

Original Research Article

Long term effect of different exercise intensities on serum cortisol level in

osteoarthritis patients.

Abstract

Purpose: to compare between the effect of different intensity of aerobic exercises training on serum cortisol level, knee pain, stiffness and difficulty performing ADL activities in over weight osteoarthritic patients. **Methods:** forty overweight, knee osteoarthritic patients were selected between Jan and Mar 2016 from Elmenia University Hospitals their ages ranged from 45- 50 years. Patients were assigned randomly into two equal groups. Serum Cortisol level and WOMAC questionnaire were assessed before the study and after 4 weeks of training. All groups received aerobic exercises for 30 min / 3 sessions/week for 4 weeks with different intensities. Group A received aerobic exercises intensity 45% to 60% of maximum heart rate (MHR) Group B received aerobic exercises intensity 65% to 75% of MHR **Results:** Serum Cortisol level after training in comparison to before training significantly decreased in Group A ($P=0.000$) and significantly increased in Group B ($P\text{-value} = 0.000$). Also WOMAC questionnaire about pain, stiffness and difficulty performing daily activities (ADL) sections show statistically significant decrease after 4 weeks of training in both groups ($P\text{-value} = 0.000$). There was no significant difference in post training serum cortisol level, pain, stiffness or difficulty performing ADL activities between all groups ($P>0.05$). **Conclusion:** High intensity exercise cause significant increase in Serum Cortisol level while low high intensity exercise causes significant decrease in Serum Cortisol level. Both low and high intensity aerobic exercises are effective in improving Knee OA symptoms

Key words (Serum Cortisol level, overweight, exercise intensity, knee osteoarthritis).

Introduction

Osteoarthritis is the most common condition affecting synovial joints. Osteoarthritis of the knee causes substantial pain and disability, especially in the elderly, resulting in a significant burden on health care provision. The majority of patients with osteoarthritis are managed in primary care, and the prevalence of knee osteoarthritis is such that simple interventions which are effective in a community setting are necessary. Treatment of osteoarthritis aims to reduce pain and disability [1].

Osteoarthritis (OA) is the most common cause of joint disease worldwide, with a tremendous impact both due to the number of people affected and the disabling consequences for those who develop symptomatic disease. The lifetime risk of developing knee OA is around 46 % and it is estimated that symptomatic disease occurs in 10 % of men and 13 % of women aged 60 years or over [2].

Recent guideline for the management of knee osteoarthritis emphasise the central role of exercise. Aerobic walking exercises have been shown to reduce pain and disability in subjects with knee osteoarthritis [3].

Exercise causes specific changes in the body. These changes are mainly stress adaptations of the body that usually have general common findings, although they are affected by several factors such as age, gender, genetic predisposition, nutrition and circadian pattern. The most prominent adaptations are in the neuromuscular and endocrine systems. The hormones of the endocrine system are the regulators of metabolic functional changes of the body during restructuring of tissues by exercise. The catabolic process causes tissue destruction within the body during resistance exercise, while the anabolic process predominates and leads to growth and tissue repair during the rest period [4].

Cortisol levels increase in response to psychological and physical stressors such as life changes, extreme temperatures, negative energy balance, and physical exercise. In response to the stress of exercise, cortisol has many specific functions helping the body modify and adapt to the stress, including: the mobilization of free fatty acids (FFA) from adipose tissue, protein catabolism, stimulation of gluconeogenesis at the liver, and inhibition of glucose uptake by the working skeletal muscle. These responses act to increase exercise capacity and aid in recovery and adaptation [5].

The type and intensity of exercise in relation to individual training levels provoke alterations in hormone responses, making it somewhat difficult to identify them [6].

Therefore, this study was aimed to assign the best exercise intensity to gain results with high efficacy, safety, and tolerability for knee OA patients and improve their quality of life, increase tolerance to psychological and physical stress. The study also clarified the contradiction about the exercise intensity that induce a hormonal change or in another word the physical stress that targeted the increase in serum cortisol level. The study also showed the possibility of using of cortisol as a marker of physical stress.

