EFFECT OF AEROBIC EXERCISE ON INFLAMMATORYCYTOKINE LEVELS INPOST-MENOPAUSAL WOMEN

Reham S. Ebrahim*, Soheir M. Elkosiery**, Engy M. El Nahas***, Gihan F. Abdel Aziz****

*' **' ***Department of Physical Therapy for Woman's Health, Faculty of Physical Therapy, Cairo University, Cairo, Egypt.

**** Department of Obstetrics and Gynecology, El Sheikh Zayed General Hospital, Cairo, Egypt.

Corresponding author: Reham S. Ebrahim– Master Degree – Department of Physical Therapy for Woman's Health

ABSTRACT

Objective: To evaluate the effect of aerobic exercise on inflammatory cytokine levels in post- menopausal women. **Methods:** Thirty post-menopausal women were selected from Ain shams University. Their ages ranged from 44 to55 years, they were divided randomly according to closed envelop into two groups equal in number, study group (group A) who performed aerobic exercises in form of walking on treadmill for 30 min/day, 3 times per week for 12 weeks, at 55% of maximum HR. And control group (group B) who didn't perform any kind of aerobic exercise and instructed to maintain their current physical activity levels during the study. Before starting and at the end of study, all participants were assessed by measuring the level of pro-inflammatory IL6 and FSH levels. **Results:** Pretreatment, there was a non statistical significant difference in the IL6 and FSH levels between both groups (A&B). While, post treatment there was a highly statistical significant difference in IL-6 and FSH between both groups (A&B), where the p value was 0.001, in favor of group (A). **Conclusion:** Aerobic exercise is effective in decreasing pro-inflammatory cytokine levels in postmenopausal women.

Keywords: postmenopausal, inflammatory cytokine levels, aerobic exercise.

Introduction

Menopause is a defining moment in each woman's life, the final episode of menstrual bleeding related with suspension of the of ovarian follicle. action the resulting in permanent cessation of menstruation. The onset of menopause is connected with a hormone lack, which is a contributory element for the increased incidence of cardiovascular osteoporosis, diseases, vasomotor disturbances and cognitive deterioration[1].

Postmenopausal women show an inflammatory immune response which reduces ability to respond to pathogens or stimuli and decreased cytotoxic activity of natural killer (NK) cells. Higher chronic pro-inflammatory cytokines productionand the infections are more common as a result of attenuated immune response and higher susceptibility to pathogenic invasion[2].

Cytokines can be divided into pro- and anti-inflammatory in which the harmony between these decides result of the an inflammatory response. <u>IL-1β</u>, <u>IL-</u> 8, and IFN- γ for instance are proinflammatory cytokines required early reactions and the in intensification of inflammatory reactions. while, antiinflammatory cytokines like ILand IL-13 restrict 4, IL-10, inflammatory responses[3].

Anti-inflammatory IL-6 appear in muscle tissue in and the circulation during exercise at levels up to one hundred times basal rates, as noted, and is viewed as a beneficially affecting on health and bodily functioning when raised in response to physical exercise[4].

In a randomized control trail studying the impact of exercise on inflammatory cytokine level, in postmenopausal women. the exercise group demonstrated a huge decline in pro-inflammatory cytokines interleukin -1B (IL-1B), IL-6 and tumour necrosis factor - α (TNF – α) and thus diminish in inflammation [5].

Subjects, Instrumentations and Methods Subjects:

Recruitment

A sample of thirty post-menopausal women was enrolled into this study. They were selected from Ain shams Universityduring the period between February, 2017, and July, 2017. They were divided randomly into two groups equal in numbers, study group (group A) who asked to perform aerobic exercises in form of walking on treadmill for 30 min/day, 3 times per week for 12 weeks, at 55% of maximum HR and control group (group B)who did not perform any kind of aerobic exercise and be instructed to maintain their

current physical activity levels during the study.

All participants were be given a full explanation of the assessment procedures and informed consent form was be signed from each subject before participating in this study. This study was approved by the Research Ethical Committee of the Faculty of Physical Therapy, Cairo University

(P.T.REC/012/001498).

