

Original Article



The effect of resistance training on blood pressure, apelin, ANP, PON1, adiponectin, H₂O₂, and ET-1 in hypertensive men

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Abstract

Background and aims: Primary hypertension, an unexplained increase in blood pressure (BP), accounts for 90% of the cases of hypertension and remains a critical public health challenge. This study aimed to investigate the effects of 12-week resistance training (RT) on some vasodilators and vasoconstrictors in hypertensive men.

Methods: This is a semi-experimental study. A total of 40 middle-aged men (45.3±3.2 years) with moderate hypertension (systolic BP [SBP] 140.5±0.3 and diastolic BP [DBP] 90.7±0.0 mm Hg) were randomly divided into the RT (n=20) and non-exercise control (n=20) groups. The 12-week dynamic RT program was performed at an intensity of 80% of one repetition maximum for 3 days per week (3 sets of 8 repetitions/3 days a week). Blood samples were taken from both groups at baseline and weeks 4, 8, and 12.

Results: SBP and DBP decreased by -8.19±2.46 mm Hg ($P=0.039$) and -1.19±0.02 mm Hg ($P=0.033$) from baseline at week 12 in the RT group, respectively, compared to the control group (SBP; 8.22±2.49, $P=0.04$; DBP; -1.19±0.03, $P=0.032$). Adiponectin, apelin, atrial natriuretic peptide (ANP), and paraoxonase-1 (PON-1) serum levels increased from baseline at weeks 8 ($P=0.01$) and 12 ($P=0.01$), while endothelin-1 (ET-1) and H₂O₂ decreased from baseline at weeks 8 ($P=0.01$) and 12 ($P=0.01$) in the RT in comparison to the control group.

Conclusion: Overall, 12-week RT led to an increase in apelin, ANP, PON-1, and adiponectin. Increasing these markers reduces H₂O₂ and ET-1, thus decreasing SBP and DBP in hypertensive men.

Keywords: Oxidative stress, Blood pressure, Adipokine, Resistance training, ANP

Received: June 20, 2022, Accepted: September 20, 2022, ePublished: November 21, 2022

Introduction

Essential hypertension (EH) increases the risk of brain, heart, and kidney diseases. The prevalence of hypertension among adults is higher in low- and middle-income (31.5%, 1.04 billion) than in high-income (28.5%, 349 million people) countries (1).

Some factors affect the dilation or contraction of blood vessels and thus affect blood pressure (BP). Oxidative stress (OS) is implicated in the etiology of EH since EH is associated with increased reactive oxygen species (ROS) production by various organs, including the brain, arteries, and kidneys (2). Individuals with hypertension also have unfavorable alterations in vascular reactivity. The endothelium regulates the tone of the arteries by releasing endothelial-derived relaxing and endothelial-derived contractile factors (2). OS causes an imbalance in the production and bioavailability of these molecules favoring vasoconstriction that can lead to endothelial dysfunction (2). Some studies have reported that OS increases the production of endothelin 1 (ET-1), a potent

vasoconstrictor, and the activity of autocrine ET-1 in vascular smooth muscle cells (3).

Atrial natriuretic peptide (ANP) is an antihypertensive hormone produced by the heart that regulates water and salt balance and BP by enhancing the excretion of sodium and kidney water and stimulating vasodilation (4). Adiponectin is a protein hormone and has beneficial effects on vascular disorders by having a direct effect on vascular tissue components (5). Orlando et al (6) reported that lower adiponectin levels were associated with high systolic BP (SBP) and diastolic BP (DBP). Paraoxonase-1 (PON-1) is another marker that can have antihypertensive effects (7). PON-1 activity showed a direct relationship with brachial flow-mediated vasodilation and BP (8). Decreased adiponectin and PON-1 activity may lead to an imbalance in oxidants and antioxidants and cause oxidative damage (9). Apelin also belongs to the adipokine family and is a biologically active mediator released by adipose tissues (10) to eliminate disorders caused by OS in the expression of anti-oxidant and pro-oxidant

enzymes, biogenesis, and mitochondrial function, and the release of pro- and anti-inflammatory adipocytokines (11). Reduced apelin levels may enhance vasoconstriction to increase BP and the work of the heart in EH and acute coronary syndrome (12).