Subjects and Methods

Subjects

The study was conducted on in the period between Jan and Mar 2016. Forty both sexes (22 female and 18 male) patients were selected to participate in this study from Elmenia University Hospitals, their ages ranged from 45- 50 years with mean value 47.34 ± 1.51 years. Inclusion criteria were as follows: age between 45 and 50 years; OA classified as grade II and over based on the Kellgren & Lawrence radiological classification; and knee OA diagnosed according to the American College of Rheumatology criteria [7]. The exclusion criteria were as follows:

pacemaker use; unstable heart conditions; to participate in another physical activity program; inability to walk on a treadmill; previous knee or hip arthroplasty; diagnosis of fibromyalgia; epilepsy; and presence of a tumor or cutaneous lesion that could interfere with the procedure. All patients were given a full explanation of the treatment protocol and a written informed consent form giving agreement to participation and publication of results was signed by the patients.

Study Design

This was randomized, pre-test and post-test design study. Patients who met the selection criteria were divided randomly into two equal groups, Low intensity exercise group (Group A) or High intensity exercise group (Group B). Randomization was allocated using the numbered envelopes method. Subjects were blinded about which group they were allocated. Group A including 20 patients received aerobic exercises training program with intensity of maximum heart rate 45% to 60%, 3 sessions per week for 4 weeks and Group B including 20 patients received aerobic exercises training program with intensity of maximum heart rate 65% to 80% only, 3 sessions per week for 4 weeks.

Assessment

All medical and demographic data of subjects was collected and the role of physical therapy importance in improving their condition was explained.

Resting heart rate (HR_{rest}) and maximum heart rate (HR_{max}) was determined to determine the target heart rate that used in exercise for every patient.

Each subject intensity was calculated as target heart rate (THR) based on his maximum, and resting heart rate according to karvonen formula [8] as follow.

$$\text{THR} = \text{HR}_{\text{rest}} + (\text{HR}_{\text{max}} - \text{HR}_{\text{rest}}) \text{ TF}$$

Where HR_{rest} = resting heart rate in bpm

$HR_{max} = 220 - \text{age}$

TF = training fraction, it was 60% to 65% in low training intensity

The pre- and post-intervention assessments were the serum cortisol level, TUG test and the self-reported WOMAC aspects of functionality, pain, and stiffness. The assessment was carried out before start of training and after 4 weeks at the end of training program.

Blood sample and Cortisol Level evaluation method:

Blood samples were collected using a 3-cc syringe for all subjects at 8:00 am (time of measurement is affixed time). Total serum cortisol concentrations were measured with immunoassay method and using Cortisol Im 1841 RIAKIT REF made in the Czech Republic. It is important to determine reference values and be aware that they vary depending on collection time. When collected at 8:00 am, the proposed value ranges between 5.0 and 25.0 $\mu\text{g/dl}$, at 4:00 pm cortisol values should decline by more than 35% of the morning value, while at 6:00 pm the drop should be greater than 50% [9].

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

The WOMAC questionnaire contains 17 questions regarding the degree of difficulty to perform daily activities, such as stair use, to assess the physical function of patients. Patients are asked to rank the degree of difficulty in the last 72 hours in a scale from 0 (none) to 4 (severe). The individual score for the 17 questions is added up to a score that can range from 0-68. The greater the score, the worse the function. The WOMAC questionnaire also includes questions about pain, stiffness and difficulty performing daily activities (ADL). In this study, the WOMAC scores of pain, stiffness, and difficulty performing ADL activities were analyzed separately [10].

Treatment

Preparatory procedures

Each patient was informed about experimental process as well as the significance of study and write a consent. All equipments were checked up, calibrated and prepared before application

Exercise procedures

Both groups received 30 min of aerobic exercises in form of walking on a treadmill (figure 1) as following.

Using a program of exercise with intensity of maximum heart rate 45% to 60% for group A and, 65% to 80% of maximum heart rate for group B and frequency of 3 times/week for 4 weeks. The session consists of 5 minutes warm-up performed on the treadmill at low load followed by training period for 30 minutes and ended by 5 minutes cool down as following:

Warming up exercise:

The aerobic training program included a 5-min warm-up consisting of fast walking, slow running and stretching.

Exercise Phase

Group A:

After warming up, continuous running was performed started by walking ~2.0 mph increased gradually every 2 min [11] to reach intensity of 45% to 60% of the maximum heart rate of the participant . The running period was 15 min for the first session, and every two sessions 2 min was added to the running period in a stepwise manner until the running period reached 30 min. [12].

Group B:

After warming up, continuous running was performed started by walking ~2.0 mph increased gradually every 2 min [11] to reach intensity of 65% to 80% of the maximum heart rate of the participant . The running period was 15 min for the first session, and every two sessions 2 min was added to the running period in a stepwise manner until the running period reached 30 min. [12]

Cool down exercise:

At the end of each session, there was a cool-down period consisting of slow running and stretching for 5 min.



