

EXPERIMENTAL STUDY

Exercise training and detraining process affects plasma adiponectin level in healthy and spontaneously hypertensive rats

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ABSTRACT

BACKGROUND: Adiponectin levels with long-term swimming exercise have been never investigated in spontaneously hypertensive rats (SHR).

OBJECTIVE: This study was aimed to investigate the effects of exercise and detraining process on the adiponectin plasma levels of spontaneously hypertensive rats (SHR) and healthy Wistar-Kyoto rats (WKY).

MATERIAL AND METHODS: The rats in the exercise groups were swimming for 10 weeks, 5 days/week, one hour in a day. The detraining rats were left to be sedentary in their cages for 5 weeks after 10 weeks of exercise period.

RESULTS: The plasma adiponectin levels decreased in E and SHRE groups compared to the SC and the SHR groups, respectively. In addition, blood pressure was decreased in the exercise groups vs their controls. The adiponectin level was not found to be significantly different in ED and SHRED groups compared to their controls. The blood pressure did not differ between SDC and ED groups, although in the SHRED group it was found to be lower than in SHRS group rats.

CONCLUSION: The results of this study showed that exercise reduced plasma levels of adiponectin in healthy and spontaneously hypertensive rats. However, this difference disappeared at the end of the training processes. Our results suggest, that changes in plasma adiponectin levels are not responsible for changes in blood pressure (Tab. 2, Fig. 2, Ref. 43). Text in PDF www.elis.sk.

KEY WORDS: adiponectin, spontaneously hypertensive rats (SHR), blood pressure.

Introduction

Hypertension (HT) is a well-known risk factor for cardiovascular disease, associated with high mortality and morbidity, a disease that requires pharmacological and non-pharmacological treatment (1, 2). The endothelial dysfunction plays a key role in the development of hypertension and cardiovascular diseases (3). Spontaneously hypertensive rat (SHR) is a good animal model for human essential hypertension and is widely used in the study of cardiovascular disease. As in humans, hypertensive response begins with advancing age in SHR and the main reason for the increase in blood pressure is not known (4, 5). Physical exercise has widespread beneficial effects on the body, cardiovascular system, and risk factors. Previous experimental and clinical studies showed, that acute and chronic exercise has beneficial effects on the blood pressure (2, 6). Exercise practice is a non-pharmacological treatment for a series of diseases. Further, there is an evidence from literature that an aerobic exercise training program has favourable

effects on cardiovascular risk factors and endothelial pathophysiology in persons with hypertension (7, 8).

Adiponectin, a circulating cytokine derived from white adipose tissue and cardiomyocyte (9), has been suggested to possess cardioprotective properties, as an anti-inflammatory, anti-atherogenic, anti-hypertensive and insulin sensitizing agent (10, 11). The adiponectin levels are reduced in conditions such as: obesity, type 2 diabetes, metabolic syndrome, and ischemic heart disease (12, 13). A large-scale study on adiponectin and coronary artery diseases found a considerably lowered risk of the myocardial infarction (MI) in subjects with higher adiponectin concentrations (14). The role of adiponectin in development of the cardiac diseases is not well known, as well as metabolic disorders. Initial evidence from clinical studies showed, that angiotensin II receptor blockers increased circulating levels of adiponectin. Ran et al have shown, that the induction of hypertension with angiotensin II injection led to a decrease in plasma adiponectin concentration (15). Clinical studies performed to explain the relationship between adiponectin and hypertension has shown, that hypo adiponectinemia is a risk factor for hypertension independent of insulin resistance and diabetes (16, 17).

As for adiponectin and exercise, some researchers have reported an increased adiponectin level with exercise intervention (18), others did not find such significant changes (19, 20). On the other hand, the study of obese female teenagers reported an insignificant change in blood adiponectin without a change in body

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weight after 12 weeks of aerobic exercise (21). Thus, the effect of exercise on adiponectin levels is still unclear, though the data perhaps suggest, that more intense the exercise is, the more likely it is to influence adiponectin levels. The mechanisms, by which adiponectin levels are regulated during exercise, are unknown (22). In the light of the information summarized above, in this study, we investigated the potential effects of the low-moderate intensity swimming exercise during ten weeks and subsequent detraining protocol (5 weeks) on plasma adiponectin levels of the SHR and healthy Wistar-Kyoto rats.