Exercise training is a key non-pharmacological treatment for hypertension. In recent years, resistance training (RT) recommended alongside aerobic exercise training as an effective tool for decreasing BP (13). Sousa et al concluded that RT alone reduces SBP and DBP in pre-hypertensive and hypertensive subjects (13). However, the effect of RT on BP in hypertensive individuals with an emphasis on these markers is unclear. This study sought to investigate the effects of 12-week RT on these vasodilators and vasoconstrictors in men with hypertension.

Materials and Methods

Subjects

The population of this semi-experimental study consisted of 45- to 50-year-old men with moderate hypertension living in Tabriz, Iran in 2021. To determine whether they were eligible for the study, potential volunteers were asked to complete a physical activity and medical history questionnaire (14). The inclusion criteria were a body mass index (BMI) $>26 \text{ kg/m}^2$, a heart rate (HR) $>82 \text{ bpm}$, an SBP and DBP $\geq 140/90 \text{ mm Hg}$ but $\leq 180/110 \text{ mm Hg}$, and no history of regular exercise. On the other hand, the exclusion criteria were age <45 and >50 , a history of regular exercise, an HR <82 , SBP and DBP $>140/90$ and $>180/110$, BMI $<26 \text{ kg.m}^2$, myocardial infarction, stroke or angina within 6 months, and symptomatic failure heart congestive or ejection fraction $<35\%$. The other exclusion criteria were known renal insufficiency – creatinine $\geq 2 \text{ mg/dL}$ and a need for diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors, or α -blockers for reasons other than hypertension (15).

The subjects were treated under the supervision of a specialist doctor and took BP medicine. To measure the HR and BP, the subjects were asked to sit for 30 minutes and not to consume caffeinated beverages for 2 hours before that. After completing the informed consent form, physiological characteristics were checked, and the subjects were advised to avoid caffeine, nicotine, alcohol, and intense sports. These physiological measurements included HR with OPTIMA SE-315 (South Korea), SBP and DBP with OPTIMA SE-315 (South Korea), and BMI with weight and height.

Although the sample size was calculated based on the feasibility of the study, a sample size of 20 per group was selected as this was thought to provide sufficient statistical power. Accordingly, the participants were then randomly divided into the dynamic resistance RT ($n=20$) and the non-exercise control (Con, $n=20$) groups. Subjects had a random chance to be placed in each group (Figure 1).

Blood sample collection

Baseline physiological parameters were measured again,

and venous blood samples were taken after 10 and 12 hours of overnight fasting to assess the serum levels of PON-1, H₂O₂, as well as serum adiponectin, ANP, apelin, and ET-1 at weeks 4, 8, and 12 (48 hours after the last exercise).

RT protocol

The participants of the exercise group participated in a 12-week program, including dynamic RT with an intensity of 80% of a maximum of one repetition (3 sets of 8 repetitions/3 days per week). The subjects of the control group were asked not to exercise regularly during the study period.

The RT program included performing the front leg movements of the device, the back of the device's foot, the chest press, the armpit of the lat, and the back of the arm standing with the device. This program is in compliance with the principle of added time in 3 sets of 8 repetitions at 80% of one repetition maximum and a 2-minute rest interval between sets and 3 minutes between exercises. At the end of each week of the test, a maximum repetition of all movements was performed again, and the intensity was adjusted to maintain 80% of one repetition maximum. The RT program lasted about 40 minutes per session.

Measurement of adiponectin

The plasma adiponectin level was measured by enzyme-linked immunosorbent assay (ELISA) using an adiponectin kit (AdipoGen Company, South Korea) with a sensitivity of $0.1 \mu\text{g/mL}$.

Measurement of apelin

The concentration of apelin plasma was also measured by ELISA with human kits (Phoenix CA, USA) with a sensitivity of ng/mL . The coefficient of change within the test was less than 5%.

Measurement of PON-1

PON-1 activity was determined using a paraoxon substrate (Sigma Chemical Company). For this purpose, the serum ($20 \mu\text{L}$) was added to ris/HCl buffer (100 mmol , $\text{pH}=8$) containing 2 mM calcium chloride (CaCl_2) and 2 mM paraoxon. The rate of the hydrolysis of Paraoxon was measured using a spectrophotometer at 412 nm and the release of p-nitrophenol at 37°C . Enzyme activity was also calculated with the extinction coefficient of 18290 mol/liter and checked in terms of nmol/min/mL of serum.

Measurement of ANP

The plasma ANP concentration was measured using ELISA with human kits (Abnova, Taiwan). The sensitivity of the measurement method was 0.26 ng/mL . The kit's internal and external measurement changes were 7.6% and 6.6%, respectively.