Figure (1): Exercise training on the treadmill .

Statistical Analysis

Statistical analysis was conducted using SPSS for windows, version 18 (SPSS, Inc., Chicago, IL). The current test involved two independent variables. The first one was the (tested group); between subject factor which had two levels (Low intensity group and High intensity group). The second one was the (training periods); within subject factor which had two levels (pre, post). In addition, this test involved two tested dependent variables (Serum cortisol level and WOMAC scores of pain, stiffness, and difficulty performing ADL activities. Accordingly, "paired t test" was used to compare between "pre" and "post" t-tests for all dependent variables for each group. "Unpaired t test" was conducted to compare Serum cortisol level and WOMAC scores of pain,

stiffness, and difficulty performing ADL activities between both groups in the “pre” and “post” tests with the alpha level .05.

RESULTS

Baseline and demographic data

There were no statistically significant differences ($P>0.05$) between subjects in both groups concerning age, weight, height, and BMI (Table 2). There were also no statistically significant differences between groups for any outcome variables at baseline (pre-intervention).

Table (1):General characteristics of all patient

	Age (years)		Height (c.m)		Weight (k.g)		BMI	
Group	Group (A)	Group (B)	Group (A)	Group (B)	Group (A)	Group (B)	Group (A)	Group (B)
Mean	46.97±1. 53	47.72±1. 42	172±2. 92	173.05± 5.7	83.65±7. 17	83.8±7. 25	28.28±1 .8	27.99±1. 54
t- value	-1.622		0.7332		0.06579		0.5475	
<i>P</i>	.113		.4679		.9479		.5872	

* : significant difference

Serum cortisol level:

As indicated at table (2) and illustrated at figure (2) "Paired t test" revealed that there was a significant reduction of serum cortisol level (t-value= 8.125, $P < 0.001$) at group A. In addition, "Paired t test" revealed that there was significant increase of serum cortisol level (t-value= - 8.045, $P < 0.001$) at group B. Considering the effect of the tested group (first independent

variable) on serum cortisol level, "unpaired t test" revealed that the mean values of the "pre" treatment between both groups showed there was no significant differences (t-value= 1.94, $P=0.064$). Also, the mean values of the "post" treatment between both groups showed there was no significant difference of serum cortisol level (t-value= -0.698, $P=0.494$).

Table (2): Serum cortisol level pre and post treatment comparison in both groups and between groups pre and post treatment.:

Serum Cortisol	Before treatment	After treatment	t_p value	P-value
	Mean $\pm$ SD	Mean $\pm$ SD		
Group A	13.17 $\pm$ 4.004	10.88 $\pm$ 3.88	8.125	.000*
Group B	9.91 $\pm$ 3.35	11.99 $\pm$ 3.21	-8.045	.000*
t_p value	1.976	-0.698		
P	.064	.494		

