



Effect of Eight Weeks of Aerobic Exercise on the Plasma Levels of Matrix Metalloproteinase in Life Guards: A Pilot Study

ARTICLE INFO

Article Type

Original Research

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How to cite this article

Rashidlamir A, Fazolahzade-Mousavi R, Mohammad Rahimi Gh R. Effect of Eight Weeks of Aerobic Exercise on the Plasma Levels of Matrix Metalloproteinase in Life Guards: A Pilot Study. Health Education and Health Promotion. 2019;7(2):59-63.

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Article History

Received: November 06, 2017

Accepted: February 20, 2019

ePublished: April 09, 2019

ABSTRACT

Aims Matrix Metalloproteinases (MMPs) are a group of proteinases in charge of extracellular matrix decomposition. The present research aimed at investigating the effects of 8 weeks of aerobic training on MMP plasma levels in lifeguards.

Materials & Methods This study was a quasi-experimental one with 19 volunteer participants who were randomly assigned to either the control group (n=8) or the experimental group (n=11). The latter did aerobic exercises in water for 8 weeks at 65 to 75% of their reserved heart rate. Fasting blood samples (10cc) were collected from the brachial vein before and after the training protocol. MMP plasma level was determined by applying ELIZA (Enzyme-Linked Immunosorbent Assay) method and the data were analyzed using SPSS 16 software. The significance level was set at $p < 0.05$.

Findings Results showed a significant increase in MMP-2 level in the experimental group as compared to the control group.

Conclusion Increasing MMP levels due to 8 weeks of aerobic exercise in water may play an important role in physiological functions and tissue homeostasis. It may indicate remodeling of muscle fibers and connective tissue.

Keywords Exercise; Matrix Metalloproteinase; Pilot Study

CITATION LINKS

[1] Matrix metalloproteinases and skeletal muscle: A brief review [2] Matrix metalloproteinases and their function in myocardium [3] MMP-2, jumping exercise and nandrolone in skeletal muscle [4] The Matrix Metalloproteinase (MMP) and Tissue Inhibitor of Metalloproteinase (TIMP) genes [5] Kelley's textbook of rheumatology [6] Physiological hypertrophy of the FHL muscle following 8 weeks of progressive resistance exercise in the rat [7] Role of matrix metalloproteinases in skeletal muscle: Migration, differentiation, regeneration and fibrosis [8] Adipocyte produces matrix metalloproteinases 2 and 9: Involvement in adipose differentiation [9] High intensity exercise increases expression of matrix metalloproteinases in fast skeletal muscle fibres [10] Effects of age, gender, ethnicity, diurnal variation and exercise on circulating levels of Matrix Metalloproteinases (MMP)-2 and -9, and their inhibitors, Tissue Inhibitors of Matrix Metalloproteinases (TIMP)-1 and -2 [11] Effects of resistance training volume on MMPs in circulation, muscle and adipose tissue [12] Effects of resistance training on matrix metalloproteinase activity in skeletal muscles and blood circulation during aging [13] Acute exercise induced changes in rat skeletal muscle mRNAs and proteins regulating type IV collagen content [14] Expression of matrix metalloproteinases 2 and 9 in regenerating skeletal muscle: A study in experimentally injured and mdx muscles [15] The effect of L-Carnitine supplementation on IL-6 and CRP during swimming training period in male swimmers [16] The expression of MMP-2 following immobilization and high-intensity running in plantaris muscle fiber in rats [17] Changes in matrix metallo-proteinases 2, 9 and Tissue Inhibitor of matrix metalloproteinase 1 to synchronized exercise training and celery, as an herbal supplement, in overweight women [18] Endurance training reduces circulating inflammatory markers in persons at risk of coronary events: Impact on plaque stabilization? [19] Exercise training ameliorates matrix metalloproteinases 2 and 9 messenger RNA expression and mitigates adverse left ventricular remodeling in streptozotocin-induced diabetic rats [20] The influence of repeated arthrocentesis and exercise on matrix metalloproteinase and tumour necrosis factor alpha activities in normal equine joints [21] Physical exercise can influence local levels of matrix metalloproteinases and their inhibitors in tendon-related connective tissue [22] Extracellular matrix adaptation of tendon and skeletal muscle to exercise [23] Role of extracellular matrix in adaptation of tendon and skeletal muscle to mechanical loading [24] Type IV collagen and its degradation in paralyzed human muscle: Effect of functional electrical stimulation [25] Serum concentrations of collagen degrading enzymes and their inhibitors after downhill running [26] Matrix metalloproteinase and tissue inhibitor of metalloproteinase responses to muscle damage after eccentric exercise