Measurement of H₂O₂

H₂O₂ was determined by the iron-xylylene-orange (FOX-1) oxidation method using the following method:

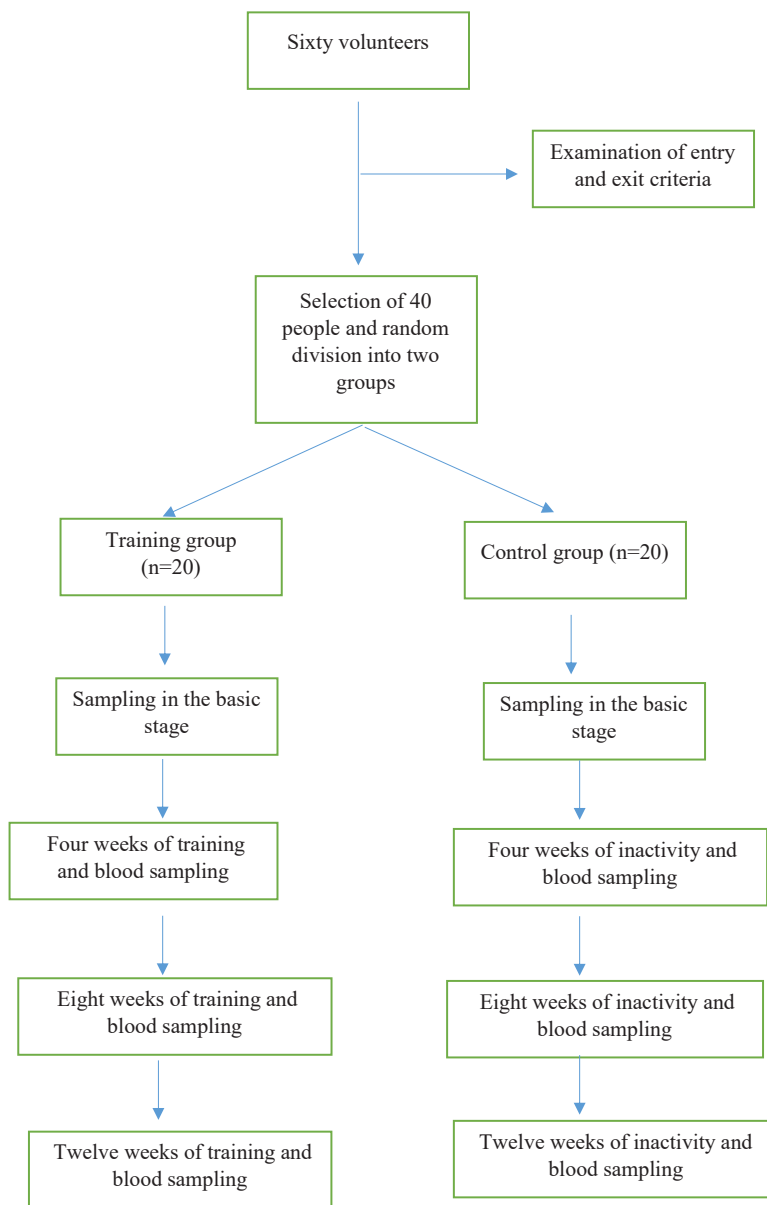


Figure 1. CONSORT diagram

First, 250 µmol of ammonium iron sulfate, 100 µmol of the FOX-1 reagent (xylenol orange), 25 µmol of sulfuric acid, and 100 µmol of sorbitol were prepared, and then, a microtube containing 1.5 mL Eppendorf was used to mix 50 mL of the prepared sample with 950 mL of the FOX-1 reagent in a vortex apparatus. The prepared mixture was incubated at 40°C (carbon dioxide incubator) for 30 minutes, and the absorbance of the sample was recorded using a spectrophotometer at 650 nm.

Measurement of endothelin-1 (ET-1)

ET-1 was measured by ELISA with human kits (Cayman Chemical Company, Ann Arbor, MI, USA) with a measurement accuracy of 1.5 pg/mL and a coefficient of change within the test of less than 5%.

Statistical analysis

Kolmogorov-Smirnov test was used to check the normality

of data distribution, and repeated measurements and the Bonferroni post hoc test were employed to compare the markers measured in different stages with their baseline values. A *t* test was applied to determine the comparison between groups. A linear mixed model was used to investigate the relationship between markers. All data were analyzed using SPSS software, version 28 (Chicago, IL, USA), and $P \leq 0.05$ was considered statistically significant.

