The effects of preceding exercise on myocardial damage in rats

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Abstract. [Purpose] The purpose of this study was to investigate the effects of exercise on myocardial injury in male Sprague-Dawley rats. Two groups of rats were trained with either moderate- or high-intensity treadmill running for four weeks. Subsequently, the concentrations of cardiac troponin and the N-terminal of prohormone brain natriuretic peptide (NT-proBNP) were examined following a single bout of prolonged intensive exercise (lasting 3 h). [Subjects and Methods] The study included 40 six-week-old male Sprague-Dawley rats weighing 150–180 g each. The aerobic exercise group was divided into high-intensity (28 m/min) and moderate-intensity (15 m/min) subgroups. Both subgroups were trained for 35 min daily for six days per week (excluding Sunday) over a four-week period. Following training, the high- and moderate-intensity exercise groups and a nonexercise group performed one bout of prolonged treadmill exercise for 3 h at a speed of 15 m/min. [Results] The cardiac troponin and NT-proBNP levels differed significantly between the groups. [Conclusion] The exercise groups showed lower levels of cardiac troponin and NT-proBNP than the nonexercise group after the bout of prolonged intensive exercise.

Key words: Myocardial damage, Treadmill exercise, Preceding exercise

INTRODUCTION

Exercise facilitates metabolic functions in the human body and benefits physical health by preventing disease, controlling weight, and maintaining homeostasis1). The American Heart Association reported that a lack of exercise is one of the main factors of heart disease (along with high blood pressure, hyperlipidemia, and smoking) and recommended regular exercise to treat and prevent heart-related disease2).

Measuring the blood biochemical indicators of myocardial damage is conventionally divided into a traditional method that measures creatine kinase myocardial band isoenzyme (CK-MB) and a cardiac enzyme test that measures cardiac troponin (cTn). An increase in these elements indicates a strong possibility of acute cardiac infarction3). Of these elements, cTn is an enzyme specific to the heart that increases in response to very small cardiac damage4). Therefore, cTn is a standard biochemical index used for diagnosing myocardial necrosis in patients with coronary artery disease5). The N-terminal of prohormone brain natriuretic peptide (NT-proBNP) is an indicator that is useful for diagnosis, the evaluation of treatment effects, and the prediction of the prognosis of patients with cardiac insufficiency. NT-proBNP is also known to be effective for predicting a malfunction of the left ventricle after cardiac infarction6). The material reflects cardiac stress in clinics and has been reported to be excessively expressed over the normal range during serious exercise, such as an ultra-marathon7). Performing regular exercise before fierce endurance exercise is effective for preventing myocardial and muscular tissue damage during the fierce endurance exercise. However, few studies have examined the physiological indicator in cases of one-off high-intensity exercise after moderate- or high-intensity endurance orientation training. Therefore, the purpose of this study was to investigate differences in the concentrations of cTnI, NT-proBNP, and CK-MB in male Sprague-Dawley rats during one bout of

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prolonged treadmill exercise (lasting 3 h) following different training and non-training regimens.

SUBJECTS AND METHODS

Forty male Sprague-Dawley rats (age: six weeks, weight: 150–180 g each) were used in this study. All animals were housed (three rats per cage) at 23 ± 2 °C and 50 ± 5% humidity with a 12-hour light–dark cycle. The rats were given a seven-day period for adapting to the environment before the experiment. Pellet feed and water were periodically provided during the experimental period. The rats were randomly divided into four groups (n=10 in each group): control, high-intensity exercise, moderate-intensity exercise, and nonexercise. This study was approved by the Institution of Animal Care and Use Committee of Daegu University, and the experimental procedure complied with the management guidelines for experimental animals.

The exercise intensity levels used in this study were set on the basis of the results of a study by Shepherd and Gollnick (1976), in which the maximal oxygen uptakes of white Sprague-Dawley rats were measured using a metabolic rate-measuring instrument and a treadmill. As a result, the levels were set at 15 m/min (i.e., approximately 65% of the maximal oxygen uptake) and 28 m/min based on the reference data that defined the relevant velocity as being approximately 82% of the maximal oxygen uptake. This study’s aerobic exercise groups first performed a preliminary aerobic adjustment exercise for 20 min daily for four days and then performed their main treadmill training for 35 min/day six days per week (except Sunday) for four weeks. The high- and moderate-intensity exercise groups maintained intensity levels of 28 m/min and 15 m/min, respectively, but, non-exercise group carried out preceding exercise for four days and since then didn’t carry out intensive aerobic exercise. After the training, the high- and moderate-intensity exercise groups and the nonexercise group simultaneously performed one bout of prolonged treadmill exercise at 15 m/min for 3 h.

