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Long Term Effect of Different Exercise Intensities on Serum Cortisol Level in Osteoarthritis Patients

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Original Research Article

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ABSTRACT

Background: Exercise intensity has a significant impact on the levels of several hormones such as cortisol, adrenalin and testeseron.
Purpose: To compare between the effect of low intensity (40-60%) and high intensity (65-80%) 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. Group A received aerobic exercises intensity 45% to 60% of maximum heart rate (MHR) and Group B received aerobic exercises intensity 65% to 75% of MHR. Both groups received aerobic exercises for 30 min / 3 sessions/week for 4 weeks. Serum Cortisol level and WOMAC questionnaire were assessed before the study and after 4 weeks of training.
Results: Serum Cortisol level after training in comparison to before training significantly decreased in Group A (P-value < 0.001) and significantly increased in Group B (P-value < 0.001). Also WOMAC questionnaire pain section, stiffness section and difficulty performing daily activities (ADL) section show statistically significant decrease after 4 weeks of training in both groups (P-value < 0.001). There was no significant difference in post training serum cortisol level, pain, stiffness or

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difficulty performing ADL activities between all groups (P-value > 0.05).
Conclusion: High intensity exercise (65-75%) significantly increased Serum Cortisol level while low intensity exercise (45-60%) significantly decreased Serum Cortisol level. Both high and low intensity aerobic exercises are effective in improving Knee OA symptoms

Keywords: Serum cortisol level; overweight; exercise intensity; knee osteoarthritis.

1. INTRODUCTION

Osteoarthritis (OA) 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. Treatment of osteoarthritis aims to reduce pain and disability [1]. Overweight and Obesity is a modifiable risk factor for the development and progression of knee OA. Epidemiologic evidence suggests that weight loss may prevent the incidence of knee OA and alleviate adverse symptoms accompanying the onset of the disease [2]. 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 [3]. Recent guideline for the management of knee osteoarthritis emphasized on the central role of exercise. Aerobic walking exercises have been shown to reduce pain and disability in subjects with knee osteoarthritis [4].

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 [5].

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 [6].

As regarding the Threshold intensity that results in significant elevations in circulating cortisol, Exercise intensity of 50-60% of VO_{2max} must be reached for cortisol to be increased and the absolute levels attained during exercise are dependent on the total duration of the exercise bout. Salivary cortisol levels have been shown to increase following acute exercise with the response dependent on the intensity and duration of activity [7,8].

Moderate to high intensity (60% and 80% of maximal oxygen consumption [VO_2 max]) exercise augmented circulating cortisol levels in moderately trained men. These increases were resulted from acombination of hemoconcentration and HPA axis stimulus ACTH. Conversely, low intensity exercise (40% of VO_2 max) did not result in significant increases in cortisol levels, actually reducing cortisol concentrations when accounting for plasma volume changes. So Moderate to high intensity exercise provokes increases in circulating cortisol levels. These increases seem due to a combination of hemoconcentration and HPA axis stimulus (ACTH). In contrast, low intensity exercise (40%) does not result in significant increases in cortisol levels, but, once corrections for plasma volume reduction occurred and circadian factors were examined, low intensity exercise actually resulted in a reduction in circulating cortisol levels [9].

Another study concluded that there was a significant difference between the salivary cortisol responses immediately following the high and low intensity exercise protocols. This study has demonstrated that salivary measures of cortisol can be used to delineate between high and low intensity workouts. The results of this study have also shown that rating of perceived exertion RPE is a reliable and useful tool of estimating the intensity of a resistance training during session. This scale would be a beneficial tool for researchers, strength coaches, recreational weightlifters, and athletes as they strive to rate the work intensity of a resistance training session [10].

Cortisol levels increase in response to psychological and physical stressors such as life changes, extreme temperatures, negative energy balance, and physical exercise. Most previous exercise studies investigating cortisol responses are in agreement that there is a "threshold intensity" of one's maximal oxygen uptake (VO2max) that results in significant elevations in circulating cortisol [11]. Type and intensity of exercise in relation to individual training levels provoke alterations in hormone responses, making it somewhat difficult to identify them [12].

Therefore, this study was aimed to compare between the long term effect of high intensity (65-80%) and low intensity (40-60%) aerobic exercise on serum cortisol level, knee pain, stiffness and difficulty performing ADL activities in over weight osteoarthritic patients after 4 weeks of tanning with frequency of 3 sessions per week.

2. SUBJECTS AND METHODS

2.1 Subjects

The study was conducted between Jan and Mar 2016. A sample size of 40 patients was determined for this study by a preliminary power analysis [power (1–α error P) = 0.85, α = 0.01, effect size = 0.5]. This effect size was chosen because it yielded a realistic sample size. The forty (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 [13]. The exclusion criteria were as follows: pacemaker use; unstable heart conditions; participating 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.