Results

Subjects

Subjects were forty 45- to 50-year-old men with hypertension. The participants were overweight and had below average physical fitness. The SBP, DBP, BMI, and HR responses before training and after training are provided in Table 1.

Table 1. Effect of 12-week resistance training on physiological characters in RT and control groups

Markers	Groups	Research Stage				P* (Intragroup)		P* (Between group)
		Basal	Week 4	Week 8	Week 12	Exercise	Control	
Weight (kg)	Exercise	84.12±4.11	83.19±3.1	81.18±2.11	79.1±2.1	$P_1=0.843$ $P_2=.0151$ $P_3=0.049^*$	$P_1=0.688$ $P_2=.0109$ $P_3=0.048$	$P_3=0.85$ $P_4=0.99$ $P_5=0.09$ $P_6=0.032$
	Control	83.18±5.11	83.23±5.13	85.32±4.14	86.34±3.18			
BMI (kg/m ²)	Exercise	27.85±1.14	27.55±1.3	26.88±0.99	26.19±0.5	$P_1=0.87$ $P_2=.0079$ $P_3=0.05^*$	$P_1=0.891$ $P_2=.0509$ $P_3=0.077$	$P_3=0.99$ $P_4=0.82$ $P_5=0.08$ $P_6=0.04$
	Control	27.18±1.27	27.19±1.28	27.88±2.5	28.21±3			
Rest heart rate (beats/minutes)	Exercise	89±2.22	87±3.10	82±1.42	79±1.1	$P_1=0.177$ $P_2=.0049$ $P_3=0.021^*$	$P_1=0.478$ $P_2=.0221$ $P_3=0.112$	$P_3=0.85$ $P_4=0.99$ $P_5=0.09$ $P_6=0.032$
	Control	88±3.19	87±2.53	86.5±2.41	86.2±2.61			

Note. RT: Resistance training; BMI: Body mass index; Data are expressed as mean±SD # $P\leq 0.05$, by repeated measure. P_1 4-week vs. basal, P_2 8-week vs. basal, and P_3 12-week vs. basal.

BMI, Body Weight, and HR

RT significantly body weight ($P=0.049$) at the 12th week compared to the basal state in hypertensive men. RT also led to a significant decrease in the resting HR at the 8th ($P=0.049$) and 12th ($P=0.021$) week. No significant change was observed in BMI, weight, and HR in the control group (Table 1).

RT reduces SBP and DBP

SBP ($P=0.039$) and DBP ($P=0.033$) decreased by -8.19 ± 2.46 and -1.19 ± 0.02 from baseline at week 12 as a result of RT, yielding a difference between the RT and control groups at week 12 of -8.22 ± 2.49 and $-1.19\pm .03$ for SBP and DBP (Figure 2).

RT increases PON-1

Based on the results (Figure 3), resistance exercise led to a significant increase in PON-1 serum levels at the 8th ($1.75\pm .73$, $P=0.001$) and 12th ($2.04\pm .7$, $P=0.001$) week compared to the basal state in hypertensive men. Further, there was a significant difference between the RT and control groups in the 8th ($1.91\pm .77$, $P=0.001$) and 12th ($2.79\pm .49$, $P=0.001$) week.

RT increases adiponectin

Resistance exercise could significantly increase Adiponectin levels at the 8th (0.62 ± 0.22 , $P=0.001$) and 12th (1.32 ± 0.22 , $P=0.001$) week compared to the basal state in hypertensive men. Moreover, a significant difference was observed between the RT and control groups in the 8th (0.67 ± 0.21 , $P=0.001$) and 12th (1.39 ± 0.22 , $P=0.001$) week (Figure 3).

RT increases apelin

Resistance exercise increased apelin levels in the 8th (1.42 ± 0.03 , $P=0.001$) and 12th (2.69 ± 0.17 , $P=0.001$) week in comparison to the basal state in hypertensive men. A significant difference was found between the RT and control groups in the 8th (1.56 ± 0.08 , $P=0.001$) and 12th ($3.13\pm .13$, $P=0.001$) week (Figure 4).

RT Increases ANP

RT caused a significant increase in ANP levels in the 8th (0.7 ± 0.6 , $P=0.001$) and 12th (0.92 ± 0.58 , $P=0.001$) week compared to the basal state in hypertensive men. The results also revealed a significant difference between the RT and control groups in the 8th (0.7 ± 0.21 , $P=0.001$) and 12th ($0.92\pm .65$, $P=0.001$) week (Figure 4).

