Effect of 8 weeks regular endurance training on galectin-3 changes after a strenuous aerobic exercise

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Abstract

Introduction: Galectin-3 (gal-3) is a member of the lectin family that is associate with heart failure, including myofibroblast proliferation, fibrogenesis, tissue repair, inflammation, and ventricular remodeling. Although gal-3 increases after high intensity exercise, regular training may attenuate these conditions. The aim of present study was to investigate the effect of 8 weeks regular endurance training on galectin-3 changes after a strenuous aerobic exercise.

Material and Methods: Eleven healthy young men (aged: 20.8 ± 1.8 years; ± SD) volunteered to participate in this study. All the subjects were performed Repeated High-Intensity Endurance Test (RHIET) as a strenuous aerobic exercise. Thereafter, the subjects were performed endurance training 3 days a week for 8 weeks at an intensity corresponding to 60-
75% individual heart rate reserve (HRR) for 30-45 min. After the 8 weeks intervention, the RHIET was performed a gain. Blood samples were taken at baseline (1st step), immediately after the RHIET (2nd step), 48h after 8 weeks intervention (3rd step) and immediately after the second RHIET (4th step).

**Results:** The results showed that gal-3 level was increased after the first strenuous aerobic exercise (P<0.05). After 8 weeks exercise training, gal-3 was decreased compared to 2nd step of blood sampling (P<0.05) and no significant change was observed in gal-3 in this step compare to the baseline. The results indicated that gal-3 level was lower after the second strenuous aerobic exercise than compare to the after the first strenuous aerobic exercise (P<0.05).

**Conclusions:** The results suggest regular endurance training with specific intensity and duration utilized in this study, attenuate gal-3 changes after single session of strenuous aerobic exercise.

**Key words:** Regular training, Galectin-3, Strenuous aerobic exercise, Heart failure

1. Introduction

Galectins are a family of galactoside-binding proteins that share a consensus sequence in the carbohydrate recognition domain (1). Galectin-3 (gal-3) is the most widely studied family member and can be found in the cellular cytoplasm and nucleus, as well as extracellularly in various tissues (2). Gal-3 is found in macrophages, monocytes, dendritic cells, eosinophils, mast cells, nature killer cells, and T- and B-cells. Differences in cell type, external stimuli, and environmental conditions may alter the expression level of galectin-3 (3).

The effects of gal-3 clearly depend on cellular or tissue localization. In order to identify therapeutic targets, recombinant gal-3 has been used in distinct experimental models, including heart failure and liver diseases where it can mimic the extracellular functions of this molecule (4). Functions of endogenous gal-3 have been widely studied in tumors,
where gal-3 seems to play a role in cell transformation, proliferation, metastasis and apoptosis (5).

Gal-3 is a new and promising biomarker for heart failure and myocardial fibrosis and exercise has been shown to have beneficial effects on cardiovascular disease prevention. Although the changes in gal-3 levels might be an important clue for understanding the beneficial effects of exercise, a little data on exercise-induced changes of gal-3 have been reported. Previous studies indicated that gal-3 concentration increases after a single bout of endurance exercise (6-8). For example, Salvagno et al. (2014) reported that gal-3 level increased after 60-km ultramarathon run in trained athletes (7). Although it has been reported that gal-3 concentration increases after acute and high-intensity exercise, there is a distinct lack of research examining the effect of regular exercise on blood gal-3 level. On the other hand, the effect of regular training on acute exercise-induced gal-3 level is not clear. Therefore, we evaluated the effect of 8 weeks regular endurance training on gal-3 changes after a strenuous aerobic exercise.

2. Material and Methods

Subjects
Eleven healthy young men (aged: 20.8 ± 1.8 years; ± SD) volunteered to participate in this study. All the subjects were asked to complete a personal health and medical history questionnaire, which served as a screening tool. The subjects were given both verbal and written instructions outlining the experimental procedure, and written informed consent was obtained. Our participants were not engaged in any systematic exercise programs at least 6 months before the study, none of them had any disease or had been consuming any drugs. The study was approved by the Marvdasht branch, Islamic Azad University Ethics Committee.

