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# Effect of 6 months moderate aerobic training on CD25, IL-2 and salivary IgA concentration in elderly men

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## ABSTRACT

*This study examined the effect of 6 months moderate aerobic training on $VO_{2max}$, Interlukin2 receptor (CD25 cells), Interlukin-2 and salivary secretary IgA concentration in elderly men. 40 sedentary and healthy aged males (mean ± SD age 65 ± 2 years and weight 74±12 kg) were randomized to experimental (N=20) and control (N=20) groups. Experimental group performed moderate aerobic training (three times per week) for 6 months, while the control group did not perform any regular training exercise. The variables analyzed and statistical analyses carried out on data by repeated measures ANOVA and T student tests ($p \leq 0.05$). The result showed amount of $VO_{2max}$, CD25 and IL-2 and sIgA concentration in experimental group increased significantly ($p<0.05$). The results confirmed that regular moderate exercise increases $vo2_{max}$, number of CD25 cells, IL-2 and sIgA concentration in elderly subjects. Moderate aerobic exercises increase $vo_{2max}$ and the number of CD25 cells and IL-2 and SIgA concentration in healthy elders if persists at least for 6 months; improving immune system function to protect them against immune-system dependent aged men.*

**Key words**: aerobic training, $VO_{2max}$, Interlukin-2 receptor, Interlukin-2, Immunogolobin A.

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## INTRODUCTION

A lot of variables associated with aging will drop in people and symptoms appear with aging which include nutritional deficiencies, lock of physical mobility, weight gaining and increased fat amount and prevalence of specific diseases that each of those factors might indirectly affect immune system function(1, 2). It's generally believed that immune system function will drop in elderly people compared with youths and these people show loss resistance against pathogenic microorganisms(3). So aging is associated with decreased immune system function and as a result, increased incidence of cancer, infectious diseases and self immune diseases (4). Aging

affects on immune system function which include fall of proliferate response of T-cells to mutagen stimulation, decreased interleukin 2 production (IL-2) by T-cells, decreased number of T-cells producing.

Interleukin 2 (IL-2), decreased affinity of Interleukin 2 receptor ($CD_{25}$), a drop in the B cells performance due to change in T-cells stimulation, decreased sIgA and finally increased risk of infection. And $CD_4$ lymphocytes which produce Interleukin 2 and express Interleukin 2 receptor (IL-2R) will be decreased with aging that leads to the decreased T-cells proliferation activity(5, 6).

In most countries, the proportion of aged population is growing and due to aged population (and relative drop in younger population) healthcare and treatment costs will be raised. Therefore, finding inexpensive non-medical approaches to increase lifelong healthcare in aged people and preventing many aged-old diseases have been considered (7). So, a survey on the effect of long – term regular training exercise on immune system performance has a wide application to develop public health and prevention (1). Some researches have shown that regular moderate training exercises play an important role in disease prevention and treatment such as hypertension, osteoporosis, cardiovascular diseases and non-insulin dependent diabetes (1, 6, 8). At present researches have and those related to the life style. In addition, there are evidences that show physical activities help to reduce the risky diseases such as cancer and those related to the life style. In addition, there are evidences that show physical activities help to reduce the risk of special cancers (6). Recent researches show that reduced sIgA in the elderly can increase upper respiratory tract infection while taking some moderate aerobic exercises can improve individual immunity responses through increased IgA concentration and increased $CD_4$ proliferation(4, 5). There is a hypothesis that moderate exercise compared to high-intensity exercise and inactivity can reduce infection rates in all aged groups (9), and the relationship between infection and activity intensity shown in J curve indicates that upper respiratory intensity and volume (9)and some evidences are emerging that regular aerobic exercise may improve immune function and thus will reduce the increased incidence of chronic diseases. One of the intracellular mechanisms that can improve people's ability to proliferate lymphocytes (6, 10) is expression of Interleukin 2 receptor (the number of $CD_{25}$ cells) and Interleukin 2 production. These 2 factors are crucial parts of the chain of $CD4^+$ cell proliferation, so through measuring the amount of Interleukin 2 production and expression of Interleukin 2 receptor, we can introduce a good index to study the ability of $CD4^+$ cells reproduction stimulated by mutagen and by measuring the saliva IgA concentration, as well, which reduces upper respiratory tract infection, we can assess mucosal immune function. Susan Louis Shor (1998) and Broadbent and et, al respectively studied the effects of 12 weeks and 12 months moderate aerobic training on the expression of Interleukin 2 in the elderly and found that the expression of Interleukin 2 receptor has been increased (2, 11, 12). While Bream et al (1996) and Kimora et al (2005) respectively studied 12 week aerobic training with low intensity on the elderly immune system and found no change in $CD_{25}$ expression percent and the number of CD4 and CD8 in trained aged men compared to untrained ones and only in kimora's research and his colleagues increased salivary IgA concentration was found(13, 14). There are some evidences that show in aged people with exercise training, higher levels of simple CD4+ cells and increased Interleukin 2 production can be seen and lymphocyte response to proliferation is stronger than those of the same age who were sedentary (4, 6, 15). Shinkai and et al (1995), Drela and et al (2004) and Arai and et al (2006) have done some researches on the elderly and have seen increase Interleukin 2 production in active aged people compared with inactive ones (16-18). however, due to conflicting results about the effects of aerobic activity on the elderly's immune system and the differences in fitness level, the gender and the age of the subjects and their exercise plan in performed research and few researches that

