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Effects of Ramadan fasting and Regular Physical Activity on Serum Myostatin and Follistatin Concentrations

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ABSTRACT:

Purpose: So far, about the affect of fasting and physical activities on Myostatin and follistatin levels of athletics have not do a particularly studies. The aim of this study was investigated the effects of fasting with regular physical activity training on serum Myostatin and Follistatin levels in elite wrestlers. Methods: Nine elite male wrestlers with an average age of 22.55±1.87 years which were selected by convenience sampling method to take part in this semi-experimental study. The wrestlers participated in selected training for a period of one month consisting of six days a week and include two sessions' wrestlers training, a special technical review session, a session of aerobic exercise and resistance training. Blood samples were taken once before the first day, on the second week, on the fourth week and two weeks after fasting month. For within-group mean difference repeated measures test were used. The level of significance was set at $p<0.05$. Results: the result show that weight during Ramadan reduced significantly. However, the levels of serum Myostatin and follistatin also (12 and 10.33 percent respectively) reduced but not significant. Conclusion: According to this result, the levels of serum Myostatin and follistatin also reduced but not significant. Season, intensity, duration, exercise and fitness athletes are the factors that affect on Myostatin and follistatin. Despite the differences in the results of different studies, researchers believe that resistance training lead to reduce the levels of serum Myostatin and follistatin which can reduce muscle atrophy and increase hypertrophy.

KEY WORDS: Fasting, Regular Physical Activity, Myostatin, Follistatin

INTRODUCTION

Ramadan is the most important lunar month for Muslims around the world which some limitations of eating, drinking and smoking are applied in it [1]. This month is one of lunar months and since lunar year is 11 days less than solar year, this month will circulate during solar month; therefore different hours of fasting (11 to 17 hours) are experienced in different seasons [2]. With its special features, this month creates some changes in food habits, the amount of energy intake, sleep and routine physical activity and might cause physiologic changes such as hematological, biochemical and hormonal of blood [3-5]. Doing exercises in Ramadan generally facilitate metabolism, prevent accumulation of fat in the body and on the other hand it has

been stated that athlete fasting people would less suffer from digestive problems and changes in blood sugar [6]. From hormones which are affected by fasting, Myostatin and Follistatin can be named [7-8].

Myostatin is the new member in big family of transforming growth factor of beta (TGF- β2) form that its expression negatively will set the growth of skeletal muscle [9] and increasing of this hormone has been observed in the conditions of muscular atrophy or dystrophy while it has been decreased in responding muscular overload after atrophy period [10]. According to these studies in this field, in some periods which body doesn't get food adequately, it can cause the emergence of muscular atrophy and some changes in body protein synthesis and ultimately pure mass through analyzing muscles' proteins and making available them to develop the metabolic cost that inactivity will be intensification of this process [7, 11]. In performed researches related to physical activity and Ramadan, participants' weight loss is often mentioned [12]. Although changes in active participants' bodies usually happen because of their fat mass reduction [13], but these changes in inactive participants, this weigh loss has been done because of body's fat mass as well as fast mass [14]. In investigating elite athletes in Ramadan in this field, weight loss and changes in body composition have been reported [6, 15]. Myostatin also is secreted and expressed more by muscular cells and also in lower values in different parts such as brain and fat tissue [16-17]. Due to this, Myostatin actions can be affected by other interactional factors such as Follistatin, quasi-gene of Follistatin, serum proteins associated with growth factor and differentiation and receiver of Myostatin (Activin llb) too [18].

Follistatin is a Glycoprotein that is almost expression in all mammals' tissues and its most important duty is neutralization of the actions of proteins in TGF-β family such as Myostatin. In the presence of Follistatin, Myostatin cannot connect to its receptor and created muscular analyzing by Myostatin can be prevented [18-19]. Myostatin expression during inactivity periods of skeletal muscle increases [20] or serum Myostatin restrain causes increasing the power and muscular mass [21]. Therefore it seems that resistance training causes reduction of Myostatin expression. In spite of the importance of Myostatin in setting skeletal muscular mass, the response of this limiting factor for growth to resistant training is not clear[22]. Resistant trainings because of overload and increasing power and muscle hypertrophy cause the reduction of Myostatin expression. The presence of this protein in effective factor affects tendons' resistance and their flexibility and lead to weakness and reduction of tendons' resilience. After being synthesized in skeletal muscle as precursor protein, Myostatin passes two proteolysis processes and achieve the main goal of messaging that is suppression of satellite cell proliferation and differentiation and ultimately inhibit muscle growth [23].