Strenuous aerobic exercise
All the subjects were performed Repeated High-Intensity Endurance Test (RHIET) as a strenuous aerobic exercise. Each subject was allowed 10 minutes to complete his own specific warm-up. Four beacons were
placed 5 meters apart in a straight line to cover a total distance of 15 meters. Subjects were instructed to avoid pacing and perform with a maximal effort throughout the whole test. Each subject started the test in line with the first beacon, and upon an auditory signal sprinted 5 m to a second beacon, touched the ground adjacent to the beacon with their hand and returned back to the first beacon, touching down on the ground adjacent to the beacon with the hand again. The subject then sprinted 10 m to the third beacon, and back to the first beacon etc. until an exercise period of 30 seconds had elapsed. No instruction was given as to which hand should touch during each turn. The subjects performed 43 repeat bouts of this protocol with a 30 second rest between bouts.

**Exercise Training Protocol**

The 8 weeks exercise training program included 3 training sessions per week. During the 8 weeks intervention, the subjects were trained for 30-45 min per session at a heart rate corresponding to 60-75% individual heart rate reserve (HRR). Each participant was equipped with a heart rate monitor (Polar, FS3c, Finland) to ensure accuracy of the exercise level. Each training session was followed by cool-down. At the end of study, the strenuous aerobic exercise trial was performed as same as before.

**3. Measurements**

*Anthropometric and body composition measurements*

Height and body mass were measured, and body mass index (BMI) was calculated by dividing body mass (kg) by height (m²). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm) (9). Body fat percentage was assessed by skinfold thickness protocol. Skinfold thickness was measured sequentially, in chest, abdomen, and thigh by the same investigator using a skinfold caliper (Harpenden, HSK-BI, British Indicators, West Sussex, UK) and a standard technique (9).
Biochemical analyses
Blood samples were taken at baseline (1\textsuperscript{st} step), immediately after the first strenuous aerobic exercise trial (2\textsuperscript{nd} step), 48h after 8 weeks intervention (3\textsuperscript{rd} step) and immediately after the second strenuous aerobic exercise trial (4\textsuperscript{th} step). Blood sample was obtained by venipuncture. Gal-3 levels were determined in duplicate via an enzyme-linked immunosorbent assay (ELISA) kits (Hangzhou Eastbiopharm Co., LTD, China) with a sensitivity of 2.49 pg/ml.

Statistical Analysis
Results were expressed as the mean ± SD and distributions of all variables were assessed for normality using kolmogorov-smirnov test. Paired t-test was used to compute mean (± SD) changes in the variables pre and after the 8 weeks intervention. 1 × 4 Repeated measures ANOVA was used to evaluate time-course change in variables. Post hoc analyses (Bonferroni) were then performed when warranted. Data were analyzed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL) and the significance level of this study was set at P< 0.05.

4. Results
Anthropometric parameters of the subjects before and after the 8 weeks intervention are presented in the table 1. As shown in the table 1, body fat percentage and WHR decreased after 8 weeks endurance training (P<0.05), however no significant change for body weight and body mass index were observed.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pretraining</th>
<th>Posttraining</th>
<th>t</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>69.4 ± 13.0</td>
<td>68.6 ± 12.2</td>
<td>2.04</td>
<td>0.06</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>22.2 ± 3.2</td>
<td>22.0 ± 3.0</td>
<td>2.09</td>
<td>0.06</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>8.2 ± 2.7</td>
<td>7.9 ± 2.6*</td>
<td>3.5</td>
<td>0.003</td>
</tr>
<tr>
<td>WHR</td>
<td>0.83 ± 0.1</td>
<td>0.82 ± 0.1*</td>
<td>3.8</td>
<td>0.005</td>
</tr>
</tbody>
</table>

* Significant differences (P<0.05)

Changes of gal-3 level during the study were shown in the figure 1. The results demonstrated that gal-3 level was increased after the first
strenuous aerobic exercise (P<0.05). After 8 weeks exercise training, gal-3 was decreased compared to 2nd step of blood sampling (P<0.05) and no significant change was observed in gal-3 in this step compare to the baseline. The results indicated that gal-3 level was lower after the second strenuous aerobic exercise compare to the first strenuous aerobic exercise (P<0.05) but no significant change was observed in gal-3 in this step compare to the baseline.