Materials and methods

Animals

Five weeks old male spontaneously hypertensive rats (SHR) were randomly divided into the two groups ($n = 14$ in each group): Sedentary and Exercised. SHR Sedentary were further divided into two as “control SHR group 1 (SHRC1)” and “control SHR group 2 (SHRC2)”, while the SHR exercised were divided as exercise “exercise SHR group (SHRE)” and detrained groups “exercise detraining SHR group (SHRED)” ($n = 7$ in each group). In addition, age-matched Wistar-Kyoto rats (WKY) were divided into two groups ($n = 14$ in each group): Sedentary and Exercised. WKY Sedentary were further divided into two as “control WKY group 1 (SC1)” and “control WKY group 2 (SC2)”, while WKY exercised were divided as exercise “exercise WKY group (E)” and detrained groups “exercise detraining WKY group (ED)” ($n = 7$ in each group). The rats in the sedentary groups for 10 weeks and sedentary detraining groups for 15 weeks were allowed to roam their cages freely. Blood samples of the animals in control groups (SC1 and SHRC1) were obtained 10 weeks after the beginning of experiments, simultaneously with the exercise groups (E and ESHR) and control groups (SC2 and SHRC2) 15 weeks after the start, simultaneously with the detrained animals (ED and SHRED). All animals were housed at a temperature of 23 ± 1 °C in individual cages and freely fed a regular pellet diet ad libitum. All rats were subjected to alternate 12 h periods of dark and light (lights on 6:00 a.m.–6:00 p.m.). Principles of laboratory animal care (NIH publication No. 86–23, revised 1985) were followed, as well as Pamukale University Ethics Committee of Animal Care and Usage.

Exercise training protocol and detraining protocol

The exercise protocol conformed to the American Physiological Society’s Resource Book for the Design of Animal Exercise Protocols (23). Swimming pools were stainless steel cylinders with a diameter of 150 cm and 60 cm high and filled to a height of 45 cm with water (31.0 ± 2.0 °C). For adaptation, swimming training was limited to 10 min on the first day and increased by 10 min each day, until 60 min was reached. Rats were subjected to daily swimming sessions for 10 weeks, 5 days/week, one hour in a day. During the exercise period, the age matched sedentary control group swam 10 minutes/week in same swimming pools and exposed to similar noise and handling (24). This protocol is defined as an aerobic endurance training and moderate intensity exercise and corresponds to the intensity below the anaerobic threshold in

rats (25). Swimming rats were individually observed. One of the WKY rats drowned while swimming. The rats in sedentary and detraining groups swam once a week for 10 minutes. The rats in the detraining groups underwent the same training protocol and then discontinued training during next five weeks (detraining groups).

Blood pressure measurements

Systolic blood pressures (SBP), diastolic blood pressures (DBP) and heart rate (HR) of the animals, values were measured using the Commat May NIBP 200-A, noninvasive blood pressure system (Biopac Systems, Inc) biweekly during the experimental period. Rats were kept up until they calmed down in animal holders at 34 °C. All animals were placed in a restrainer for 15 minutes, they should be quiet and still to prevent the excessive stresses. Most animals showing compliance at the end of the acclimatization period, learned to enter the cage themselves. A cuff was attached to their tail; SBP and HR, were then recorded. All measurements were performed without anaesthesia in a silent room. Three findings were observed from each rat and averaged. The blood pressure of the animals averaged after 18 hours from the end of the exercise and always has been made before swimming exercise that day.