Wrestling is a part of active and dependent sports on athlete's weight that in terms of metabolic and physiologic, elite wrestlers achieve many features (such as increasing lactate tolerance) [24]. The athletes of this field also require high power of muscular ability that considering the limitation of weight in this field, athlete body composition is very important so in addition to quality and intensity of exercise, the kind of athlete's nutrition is totally important as well as his nutrition patterns. In this field Mirzaei et al (2012) have observed the weight loss and body's fat reduction in university wrestlers after Ramadan [24]. Considering the features of wrestling exercises and power nature of this sport field; based on performed studies that have investigated the effectiveness of strength training on serum Myostatin levels, Roth et al (2003) concluded in a research that 9 weeks resistant exercise in 8 young men and women led to 37 percent reduction of mRNA Myostatin in human participants [25]. On the contrary, Willoughby et al (2004) reported the increase of serum Myostatin levels in responding to 12 weeks of resistant exercise [26]. Raue et al (2006) reported the reduction of Myostatin levels through 12 weeks of resistant exercises on human participants [27]. Saremi et al(2010) investigated the effect of 10 weeks, each week three sessions with intensity of 60 to 70 percent of one maximum repetition on muscular strength, lean body mass, serum levels and Myostatin serum level and concluded that resistant exercise increased lean body mass and muscle strength significantly, simultaneously Serum concentration of Myostatin in response to resistance training also decreased significantly[28].

Studies that have been performed related to this issue in Muslim countries and all over the world haven't achieved united results and there are also some ambiguities in the field of sport activity's effect in Ramadan and increasing the time of fasting in hot summer [29-30],so simultaneous investigation of fasting with regular sport activity has got great value. in short considering the importance of fasting especially fasting with sport activities and also better perception of athletes' physiologic conditions during Ramadan have made researchers to accomplish a research with the goal of one month fasting's effect with wrestling exercises on serum levels of Myostatin and Follistatin in elite wrestlers.

METHODS

Subjects

The present research was semi-practical, and it was done by doing repetitive tests on professional male athletes. This research took place in Ramadan of 2014, which corresponded with the summer months of July/August (25). The sample rate for this test was 9 and these were athletes with a minimum of eight years of consistent training experience. The sample for this research was designated by the "choice sampling technique".

Study Design

During this research, the health and medical history of the sample group were established through questionnaires. After agreeing on taking part in the research, the sample group was given further information on the methods and procedure which had to be followed in the research tests. They were also given instructions on observing vital points regarding physical exercise, diet, any possible use of medication, smoking habits and any possible use of sports supplements. To

determine sample size with considering the power of 0.8 and alpha 0.05 with a mean change of 5 units, by using equation to estimate the sample size felis (1981), 8.81 samples was obtained. That more cautious among wrestler's volunteers, 9 elite healthy wrestlers. These were athletes with a minimum of eight years of consistent training experience.

Training Protocol

The exercise program used for this research was the same as the last one which was used for the professional national wrestling champions. This comprised of a one-month period; six days per week and two wrestling sessions, two sessions of review for wrestling techniques and one session of aerobic exercise and one of weightlifting. A) The Saturday to Wednesday exercises included a general rule of a 15-minute warm-up and 10-15 minutes of specialized warm-up. Three times of three minutes of real wrestling practice with a 30 second break between each session. Then two 30- second rounds at the ground mode, 4 minutes of rest before the start of the next episode, three 2-minute drill wrestling with a 30-second timeout for wrestlers to cool down. Then again, two times of 30-second rounds at the ground mode and for 5 to 10 minutes of cool-down. B) For Sunday's timetable, aerobics was practiced for 45 minutes with an intensity of 60-80% in the form of continuous or interval methods. C) On Monday and Thursday, the wrestlers spent 45 minutes reviewing techniques with medium intensity. Tuesday included weightlifting exercises; for example two-stage lifting 3×10, chest press 3×10, squat 3×10, Shoulder blade 3×10 and lifts 3×10 respectively[5].