SD: Standard Deviation

t_p : paired t-test

* = Significant

N.S. = non-significant

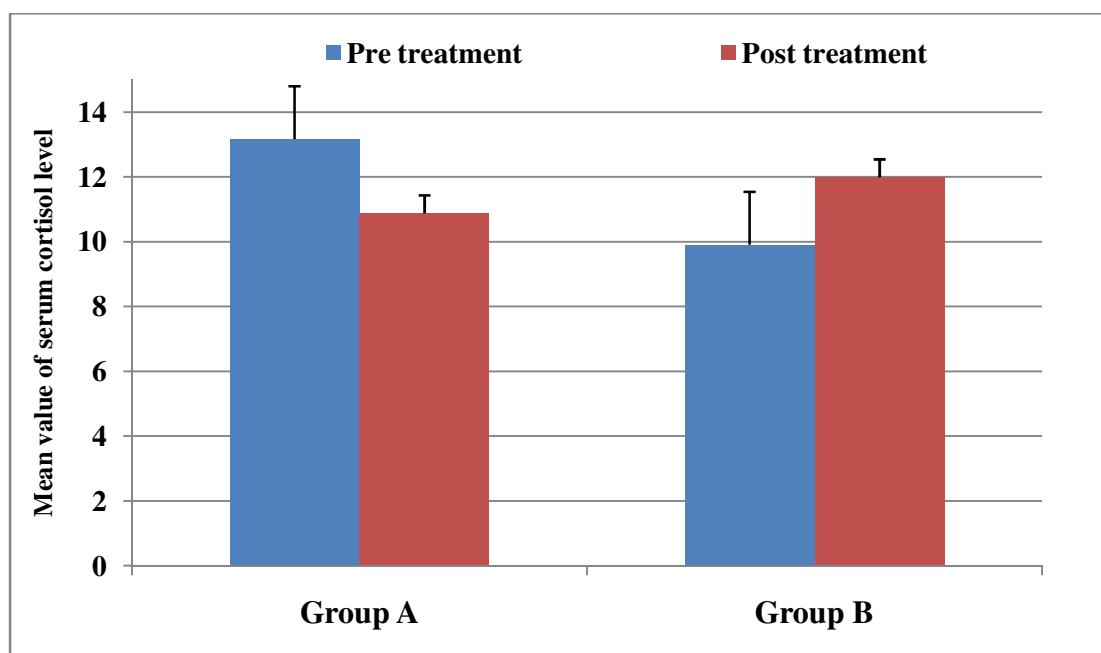


Figure. (2): Mean $\pm$ SD values of serum cortisol level of pre test and post test in both groups.

WOMAC scores of pain, stiffness, and ADL:

As indicated at table (3) and illustrated at figure (2) "Paired t test" at group A revealed that there was a significant reduction in Pain (t-value= 12.964, $P < .001$), stiffness t-value= 10.239, $P < .001$) and difficulty performing ADL activities (t-value= 13.307, $P < .001$). In addition, "Paired t test" at group B revealed that there was a significant reduction in Pain (t-value= 8.510, $P < .001$), stiffness t-value= 8.510, $P < .001$) and difficulty performing ADL activities (t-value= 13.307, $P < .001$). Comparison between both groups pre treatment and post treatment, "unpaired t test" revealed that there was no significant differences in pin pre treatment (t-value= -0.54, $P = .59$) or Pain post treatment (t-value= -1.07, $P = .29$), stiffness pre treatment (t-value= -0.47, $P = .64$) or stiffness post treatment (t-value= 0.34, $P = .73$) and Difficulty performing ADL activities pre treatment (t-value= 0.68, $P = .50$) or difficulty performing ADL activities post treatment (t-value= -1.00, $P = .32$).

Table (3): WOMAC scores of pain, stiffness, and ADL function pre and post treatment comparison in both and between groups pre and post treatment.

		Before treatment	After treatment	t _p value	P-value
		Mean± SD	Mean± SD		
Pain	Group A	12.12±0.828	8.47±0.893	12.964	.000*
	Group B	12.27±0.892	8.75±0.776	12.942	.000*
	t _p value	-0.54	-1.07		
	P-value	.59	.29		
Stiffness	Group A	4.56±0.876	2.03±0.517	10.239	.000*
	Group B	4.69±0.924	1.97±0.595	11.092	.000*
	t _p value	-0.47	0.34		
	P-value	.64	.73		
Difficulty performing ADL activities	Group A	41.47±1.404	35.50±1.250	13.307	.000*
	Group B	41.17±1.307	35.90±1.312	13.108	.000*
	t _p value	0.68	-1.00		
	P-value	.50	.32		

SD: Standard Deviation t_p: paired t-test

* = Significant

N.S. = non-significant

Discussion

This study investigated the effect of different aerobic exercise intensities on serum cortisol level and WOMAC scores of pain, stiffness, and function in overweight with knee OA adult people.

Aerobic exercise intensities include two types; low intensity 45% to 60 % of maximum heart rate and high intensity 65% to 80% of maximum heart rate.

The findings of this study indicated significant decrease in the Serum Cortisol level mean values after training in comparison to before training mean values in Group A ($P=0.000$). Serum Cortisol level mean values after training in comparison to before training mean values in Group B showed significant increase with ($P\text{-value} = 0.000$).

The findings of this study indicated no significant difference between Group A, and Group B post treatment values of Serum Cortisol level.

Therefore, the results of current study showed that there was a significant increase in Serum Cortisol level with high intensity exercise and significant decrease in the Serum Cortisol level in low intensity exercise with no significant difference Serum Cortisol level between both groups after training.