1- Background

The extracellular matrix (ECM) surrounding skeletal muscle fibers provides structural support, protection, and maintenance of the functional integrity of skeletal muscle through several mechanisms, including the transmission of lateral strength between fibers and fascicles and the passive elastic response in the muscle contraction process [1]. Remodeling of ECM is one of the components involved in cardiac remodeling and is the result of increased synthesis and deposition of ECM components [2]. The modulation of function is controlled by matrix metalloproteinases (MMPs). MMPs are a family of zinc- and calcium-dependent enzymes that promote the degradation and synthesis of ECM components, such as collagen, proteoglycans, and glycoproteins during normal and pathological tissue remodeling [3]. In human, this family includes at least 18 members which are divided into the following 5 subgroups according to their structural similarities and substrate specifications: Collagenases, Gelatinases, membrane Metalloproteinases, and others, including Matrilysin, Metalloelastase, and Enamelysin. Among these subgroups the collagen type IV (72 and 92KD) called MMP-2 and MMP-9 respectively, are the most widespread and active of all [4, 5].

The MMP-2 and MMP-9 are crucial to the maintenance of different tissues during embryonic development, remodeling and growth. Evidence suggests that MMP-2 promotes positive effects in skeletal muscle, such as the release of local growth factors [6] and the stimulation of proliferation, differentiation, and migration of satellite cells to sites of injury, where they fuse to each other, which allows tissue regeneration [7]. Furthermore, MMP-2 plays an important role in angiogenesis and differentiation of preadipocytes into mature adipocytes that could result in adipose mass expansion [8]. Higher levels of MMP-2 and -9 in the circulation are associated with an inflammatory condition, tumor progression and apoptosis [3].

Nevertheless, MMP-2 and MMP-9 can also play an important role in adaptation to exercise [3, 9]. In a recent systematic review, it was demonstrated that concentrations of MMP-2 and -9 in the circulation provide important information on the influence of exercise and inflammatory state in humans, while the findings in the circulation may not be an accurate reflection of tissue adaptations in response to exercise [3]. Furthermore, another study has shown an increase in MMP-2 activity following an intense Bruce protocol [10]. As well as, de Sousa Neto *et al.* suggest that higher volume exercise up-regulates MMP-2 activity in skeletal muscle, while down-regulating MMP-2 in visceral adipose tissue. Moreover, it induces a decrease of MMP-2, 9 activities in circulation. Different tissue and circulatory MMP responses to exercise may result in

specific remodeling and it also may be a useful tool for the maintenance of ECM remodeling [11, 12].

Muscle damage induced by exercise increases the activity of MMPs; however, the correlation between exercise intensity and muscle MMP activity is not well understood [9]. Intense eccentric exercise induced an increase of MMP activity that is responsible for collagen IV degradation in the skeletal muscle [13]. Low-intensity running (~40% of the VO₂max) did not change the MMP-2 expression in the gastrocnemius, soleus and quadriceps muscles of rats [9]. On the other hand, in high-intensity running (70–75% of the VO₂max), MMP-2 protein expression was increased in the gastrocnemius and superficial portion of the quadriceps [14].

2- Objective

As MMPs, their types, and their roles as the front line of inflammation mediators to exercise have recently become a matter of interest to the researchers and that the limited existing research has not brought about consensus in this regards, the present research aimed at investigating the effects of 8 weeks of aerobic training on the plasma levels of MMPs.

3- Materials and Methods

The present research was a quasi-experimental one with an experimental and a control group. Nineteen females, life guards who voluntarily took part in this study were randomly assigned to either the experimental group (n=11) or the control group (n=8). None of the participants suffered from injuries or illness, smoked, drank alcohol, had been taking any kinds of medicine 6 months before the study, or took part in regular aerobic activities for at least 3 months before the study.