The intensity of the exercises was decreased by 10% after the first week of Ramadan fasting compared to that of before Ramadan, while, the volume of the training was stable. In the second week of training intensity and volume of exercise was constant. In the third week the intensity of training, 5% increased and the volume of the training was stable. The intensity of the exercises in the fourth week 5% increased and the volume of the training were stable. In the fifth week of training the intensity of the training 5% more than before Ramadan[5]; the exercise intensity was controlled using the "Borg Scale".

Obtaining blood sample

All the variables associated with this research (serum Myostatin and Follistatin levels and body composition) were carried out in four stages 1) Three days before the start of Ramadan 2) After 14 days of fasting 3) After 28 days of fasting 4) Two weeks after the end of Ramadan in identical sampling conditions. Participants were asked to avoid for 24 hours before all visits intense physically activities like cycling, running and walking lasting more than 15 min. Blood samples in all related studies were collected by venepunction from forearm vein after at least 15 minutes of sitting at rest or in the supine position.

Assays

Serum levels of Myostatin and Follistatin of all subjects before and after the training period were measured using Enzyme-Linked Immunosorbent Assay methods, USA Glory Science Co.

Statistical Analysis

The SPSS software version 15 was used at the end of the experiment to analyze the given data. After ensuring that the data was not corrupt and was deemed logical (statistical Shapiro-wilk) and upon checking the variances (Leven analysis), Statistical analyses of the data were carried out using ANOVA for repeated measure to compare the various changes that occurred within each group and were specified for use with the results of levels (P<0 05).

STATISTICAL RESULTS

The mean and standard deviation of age, height, weight and BMI were 22.55±1.87 years, 1.71±5.72 m, 71.15±10.81 kg and 24.27±3.03 kg/m2, respectively. A significant reduction of body weight was observed after Ramadan fasting compared to that of before Ramadan (P<0.001). The changes in BMI and body fat percent before and after Ramadan were not significant (P >0.05) (Table 1). According to Table 2, the mean concentrations of all these parameters (Myostatin and Follistatin) showed not significant changes when compared before and after Ramadan (Figure 1 and 2).

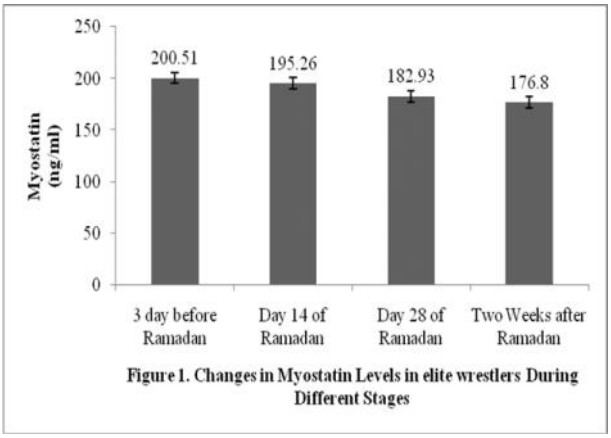

Figure 1. Changes in Myostatin Levels in elite wrestlers During Different Stages

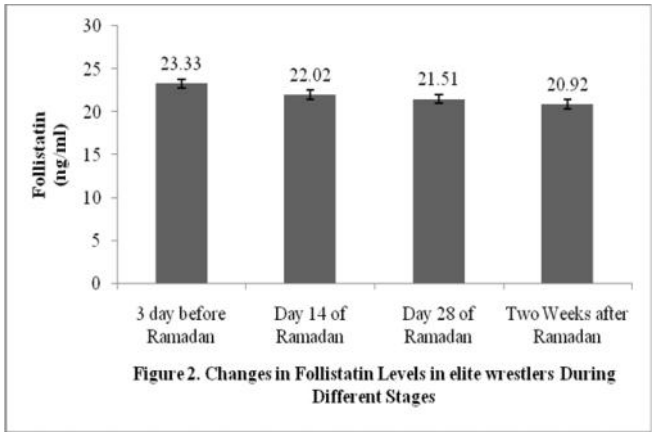

Figure 2. Changes in Follistatin Levels in elite wrestlers During Different Stages

