

## Galectin-3 concentrations in response to an exhaustive aerobic exercise

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### Abstract

*Introduction:* Elevated levels of galectin-3 have been found to be significantly associated with higher risk of death in both acute decompensate heart failure and chronic heart failure populations. Although endurance exercise is a crucial element in cardiovascular disease prevention, the relationship between exercise and plasma levels of galectin-3 is still unknown. The aim of this study was to determine the effect of an exhaustive aerobic exercise on galectin-3 levels in healthy males.

*Material & Methods:* Fifteen healthy male (aged:  $22.2 \pm 2.3$  years;  $\pm$  SD) volunteered to participate in this study. The subjects were performed Bruce protocol as the exhaustive aerobic exercise. The blood sample was taken before and immediately after the completion of the exhaustive aerobic exercise. Wilcoxon test and Spearman correlation test were used to analyze the data.

*Results:* The results demonstrated that galectin-3 had no significant changes in response to the exhaustive aerobic exercise ( $297.6 \pm 180.5$  vs.  $294.9 \pm 190.3$  pg/ml). No significant correlation was observed between the post-exercise levels of galectin-3 with body mass ( $r = 0.1$ ,  $P = 0.7$ ), BMI ( $r = -0.1$ ,  $P = 0.7$ ), body fat percentage ( $r = 0.06$ ,  $P = 0.8$ ), WHR ( $r = 0.02$ ,  $P = 0.9$ ), or  $VO_{2\max}$  ( $r = 0.2$ ,  $P = 0.4$ ).

*Conclusions:* In conclusion, the exhaustive aerobic exercise had not significant effects on galectin-3 concentrations in healthy individuals.

**Keywords:** Galectin-3, Biomarker, Exhaustive aerobic exercise, Heart failure

## 1. Introduction

Galectin-3 is a 26-kDa beta-galactoside-binding protein belonging to the galectin cluster (1). It consists of one carbohydrate recognition domain (CRD) and one regulatory domain with repeated collagen-like regions (2). Galectin-3 is produced by a variety of cell types including macrophages, mast cells, eosinophils and neutrophils (3). In murine tissues, Galectin-3 is amply expressed in, for example, lung and colon, and at lower levels in, for example, heart and liver (4). Many biological activities have been attributed to Galectin-3 depending on cell type including effects on apoptosis, cytokine production, cell migration and adhesion (5). Within recent years, Galectin-3 has been implicated in the pathophysiology of heart failure by modulating cardiac remodelling and fibrosis (6). Moreover, Galectin-3 in serum is increased in patients with heart failure (7), and elevated Galectin-3 is associated with cardiovascular and all-cause mortality in elderly people (8). Galectin-3 levels are also increased in certain malignant tumors, thyroid (9) and colonic (10) in particular, and circulating Galectin-3 holds promise as a useful seromarker of disease dissemination (11).

Endurance exercise is one of the most effective tools to prevent and to treat heart failure (12,13) However, experimental data suggest that exercise exceeding general recommendations may induce acute and

chronic effects on the heart, specifically fibrotic changes on myocardial tissues (14-16). These observations are supported by reports of cardiac fibrosis and arrhythmias after long-term strenuous endurance exercise (16-19). Although regular endurance exercise improves cardiovascular system, the effect of exhaustive aerobic exercise on cardiac muscle is not well known. Ilbeigi et al. (2017) reported that Galectin-3 increases after the exhaustive endurance exercise in male runners (20). Khajeian and Moghadasi (2017) also noted that Galectin-3 increases after a strenuous aerobic exercise (21). Thus the purpose of this study was to investigate the effect of an exhaustive aerobic exercise on galectin-3 levels in healthy males.

