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Review Article

Antiatherosclerotic effect of exercise on the antioxidant properties of paraoxonase – A preliminary examination

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ABSTRACT

Introduction: The positive impact of properly performed exercise on the human body is well known. In this study, the effect of maximal exercise on the antioxidant activity of the blood enzyme, paraoxonase (PON), was determined.

Aim: The aim of this study was to determine the influence of a single bout of maximal physical exercise on PON activity and to investigate the correlation of this activity with chosen biometric parameters and physical activity levels.

Materials and methods: In total, 15 subjects participated in this study. The average age of the subjects was 18 years (±2.74 years). Participants were subjected to maximum efforts on a treadmill until complete exhaustion resulted. They had their blood taken for analysis at three time points – before, at the end, and 2 h following the end of exercise. PON activity was determined by the ability to dispose of paraoxon. The subjects also filled in questionnaires in which they determined the amount and form of training carried out. Basic biometric data were collected from the subjects.

Results and discussion: This study demonstrates that the enzyme activity at the maximal effort is higher than at rest; however, it does not depend on the level of physical activity. PON activity 2 h following exercise, though higher than at rest, was not statistically significant. No relationship was found between PON activity and chosen parameters such as age, weight, BMI, lean, body mass.

Conclusions: A single bout of maximal exercise increases PON activity. A positive trend was also observed with respect to the impact of the physical activity level on PON activity at rest.

1. Introduction

1.1. *Paraoxonase and atherosclerosis*

Paraoxonase (PON) is an enzyme associated with a high density lipoprotein (HDL) fraction in serum. It has a protective effect against blood vessels, due to its antioxidant properties.

PON activity primarily depends on its genotype; PON1 and PON2 are found in the blood.[12] They exhibit their activity by different enzymatic paths. Available studies[1,6,7] demonstrate that the intake of antioxidant vitamins, saturated fatty acids, smoking tobacco and the use of hypolipidemic drugs can modify the antioxidant capacity of PON. Diets rich in

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fruit and vegetables increase the activity of PON1, which is associated with the presence of antioxidant vitamins in vegetables (vitamin E and C). Alcohol consumption causes a moderate increase in PON1 activity, while serum enzyme activity decreases in patients demonstrating alcohol addiction.

The activity of PON1 lasts significantly longer than the effect of antioxidant vitamins. This substance is a better protector against low density lipoprotein (LDL) peroxidation. Low PON1 activity has been shown in patients with clinically confirmed myocardial atherosclerosis. PON activity below normal is seen in: family hypercholesterolemia, systemic and local inflammation, myocardial infarction, stroke, and diabetes.[9,11]

A correlation exists between PON1 and LDL. PON1 is inactivated during the formation and accumulation of oxidized LDL (oxLDL). Oxidation of LDL is inhibited in 42–65% by PON1.

PON is involved in the degradation of hydrogen peroxide (peroxidase role, mainly PON1) and hydrolyzes esters in phospholipid peroxides and hydrogen peroxides cholesterol esters (the role of esterases, especially PON2). Acting as an esterase, it catalyzes the distribution of aryl esters: phenyl acetate and paraoxon. It also acts as an aryl esterase, carbamates hydrolase and "-oxons" (paraoxon, diazoxon, chlorpyrifoxon, soman and sarin). It can also decompose peroxides of fatty acids in oxidized phospholipids.[7,9]

The presence and activity of PON1 has been observed in various tissues. Its most extensive activity is found in the liver, where it is synthesized. Then it passes further into the serum. It is active and is also generated in kidneys, heart, small intestine, lungs and brain.

LDL oxidative action within the wall of blood vessels contributes to the development of atherosclerosis. This is due to an inactivation of the nitric oxide and the formation of foam cells. These processes, in return, release proinflammatory substances. HDLs inhibit LDL oxidative activity. They hydrolyze lipid peroxydation products and prevent LDL oxidation. HDLs cause detoxification of oxidized phospholipids generated during lipid peroxidation. Antioxidant effect is possible thanks to apolipoprotein A-I properties, the presence of PON1 enzyme and the platelet activating factor acetylhydrolase (PAF-AH), which all hydrolyze lipid peroxidation products.

Factors increasing HDL levels are as follows: low body weight, being female, physical activity (mainly of endurance type), the consumption of red wine in small quantities, estrogens and glucocorticoids. Factors causing a decline in HDL concentration include: obesity, low physical activity, being male, smoking, high carbohydrate diet, diabetes, kidney disease, and liver failure.[4]

It is assumed that atherosclerosis is caused by chronic inflammation of the arteries. Hypercholesterolemia may promote endothelial dysfunction. These disorders can be drawn forth by the creation of active oxygen species and the oxidation of lipids.[8]

Bearing in mind the risk factors leading to atherosclerosis, several forms of primary and secondary preventive measures which could halt the formation of atherosclerosis have been found. These include: giving up smoking, weight reduction, control of BMI, regular exercise and diet.[8]

2. Aim

Regular physical activity promotes an increase in PON activity and reduces the risk of atherosclerosis and cardiovascular diseases. A single bout of physical exercise causes oxidative stress in the body. Adaptive mechanisms react to this situation by running a number of antioxidative substances, including PON. Frequent disturbances of homeostasis lead to enzymatic activation. The purpose of this study was to determine the impact of a single bout of exercise on PON activity and to investigate the quantitative relationships between chosen biometric parameters and parameters of the physical fitness and activity of the enzyme.

3. Materials and methods

3.1. Material

In total, 15 subjects participated in this study with an average age of 18 years ($\pm$2.74 years). The majority (10 subjects) were school pupils attending a sport profile class. The remaining (5 subjects) were students born in the years 1983–1986 from the universities located in Łódź. The study group comprised 13 men and 2 women.

3.2. Methods

Maximum effort was achieved in an exercise test carried out on a Trackmaster treadmill. The exercise intensity was regulated by increasing treadmill speed and inclination according to the Bruce protocol modified to meet the requirements of the experiment. Subjects' fitness expressed by maximal oxygen consumption (VO_{2max}) was assessed directly by measuring the respiratory gases. Heart rate was also recorded. Subjects ran until they refused to exercise due to fatigue. Maximum heart rates (HR_{max}), VO_{2max} and the maximal carbon dioxide excretions (VCO_{2max}) were recorded employing the VO2000 MedGraphics Cardiorespiratory Diagnostic Systems (Medical Graphics Corporation, USA), which worked compatibly with Breeze suite 6.2A MedGraphics software.

Blood samples were collected at three time points: T_1 – before exercise, T_2 – at the end of exercise, and T_3 – 2 h following exercise. Blood samples were taken from the antecubital vein into Vacutainer tubes containing lithium heparin.

Blood samples were centrifuged (3000 rpm) for 20 min. Isolated plasma was frozen in 0.5 mL tubes at -80°C.

Questionnaires were completed in order to assess the level of physical activity concerning the examined subjects. The level of physical activity was rated utilizing a 5-point scale depending on the number of trainings performed per week, time of training, the type of activity involved and the loads that were undertaken (Table 1).

3.3. Chemicals

The majority of chemicals were purchased from Sigma-Aldrich Chemical (St Louis, MO, USA). Trizma base was purchased from Fluka Chemie (Buchs, Switzerland).