The inclusion and Exclusion criteria:

To be included in the study, all females were post-menopausal women. Their ages ranged from 44 to55 years. Their BMI were less than or equal to 28 kg/m². The participants were excluded if they weresmokers, hypertensive, obese and havingosteoarthritisorco-morbid conditions that would impact inflammatory markers and any known cardiovascular, respiratory, endocrine, metabolic disorders or conditions that might alter reproductive hormones.Also, who took any medications known to influence the immune system (for at least 12 months). The postmenopausal women should not start the practice of the sports at least one year before the onset of menopause.

Anthropometric measures:

Weight-Height scale was used to measure the weight and height of each female in the two groups. Then, the body mass index (BMI) was calculated by dividing weight by height squared (Kg/m²).

Sphygmomanometers:

It was used for measuring blood pressure for each subject before starting the study (to exclude data).

Laboratory investigation

Before starting and at the end of study, the subject was asked to lie in half lying position, with well supported back and arm. The anticubital area had been cleaned with alcohol. Blood sample of about 20 ml was drawn from the anticubital vein from all subjects by disposable sterile syringe by vein puncuture, the sample was collected between 7 and 8 hours o'clock. Participants were fasting (except for water) for 12 hours and free of vigorous exercise for a minimum of 24 hours prior to sampling. Samples to measure IL-6 and FSH were collected in serum tubes.

Statistical analysis:

Results are expressed as mean ± standard deviation. Test of normality, Kolmogorov-Smirnov test, was used to measure the distribution of data measured pretreatment. Accordingly, comparison between variables in the two groups was performed using unpaired t test. Comparison between variables measured preand post-treatment in the same group was performed using paired t test.Difference was calculated as follows: - pre-treatment – posttreatment.Percent change was calculated as follows: - [(pretreatment – post-treatment)/pretreatment] x 100.Statistical Package for Social Sciences (SPSS) computer program (version 19 windows) was used for data analysis. P value ≤ 0.05 was considered significant.

RESULTS

Baseline characteristics

The participants' anthropometric data are summarized in (**Table 1**), There was a non-statistically differences between both groups (A and B) in their ages, weight, height and body mass index, where their t and P values were (1.613, 0.118), (0.734, 0.469), (0.657, 0.517) and (0.539, 0.594), respectively.

Items	Group (A) Study	Group (B) Control	t value	P value
	(n =15)	(n = 15)		
Age (yrs.)	48.53 ± 2.26	49.87 ± 2.26	1.613	0.118 (NS)
Weight (Kg.)	71.87 ± 5.01	73.20 ± 4.93	0.734	0.469 (NS)
Height (cm.)	163.40 ± 5.14	164.60 ± 4.87	0.657	0.517 (NS)
BMI (kg/m ²)	26.91 ± 0.71	27.08 ± 0.97	0.539	0.594 (NS)

Table 1.Baseline characteristics of study and control groups.

Pro-inflammatory interleukin 6 (IL-6) level

Pre-treatment, there was anon statistical significant difference between mean value of IL-6 of study group (2.53 ± 0.31) and its corresponding value in control group (2.39 ± 0.29) with t value = -1.287 and p value = 0.209.

While post-treatment, there was a highly statistical significant decrease in mean value of IL-6 of study group (1.97 ± 0.27) when compared with its corresponding value in control group (2.49 ± 0.48) with t-value=3.705 and p-value = 0.001,(**Table 2**).

Table (2): Comparison between pro-inflammatory interleukin 6 in bothgroups (A&B) measured pre- and post-treatment.

Pro- inflammatory interleukin 6 (pg/ml)	Group (A) Study group)((n= 15)	Group(B) (Control group) (n=15)	t value	P value
Pre-treatment	2.53 ± 0.31	2.39 ± 0.29	-1.287	0.209 (NS)
Post-treatment	1.97 ± 0.27	2.49 ± 0.48	3.705	0.001 (HS)

Follicle-Stimulating Hormone level

Pre-treatment there was anon statistical significant difference between mean value of FSH of study group (2.62 ± 0.34) and its corresponding value in control group (2.43 ± 0.45) with t value = -1.278 and p value = 0.212.

While post-treatment, there was a highly statistical significant decrease in mean value of FSH of study group (1.75 ± 0.26) when compared with its

corresponding value in control group (2.73 ± 0.32) with t-value=9.209 and p-value = 0.001, (**Table 3**).