The result of the current study supported by Alghadir, Gabr [13] who evaluated the effect of 4 weeks moderate aerobic exercise on outcome measures of saliva stress hormones and lactate levels on Sixteen healthy students volunteers. The participants performed an exercise test of moderate intensity for 4 weeks, three times per week. The exercise was treadmill walking. Saliva concentrations of cortisol, testosterone and lactate dehydrogenase (LDH) were measured before and after the 4 weeks of moderate aerobic training. After 4 weeks of exercise, there were significant increases in cortisol. So the results suggest that four weeks exercise of moderate intensity significantly affects the salivary stress hormones of young healthy volunteers. The data support the importance of salivary stress hormones as potential biological markers especially for older ages.

The result of this study came in accordance with Mohebbi, Azizi [14] who investigated the effect of 8 weeks resistance training with different intensity on leukocyte count, IgG, cortisol and lactate concentration in untrained men. 24 untrained male were selected and randomly divided into three groups: high-intensity (80%1RM)(n=8), low-intensity (50%1RM)(n=8) and control (n=8) groups. Result showed that Cortisol concentration in high-intensity group increased significantly. Cortisol concentration in low-intensity group decreased significantly.

In agreement with this study Beni, Akbari [15] who investigated the effect of selected aerobic training on serum immunoglobulin levels, testosterone and cortisol hormones in young men. The experimental group underwent aerobic training consisting of three sessions per week for 8 weeks (3 sessions per week with intensity between 65 and 75% of the maximum heart rate), while the control group did not participation in the training program during the study period. The findings showed that aerobic training led to significant decrease of cortisol ($p= 0.007$) in the experimental group compared with the control group.

On the other hand, the results of this study contradict the study of Bijeh, Moazami [16] who investigated the effect of six months aerobic exercise on serum leptin, cortisol, insulin and glucose levels on 19 healthy middle-aged women. The Exercise protocol included aerobic exercise for 6 months and 3 sessions per week and every session lasted 60 minutes with intensity of 60-70% of heart rate reserve. Results shows that six months of aerobic exercise does not induce significant change in serum levels of leptin, cortisol, insulin and glucose in thin middle-aged women.

In disagreement with this study Khorshidi, Assarzadeh [17] who examined the effect of 12-week aerobic exercising on the serum levels of leptin, testosterone, insulin, glucose, cortisol and growth hormone in thirty obese men. The experimental group performed an aerobic training

for 3 days per week which lasted for 12 weeks. Cortisol were measured before and 48 h after the training program. Results shows no significant differences in the serum levels of cortisol after the training.

This study also, came in contradiction with Yazdanparast, Azarbayjani [18] who examined the effect of different exercise intensity (low, medium and high) on the salivary concentration of Cortisol in elite 10 young female swimmers. The subjects participated in a 6-week exercise program. The exercise program was divided into three time segments: the basic endurance session during the first two weeks, special endurance session during the second two weeks and hard exercise session during the last two weeks. Saliva samples were collected at the end of each two weeks before and immediately after exercise from the study group. The findings of the research show that: exercise with low, medium and high intensity does not have a significant effect on the concentration of cortisol level of elite girl swimmers.

The result of this study came in contradiction with the three previously mentioned studies may be due to differences in subject characteristics (younger age or normal or elite subjects) and longer training period (more than 4 weeks)

Also the results for WOMAC scores of pain, stiffness and Difficulty performing ADL activities showed significant improvement in both groups in comparison to pre treatment values with no significant difference between both groups pre or post treatment

So the results of our study also came in accordance with Kovar, Allegrante [19] compared the effects of 8 weeks of fitness walking with a usual-care intervention in a sample of 102 older adults. The exercise intervention involved 90-min sessions of supervised walking and psychoeducational training performed three times per week. Participants walked for up to 30 min during each of the three weekly exercise sessions. Pain was assessed using the arthritis-pain

subscale of the Arthritis Impact Measurement Scale. Results revealed that the fitness-walking intervention resulted in a greater reduction in pain than did the usual-care treatment. In addition, participants assigned to the walking intervention experienced greater improvement in pain when compared with baseline than did those undergoing usual care.

Mangione, McCully [20] examined the effect of 10 weeks of high- and low intensity aerobic training in a sample of 54 older knee-OA patients. Participants completed 25 min of stationary cycling at either 70% or 40% of heart-rate reserve three times per week. A total of 39 participants (72%) completed the study. Pain symptoms were assessed using the pain subscale of the AIMS-2. Analysis revealed no significant post treatment differences in pain between the high- and low-intensity exercise groups. Nonetheless, pain symptoms improved significantly when compared with baseline values with both high-intensity and low intensity exercise.