have studied the effect of long-term aerobic exercises on the number of CD-25 cells and Interleukin 2 concentration and salivary IgA in the elderly as well and the absence of convincing evidences regarding the effect, of long-term exercise training on immune system performance and intracellular reactions in aged people and try to answer to this question that how long aerobic plan can be effective in inactive aged people with no regular exercise training. This research is trying to study the effect of 6-month selected aerobic exercises on Interleukin 2 concentration and the number of CD 25 cells and mucosal immune system (salivary IgA) in aged males because Interleukin 2 concentration and CD 25 cells number play an important role in expressing the rate of lymphocyte T-cells proliferation and performance of other immune cells and variety of immune responses.

## MATERIALS AND METHODS

### Subjects

The call for volunteers was sent out by First Call Research at the University of Qom for elderly men aged 60 to 70 who were willing to take part in the research. A total of 109 elderly men volunteered. After the volunteers were informed of the objectives of the study, they underwent medical examination. A medical history questionnaire and a physical activity readiness questionnaire were accomplished for 83 people comprising healthy elderly and non-athletes.

40 subjects were randomly selected with replacement. Subjects were randomly assigned in to two control and training groups of 20 people. They completed the forms of consent which indicated their readiness to participate in this study for 6 months. The experimental group was trained during the study duration, while the control groups were not given any exercise routine and were allowed to resume their daily routine. The profiles of both groups are presented in Table 1.

**Table 1.Subject characteristics**

| | **Aerobic** | **Control** |
|---|---|---|
| **Age(year)** | 62±2 | 66±3 |
| **Weight (kg)** | 86±12 | 84±12 |
| **Fat (%)** | 25.23±2.2 | 25.82±2.38 |
| **Lean body mass** | 64.33±2.29 | 62.3±1.72 |
| **$Vo_{2max}$(ml.kg.min)** | 31.9±3.1 | 61.7±3.5 |

### Calculated Maximum oxygen consumption

To estimate aerobic power of subjects, we conducted a Walking 1 mile Rockport test (10). Aerobic power of subjects was calculated using the following equation:

VO2max (mL•kg-1•min-1) = 132.853 (0.0769 x *155.5*) (0.3877 x *30.0*) + (6.315 x *0*) (3.2649 x*13.56*) (0.1565 x *145*)

### Training program

The aerobic exercise group followed a training protocol, three sessions a week for 6 months. Each session includes 8-minute warm-up exercise and cool down in the first three months, 20 to 30 minutes jogging with 35-45 percent of maximum heart rate reserve intensity (MHRR). Second in 3-6 months training period from 30 to 40 minutes of running with 45 to 60 percent increased maximum heart rate reserve. To suit each stage of the work for subjects exercise intensity was controlled using a watch heart rate monitor Polar.

The subjects in the control group did not do any training program and proceeded with their normal daily routine. All protocols were approved by the Graduate Council of faculty of Physical Education and Sports Science, Islamic Azad University Central Tehran branch.

**Blood sampling**

To measure the number of cd4 and cd8 cells, blood samples were taken before the training, 3 months after the training and 6 months after the training. Before blood extraction, all subjects undertook 12 hours of fasting (from 7 pm to 9 am), ten (10 ml) venous blood was extracted from a vein of the anticubital in the spine and collected in a sterile tube containing a blood anticoagulant (EDTA) before laboratory transfer.

**Assessment of CD25 and IL-2**

The number of CD25 cells were evaluated using device flow cytometric analysis, made in Becton, Dickinson company, USA,(model FACS CLAIBAR) and monoclonal Antibody Phycoergthrin (mAB PE) to assess IL-2 concentrating, the lab method of ELISA Immonometric kit (ELISA) manufactured in English company Rend ox and Hitachi 902 automatic processor (manufactured by Roach in Germany).

