the organism’s response to IHT are poorly studied. At the same time, it is known that hypoxia may cause increased accumulation of the reactive oxygen species and peroxidation products (i.e., induce oxidative stress) [7], thus increasing gene expression of the main antioxidant enzymes—superoxide dismutase (SOD), catalase, and glutathione peroxidase (GP) [8]. We proposed, therefore, that an increase in the antioxidant enzyme activity caused by the intermittent oxidative stress may be one mechanism of the organism’s response to IHT.

Notably, oxidative stress is typical of pathogenesis of more than 100 diseases and pathological states, including essential hypertension (EH) [9]. According to recent findings, reactive oxygen species are responsible for arterial dysfunctions and impaired arterial structure in the case of EH, because they inactivate nitric oxide and thus decrease its vasodilating effect, irreversibly damage the vascular wall by way of peroxidation, and stimulate the remodeling of vessels. It is believed that oxidative stress in the case of EH is caused by not only the increased production of reactive oxygen species by certain enzyme systems in the vascular wall cells, but also inactivity of the antioxidant enzyme system [10]. Hence, the objective of this paper was to study the metabolism of reactive oxygen species in response to IHT both in healthy subjects and in patients with EH.

METHODS

The study included 20 virtually healthy subjects (6 males and 14 females at the age of 40 ± 2 years) and 20 patients (7 males and 13 females at the age of 43 ± 3 years) with I–II degree EH (according to the 1996 WHO classification). In all patients receiving standard antihypertensive therapy, the arterial pressure was not higher than 145/85 mm Hg during the previous two to three months. This allowed us to correctly reveal the effect of the IHT, which would be difficult to do in case of EH decompensation necessitating a quick change in the drug therapy.

The Bio-Nova-204 instrument was used for the IHT. The IHT course consisted of 14 daily 1-h sessions. During a session, the subjects alternated 1- to 5-min inhalation of the hypoxic gas mixture (10–12 vol % oxygen) with atmospheric air.

Prior to the course of IHT and after the last session (on the first day and three to four days later), the degree of oxidative stress was estimated in the plasma by two indices: the concentration of thiobarbituric acid reactive substances (TBARS) and oxidative stress markers, including total prooxidant activity and plasma concentration of thiobarbituric acid reactive substances, in response to 14-day interval hypoxic training (IHT). The study included healthy subjects and patients with essential hypertension, who had a decreased activity of the main antioxidant enzymes due to a marked oxidative stress, as revealed by previous studies. In all subjects, the oxidative stress markers decreased and the enzyme activity increased in four days after the IHT course. However, the differences in metabolism of the reactive oxygen species between the patients and the healthy subjects persisted. It is suggested that, even with a different antioxidant enzyme system baseline, IHT may contribute to adaptive activity of this system.
RESULTS AND DISCUSSION

It was shown that, prior to the IHT course, the patients with EH had a significantly elevated TPA (by a factor of 1.8) and TBRP concentration (by a factor of 1.7) compared to those in the healthy subjects. This evidenced marked oxidative stress in the patients, which was associated with decreased activity of the antioxidant enzymes under study. These findings, as well as previously obtained data, showed that the antioxidant enzyme activity was inadequate to the rate of production of reactive oxygen species in patients with EH [10].

As seen from Tables 1 and 2, the IHT course significantly affected all metabolic parameters of the reactive oxygen species in both healthy subjects and patients with EH. The behavior of these parameters was similar in both groups for several days after the end of the IHT. During the first day after the last IHT session, the oxidative stress markers increased and then decreased. This was followed by a moderate transitory decrease in SOD, catalase, and GP activity and a subsequent increase in the same. These changes showed that the IHT caused the enhanced generation of the reactive oxygen species and, thus, the activation of the antioxidant enzyme system. Notably, the activity of antioxidant enzymes in subjects preconditioned by hypoxia has been described in [14, 15]. Considering the possibility of substrate-induced biosynthesis of these enzymes, it can be concluded that the increased activity of the reactive oxygen species is due to accumulation of these forms.

Thus, the direction of changes in metabolism of reactive oxygen species in response to the IHT were similar in both groups of subjects. However, compared to healthy subjects, the patients with EH had higher values of TPA and concentration of TBRP and lower antioxidant enzyme activity during the first day after the IHT course and on the third to fourth day. It is likely that the higher values of the oxidative stress markers in patients with EH were due to a hypoxia-induced increase in the production of reactive oxygen species combined with the preexisting oxidative stress. Note that these metabolic changes caused no changes in the blood pressure and had no adverse health consequences. An important fact for understanding the pathogenesis of EH is the increase in enzyme activity observed in patients on the third to fourth day after the IHT. It was within this period that the metabolism of reactive oxygen species in the patients with EH almost corresponded to that in the healthy subjects prior to the IHT.

CONCLUSION

The findings prove that, even with a different baseline of the antioxidant enzyme system, IHT may increase the activity of this system. This mechanism is