Following this bout of prolonged treadmill exercise, the animals were weighed. They were anesthetized using ether as an inhalation anesthetic. Each animal’s abdominal cavity was dissected immediately, and 10 ml of blood was collected from the main artery using a syringe. The collected blood was put into an Eppendorf tube and centrifuged at 18,000 rpm at 4 °C for 18 min. The collected sera were stored in a freezer at −70 °C prior to analysis. The cTnI and NT-proBNP concentrations of the animals were measured. A Dimension Xpand Pluse (Siemens, Ltd., USA) was used as a measurement device, and a Dimension® MMB FlexTM Reagent Cartridge was used as a reagent. The blood threshold applied to each experiment was under 0.6 ng/ml and 125 pg/ml for cTnI and NP-proBNP, respectively.

A one-way analysis of variance test was performed using PASW (version 18.0 for Windows) to investigate intergroup differences. The Bonferroni post hoc test was used to perform the post hoc comparisons. The significance level was set at 0.05.

RESULTS

Table 1 presents the weights of the rats measured in each exercise group after one bout of prolonged treadmill exercise. The cTnI levels differed significantly between the groups: 0.01 ± 0.00 ng/ml for the control group, 0.08 ± 0.02 ng/ml for the high-intensity exercise group, 0.59 ± 0.40 ng/ml for the moderate-intensity group, and 1.54 ± 0.74 ng/ml for the non-exercise group (p<0.05). The post hoc analysis showed that the high- and moderate-intensity exercise groups had significantly higher cTnI levels than the control group (p<0.05), and the high- and moderate-intensity exercise groups had significantly lower cTnI levels than the non-exercise group (p<0.05) (Table 1).

The NP-proBNP levels differed significantly between the groups: 27.8 ± 8.7 pg/ml for the control group, 29.7 ± 10.5 pg/ml for the high-intensity exercise group, 38.5 ± 12.8 pg/ml for the moderate-intensity exercise group, and 58.5 ± 15.3 pg/ml for the non-exercise group (p<0.05). The post hoc analysis showed that the non-exercise group had significantly higher NP-proBNP levels than the control group (p<0.05), and the high- and moderate-intensity exercise groups had significantly lower NP-proBNP levels than the non-exercise group (p<0.05) (Table 1).

DISCUSSION

This study examined the impact of four weeks of moderate- and high-intensity treadmill warming-up exercise on the heart’s condition during serious aerobic exercise using a sample of Sprague-Dawley white male rats.
In this study results, the blood cTnI levels of the non-exercise group and the moderate-intensity training group increased significantly after long-distance running compared to the control group, which did not perform long-distance running. However, the high-intensity training group did not show a significant increase, indicating that high-intensity training in advance of long-distance running is effective at preventing myocardial damage during long-distance running. This result is consistent with the results of a study by Chen et al.\textsuperscript{9}, in which cTnT concentrations in white rats decreased remarkably in an experiment group that performed high-intensity warm-up swimming training with an extra weight compared with an experiment group that swam without a weight. The study argued that performing preliminary exercise before high-intensity training can decrease myocardial damage or negative impacts in the body in case of fierce exercise. In the current study, a significant increase in NT-proBNP, which is used as an indicator of cardiac insufficiency, was observed in the nonexercise group.

Several studies reported that elite athletes, non-elite athletes, and leisure players can show a short-term increase in NT-proBNP after intense and severe long-term exercise. Moreover, NT-proBNP concentration increases after long-term exercise or fierce endurance exercise\textsuperscript{10, 11}. However, NT-proBNP concentrations at rest do not increase among trained athletes compared to untrained people in the same age group\textsuperscript{10, 12}. In the current study, the moderate- and high-intensity exercise groups showed a significant decrease of indicator for myocardial damage compared to the non-exercise group when implementing serious long-distance running. Among the exercise groups, the prevention effects were larger the high-intensity training than the moderate-intensity training. This implies that performing high-intensity training before severe aerobic exercise is effective at preventing myocardial damage. Wannamethee et al.\textsuperscript{13} noted that the implementation of regular exercise reduced exercise-induced inflammatory responses; this was attributed to adaptive responses to the exercise and to anti-inflammatory effects.

The current study found that, compared to the nonexercise group, rats that underwent preceding exercise showed less cardiac muscle damage and inflammatory responses during prolonged intense exercise. In particular, the effects were greater after one bout of intense exercise following high-intensity training than moderate-intensity training.

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