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The Effect of Endurance Training on The Serum and Cardiac Levels of Malondialdehyde in the High Fat Fed Male Rats

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ABSTRACT

Introduction: Malondialdehyde (MDA) is known as an important biomarker for assessing oxidative stress, which exert many pathological effects. The present study sought to investigate the effect of endurance training on the serum and cardiac levels of malondialdehyde (MDA) and lipid profile in the high fat fed male rats.

Materials and Methods: For the 21 male Wistar rats (weighing 200-250g) randomly assigned in three equal groups including the control (C; received normal diet), 60% high-fat diet (HF), and 60% HF + endurance training group (HFE). The HF and HFE groups received 60% calories from fat for 12 weeks. Subsequently, endurance training program performed for six weeks (5 session per week) by the HFE group. Following completing intervention, blood and heart tissue samples collected, and the MDA and lipid profile were measured. Data were analyzed by SPSS-24 software, using one-way ANOVA test.

Results: Serum MDA in the C and HFE groups was significantly lowered compared to the HF group ($P < 0.05$). Cardiac MDA also represented a significant decrease in the C and HFE groups compared to the HF group ($P < 0.05$). Moreover, endurance training result in significant improvement in the lipid profile compared to the HF group ($P < 0.05$).

Conclusion: It seems that exercise training can be considered as an effective strategy for ameliorate the pathological effect of high fat feeding, partly exerted by downregulation of serum and cardiac MDA levels and the lipid profile improvement.

Keywords: High fat diet, Endurance training, Malondialdehyde

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Introduction

Obesity is characterized by chronic low-grade inflammation with permanently increased oxidative stress, which is associated with different pathological condition including cardiovascular disease, metabolic syndrome, diabetes mellitus, fatty liver diseases, and different type of cancer, and its suggested that over-expression of oxidative stress damages cellular structures together with under-production of anti-oxidant mechanisms, leading to the development of obesity-related complications (1). It has also been demonstrated that obesity per se can induce systemic oxidative stress: indeed, fat accumulation increases Nox activity and endoplasmic reticulum (ER) stress in adipocytes that lead to increased reactive oxygen species (ROS) production (2, 3). Other factors that contribute to oxidative stress in obesity are abnormal post-prandial ROS generation, hyperleptinemia, chronic inflammation, tissue dysfunction, and low antioxidant defenses (4). In the animal studies, its suggested that consumption of high fat diet can induce and aggravates the oxidative stress in the rat heart and liver tissues (5).

Oxidative stress is the state of imbalance between the ROS and the ability of a biological system to detoxify readily the reactive intermediates (6). Many researches indicated that oxidative stress impairs glucose uptake in the different tissues of body including muscle and adipose tissue and decreases insulin secretion from pancreatic β cells. Increased oxidative stress also underlies the pathophysiology of hypertension and atherosclerosis by directly affecting vascular wall cells (2). At the cardiac level, the main sources of ROS are the mitochondrial electron transport chain, the xanthine oxidase, the NADPH oxidases (NOX), and the nitric oxide (NO) synthases (7). The measurement of malondialdehyde (MDA) levels has long been considered as a lipid peroxidation marker in studies related to oxidative stress and redox signaling (8). MDA has been used in both in-vivo and in-vitro studies as a key biomarker for various disease patterns including hypertension, diabetes, atherosclerosis, heart failure and cancer (9). Despite adverse effect of oxidative stress and its related increase in the levels MDA, Oxidative stress may be corrected by improving antioxidant defenses through reduction of adipose tissue mass via surgery, pharmacological agents, exercise and/or dietary modification (10). Supporting this statement, trained men and women was observed to has a lower oxidative stress, particularly regarding MDA levels (11). Therefore, exercise training considered as an effective antioxidant strategy which cause to upregulation of superoxide dismutase (SOD1, SOD3) and downregulation of NAD(P)H oxidase, which likely blunts the effects of oxidative stress (12). However, the exact mechanism for exerting the antioxidant effects of various type of exercise training including in obese subjects is remarkably unknown and should be determined in the future studies. Accordingly, the effect of endurance training for six weeks on the MDA levels in the serum and heart tissue of high fat fed male rats have been investigated in our study.

Materials and Methods

Animals

In this experimental study, the 21 male Wistar rats weighing 200-250 g were purchased from Kerman medical university. All animals were housed in the laboratory animal care center, including 4 rats in each separate cages at an ambient temperature of 23 °C, humidity between 45–60%, and in a 12:12 h light–dark cycle.