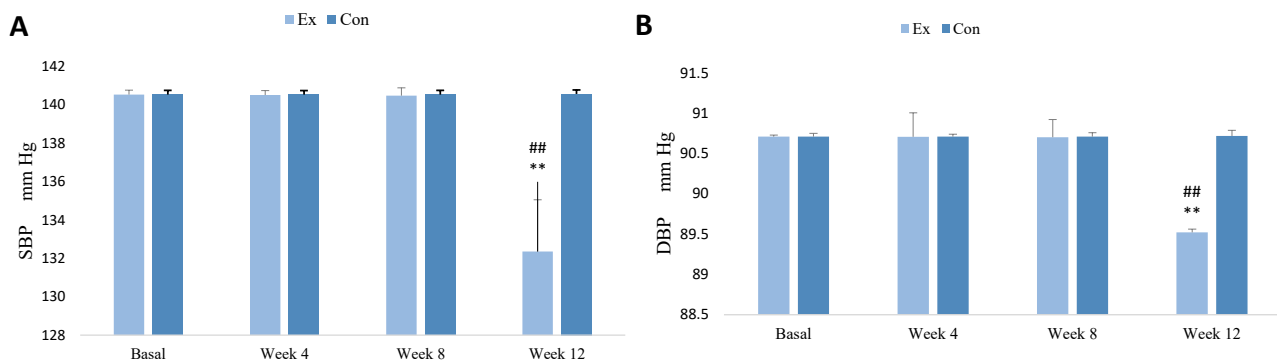


Figure 2. Effect of 12-week resistance training on SBP and DBP in middle-aged hypertensive men. Note. SD: Standard deviation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure. The values of SBP and DBP are specified in Sections A and B, respectively. Data are expressed as the mean±SD. ## $P\leq 0.001$ vs. basal, ** $P\leq 0.001$ vs. control groups by repeated measure

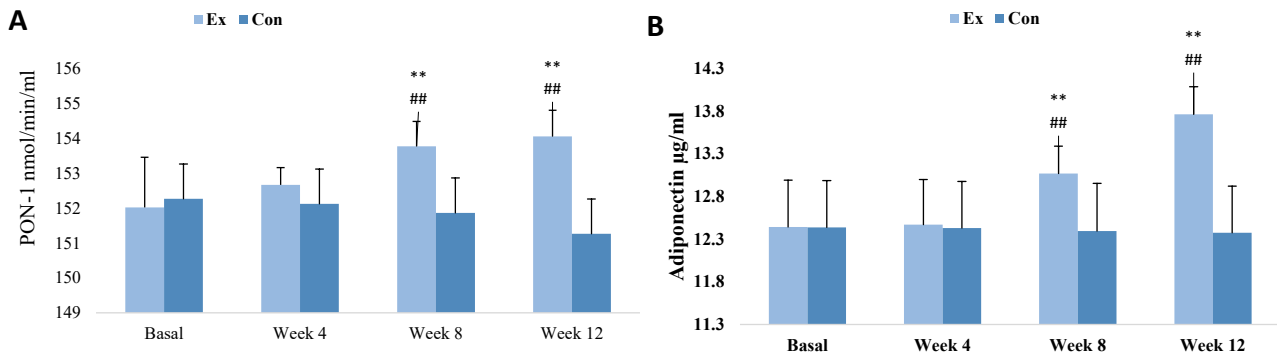


Figure 3. Effect of 12-week resistance training on PON-1 and adiponectin in middle-aged hypertensive men. Note. PON-1: Paraoxonase-1; SD: Standard deviation. The values of PON-1 and Adiponectin are specified in Sections A and B, respectively. Data are represented as the mean ± SD. ** $P \leq 0.001$ vs. basal and ** $P \leq 0.001$ vs. control groups by repeated measure