2.2 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 envelops 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%, 3 sessions per week for 4 weeks.

2.3 Assessment

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

Resting heart rate (HRrest) and maximum heart rate (HRmax) was determined to calculate the target heart rate that was used in exercise for every patient.

Each subject intensity was calculated as training heart rate (THR) based on his maximum, and resting heart rate according to karvonen formula [14] as following.

$$THR = HRrest + (HR\ max - HR\ rest)\ TF$$

Where

HRrest = resting heart rate in bpm
HRmax = 220 - age
TF = training fraction, (was 45-60% in low training intensity and 65-80% low training intensity)

The pre- and post-intervention assessments were the serum cortisol level 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.

2.3.1 Blood sample and cortisol level evaluation method

Blood samples was collected using a 3-cc syringe for all subjects at 8:00 am (time of measurement is affixed time) pre and post exercise training program. 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 µg/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% [15].

2.3.2 Western Ontario and Mcmaster Universities Osteoarthritis Index (WOMAC)

The WOMAC questionnaire was used 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 WOMAC comprises 3 subscales: pain (2 items), stiffness (2 items) and function (17 items). Raw scores for each subscale were analyzed without transfor-mation.. Each subscale is summed, 0-20 for pain, 0-8 for stiffness, and 0-68 for function (numerical data). The greater the score, the worse the function [16].

2.4 Treatment

2.4.1 Preparatory procedures

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

2.4.2 Exercise procedures

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

Using a program of exercise with 45% to 60% of maximal heart rate reserve for group A and, 65% to 80% of maximal heart rate reserve 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:

2.4.2.1 Warming up exercise

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

2.4.2.2 Exercise phase

After warming up, both groups performed continuous running started by walking ~2.0 mph increased gradually every 2 min [17] to reach intensity of 45% to 60% of maximal heart rate reserve for group A patients and to reach intensity of 65% to 80% of maximal heart rate reserve for group B patients. 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 [9].

2.4.2.3 Cool down exercise

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

Fig. 1. Exercise training on the treadmill

2.5 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 subjects factor which had two levels (group A and group B). The second one was the (training periods); within subjects 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. The distributions variables were assessed for normality by Kolmogorov-Smirnov test. WOMAC scores of pain, stiffness, and difficulty performing ADL activities data were not normally distributed. "paired t-test" was used to compare between “pre” and “post” tests for Serum cortisol level variable while Wilcoxon test was used to compare between “pre” and “post” tests for WOMAC subscales scores in each group. "Unpaired t-test" was conducted to compare Serum cortisol level while Mann-Whitney U was conducted to compare WOMAC subscales scores between both groups in the “pre” and “post” tests with the alpha level 0.05.

3. RESULTS

3.1 Baseline and Demographic Data

There were no significant differences (P>0.05) between subjects in both groups concerning age, weight, height, and BMI (Table 1). There were also no significant differences between groups for any outcome variables at baseline (pre-intervention).

3.2 Serum Cortisol Level

As indicated in Table 2 "Paired t-test" revealed that there was a significant reduction of serum cortisol level (t-value = 8.125, P <0.001) in group A. In addition, "Paired t-test" revealed that there was significant increase of serum cortisol level (t-value = -8.045, P <0.001) in group B. Comparison of serum cortisol level between groups "pre" treatment using "unpaired t-test" showed no statistically significant differences (t-value= 1.94, P=0.064). Also, "post" treatment values of serum cortisol level between both groups showed no significant difference (t-value= -0.698, P=0.494).

3.3 WOMAC Scores of Pain, Stiffness and ADL

As indicated in Table 3 "Wilcoxon test" in group A and group B revealed that there was a significant reduction in Pain, stiffness and difficulty performing ADL activities (P < 0.001). Comparison between both groups pre treatment and post treatment, " Mann-Whitney U" revealed that there were no significant differences between both groups in pain pre treatment (P= 0.565) or Pain post treatment (P= 0.242), stiffness pre treatment (P = 0.565) or stiffness post treatment (P = 0.820) and Difficulty performing ADL activities pre treatment (P = 0.547) or difficulty performing ADL activities post treatment (P = 0.277).

4. 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 adult patients with knee OA. Aerobic exercise intensities in this study include two types; low intensity 45% to 60% of maximal heart rate reserve and high intensity 65% to 80% of maximal heart rate reserve.