After signing a written consent form and getting checked up by a physician, the participants were familiarized with the training protocol. Their body fat percentage and BMI were assessed using Inbody (K720), their heights were measured with a measuring tape (With an accuracy of 1cm) installed on a wall. The duration of training was measured using a digital chronometer with an accuracy of 0.01 seconds. The participants' heart rates were determined manually from their carotid artery pulse and their aerobic power was assessed applying the Bruce test. 10cc of blood was drawn from the brachial vein of the participants in a sitting position after an overnight fast. The samples were collected in tubes containing anti-coagulant EDTA and were immediately processed for plasma preparation and were stored at -80°C for further analysis. MMPs' levels were measured using ELISA kit (R&D Systems, Minneapolis, MN, USA).

While the control group remained inactive during the study, the experimental group exercised with 65 to 75% of their reserved heart rate, two times a

week, 1.5-2.5 hours each session for 8 weeks. Training started with a general warm up of 100m, followed by 100m of specialized swimming warm up. The session then continued with a combination of 100, 200, and 400m swimming so that after the initial 100m, the participants swam 5 sets of 200m, 2 sets of 400m and a final 100m for recovery. There were 5 -7 minutes of active recovery between the sets. The participants began the training protocol with swimming 2000 meters in the initial sessions and ended up with 3000-3500 meters, as the swimming distance increased 200-400 meters every week [15].

SPSS 16 software was used for data analysis. Normality of data distribution was approved by Kolmogorov-Smirnov test. Dependent and independent t-tests were applied in order to study the intra- and inter-group changes respectively and the significance level was set at $p < 0.05$.

4- Findings

The two study groups were homogeneous regarding their age, height, weight, BMI, and body fat percentage (Table 1). Results showed that 8 weeks of aerobic training in water significantly increased the MMP level of the experimental group as compared to the control group (Table 2).

Table 1) Anthropometric characteristics of the participants before and after the training protocol

Variables	Pre-test	Post-test	P*	P**
Age (Years)				
Control	23.71±1.49	-	-	-
Experimental	25.63±3.17	-	-	-
Height (Cm)				
Control	163.57±5.27	-	-	-
Experimental	163±4.05	-	-	-
Weight (Kg)				
Control	59.88±7.99	60.61±8.56	0.106	0.079
Experimental	60.15±4.36	59.99±4	0.587	
BMI (Kg/m²)				
Control	22.37±2.71	22.84±2.91	0.061	0.813
Experimental	22.15±2.16	22.49±2.10	0.447	
Body Fat Percentage (%)				
Control	28.52±4.47	28.95±4.58	0.398	0.796
Experimental	28.58±5.23	28.32±5.16	0.675	

*Paired sample t-test; **Independent sample t-test

Table 2) Changes in the MMPs' levels of the two study groups

Group	Experimental	Control
Pre-test	62.88±3.05	60.30±2.80
Post-test	67.93±2.86	61.26±2.87
P*	0.046*	0.151
P**	0.016**	

**Independent sample t-test; *Paired sample t-test

5- Discussion

The present research aimed at investigating the effects of 8 weeks of aerobic training in water, on MMP plasma levels of life guards. The result from the present research showed that 8 weeks of aerobic

training in water could significantly increase the MMP levels in life guards.

The results of the current study are in agreement with previous investigations that evaluated the influence of exercise training on MMP activity. For instance, Carmeli and Haimovitch displayed that high-intensity running and 2 weeks of immobilization are required to promote the expression of MMP-2 in the plantaris muscle. Moreover, their results indicated that 2 weeks of high-speed running or 2 weeks of immobilization promote muscle fiber changes and that changes involve degradation and synthesis of ECM [16]. On the other hand, Seidanloo and Farzanegi showed that pilates training significantly decreased MMP-2 and MMP-9 in overweight women [17]. Niessener *et al.* demonstrated that MMP-9 activity decreased in the participants with coronary disease, following 12 months of endurance training [18]. Silva Flavio *et al.* also showed that attenuation of MMP-2 down-regulation and reduction in MMP-9 mRNA expression may constitute an underlying mechanism by which exercise training counteracts progression of adverse left ventricular remodeling in type I diabetes [19]. De Sousa Neto *et al.* demonstrated that manipulation of resistance training volume resulted in different responses of MMPs activity in skeletal muscle, visceral adipose and circulating plasma of rats. These results suggest that a higher volume resistance training upregulates MMP-2 in skeletal muscle and downregulates MMP-2 in visceral adipose tissue. Moreover, higher resistance training volume induces a decrease of activity MMP-2 and -9 in circulation. The discrepancy between these results may be due to differences in intensity, volume, type, and duration of the training protocols employed [11, 12].