Conclusion

The results of current study showed that both low and high intensity aerobic exercises are effective in improving Knee OA symptoms weight patients but low intensity exercises had a reducing effect on serum cortisol level while high intensity exercises had an increasing effect on serum cortisol level after 4 weeks of training.

References

1. Roddy, E., W. Zhang, and M. Doherty, *Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review*. Annals of the rheumatic diseases, 2005. **64**(4): p. 544-548.
2. Zhang, Y. and J.M. Jordan, *Epidemiology of osteoarthritis*. Clinics in geriatric medicine, 2010. **26**(3): p. 355-369.
3. Deveza, L.A. and D.J. Hunter, *Pain Relief for an Osteoarthritic Knee in the Elderly: A Practical Guide*. Drugs & aging, 2016. **33**(1): p. 11-20.
4. Kraemer, W.J. and N.A. Ratamess, *Hormonal responses and adaptations to resistance exercise and training*. Sports Medicine, 2005. **35**(4): p. 339-361.
5. Viru, A. and M. Viru, *Cortisol-essential adaptation hormone in exercise*. International journal of sports medicine, 2004. **25**(06): p. 461-464.
6. Hansen, D., et al., *Effect of acute endurance and resistance exercise on endocrine hormones directly related to lipolysis and skeletal muscle protein synthesis in adult individuals with obesity*. Sports Medicine, 2012. **42**(5): p. 415-431.
7. Kellgren, J. and J. Lawrence, *Radiological assessment of osteo-arthritis*. Annals of the rheumatic diseases, 1957. **16**(4): p. 494.
8. Goldberg, L., D. Elliot, and K. Kuehl, *Assessment of exercise intensity formulas by use of ventilatory threshold*. CHEST Journal, 1988. **94**(1): p. 95-98.
9. Fischbach, F.T. and M.B. Dunning, *A Manual of Laboratory and Diagnostic Tests*. 2009: Wolters Kluwer Health/Lippincott Williams & Wilkins.

10. Bellamy, N., *Validation study of WOMAC: a health status instrument for measuring clinically-important patient-relevant outcomes following total hip or knee arthroplasty in osteoarthritis*. J Orthop Rheumatol, 1988. **1**: p. 95-108.
11. Keteyian, S.J., *Graded exercise testing and exercise prescription*, in *Clinical Exercise Physiology*, J.K. Ehrman, et al., Editors. 2013, Human Kinetics. p. 61-88.
12. Hill, E., et al., *Exercise and circulating cortisol levels: the intensity threshold effect*. Journal of endocrinological investigation, 2008. **31**(7): p. 587-591.
13. Alghadir, A.H., S.A. Gabr, and F.A. Aly, *The effects of four weeks aerobic training on saliva cortisol and testosterone in young healthy persons*. Journal of physical therapy science, 2015. **27**(7): p. 2029.
14. Mohebbi, H., M. Azizi, and H. Moradiani, *Effect of 8 weeks low and high intensity resistance training on leukocyte count, IgG, cortisol and lactate concentration in untrained men*. Appl Sci, 2012. **16**(7): p. 949-54.
15. Beni, M.A., et al., *The Effect of Selected Aerobic Training on Serum Immunoglobulin Levels and Testosterone and Cortisol Hormones in Young Men*. International Journal of Sport Studies, 2013. **3** (9): p. 956-962.
16. Bijeh, N., et al., *Effect of 6 months of aerobic exercise training on serum leptin, cortisol, insulin and glucose levels in thin middle-aged women*. Trauma Monthly, 2011. **2011**(1, Spring): p. 53-59.
17. Khorshidi, D., et al., *The effect of a period of selective aerobic exercise on serum level of leptin and some hormones in obese men*. Annals of Biological Research, 2012. **3**(3): p. 1415-1423.

18. Yazdanparast, B., et al., *The effect of different intensity of exercise on salivary steroids concentration in elite girl swimmers*. Facta universitatis-series: Physical Education and Sport, 2009. **7**(1): p. 69-77.
19. Kovar, P.A., et al., *Supervised fitness walking in patients with osteoarthritis of the knee: a randomized, controlled trial*. Annals of internal medicine, 1992. **116**(7): p. 529-534.
20. Mangione, K.K., et al., *The effects of high-intensity and low-intensity cycle ergometry in older adults with knee osteoarthritis*. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 1999. **54**(4): p. M184-M190.