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Original Research Article

Effect of physical training on indices of platelet aggregation and fibrinogen concentration in patients with chronic heart failure

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ABSTRACT

Objective: The aim of this study was to determine the effect of long-term physical load on the changes in the fibrinogen concentration and platelet aggregation.
Material and methods: Platelet aggregation was investigated in 144 patients while fibrinogen concentration in 138 patients with CHF. The patients were divided into the groups of the trained patients and the controls and were investigated as follows: on admission to the hospital (stage 1); after treatment in the hospital (stage 2); after 3 months (stage 3); after 6 months (stage 4); and after 1 year (stage 5). The indices were investigated before and after physical load.
Results: It was determined that fibrinogen concentration significantly increased after physical load in all the treatment stages in both groups of the patients ($P = 0.045$). In the course of the treatment, fibrinogen concentration gradually decreased in the group of the trained patients ($P = 0.02$). Platelet aggregation investigated with ADP significantly increased after physical load in all the stages in both groups of the patients and decreased during the different investigation stages in the groups of the untrained ($P = 0.02$) and trained patients. Platelet aggregation investigated with ADR consistently decreased before physical load during the different investigation stages in the groups of the trained (difference is not significant) and untrained patients ($P = 0.02$).
Conclusions: Physical training reduces fibrinogen concentration in patients with CHF. It remains unclear whether physical training can have an effect on the decrease in platelet aggregation in patients who have long-term physical training applied.

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1. Introduction

It has been proven that adrenalin influences a higher fibrinogen concentration and noradrenalin activates platelet [1]. Exercise training attenuates neurohormonal stimulation [2] and improves quality of life of patients [3]; however, it is not clear which organ systems and which changes in particular have an impact on these processes.

The data of research studies about the importance of physical training on the indices of the hemostasis are controversial. According to some authors, platelet activity does not depend on physical training [4]. Other studies report that moderate exercises reduce platelet activity [5,6]; meanwhile, those of high intensity increase it [5–9]. Some studies have proven that physical training of low [9] and moderate intensity activates platelet [10]. Yet other authors claim that moderate physical load does not affect platelet activity [6]. It is rather complicated to assess and compare these studies since not all the authors provide details about the methods and regimen of the chosen intensity of physical training; they also use different research methods of platelet aggregation. The time period between exercise and investigations was also different, and the results of the studies were influenced by a small number of investigated subjects as well. No scientific studies about the remote effect of physical load on platelet aggregation in patients with chronic heart failure (CHF) have been found.

Fibrinogen is one of the markers of a systemic inflammation, and its level is found to be increased in the blood of the patients with CHF in comparison with healthy subjects [1,11]. It is a risk factor of cardiovascular diseases [12] and one of the factors conditioning the hypercoagulable state [1]. It has been determined that fibrinogen significantly decreases in the blood of patients with CHF if they exercise [12,13]. No significant difference in the fibrinogen concentration has been found when healthy subjects exercising for 6 or 12 weeks were investigated [14]. No data about the influence of long-term physical training on the changes in the fibrinogen concentration in patients with CHF have been found in literature sources.

Thus, the aim of the study was to determine how long-term physical training influenced the changes in the hemostasis indices, i.e., fibrinogen concentration and platelet aggregation.

2. Material and methods

Platelet aggregation was investigated in 144 patients and fibrinogen concentration in 138 patients with CHF (class II–IV according to the NYHA (New York Heart Association)). The diagnosis of CHF was made following the guidelines for the diagnostics and treatment of heart failure approved by the European Society of Cardiology [1]. The inclusion criteria were as follows: 18- to 80-year-old patients who agreed to participate in the study; class II-IV heart failure according to the NYHA with ischemic, dilated, or hypertensive cardiomyopathy; left ventricular ejection fraction (LVEF) of <35%; VO_2 max <20 mL/kg/min; the level of aerobic activity not lower than 3 min as determined by spiroergometry; and patients with a stable clinical state, without inflammation and receiving adequate treatment with medications. The clinical state was considered stable if there were no changes in the clinical state, functional class according to the NYHA, weight, and used medications during the past 3–4 weeks, nor were there new heart failure symptoms.

The patients were randomly divided into 2 groups, i.e., intervention group and controls, at a ratio of 1:1. The patients in both groups were given optimal treatment following the guidelines for the diagnostics and treatment of heart failure approved by the European Society of Cardiology [15]. The aerobic physical training method was applied to the patients in the intervention group, i.e., the intensity of physical load was 10% lower than their anaerobic threshold registered during spiroergometry. During aerobic physical exercise, the load was gradually increased by prolonging the duration of exercise and later by increasing load intensity. Everyday physical activity of 30 min was recommended for the patients in the control group as well.

The patients were investigated in the following treatment stages: on admission to the hospital (1); after the treatment in the hospital (2); after 3 months (3); after 6 months (4); and after 1 year (5). Except for the first stage, the indices were analyzed before and after physical load. During the first stage in the hospital, the patients in the intervention group had physical training for 5–10 min twice a day, i.e., in the morning and afternoon, until they were discharged from the hospital. During the second stage, ambulant physical training for 10–30 min twice a week in a clinic and 3 times a week at home was continued. Later, the patients continued individual home training programs. When the diaries prepared for this study and filled out by the patients were checked during different study periods, it was observed that 90% of the patients adhered to the program. The mean training duration was 32 min a day.

Hematological parameters (hematocrit and complete blood count), platelet aggregation and fibrinogen concentration of every study participant were analyzed during all five stages of the study. Blood for hematocrit and complete blood count testing was taken from the forearm vein into 4.5-mL vacuum tubes with EDTA (ethylene-diamine-tetra-acetic acid) and was put into hematological analyser COULTER LH 780 (USA, Brea, CA). Before inclusion in the study, CRP levels of every patient were tested. C-reactive protein concentrations were quantified using ''Synchron'' analyzer based on turbidimetry (Beckman Coulter, USA, Brea, CA). Patients with CRP levels exceeding 7.5 mg/L were not included in the study due to the presence of inflammation.

In order to investigate platelet aggregation, blood was taken from the forearm vein into 5-mL vacuum tubes with 3.8% sodium citrate. In order to prepare the platelet-rich plasma blood was centrifuged at 1000 rpm ($100 \times g$) for 15 min at room temperature. Platelet-poor plasma was obtained when the rest of blood was centrifuged at 3000 rpm ($1000 \times g$) for 30 min. Platelet aggregation was investigated in platelet-rich plasma using the aggregometer (Chrono-Log, USA) by the standard Born method [16]. ADP (3.8 mmol/L, Chrono-log P/N 384), collagen (2 μmol/L, Chrono-log P/N 385) and adrenalin (ADR, 4.5 mmol/L) were used for aggregation induction. Spontaneous aggregation (SP) was registered without using an inductor.

Fibrinogen concentration was investigated by the Clauss method using a semiautomatic analyzer Bios-4 (France) and