Biochemical parameters

Twenty four hours after the last training session, the blood samples were collected from the abdominal aorta of rats under Ketamin/XylazineHCl (75 mg/kg/10 mg/kg) anesthesia and anticoagulated with EDTA (1.5 mg/ml) and used for the determination of adiponectin levels. Plasma was separated by centrifugation (7660 rpm, 5 min) and stored at -80 °C. Plasma adiponectin were determined by ELISA (Biocompare, San Francisco, CA, USA).

Body weight

Body weight of SHR and WKY rats was measured biweekly.

Statistical analyses

The results were expressed as the means \pm standard deviation (mean \pm SD). “Kruskal-Wallis Variance Analysis” and “Mann-Whitney U test” were used for statistics, with p values ≤ 0.05 accepted as statistically significant. All analyses were carried out with the computerized SPSS 15.0 program (Statistical Package for Social Sciences, SPSS Inc).

Results

Heart rate (HR), systolic and diastolic blood pressure of the groups were found to be significantly different among SC1, E, SHRC1 and SHRE groups ($p < 0.001$) (Tab. 1). HR, systolic and diastolic blood pressure of the SHRC1 and the SHRE groups were higher than the SC1 and the E groups ($p < 0.001$), whereas HR and systolic blood pressure of SHRE group was lower compared to the SHR control ($p < 0.05$) (Tab. 1). HR and diastolic blood pressure of the SC1 group were found to be significantly higher than the E group ($p < 0.05$) (Tab. 1).

Table 1 shows body weight of the groups. Body weight of the SC1 and the E groups were significantly different compared to the

Tab. 1. Effect of 10 weeks exercise on blood pressure, heart rate and body weight.

	SC1	E	SHRC1	SHRE	p
SBP (mmHg)	122.60±3.16	118.57±10.14	173.71±2.69****†	149.40±8.09****††††	0.000
DBP (mmHg)	81.90±2.76	74.66±4.17**	94.28±2.36****†	89.00±2.66****††††	0.000
HR	336.30±10.93	292.14±9.87**	399.85±57.58****†	340.10±16.16****††	0.000
BW (gr)	305.85±19.50	277.14±7.74**	261.94±1.33**†	258.50±9.31****	0.0001

Data are given as the mean ± standard deviation. SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, BW: body weight, †: Difference from SC, ††: Difference from E, †††: Difference from SHRC, *,†,††: p < 0.05, **,††,†††: p < 0.01, ****,†††,††††: p < 0.001

Tab. 2. Effect of detraining process on blood pressure, heart rate and body weight.

	SC2	ED	SHRC2	SHRED	p
SBP (mmHg)	122.33±4.87	120.22±1.71	184.57±5.06****†	152.50±9.51****††††	0.000
DBP (mmHg)	79.88±1.05	76.55±4.50	97.57±1.71****†	92.87±3.39****††††	0.000
HR	344.88±18.07	323.88±15.83*	429.14±22.93****†	369.00±28.20****††††	0.000
BW (gr)	344.50±8.80	334±14.67	282.85±13****†	293.42±10.73****†	0.000

Data are given as the mean ± standard deviation. SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, BW: body weight, †: Difference from SC, ††: Difference from E, †††: Difference from SHRC, *,†,††: p < 0.05, **,††,†††: p < 0.01, ****,†††,††††: p < 0.001

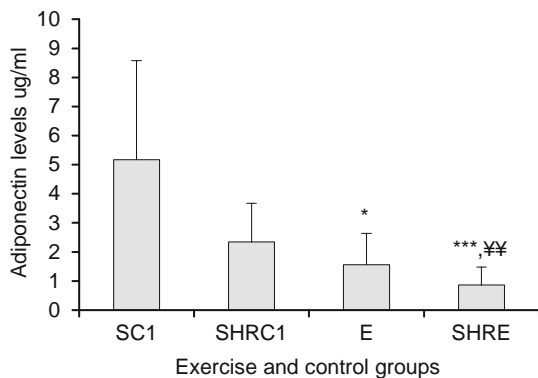


Fig. 1. Effect of 10 weeks exercise on adiponectin plasma level. Data are given as the mean ± standard deviation. †: Difference from SC, ††: Difference from SHRC, * p < 0.05, ††: p < 0.01, *: p < 0.001.**