Grouping of Animals

The animals were familiarized with the new environmental conditions for one week, subsequently the rats assigned in the three

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equal groups including normal diet (C), high fat diet group (HF), and high fat diet group + endurance training group (HFE). Rats (14 rats) initially were feed by high fat diet (60% calories from fat) for 12 weeks and then were randomly divided into following groups consist of HF and HFE groups. However, the rats in the normal diet group (7 rats) were fed for 12 weeks by the standard food. In the next step, six weeks intervention (exercise training or sedentary lifestyle) were exerted and animals continued their previous diet (normal diet or high fat diet) during this period. All animals had free access to rat-specific water and food during intervention (high fat diet for HF and HFE groups and normal diet for C group).

Exercise Training Protocol

Present study exercise training program was endurance type, which was performed on a rodent specific treadmill with a zero-degree slope, 5 days per week for six week and each session lasted 70 minutes. The treadmill speed was 15-18 meters per minute ($m.min^{-1}$) at the first week and the training intensity progressively increase, as in the final week of training program the treadmill speed reach 26 $m.min^{-1}$. Each training session consist of 10 min warming up with 10-12 $m.min^{-1}$, 50 minutes main part of endurance training session (15-26 $m.min^{-1}$) and 10 minutes of cooling down with 10 $m.min^{-1}$ (13). Endurance training protocol properties during six weeks represented in the Table 1.

Table 1. Endurance training program for the rats in the study.

	10 minutes Warming up (Meter per minute)	50 minutes main part of training (Meter per minute)	10 minutes cooling down (Meter per minute)
Week 1	10	15-18	10
Week 2	10	18-22	10
Week 3	12	23-25	10
Week 4	12	26	10
Week 5	12	26	10
Week 6	12	26	10

Sampling (serum and heart tissue) and Measurement of Variables

The 48 hours after last training session (in order to eliminating the acute effect of last training session) and following 12 to 14 hours of fasting, all rats were sacrificed. For this purpose, firstly animals were anesthetized with sodium thiopental (50 mg/kg). Subsequently, Blood was drawn directly from the animal's heart using a 5-ml syringe. Collected serum samples were prepared using centrifugation at 3500 rpm for 15 min. After separation, the serum was poured into microtubes and then transferred to a −80 °C freezer until used for next biochemical assays. In addition, the heart tissue was homogenized immediately after isolation and washing and supernatant were collected for MDA levels measurement. Cardiac levels of MDA were measured by thiobarbituric acid reactive species (TBARS) method. In order to measurement of lipid profile we used the Pars Azmoon (Iran) kit.

High Fat Diet

The normal diet group food consisted of a pelletized diet (Laboratory rodent base food) that were purchased from the laboratory animal care. The high fat diet food used in this study consisted of animal pelletized rodent diet that are composed of 60 percent fat, which were purchased from Royan research institute. The high fat diet consumed by HF and HFE groups for 12 weeks before endurance training and continued for six weeks after starting exercise training program. All research groups under normal diet or high-fat diet ad libitum access until the end of the study to the food and water.

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Statistical Analysis

Present study data were analyzed by means of SPSS software version 24. In order to assess normality of distribution of data, Shapiro-Wilk test were used, that represented a normal data distribution. Between group analysis performed by one-way ANOVA along with Tukey post hoc test ($P < 0.05$).

Results

The 21 male Wistar rat (7 rat in each group) completed 6 weeks intervention (endurance training or control) and included in the final data analysis. One-way Anova test for serum MDA levels represented a significant between group difference ($P = 0.009$), and Tukey's post hoc test showed that serum MDA levels in the C ($P = 0.022$) and HFE ($P = 0.015$) groups were significantly lowered compared to HF group. However, there was no significant difference between C and HFE groups for serum levels of MDA ($P = 0.999$). The serum levels of MDA in the different groups have been reported in the Figure 1.