 Table (3): Comparison between mean values of FSH in both groups

 (A & D) measured are and post treatment

FSH level (mlU/mL)	Group (A) Study group)((n= 15)	Group(B) Control group)((n=15)	t value	P value
Pre-treatment	2.62 ± 0.34	2.43 ± 0.45	-1.278	0.212 (NS)
Post-treatment	1.75 ± 0.26	2.73 ± 0.32	9.209	0.001 (HS)

(A&B) measured pre- and post-treatment

DISCUSION

The onset of menopause is associates with hormone deficiency which is related to the onset of a low systemic inflammatory status, inflammation manifested by increased serum levels of the key pro-inflammatory cytokines IL-1, IL-6 or tumor necrosis factor (TNF) α [6].

Change in serum antiinflammatory cytokine values after menopause, could be related to the of function monocytes and macrophages, a function that is impaired due to estrogen deficiency, the implications of these cytokines in the development and progression after menopause of important diseases such osteoporosis, cardiovascular as

diseases, hot flashes or depressive syndrome [6].

Physical activity involves the contraction of skeletal muscles which promote the synthesis may and of anti-inflammatory secretion cytokines and peptides from myotubes termed as 'myokines'. commonly Research indicates that a single bout of moderate to vigorous intensity aerobic exercise lasting 30-60 min in duration stimulates muscle-derived IL-6[7].

Elevated plasma concentrations of muscle-derived IL-6 subsequently initiate the secretion of IL-1 receptor agonist and IL-10 from monocytes and lymphocytes. An increase in the appearance of such anti-inflammatory cytokines promotes a range of benefits in vascular reactivity, lipid and glucose metabolism and the suppression of proinflammatory cytokines which may

incidence reduce the of disease. Exercise-induced changes in IL-6 may also promote an increase in CRP within 24 h of exercise cessation. Although CRP is largely pro-inflammatory, the immediate post-exercise antiinflammatory actions may also promote endothelial homeostasis by inhibiting cytokines involved leukocyte in activation, proliferation and endothelial dysfunction[7].

The results of our study showed that pretreatment, there was a non statistical significant difference between both groups (A&B) in proinflammatory interleukin 6 (IL-6) and FSH levels, as the P value was (>0.05). While, there was a highly significant difference statistically between both groups (A&B) post treatment, as the P value was (<0.001), in favor of group (A).

This result was in agreement with Abdollahpour et al.,[8] who randomly assigned 41 postmenopausal, sedentary women aged 50 to 74 to either an exercise or a non exercise group, the intervention involved facility-based aerobic exercise (three days/week, at 70 - 80% of the maximum heart rate, for six months),the results showed that the plasma IL-6 level decreased by 21.3% in the exercisers and by 6.9% in the non exercise, and the intervention effect was significant (P = 0.001), although the effect of exercise was not statistically significant (P = 0.28), overall, longterm aerobic exercise may result in a decreased IL-6 concentration.

These results agreed with Wang et al., [9]who conducted a study on 23 women at which (exercise group) who participated in a treadmill-exercise program for 12 weeks, whereas 23 women in a control group maintained their customary lifestyle. The result revealed that endurance exercise exerted significant beneficial effects on waist circumference, serum highdensity lipoprotein cholesterol and IL-6 levels and exercise capacity (all P < 0.05), the beneficial effects on IL-6 and exercise capacity were correlated with improvements in serum high-density lipoprotein cholesterol levels (r = -0.33, P = 0.03)and r = 0.31, P = 0.04, respectively), there results suggest that health-care providers can incorporate an exercise program in treatments to improve the health of postmenopausal women.

These results agreed with Tartibian et al., [5] in which twenty-eight healthy, sedentary post-menopausal women were randomly assigned to study (n =14) and control (Con, n = 14) groups, the study group completed lowmoderate intensity treadmill training 25-30 min/day, up to 55% of HRmax, 3–4 days/week, for 16-weeks.the control group maintained current physical activity level, baseline and week-16 serum samples evaluated interleukin-1 beta, interleukin-6, tumor factor-alpha, C-reactive necrosis protein, estradiol, luteinizing hormone and follicular stimulating hormone, the results show that Post-intervention, the study group showed a significant decrease in interleukin-1 beta, proinflammatory interleukin-6. tumor estradiol, necrosis factor-alpha, follicular stimulating hormone and luteinizing hormone levels compared to baseline values, no significant changes were observed in control ,significant correlations were observed between IL-1b, IL-6, TNF-a, and reproductive hormones, both before and after the exercise intervention.