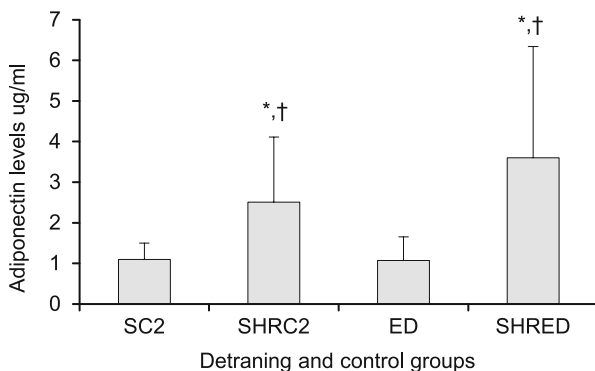


Fig. 2: Effect of detraining process on adiponectin plasma levels. Data are given as the mean ± standard deviation. †: Difference from SC, ††: p < 0.05 ††: Difference from E, *,†: p < 0.05.

SHRC1 and the SHRE at beginning and end of the experiment (p < 0.05) (Tab. 1). There was no significant difference at the level of body weight between the SC1 and the E groups at the beginning of the experiment, however, final body weight of the E group rats decreased compared to the SC1 group, p < 0.01.

Unfortunately, we did not have a chance to look at the adiponectin levels of serum at the beginning of the experiment. How-

ever, at the end of a ten-week experiment, the adiponectin levels of rats were found to be significantly different among the SC1, E, SHRC1 and the SHRE groups (p < 0.001) (Fig. 1). The adiponectin plasma levels decreased in the E and the SHRE groups compared to the SC1 group. Adiponectin plasma concentration in the SHRE group was also lower than in the SHRC1 group.

After fifteen weeks, SBP, DBP, HR, body weights and the plasma adiponectin levels of detraining and sedentary group rats were measured. SBP, DBP and body weight were not found to be significantly altered in the ED group compared to the SC2 group (Tab. 2). On the other hand, HR of ED rats was lower than the SC2 rats (p < 0.05). SBP, DBP and HR levels of the SHRC2 group rats were found to be significantly higher than the other groups (p < 0.001). There was no statistically significant difference between body weights of SHRC2 and SHRED groups (Tab. 2). However, body weights of the SHRC2 and the SHRED rats were found to be significantly lower than both sedentary detraining control and exercise detraining animals (p < 0.01).

The adiponectin plasma level of the SC2 group rats was found significantly low compared to the SC1 rats. Also, the other parameters did not show significant difference between these two groups. There was no statistically significant difference between all parameters of the SHRC2 and SHRED groups, E and ED groups. In the SHRED group, adiponectin concentration and DBP levels were significantly higher than in the SHRE group.

The plasma adiponectin concentration of the SC2 group was not different from exercise detraining rats. In addition, there was no difference between SHRC2 and SHRED groups in term of adiponectin. On the other hand, SHRC2 and SHRED animals have had high adiponectin plasma levels compared to SC2 and ED rats (p < 0.05) (Fig. 2).

Discussion

In this study, we investigated the effects of a ten-week swimming exercise program and five-week detraining process after swimming exercise on the plasma adiponectin levels of WKY and spontaneously hypertensive rats. In addition, we aimed to investigate the relationship between blood pressure and adiponectin levels.