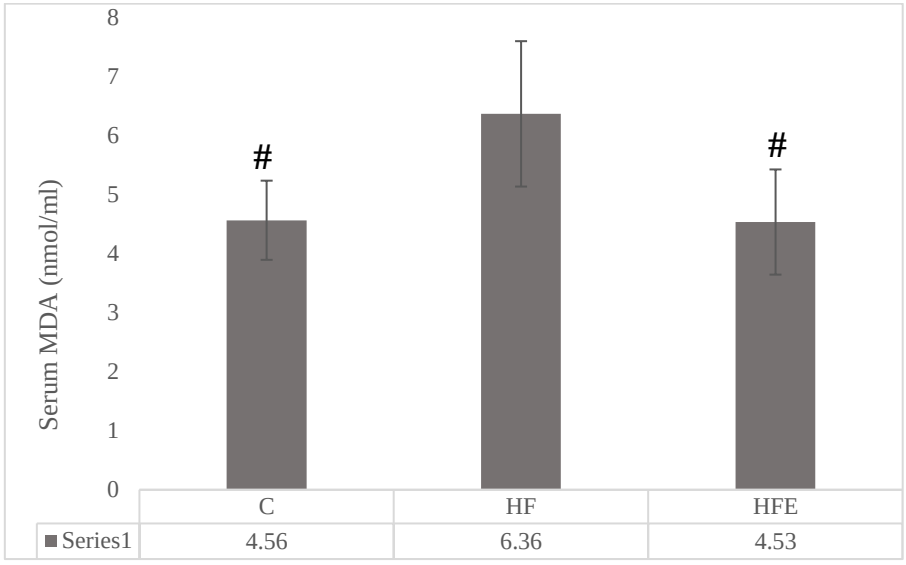


Figure 1. Serum levels of malondialdehyde (MDA) in the different treatment groups of rates. C: control, HF: high fat diet, HFE: High-fat diet + endurance training groups.
[#] Significant difference compared to the HF group.

In addition, significant between group difference were observed for cardiac MDA levels ($P = 0.005$). According to Tukey's post hoc test findings, Cardiac MDA levels significantly decreased in the C ($P = 0.013$) and HFE ($P = 0.008$) groups compared to HF group, but observed difference between C and HFE groups wasn't significant statistically ($P = 0.996$). The cardiac levels of MDA in the different groups have been reported in the Figure 2.

One-way ANOVA test indicated that observed changes between different groups for triglyceride, LDL and VLDL levels was statistically ($P < 0.001$) significant, but the HDL levels did not change significantly in the all groups ($P = 0.382$). Tukey's post hoc test indicated that triglyceride level in the HF group was significantly higher compared to C and HFE groups ($P < 0.001$). However, triglyceride level difference between the C and HFE groups was not significant ($P = 0.867$). Similarly, LDL and VLDL levels was significantly higher in the HF group compared to C and HFE groups ($P < 0.001$). However, no significant difference between C and HFE groups was observed for LDL and VLDL levels ($P = 0.896$, $P = 0.867$, respectively). The levels of triglyceride, LDL, HDL and VLDL in the different groups of the study are reported in the Table 2.

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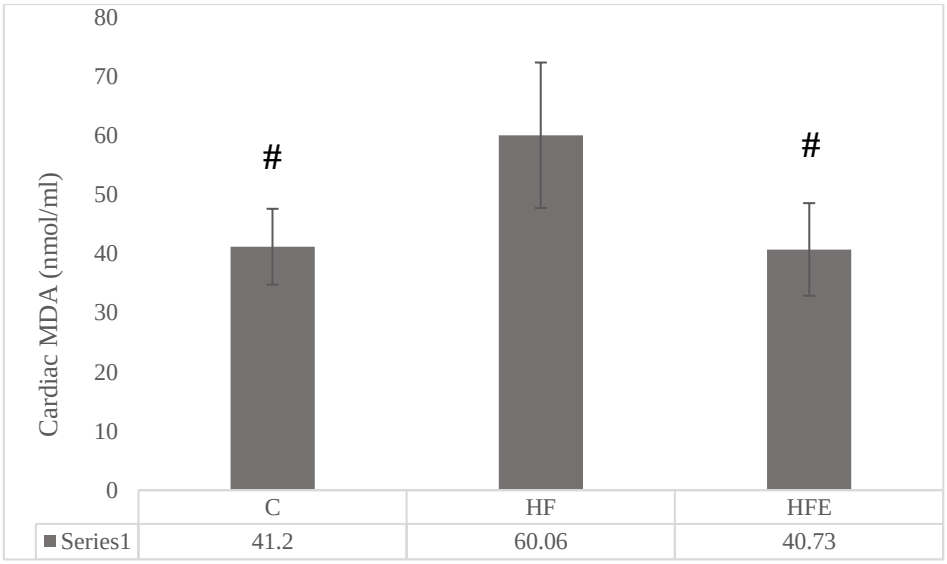


Figure 2. Cardiac tissue levels of malondialdehyde (MDA) in the different treatment groups of rates. C: control, HF: high fat diet, HFE: High-fat diet + endurance training groups.
[#] Significant difference compared to the HF group.

Table 2. The levels of triglyceride, LDL, HDL and VLDL in the different treatment groups of rates in the study.

	Variables			
Treatment group	Triglyceride (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	VLDL (mg/dl)
Control	30.16 ± 2.96	24.94 ± 3.65	42.42 ± 6.50	6.03 ± 0.59
High fat diet	69.55 ± 5.85	51.43 ± 6.05	37.78 ± 5.57	13.91 ± 1.17
High-fat diet + endurance training	28.60 ± 5.45	23.68 ± 3.60	38.70 ± 4.72	5.72 ± 1.09

Data are shown as Mean ± SD.