It has been shown that exhaustive activity may result in inflammatory responses and significant changes in MMPs (MMP-2 and MMP-9) activity, which may continue even during the day after the inflammation. So it is important not to ignore the effects of intense training on activating MMPs, as the main index of inflammation and their role in different, long-term, joint and tissue damages and many other illnesses. In addition, it was observed that long-term adaptation to exhaustive activity and inactivity are the same regarding the acute phase reactions and the changes in the following day. It is probable that the intensity and duration of the activity and the amount of myofibril damages are the factors determining the intensity of acute phase responses. The present study showed that 8 weeks of aerobic training in water at an intensity of 65 to 75% of the reserved heart rate significantly increased MMPs levels. Therefore, it may be hypothesized that long-term adaptation in athletes does not affect acute phase inflammatory responses. As tissue MMPs are produced, their inhibitors are also activated, maintaining the required balance

between the two. Any illness or physical stress, such as exercise, stimulates immune cells, inflammation, pre-inflammation cytokines secretion and eventually activation of MMPs, to which tissue inhibitors (TIMPs) react [20, 21].

The MMPs and their inhibitors in skeletal muscle have important physiological functions in the maintenance of the integrity and homeostasis of muscle fibers and of the ECM. However, little is known regarding the role of MMPs in skeletal muscle, they have been implicated in a range of developmental, functional, and pathological processes. MMPs have regulatory roles in muscle growth and development because they release local growth factors, and are also important in repair processes after traumatic injury or disuse myopathy [1, 22]. MMP-2 activity is found in tissues under constant turnover [23], and an increase in this activity is usually indicative of matrix degradation that is needed to allow tissue growth [24, 25]. One of the most important MMP associated with skeletal muscle function is MMP-2, also known as gelatinase-A, or type IV collagenase of 72kDa, which can be transformed into an active form of 62 kDa. MMP-2 regulates ECM integrity and composition of the skeletal muscle, an essential role in myofibrillar proliferation, differentiation, recovery of fibers after damage, and surrounding connective tissue maintenance [1].

Some limitations of the present study should be highlighted, such as the inability to analyze protein expression levels of MMP and inflammatory cytokines. In addition, the tissue inhibitors of metalloproteinases (TIMPs) also modulates ECM remodeling, inhibiting the enzymatic functions of MMPs. The balance between MMPs and TIMPs must be well managed to optimize damage repair post-exercise [26]. There is little evidence to illuminate the relationship between MMPs and TIMPs in response to aerobic exercise. Most of the existing studies have analyzed TIMPs in acute models and in blood circulation. Therefore, future studies should also investigate the ability of aerobic exercise to modulate TIMPs in different skeletal muscles of female life guards with different body mass index.

6- Conclusion

In conclusion, according to the results of the present research aerobic training at 65 -75% of the reserved heart rate increased the levels of MMPs that this is important to physiological functions and tissue homeostasis. It may indicate the remodeling of muscle fibers and connective tissue.

Acknowledgements: The authors wish to thank all the women who kindly agreed to participate in this study.

Ethical permissions: Before starting the study, informed consent was gained from the participants.

All subjects were participating voluntarily, and they had the right to withdraw from the study at any time. Permission was obtained from the Ethics Committee of the Ferdowsi University of Mashhad, Iran (IR.MUMS.REC.1392.203), and was carried out according to the Helsinki Protocol.

Conflicts of interests: The authors state that there is no conflict of interest.

Authors' Contribution: Rashid-lamir A. (First author), Introduction author/ Methodologist/ Original researcher/ Statistical analyst/ Discussion author (40%); Fazolahzade-Mousavi R. (Second author), Introduction author/ Methodologist/ Original researcher (35%); Mohammad Rahimi GR. (Third author), Assistant researcher (25%)

Funding/Support: The present study was not funded by any financial support.

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