According to our results, the adiponectin concentration was reduced in the exercising groups of both WKY and SHR compared to their sedentary control groups. Similar to the adiponectin levels, systolic and diastolic blood pressure values have declined in the exercising groups. In exercise studies, plasma adiponectin levels vary in the results. The results of previous studies have shown, that acute episodes of mild or moderate exercise in healthy, lean subjects did not affect the adiponectin levels (20, 26, 27). Some researchers have reported that exercise increased adiponectin levels (28, 29, 30). However, in another study performed by Kraemer et al, plasma adiponectin levels of young athletes were demonstrated to be decreased after acute strenuous rowing (31). Our findings are similar to this study. Some studies suggest, that adiponectin level is associated with a blood pressure. Tan et al have shown, that hypoadiponectinemia is associated with a lower vasodilatation and adiponectin administration increases NO production in human aortic endothelial cells (32). Previous clinical studies reported, that exposure to angiotensin II receptor blockers increases circulating levels of adiponectin (33, 34). At the same time, Tanida et al found, that adiponectin dose-dependently decreases blood pressure and sympathetic nerve activity by intravenous injection in rats (35). In our study, decrease in blood pressure was probably independent of the level of adiponectin.

Plasma adiponectin level, systolic and diastolic blood pressure did not differ between the SC1 and ED groups at the end of detraining period. The plasma adiponectin levels of SHRED group were found to be higher than SHRC2 group. However, this increment was not statistically significant. In the recent study, at the end of ten-weeks swimming exercise followed by a 3-week detraining period, the systolic and diastolic blood pressure was decreased in SHRED group compared to SHRC2 group. Nikseresht M et al found, that adiponectin was increased significantly with aerobic interval training vs nonlinear resistance training in human subjects and in both training groups after detraining, but adiponectin was decreased significantly (36). Unfortunately, we did not have a chance to determine the blood adiponectin levels of detraining rats after exercise. In this study, the plasma adiponectin levels did not show significant difference between sedentary spontaneously hypertensive rats and SHRC2. However, its' levels were observed to be increased in trained SHR group by the end of 5 week detraining period compared to SHRE group. Fatouros et al reported, that plasma levels of the adiponectin did not change among pre-training, post-training and detraining period, however moderate-intensity and high-intensity exercise had led to increment of the adiponectin levels in post-training and detraining compared to the pre-training levels (37). A recent study performed in overweight children indicated the positive effects of 12 weeks of training on body composition, serum adiponectin levels. However, the adiponectin results did not show any significant difference between 12 weeks of detraining and trainings groups (38).

Body weight of the WKY groups was significantly lower compared to the SHR groups in our study at the beginning and at the end of the experiment. Tonooka et al study showed, that body weight gain was significantly lower in the SHR groups, rather than in the WKY groups (39). As the result of this study, while the body weight of the exercise training rats was decreased compared to the

sedentary control rats, adiponectin concentration was found to be lower in the E group. On the other hand, in terms of the body weight levels of rats, no statistically significance was observed between sedentary spontaneously hypertensive rats and exercise training SHR group. In addition, a significant decrease of the adiponectin levels of SHRE rats was shown according to SHRC rats. Plasma levels of adiponectin decrease with weight gain and increase by weight loss (40). These findings are contrary to the previous reports suggesting, that weight loss is required to increase the circulating adiponectin levels (40, 41), although there are some studies that have shown, that exercise training combined with a reduction in body mass had no effect on the adiponectin concentrations (42, 43).

However, the pattern of findings from different studies indicated that it was more likely for t adiponectin to be affected by exercise training, if greater volume (frequency, intensity and duration) of exercise training leading to weight loss was employed (31). This suggests, that the conflicting results from previous studies can be attributed to differences in the volume intensity, duration, type of exercise and to the different experimental protocols. This study showed, that swimming exercise resulted in decrement of body weight, blood pressure and adiponectin levels in WKY rats and SHR. In addition, detraining did not cause any change in adiponectin levels, body weight and blood pressure between WKY rats. However, detraining positively affected body composition and the adiponectin level in the SHR group.

In conclusion, these data suggest, that exercise and detraining affect plasma adiponectin levels, body weight and blood pressure and the changes in the plasma adiponectin levels are not only responsible for increased or decreased blood pressure. We think that further studies are needed to describe the relationship between these parameters.

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