Discussion

Present study conducted aimed to investigate the effect of six weeks endurance training on the serum and cardiac levels of MDA in the high-fat-fed male rats. Our study main findings were that consumption of high fat diet (12 weeks) is associated with upregulation of serum and cardiac MDA levels compared to normal diet. In contrast, endurance training in the high fat fed rats for six weeks cause to significant decrease in both serum and cardiac MDA levels. In fact, the MDA levels as an important oxidative stress biomarkers following six weeks endurance training decreased to its normal values. Oxidative stress, defined as an excess production of reactive oxygen species relative to antioxidant defense, has been shown to play an important role in the pathophysiology of cardiac remodeling and heart failure (14). Some researchers approved present study findings and observed the increase (non-significantly) in circulation levels of MDA in the rat following six weeks high fat diet (15). On the other hand, its reported that obesity induced by HFD increase the MDA in myocardium (16). Consistent to above mentioned statement, its reported that high fat diet elicits oxidative stress in the blood and liver, and 9 weeks aerobic exercise training (including moderate-intensity continuous training and high-intensity interval training) can result in attenuate oxidative stress (17). Therefore, different type of exercise training acts as an antioxidant strategy and attracted a lot attention (18).

Similar to present study findings, the researchers recently reported that high-fat diet feeding for eight weeks in rats cause to significant increase in the cardiac MDA levels and significant decrease of antioxidant markers (SOD, GPx), and eight weeks aerobic training program can combat high fat diet induced cardiac oxidative

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stress and cause to significant downregulation of MDA and upregulation of SOD and GPx levels in the heart tissue (19). Exercise training (four weeks swimming training) is also effective in modulating serum levels of MDA in diabetic rats, and researchers introduce exercise training as an important intervention for reducing oxidative stress in diabetes (20). Moreover, positive effect of exercise training in decreasing insulin resistance attributed to the reduction of Nox4- induced ROS in the skeletal muscle and enhancement of AKT signal transduction. These researchers showed that swimming exercise training in eight weeks enhance the GSH-Px and SOD antioxidant enzymes and decrease MDA levels significantly (21). In another study, voluntary exercise training protection against oxidative stress in the heart tissue of high-fat diet-induced type 2 diabetic rats were observed during eight weeks, indicated by significant elevation in GPx, CAT, and SOD with reduction in the MDA levels in the heart (22). Confirming the positive effect of exercise training in attenuate oxidative stress, researchers found that exerting exercise training is an important intervention to decrease the diet-induced elevation in cardiac ROS content. (23). Zacarias et al (2017) confirmed present study findings and indicated that hepatic MDA levels in the rats submitted to high-fat diet significantly increased, but swimming exercise training for six weeks (1 h/day, 5 days per week) was associated with significant decrease in the hepatic MDA levels and improvement of glucose metabolism and insulin resistance were observed in the trained groups which these positive effects of swimming training attributed to increase in catalase activity as an antioxidant enzyme and activation of PPAR-γ2 (13). Unfortunately, the levels of antioxidant enzymes including catalase and SOD don't investigated in the present study. In contrast to the present findings, Rinaldi et al (2007) reported that six weeks endurance training on the rodent treadmill can't reverse the aging-induced increase in the cardiac MDA levels, but the antioxidant capacity improved significantly. These researchers concluded that prolonged exercise can partially counterbalance the age-related effects in the heart's antioxidant cellular system without altering peroxidation levels and attributed the beneficial effects on aged-related cardiovascular changes could be connected to the ''antioxidant'' effects of prolonged exercise training (24). This contradiction with the present findings can be attributed to the different characteristics of the examined samples. Although, acute exercise has different effects on cells, including an increase in the formation of oxidants and inflammatory mediators that ultimately leads to oxidative stress, but regular exercise training (different type) can modulate the oxidative stress and exert antioxidant effects (25). This reduction of oxidative stress by exercise training exerted by different mechanism, including weight loss and decreasing adipose tissue as major source of the elevated plasma ROS, decrease inflammation, improvement insulin resistance, upregulation of different antioxidant enzymes (SOD, catalase), and etc (26). However, these potential mechanisms don't determine in our study and should be investigate in the future studies.

Conclusion

It seems that exercise training can be considered as an effective strategy for ameliorate the pathological effect of high-fat-feeding, partly exerted by downregulation of serum and cardiac MDA levels and lipid profile improvement.

Acknowledgments

Present research was write based on PhD thesis findings of exercise physiology.

Conflict of Interest

The authors declare that no conflict of interest exists.

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