Table 1
Changes in anthropometric parameters in elite wrestlers During Different Stages

Variables	Stages				Variations	
	3 day before Ramadan (Mean ± SD)*	Day 14 of Ramadan (Mean ± SD)*	Day 28 of Ramadan (Mean ± SD)*	Two Weeks after Ramadan, (Mean ± SD)*	F	P Value**
Weight (Kg)	71.15±10.81	70.64±10.86	71.21±10.59	70.70±10.54	0.999	0.001‡
BMI (Kg/m2)	24.27±3.03	24.11±3.12	24.40±3.82	24.24±3.84	0.009	0.999
Body fat (%)	10.63±3.86	10.12±3.51	10.30±3.78	10.05±3.43	0.043	0.988

*Data presented as mean ± standard deviation ** P Value within group
‡The mean difference is significant at the 0.05 level.

Table 2
Changes in anthropometric indicators and Myostatin and Follistatin levels in elite wrestlers During Different Stages

Variables	Stages				Variations	
	3 day before Ramadan (Mean ± SD)*	Day 14 of Ramadan (Mean ± SD)*	Day 28 of Ramadan (Mean ± SD)*	Two Weeks after Ramadan, (Mean ± SD)*	F	P Value
Myostatin (ng/ml)	200.51±45.71	195.26±42.10	182.93±40.80	176.80±51.91	0.928	0.442
Follistatin (ng/ml)	23.33±6.19	22.02±6.35	21.51±4.36	20.92±4.48	0.656	0.587
Myostatin/ Follistatin	8.66±0.81	9.09±1.79	8.48±0.51	8.34±0.72	1.42	0.261

*Data presented as mean ± standard deviation

DISCUSSION

The aim of this study was to the effect of one month fasting and regular physical activity on Myostatin and Follistatin hormones levels in elite wrestlers. In this study, one month fasting and regular physical activity had a meaningful impact on weight, hence, during the month of Ramadan wrestlers body weight was reduced by approximately 0.63 kg. The findings from the present study are consistent with those reported in the literature [24, 31-33] and this finding was not supported by different studies [34-37]. From different reasons in researches' results, metabolic changes made of differentiation in food habits, the kind of consuming nutrition, the level of activity, climate and also reduction in metabolic process of participants' resting time [38] and also on the other hand, dehydration and major changes in hormone levels can be mentioned [39].

One of the main reasons of losing weight and body's fat mass seems to be caloric restriction for wrestlers; on the other hand change in body's weight can be related to change in moods and mental pressures of wrestlers [40]. Reducing received energy of participants can lead to reduction in body's fat percentage. This is while considering the level of participants' elitism, regular routine exercises weren't eliminated. On the other side reducing body's liquids in this month can be effective on body's weight loss[24]. The mood of dehydration, catabolism and muscular damage are also factors which have been recorded in this month[24]. These factors can have unpleasant bad effects on body's composition and athletes' performance. It is worth to note that Ramadan in current study has been accomplished in summer therefore these results can be different with the results of performed researches in fall because of difference in fasting time.

The result of present study showed that one month fasting and regular exercise could decrease Myostatin levels (approximately 12 percent) in

elite wrestlers, but no significant change was seen. This finding was supported by Laurentino et al [41] and this finding was not supported by different studies[7, 42]. Myostatin has a key role in setting skeletal muscular mass and a mutation in the Myostatin gene in human causes, muscular hypertrophy [43] and its systematic increase causes muscle's atrophy [44]. Myostatin also as a catabolic factor in skeletal muscles and an anabolic factor in fat tissue can play a min role in hormone mechanism related to weight loss. There have been limited researches about Myostatin changes in the field of physical activities up to now. The existing difference among these researches may be related to differences in time of blood sampling after exercise or related effects to differences in secretion or getting Myostatin from blood flow among participants or among exercise programs.