Table 1. General characteristics of all patient

Group	Age (years)		Height (c.m)		Weight (k.g)		BMI	
	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	
P	0.113		0.4679		0.9479		0.5872	

Table 2. Comparison of serum cortisol level within and between groups

Serum cortisol	Before treatment	After treatment	t_p value	P-value
	Mean± SD	Mean± SD		
Group A	13.17±4.004	10.88±3.88	8.125	0.000*
Group B	9.91±3.35	11.99±3.21	-8.045	0.000*
t_p value	1.976	-0.698		
P	0.064	0.494		

*SD: Standard Deviation, tp: paired t-test, * = Significant*

Table 3. Comparison of WOMAC scores within and between groups

		Before treatment	After treatment	P-value
		Mean± SD	Mean± SD	
Pain	Group A	12.12±0.828	8.47±0.893	0.000*
	Group B	12.27±0.892	8.75±0.776	0.000*
	P-value	0.565	0.242	
Stiffness	Group A	4.56±0.876	2.03±0.517	0.000*
	Group B	4.69±0.924	1.97±0.595	0.000*
	P-value	0.565	0.820	
Difficulty performing ADL activities	Group A	41.47±1.404	35.50±1.250	0.000*
	Group B	41.17±1.307	35.90±1.312	0.000*
	P-value	0.547	0.277	

*SD: Standard Deviation, tp: paired t-test, * = Significant*

The findings of this study indicated significant decrease and increase in the Serum Cortisol level mean values after training in comparison to before training mean values in Group A and B respectively (P< 0.0001). The findings of this study indicated no significant difference between Group A, and Group B post treatment values of Serum Cortisol level.

The result of the current study supported previous study that reported that aerobic training with intensity of 65 to 75% of heart rate reserve on sixteen healthy volunteer students for 4 weeks showed significant increases in saliva concentrations of cortisol [18].

Physical exercise is considered as a physiologically stressful situation to the body, so that post-exercise cortisol concentration changes seem to be due to activation of the hypothalamic-pituitary-adrenal axis. physical exercise stress stimulate the sympathetic nervous system, cause stimulation of hypothalamic-pituitary-adrenal (HPA) secretion, elevated secretion rates of corticotropin-releasing hormone which activates the anterior pituitary and stimulates the release of adrenocorticotropin hormone (ACTH). The presence of ACTH stimulates the adrenal cortex to release Cortisol [19,20]. Also this physical stress associated with hypothalamic-pituitary-adrenal (HPA) secretion which increases body temperature, changes in blood pH, hypoxia, lactate accumulation and mental stress [21]. Cortisol release seems to be affected by the type of resistance training (hypertrophic vs maximal strength), previous long- term sports participation and neuromuscular performance. The immune and endocrinological responses to exercise are dependent on its intensity and duration [21,22].

On the other hand, the results of this study came in contradiction with the previous study that mentioned 3 sessions per week for 8 weeks with intensity between 65 and 75% showed that aerobic training led to significant decrease of cortisol [23]. Also, in disagreement with this study there were previous studies that showed no significant change in cortisol level after aerobic exercise training for six months with intensity of 60-70% of heart rate reserve in thin healthy middle-aged women [24], after aerobic exercise training for 12-weeks in thirty obese men [25] and after aerobic exercise training with low, medium and high intensity in elite 10 young female swimmers [26].

The contradiction with the previously mentioned studies may be due to differences in subject characteristics as younger age subjects [25] or thin healthy subjects [24] or elite trained subjects [26] and longer training period more than 4 weeks. The difference in the results may be due to that, the biosynthesis and metabolism of cortisol are altered by the high levels of adipose tissue and the constant state of low-grade inflammation of overweight subjects [27]. Also physiological stress reaction during acute exercise in individuals who are obese is greater than the response in healthy individuals and elite trained persons, leading to a greater stimulation of skeletal muscle protein catabolism but, also, to a greater lipolytic response [12].

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.

The results of our study also came in accordance with previous study examined the effect of 10 weeks aerobic training with high 70% or and low intensity 40% of heart-rate reserve in a sample of 54 older knee-OA patients. Analysis revealed significant improvement of OA pain with no significant post treatment differences in pain between the high- and low-intensity exercise groups [28]. Many other studies showed reduction in pain intensity [29-35] reduce morning stiffness [36] and improve functional activities [37,30,38-41] with aerobic exercise and aerobic walking.

Knee osteoarthritis patient's weakness of the quadriceps muscles is caused by disuse and capsular swelling which inhibition muscle contraction. Severity of pain is directly correlated with the degree of muscle weakness. Although strong muscles may promote structural deterioration in misaligned knees. Aerobic exercise, improves muscle strength, flexibility, and balance [42]. Cartilage oligomeric matrix protein (COMP) is a matrix protein, which is currently studied as a potential serum marker for cartilage processes in osteoarthritis. Serum COMP levels increased during exercise in individuals with knee OA, whereas the levels decreased during rest [43].

5. CONCLUSION

The results of current study showed that both low and high intensity aerobic exercises are effective in improving Knee OA symptoms among overweight 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.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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