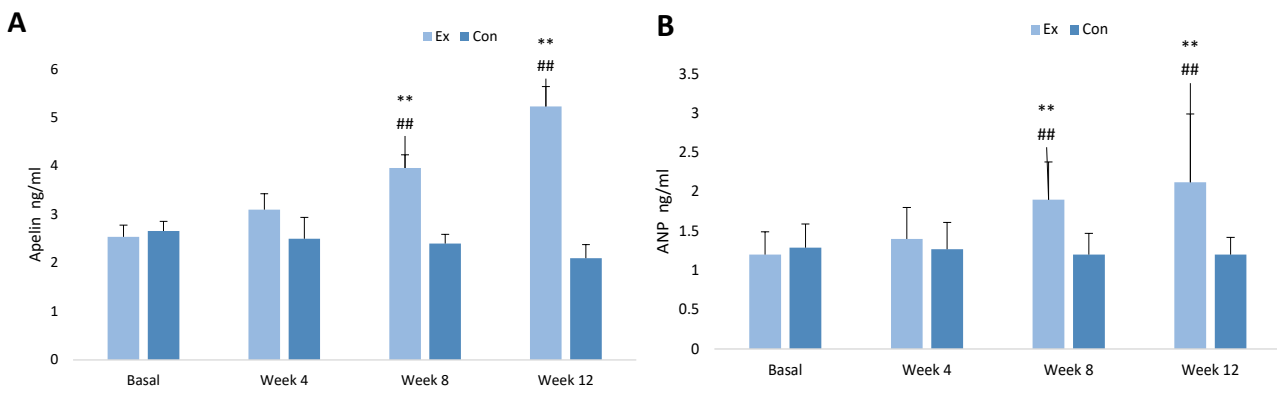


Figure 4. Effect of 12-week resistance training on apelin and ANP in middle-aged hypertensive men. Note. ANP: Atrial natriuretic peptide; SD: Standard deviation. The values of apelin and ANP are specified in Sections A and B, respectively. Data are expressed as the mean ± SD. ** $P \leq 0.001$ vs. basal, ** $P \leq 0.001$ vs. control groups

RT reduces H₂O₂ and ET-1

The findings (Table 2) demonstrated that H₂O₂ decreased from baseline at weeks 8 ($-0.32 \pm 0.1\%$, $P = 0.032$) and 12 (-0.36 ± 0.1 , $P = 0.021$) of RT in comparison to baseline as a result of RT, highlighting a difference between the RT and control groups at weeks 8 (-0.32 ± 0.01 , $P = 0.008$) and 12 (-0.37 ± 0.01 , $P = 0.002$).

Based on data in Table 2, resistance exercise decreased ET-1 levels at 8 (-0.4 ± 0.07 , $P = 0.001$) and 12 (-0.06 ± 0.07 , $P = 0.001$) weeks compared to the basal state in hypertensive men. There was a significant difference between the RT and control groups at 8 (-0.28 ± 0.11 , $P = 0.001$) and 12 ($-0.47 \pm$, $P = 0.001$) weeks.

Relationship between markers

RT resulted in a significant relationship between H₂O₂ (0.001), apelin (0.001), PON-1 (0.001), Adiponectin (0.001), ANP (0.001), and ET-1 (0.001) with SBP and DBP. There was also a significant relationship between apelin (0.001), PON-1 (0.002), Adiponectin (0.002), ANP (0.001), and ET-1 (0.001) with H₂O₂ in the RT group (Table 3).

Discussion

This study aimed to evaluate the effect of 12 weeks’ RT on

H₂O₂, apelin, ET-1, adiponectin, ANP, and PON-1 levels in hypertensive men. In the present study, SBP and DBP significantly decreased after 12 weeks of RT. Bhati et al also reported that resistance modulates cardiac autonomic control (16). The exact mechanism by which RT lowers BP is not fully understood yet. The current study focused on examining the effects of several important markers on SBP and DBP.

In the present study, H₂O₂ was significantly reduced at the 8 and 12 weeks of RT. There was also a significant relationship between H₂O₂ and SBP and DBP in the RT group. Similarly, Ribeiro et al (17) reported a significant reduction in oxidative stress as a result of eight weeks’ RT. oxidative stress produce ON- - by reacting with endothelial nitric oxide synthase (eNOS) (18). Therefore, interference with eNOS enzyme activity and a decrease in NO are among the reasons for high BP. The findings of another study demonstrated that ROS reduces the level of Tetrahydrobiopterin, which is one of the effective cofactors in the production of NO (19). However, evidence suggests that ROSs play a role in increasing growth factors and activating matrix Metalloproteinases, which are effective in raising BP (20). Various factors are effective in reducing OS following RT. However, as previously reported, changes in apelin, ANP, and PON-1 can have an effect on OS. Lv et al found that apelin can

Table 2. Effect of 12-week resistance training on systolic H₂O₂ and ET-1 in middle-aged hypertensive men