## 2. Material & Methods

### *Subjects*

Thirty sedentary male enrolled and volunteered to participate in this study. All the people were asked to complete a personal health and medical history questionnaire, which served as a screening tool. Fifteen healthy and sedentary male with a mean ( $\pm$ SD) age of  $22.2 \pm 2.3$  years selected as the subject after screening by inclusion criteria. All the subjects were completely inactive at least 6 months before the study and they were nonsmokers and free from unstable chronic condition including dementia, retinal hemorrhage, and detachment; and they had no history of myocardial infarction, stroke, cancer, dialysis, restraining orthopedic or neuromuscular diseases. The Islamic Azad University, Marvdasht branch Ethics Committee approved the study and written informed consent was obtained from all subjects.

### *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 ( $m^2$ ). 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 (cm) by hip circumference

(cm). Body fat percentage was assessed by skinfold thickness protocol. Skinfold thickness was measured sequentially, in chest, abdominal, and thigh by the same investigator using a skinfold caliper (Harpender, HSK-BI, British Indicators, West Sussex, UK) and a standard technique.

► *Exhaustive exercise and  $VO_{2max}$  measurement*

The Bruce test protocol was used as the exhaustive exercise. This test includes 7 phases. This test is done on the treadmill and started with low intensity; every 3 minutes. The speed and the gradient (slope) of the device increased up to the level in which the subject could not perform the test anymore and became totally exhausted. The length of time on the treadmill were scored and used to estimate the  $VO_{2max}$  value. During the test, heart rate, blood pressure and ratings of perceived exertion were also collected.

► *Biochemical measurement*

Blood samples were collected before and immediately after the exhaustive exercise. Plasma Galectin-3 levels were determined via an enzyme-linked immunosorbent assay (ELISA) kits (Hangzhou Eastbiopharm CO., LTD, China). The sensitivity of the kit was  $< 2.49\text{pg/ml}$ .

*Statistical analysis*

Data were analyzed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL). Wilcoxon test was used to evaluate the changes of Plasma Galectin-3 levels before and after the intervention. Spearman correlation test was used to evaluate the relationship between the variables. The significance level of this study was set at  $P < 0.05$ .

### **3. Results**

Personal characteristics of the subjects are presented in the Table 1. Our results indicated that the subjects had the normal body mass and aerobic capacity.

Table 1. Anthropometric, body composition and physiological characteristics of the subjects

| Variables  | Mean  | SD   |
|--|-------|------|
| Age (y)  | 22.2  | 2.3  |
| Height (cm)  | 176.4 | 7.2  |
| Body mass (Kg)   | 70.9  | 14.4 |
| BMI (Kg.m <sup>-2</sup> )                                    | 22.5  | 3.3  |
| WHR  | 0.84  | 0.05 |
| Body fat (%)   | 17.8  | 7.1  |
| VO <sub>2max</sub> (ml.kg <sup>-1</sup> .min <sup>-1</sup> ) | 38.3  | 6.04 |

Changes on Galectin-3 levels are presented in the Figure 1. The results demonstrated that galectin-3 had no significant changes in response to the exhaustive aerobic exercise ( $297.6 \pm 180.5$  vs.  $294.9 \pm 190.3$  pg/ml).

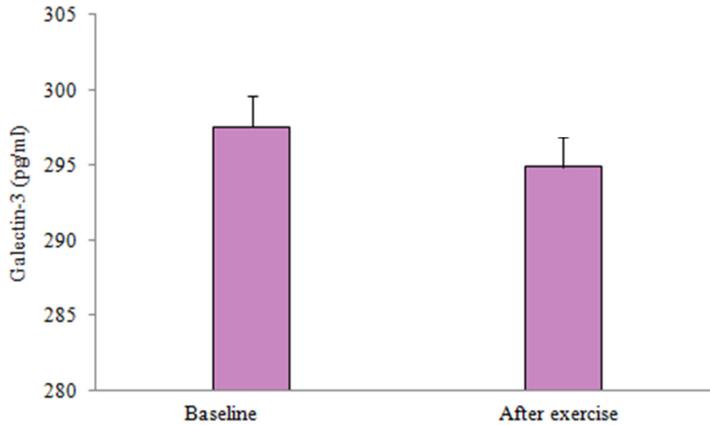


Figure 1. Change on NT-proBNP levels before and after the exhaustive exercise

There were no significant relationships between the Galectin-3 levels with body mass, BMI, body fat percentage, WHR or VO<sub>2max</sub> (Table 2).

