

ADVERSE EXERCISE-DRUG INTERACTIONS: THE CASE OF ANTIHISTAMINE MEDICATION

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Introduction: Antihistamine medication blocks the functioning of the histamine system and is widely used to treat allergies and stomach acid production. However, recent evidence suggest that activation of the histamine system could be important for the response to acute physical exercise. As exercise training is a powerful strategy to prevent and combat chronic diseases, we aimed to unravel if and how administration of antihistamine medication interacts with the beneficial adaptations to an exercise training program. **Methods:** In a randomised, placebo-controlled and double-blind study, participants were allocated to a placebo (n=9) or antihistamine (n=9) group and performed 6 weeks of cycling training. Before and after the training program, aerobic performance, whole-body insulin sensitivity and vascular function were determined, accompanied by muscle biopsies to assess mechanistic outcomes. Training-induced changes between groups were compared with linear mixed models. **Results:** Aerobic performance, as reflected by maximal power output (+12% vs +7%, $p=0.044$) and submaximal respiratory compensation point (+19% vs +6%, $p<0.001$), increased substantially more in the placebo compared to the antihistamine group. Improvements in whole-body insulin sensitivity (+26% vs +1%, $p=0.010$) and vascular function (+37% vs -14%, $p=0.017$) were completely abolished in the antihistamine group. These functional data were reflected by impaired adaptations in mitochondrial capacity, muscle capillarisation and nitric oxide bioavailability in the muscles of the antihistamine group. **Conclusion:** Blockade of the histamine system during exercise by administration of antihistamine medication blunted multiple therapeutic effects of exercise training related to cardiovascular and metabolic diseases.