Markers	Group	Time				P value –Intra group		P value- between group (Ex compare with Con)
		basal	Week4	Week8	Week12	Exercise	Control	
H ₂ O ₂ (µm)	Exercise	3.32±0.19	3.29±0.14	2.99± 0.08	2.96± 0.08	P1=0.99 P2=0.032 P3=0.021	P1=0.313, P2=.0.151, P3=0.092	P&=0.86 P*=0.88 P#=0.008 P@=0.002
	Control	3.30± 0.29	3.31± 0.29	3.32±0.41	3.33±0.41			
ET-1 (pg/ml)	Exercise	2.5±0.34	2.3±0.5	2.1±0.41	1.9±0.41	P1=0.061 P2=0.001 P3=0.001	P1=0.157 P2=0.09 P3=0.071	P&=0.36 P#=0.1 P@=0.001 P@=0.001
	Control	2.37±0.4	2.38±0.3	2.42±0.33	2.47±0.41			

Data are expressed as mean ± SD. # P≤0.05, by repeated measure and Ancona. **Intra group comparison:** P1 vs basal, P2 8week vs 4-week, P3 12-week vs 4-week. **Between group comparison:** P& vs control group in basal, P* vs control group in 4-week, P# vs control group in 8-week, P@ vs control group in 12-week.

Table 3. Relationship between markers in RT and control groups

Markers (1)	Markers (2)											
	SBP				DBP				H ₂ O ₂			
	Ex		Con		Ex		Con		Ex		Con	
	P	Est*	P	Est	P	Est	P	Est	P	Est	P	Est
H ₂ O ₂	0.001	1.61	0.99	0.12	0.001	0.33	0.89	0.01	-	-	-	-
Apelin	0.001	0.82	0.8	0.00	0.001	0.18	0.7	0.04	0.001	0.15	0.99	0.02
PON-1	0.001	0.33	0.78	0.02	0.001	0.08	0.99	0.00	0.02	0.08	0.99	0.00
Adiponectin	0.001	1.02	0.99	0.08	0.001	0.22	0.99	0.00	0.002	0.18	0.99	0.02
ANP	0.001	1.82	0.99	0.11	0.001	0.42	0.99	0.01	0.001	0.39	0.99	0.01
ET-1	0.001	2.41	0.99	0.4	0.001	0.59	0.73	0.03	0.001	0.14	0.84	0.00

Note. Ex: Exercise group; Con: Control group; RT: Resistance training; PON-1: Paraoxonase-1; ANP: Atrial natriuretic peptide; ET-1: Endothelin-1; DBP: Diastolic blood pressure. Data are expressed by the linear mixed model. Est: Estimate: A change in the value of each marker causes a change in the value of the other. In other words, the increase or decrease of each marker causes the decrease or increase of another marker. P: Significance level of the relationship between markers.

reduce OS (21). Tisato et al pointed to the role of PON-1 in reducing OS (22). Choi and Fernández also concluded that ANP stimulates antioxidant defenses in vascular and cardiac cells (23). Our result confirmed a significant relationship between apelin, ANP, and PON-1 with H₂O₂.

The results of this study represented that performing 12-week RT has significantly increased plasma apelin levels. Apelin is a secretory substance from the adipocyte tissue that can play a role in the body's metabolism (24). Performing 12 weeks of RT seems to increase the contribution of adipose tissue metabolism during exercise; as a result, the call of fatty acids is increased, causing a significant increase in the levels of adipokine produced by the adipose tissue (25). According to the results of the present study, there was a significant decrease in BMI and weight after 12 weeks of RT. Our result revealed a significant relationship between apelin with SBP and DBP. It seems that apelin phosphorylates eNOS by binding to its receptor, then helps release NO through L-arginine. NO, in turn, increases the amount of cyclic guanosine monophosphate, dilating blood vessels (26).

Based on the results of the current study, plasma ANP levels significantly increased after 8 and 12 weeks of RT. Another study indicated that RT increases the myocardial diameter and cardiac tissue hypertrophy (27). Therefore, the increase in the cardiac muscle volume under the influence of RT may lead to an increase in the tension of the heart wall, increasing ANP. The end-diastolic volume

can increase after RT, increasing the volume of the stroke and the volume of blood returned to the heart, namely, the volume of the preload (28). This, in turn, increases the tension in the walls of the atria of the heart and can increase the secretion of ANP by exercise. ANP can affect BP (29). The results of the present study represented that RT led to a significant relationship between SBP, DBP, and H₂O₂ in hypertensive men. It seems that ANP reduced SBP and DBP by decreasing H₂O₂. ANP can also have an effect on ET-1 (30).