Table 2. Relationships between Galectin-3 with body composition and physiological characteristics of the subjects

| Variables  | Galectin-3 (pmol/ml) |     |
|--|----------------------|-----|
|  | r                    | P   |
| Body mass (kg)   | 0.1                  | 0.7 |
| BMI (Kg.m <sup>-2</sup> )                                    | - 0.1                | 0.7 |
| Body fat (%)   | 0.06                 | 0.8 |
| WHR  | 0.02                 | 0.9 |
| VO <sub>2max</sub> (ml.kg <sup>-1</sup> .min <sup>-1</sup> ) | 0.2                  | 0.4 |

#### 4. Discussion

Galectin-3 is a  $\beta$ -galactoside-binding lectin that binds to glycoproteins thereby regulating their activities (22). Clinical studies have shown that high circulating Galectin-3 levels are indicative of severity of heart diseases or associated with increased risk of major adverse cardiovascular events including heart failure (7), arrhythmias (23), arterial stiffening (24), re-hospitalization post heart failure discharge (25), diastolic dysfunction (26), severity of atrial fibrosis (27) or mortality (28). However, a lack of association of Galectin-3 levels and disease severity has also been reported in some studies.

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 (29,30). The effect of strenuous and exhaustive aerobic exercise on cardiac muscle and Galectin-3 is not well known. Thus the purpose of this study was to investigate the effect of an exhaustive aerobic exercise on galectin-3 levels in healthy males. The results demonstrated that galectin-3 had no significant changes in response to the exhaustive aerobic exercise. On the other hand, there were no significant relationships between the Galectin-3 levels with body mass, BMI, body fat percentage, WHR or  $VO_{2max}$ . Previously, Ilbeigi et al. (2017) reported that Galectin-3 increases after the exhaustive endurance exercise in male runners (20). Khajeian and Moghadasi (2017) also noted that Galectin-3 increases after a strenuous aerobic exercise (21). Hättasch et al. (2013) reported that galectin-3 increases after the marathon (31). Salvagno et al. (2014) also noted that NT proBNP and galectin-3 increases after a 60-km ultramarathon (29). These discrepancy results might due to study population, exercise protocol or procedure of blood sampling and Galectin-3 analysis.

The mechanism(s) responsible for increased blood levels of Galectin-3 after strenuous exercise remains incompletely defined. Clinical studies demonstrated that while increased cardiac Galectin-3 expression was observed in human cardiac biopsies (27,32), cardiac release of Galectin-3 is not evident in patients with atrial fibrillation or severe heart failure

indicated by the absence of a trans-cardiac Galectin-3 gradient (33). A positive correlation between blood and myocardial levels of Galectin-3 was reported in one study (34), but not in another study (35). Clinical studies have consistently reported a strong and negative correlation between circulating Galectin-3 levels and estimated glomerular filtration rate, indicating that renal dysfunction is a determinant of blood Galectin-3 levels (36). Indeed, Galectin-3 levels are markedly elevated in patients with end-stage renal failure (37).

There is an increasing appreciation of the presence of inflammation contributing to heart failure (38). In patients with dilated or inflammatory cardiomyopathy, cardiac expression of Galectin-3 correlated with inflammatory cell density<sup>16</sup>. In this context, myocardial infarction is known to trigger intense regional and systemic inflammation, and in patients with acute myocardial infarction, blood levels of inflammatory biomarkers including Galectin-3 are increased (39). Another hallmark of heart disease is activation of the sympatho- $\beta$ -adrenergic system (40). Recently, Nguyen et al. (2018) indicated that activation of  $\beta$ -adrenoceptors leads to increased cardiac and circulating levels of Galectin-3 in healthy or cardiomyopathy hearts (41).

## 5. Conclusion

Our results suggested that the exhaustive aerobic exercise had not significant effects on galectin-3 concentrations in healthy individuals

**Conflict of interests:** There was no conflict of interest among authors.

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