It is also well described some mechanism which through that Myostatin can suppress muscle growth. Like most of members in TGF-β family, Myostatin (through breaking protein) in Endoplasmic reticulum is converted to one amino terminal (inactive area) and a carboxyl terminal (active one). Secreted Myostatin then will flow in a form of an inactive multi-protein complex in blood that includes non-covalent dual connection to an inactive area or other inhibitor proteins such as Follistatin. Dual active Myostatin will release through this protein inactive complex may be by analyzing enzymes which are in extracellular matrix of muscle and other tissue [45].

Then released Myostatin is connected to Activin ll or llb which utterly causes phosphorylation of a protein family Asma and mode [46], although there are some evidences that Myostatin can make muscle mass adjust without affecting SMAD. Regardless of this course, Myostatin can prevent proliferation [47] and differentiation [48] of muscle stem cells or can weaken the growth of mature muscular fibers [49] that as its result the reduction of skeletal muscular mass will appear. From the other reasons of Myostatin reduction after exercise, can be related to the muscle imbalance of growth regulators toward the positive regulators. In a normal situation in order to maintain the size of muscle fibers, there is a hemostatic balance between the positive regulators (such as IGF-1) and negative regulators (such as Myostatin) of muscle growth; but in case that muscle suffers atrophy this balance will go to negative regulators and in case that a load is applied on muscle will go to positive regulators. Although the mechanism of these regulators isn't clear enough, this relationship seems to be connected through very complex negative feedback loop [50].

Myostatin inside muscular cell has a dual performance. On one hand, the increase in FOX1 as one of the important cellular pathways, get the responsibility of increasing protein breakdown and eventually apoptosis and on the other hand it causes reducing the amount of mTOR as the most important regulator of protein synthesis intracellular. Increasing each one of these factors in negative or positive feedback loop through some factors such as PI3K, GSK3β, MuRF-1 and atropine-1 affects the value of expression and secretion of myostatin in muscle cells [51]. Therefore, one of the possible reasons of reducing the amount of Myostatin immediately after exercise can be related to the imbalance of muscular growth regulators toward positive regulators.

Also following resistant activities such as wrestling the amount of FOXO1 is reduced and the amount of mTOR increases. Therefore it seems that the other reason of reducing Myostatin after each kind of exercises is because of increasing the amount of mTOR and reducing the value of FOX1. It has been shown that changes in the value of Myostatin in responding confounders such as sport activity, with changes in number and rate of its receptor's activity in skeletal muscular. Changes in number and rate of Myostatin receptors' activity and value in skeletal muscle is because of increasing or decreasing some factors that play role in setting the number and activity of Myostatin receptors and its connection to these receptors [52]. It has been seen that after sport activity, increasing performance pioneer of increasing regulators (especially Decorin), the number of kinase receptor serine / threonine Activin IIa and IIb (especially Activin IIb receptor), Myostatin and its connection to these receptors on reduction regularities performance cause increasing more connection of Myostatin to these intramuscular receptors and finally cause reducing the value of Myostatin [52].

The results of the present study reveal that the level of Follistatin reduced, but not significantly. Several studies examined the effect of exercise on skeletal muscle follistatin expression and achieved different conclusions [53-54]. The regulation of follistatin during exercise is unclear, but it is important; Because physical activity, an important intervention for the prevention of muscle atrophy[55]. Follistatin as an important expression of Myostatin inhibitors, affect the molecular and cellular mechanism is very complex, inhibits Myostatin expression. So that Follistatin by binding to receptor binding site activin type IIb, the Myostatin binding to its receptor can prevent[56-57]. Therefore with reducing the connection of Follistatin to Myostatin receptors (Activin llb), Myostatin more than before can connect its receptors and leave its catabolic effects. These catabolic effects can lead to reducing fat-free mass in elite wrestlers and as result reducing sport performance [55].

In conclusion, based on obtained results the level of serum Myostatin and Follistatin despite having reduction but this reducing wasn't significant. Year's seasons, intensity, duration, athletes exercise and fitness scheme are the effective factors on stating Myostatin and Follistatin. Despite difference in different studies results, researchers believe that resistant exercises can reduce Myostatin and increase Follistatin that can reduce muscular atrophy process and increase hypertrophy.

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