According to the findings, ET-1 was significantly reduced under the influence of RT. Tagawa et al also reported a similar result in this regard (31). ET-1, in addition to being effective in narrowing blood vessels, is responsible for the proliferation of smooth muscle cells in the vessel wall (32). Thus, reducing the level of ET-1 under the influence of exercise can have beneficial effects on the cardiovascular system. According to other studies, ANP suppresses endothelin expression and proliferation in cardiac fibroblasts through a GATA4-dependent mechanism (30). In fact, increasing ANP for a long time reduces ET-1. Considering that ANP levels increased in this study due to RT, it is expected that ET-1 levels represent a decrease. It has also been previously mentioned that OS affects ET-1 levels. Hence, the reduction of hydrogen peroxide under the influence of RT is one of the reasons for the decrease in ET-1. Moreover, our results demonstrated a significant relationship

between ET-1 and H₂O₂ in training groups. Similarly, RT led to a significant relationship between ET-1 and SBP and DBP in hypertensive men in this study. ET-1 receptors are of A and B types; exercise increases the type B receptor and, in contrast to the type A receptor, plays a role in vasodilation and produces NO. Therefore, it seems that another reason for lowering BP during RT is the increased ET-1 B receptor and increased NO production (33).

The results of this study confirmed that the plasma levels of adiponectin significantly increased at weeks 8 and 12 of RT. Adiponectin is released from the adipose tissue and plays an important role in controlling endothelium, reducing infection, and regulating energy metabolism; however, it is also affected by changes in weight and physical activity (34). In the current study, adiponectin levels increased significantly along with weight loss. The other research reported that ANP is also effective in increasing adiponectin (35). Additionally, it was found that an increase in H₂O₂, angiotensin II, and inflammatory cytokines also leads to a decrease in adiponectin (36). Thus, reducing OS following RT can be one of the reasons for increasing adiponectin. Nonetheless, another study reported that Adiponectin inhibits the production of high glucose-induced ROS and induces the formation of endothelial NO synthase in human mesenchymal cells (37). Likewise, we found a significant relationship between Adiponectin with H₂O₂ and SBP and DBP. It is believed that adiponectin is effective in increasing the activity of AMPK (AMP-activated protein kinase) in endothelial cells through Adiponectin receptors 1 and 2 (38). Accordingly, adiponectin leads to the phosphorylation and activation of eNOS via the AMPK pathway (39). There is also evidence that Heat Shock Protein 90 (Hsp90) plays a role in the regulation of eNOS, where adiponectin produces NO by activating Hsp90 (40).

However, hydrogen peroxide can be affected by PON-1 (41). In the present study, PON-1 levels were significantly increased under the influence of eight and twelve weeks of RT. PON-1 is an enzyme that is expressed in the liver and is associated with HDL and LDL lipoproteins, leading to a reduction in the oxidation of blood lipids and thus OS (41). However, this enzyme is also affected by weight gain and a sedentary lifestyle (42). However, exercise increases its level (43). Nonetheless, we could not reach any definite results about the effect of RT on it. Conversely, some studies reported that PON-1 affects adiponectin levels. PON-1 can be effective in this process by lowering blood lipids and then H₂O₂ (22). The role of PON-1 in reducing inflammatory and pro-inflammatory cytokines is also important in this process. Inflammatory cytokines can increase OS (44). PON-1 may be effective in lowering BP by lowering OS and increasing adiponectin. In addition, our result showed a significant relationship between PON-1 with SBP and DBP in the RT group. The lack of the examination of AMPK, Hsp90, and Adiponectin

receptor is the limitation of the research.

Conclusion

The results of this study revealed that 12 weeks of RT reduced SBP and DBP in men with hypertension by increasing adiponectin, PON-1, and ANP while reducing OS and ET-1. RT reduced H₂O₂ and ET-1 and ultimately SBP and DBP in hypertensive men by increasing Adiponectin, PON-1, ANP, and apelin.

Acknowledgements

We thank the people who participated in the research.

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Conflict of Interests

The authors have no conflict of interests.

Ethical Approval

This article was approved by the Ethics Committee of Islamic Azad University and registered with the code IRCT2015060521481N2 in the Iranian Registry of Clinical Trials.

Funding/Support

This project received no funding.

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