These results agreed with<u>Shin</u> et al.,[10]which consisted of 20 postmenopausal women, who had not menstruated for at least 1 year and had follicle-stimulating hormone levels >35 mIU/L, estradiol levels<40 pg/mL, the subjects were randomly divided into two groups: control group (n=10), new sports tennis type exercise group (n=10), the exercise done in form of new sports tennis type exercise was consisted of warm up (10 min), main exercise (40 min), cool down (10 min) 3 days a per weeks for 12 weeks, new sports tennis type exercise program comprises circuit exercise including side step, cross over step, sprint & back step, running, forehand stroke drill, back-hand stroke drill, forehand and back hand running stroke drill, and approach drill, training intensity was consisted of 50 to 60% HR-max at 1-6 weeks and 61-70% HRmax at 7-12 weeks using Karvonen's equation, blood sampling was performed before the exercise, after 6 weeks and after 12 weeks, the result show FSH was significantly decreased after 12 weeks (P=0.04), FSH was lower in the exercise group than those in the control group after 12 weeks, however. interaction between group and time showed no significant difference. NTx was lower in the exercise group than those in the control group (P=0.009), however, interaction between group and time showed no significant difference.

Conclusion

Our findings demonstrate that aerobic exercise intervention decreased the level of IL-6 and FSHin postmenopausal women.

Acknowledgement

The authors are grateful to the subjects who participated in the study for without their dedication the study could not have been done.

Financial support and sponsorship Nil.

Conflict of interest

There are no conflicts of interest.

REFERENCES

1.Su H and Freeman E: Hormone changes associated with the menopausal transition. Minerva Ginecol; 2009, 61: 483-489.

2. Ghosh M, Rodriguez-Garcia M and Wira C: The immune system in menopause: Pros and cons of hormone therapy. J. Steroid Biochem. Mol. Biol. ;2014, 142: 171–175.

3. Neurath Cytokines M: in inflammatory bowel disease. Nat. Rev. Immunol. ; 2014, 14: 329–342. 4. Muñoz-Cánoves P, Scheele C, Pedersen B and Serrano A: "Interleukin-6 myokine signaling in skeletal muscle: a double-edged sword?". The FEBS Journal; 2013, 280 (17): 4131-4148.

5. <u>Tartibian</u> B, <u>FitzGerald</u> L, <u>Azadpour</u> N and <u>Maleki</u> B: A randomized controlled study examining the effect of exercise on inflammatory cytokine levels in post-menopausal women. Saga journals; 2015, 21(1): 9–15.

6.Malutan A, Costin N, Ciortea R and Mihu D: Variation of Antiinflammatory Cytokines in Relationship with Menopause. Applied Medical Informatics;2013, 32(2): 30-38. 7. Brown W, Davison G, McClean C and Murphy M: A Systematic Review of the Acute Effects of Exercise on Immune and Inflammatory Indices in Untrained Adults.Sports Medicine – Open; **2015,1(1):1**-35.

8.Abdollahpour A<u>,Khosravi</u> N, Eskandari Zand Haghighat S:

Effect of Six Months of Aerobic Exercise on Plasma Interleukin-6 and Tumor Necrosis Factor-Alpha as Breast Cancer Risk Factors in Postmenopausal Women: A Randomized Controlled Trial: Iran Red Crescent Med J; 2017,19(1):1-10.

<u>9. Wang C, Chung M, Chan P, Tsai J</u> and <u>Chen</u> F: Effects of endurance exercise training on risk components for metabolic syndrome, interleukin-6, and the exercise capacity of postmenopausal women. Geriatric nursing; 2014, 35(3): 212–218.

10.<u>ShinH</u>, <u>LeeH</u>, <u>ChoH</u>, <u>Park</u> Y, <u>Moon H</u>, <u>Lee S</u>, <u>Lee S and Kim M</u>: Effects of new sports tennis type exercise on aerobic capacity, follicle stimulating hormone and N-terminal telopeptide in the postmenopausal women. Journal of Exercise Rehabilitation; 2014, 10(2): 89-91.