![Fig 1. Gal-3 changes during the study](image)

* Significant differences with step 2 (P<0.05)

5. Discussion
Gal-3 is a new and promising biomarker for heart failure and myocardial fibrosis (10). Gal-3 levels are strongly associated with changes of left ventricular structure and function, with diagnostic specificity for predicting heart failure (11). Expression of gal-3 has been detected in several tissues, albeit its synthesis is substantially amplified by a number of conditions, which also include heart failure (12). Interestingly, gal-3 is not only being used as a reliable biomarker of cardiac dysfunction and adverse outcomes, but it is also directly implicated in a kaleidoscope of biological pathways that contribute to development and worsening of heart failure, thus including myofibroblast proliferation, collagen deposition and adverse cardiac remodeling (12). In addition, the evidence that inhibition of galectin-3 activity efficiently prevents cardiac
inflammation, fibrosis, hypertrophy and dysfunction (13), has paved the way to a number of studies that have considered the hypothesis of developing specific anti-galectin treatments in the therapy of patients with heart failure and preserved ejection fraction (14).

Previous studies indicated that strenuous aerobic exercise represents a unique and ideal model for reproducing physiological myocardial stress and studying the kinetics of cardiac biomarkers, since it is associated with a transitory condition of overload and ischemia, without generating an immediate damage to the heart (7,15). Although it has been reported that gal-3 concentration increases after acute and high-intensity aerobic exercise, the effect of regular endurance exercise on gal-3 level is not still clear. Therefore, the aim of present study was to evaluate the effect of 8 weeks regular endurance training on gal-3 changes after a strenuous aerobic exercise. The results in agreement with previous studies indicated that gal-3 concentration increase after a strenuous aerobic exercise (6-8). Hättasch et al. (2014) and Salvagno et al. (2014) noted that gal-3 increases after a strenuous run of 30-km and 60-km in healthy non-elite marathon runners and trained athletes respectively (7,8). It is well-known that inflammatory markers increase after high intensity aerobic exercise (16) and strenuous aerobic exercise is associated with myocardial stress, a transitory condition of overload and ischemia. Thus increase in inflammatory markers and myocardial stress induced by strenuous aerobic exercise might be contributed to gal-3 increases. On the other hand, intensity of endurance exercise is an important factor influencing the increase in gal-3 concentrations (8). As regards the biology of galectin-3 after vigorous aerobic exercise, it is hence plausible that such a remarkable increase of expression and release into circulation may promote a deleterious mechanism of fibrosis that may involve both skeletal and cardiac muscles, i.e., the tissues that are mostly stressed during this type of demanding physical exercise (7).

By our knowledge this is the first study to evaluate gal-3 level after regular endurance training. Our results indicated that gal-3 concentration was decreased after 8 weeks regular endurance training and gal-3 level was lower after the second strenuous aerobic exercise compare to the first strenuous aerobic exercise (P<0.05) and no significant change was observed in gal-3 in this step compare to the
baseline. Gal-3 is expressed by many tissues such as myocardium and skeletal muscles. Hättasch et al. (2014) reported that gal-3 mRNA was higher in skeletal muscle than the myocardium of the left ventricle (7). These researchers noted that skeletal muscle adapts to long-term endurance exercise, with possible reduced gal-3 release (7). On the other hand, regular exercise has the anti-inflammatory effects (17), so the decrease on inflammatory markers after the 8 weeks endurance exercise might be responsible for the decrease of gal-3. We did not measure inflammatory markers in the present study, thus further studies are needed to confirm our findings.

6. Conclusion
In conclusion, the present study suggests that regular endurance training decreases gal-3 concentration induced by strenuous aerobic exercise.

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Conflict of interests: No conflict of interests amongst authors.

References


Regular exercise and galectin-3