**Assessment of salivary IgA concentration**

To measure the salivary IgA concentration, in the 1st stage in fasting, after rinsing the mouth with distilled water 3 times, the subjects took a five- minute rest in the same position and then saliva sample was gathered by a cotton wool and was placed inside a test tube. Then the sample was centrifuged in 3000 RPM centrifuge speed for 10 minutes and was kept at -40^ centigrade, finally its concentration was identified using ELISA Method.

**Statistical analysis**

Statistical analysis of data was calculated for each group using means and standard deviation. Then Kolmogorov-Smirnov test was used to ensure normal distribution of data. The student's **t**-test was used to evaluate between-group analysis of variance with repeated measure. ANOVA[3] for within-group evaluation according to the corrective procedure Green house-Giser (GG) were used. The T-test with Bonferony amendment was used to analyze significant differences observed by determining the difference location to reduce error paired samples. The significant level was $P \leq 0.05$ for all the calculations and all the statistical tests were conducted using SPSS software (version 16, Michigan, USA).

## RESULTS

All the measured variables have shown as Mean ± Standard Deviation (SD). The results Showed that six months aerobic training caused significantly improved VO2max in aerobic group (p=0.001). After 3 to 6 months of training, VO2max significantly increased in comparison to pre value from 31.9±3.1 to 35.8±2.4, p=0.001 and 31.9±3.1 to 38.1±3.6, p=0.001 respectively. But VO2max haven't significantly changed in control group during the same time. Significantly increased in aerobic group VO2max in comparison to control group showed the results of 35.8±2.4 vs. 30.7± 6.1 after three months and 38.1±3.6 vs. 31.7±3.5 after six months (table 2).

Aerobic training caused increasing in CD25 cells count. After 6 months of training, CD25 cells count significantly increased in comparison to pre value from 320±36.2 to 379±31.6,P=0.001, while this increase was not significant after 3 months. But CD25 cells count haven't significantly changed in control group during the same time. Comprising CD25 cells count between two groups showed the elevation of CD25 cells count in aerobic group 379±31.6 vs. 343± 36.3,P=0.002 in comparison with control group after 6 months (table 2).

Interleukin 2 concentration the same pattern of changes in CD25 cells count within and between two groups (table 2).

**Table 2. Cheng Immune and physical factors in aerobic and control groups**

| | Aerobic group(n=20) | | | Control group(n=20) | | |
|---|---|---|---|---|---|---|
| | Pre test | Mid test | Pos test | Pre test | Mid test | Pos test |
| $Vo_{2max}$(ml/kg/min) | 31.9±3.1 | 35.8±2.4 $^{*+}$ | 38.1±3.6 $^{-*+}$ | 30.7±6.1 | 31.4±4.2 | 31.7±3.5 |
| $CD_{25}$(cells/µl) | 320±36.2 | 336±28.9 | 379±31.6 $^{*+}$ | 337±22.1 | 321±34.3 | 343±36.8 |
| IL-2(pg/ml) | 90.1±3.7 | 97.8±4.8 | 112.4±5.3 $^{*+}$ | 94.7±5.9 | 98.3±3.8 | 93.9±4.5 |
| IgA(µg/ml) | 25.2±2.3 | 30.5±1.8 | 32.7±2.6 $^{-*+}$ | 26.2±2.1 | 27.3±3.4 | 26.8±2.8 |

***** *Denote significant with pre test (p<0/05)*

**-** *Denote significant with mid test (p<0/05)*

**+** *Denote significant between aerobic and control groups (p<0/05)*

Six months aerobic training caused significantly improved Salivary IgA concentration in aerobic group (p=0.001). After 3 to 6 months of training, Salivary IgA concentration significantly increased in comparison to pre value from 25.2±2.3 to 30.5±1.8, p=0.001 and 25.2±2.3 to 32.7±2.6, p=0.001 respectively. But Salivary IgA concentration haven't significantly changed in control group during the same time, Significantly increased in aerobic group Salivary IgA concentration in comparison to control group showed the results of 30.5±1.8 vs. 26.2± 2.1 after three months and 32.7±2.6 vs. 26.8± 2.8 after six months (table 2).

## DISCUSSION

The project results showed that aerobic activities $VO_{2max}$ in aerobic group about 12.22 and 19.5 percent respectively from per-test to mid-test and post-test phase. While $VO_{2max}$ in control group showed no changes. Also, $VO_{2max}$ in aerobic group in mid-test and post-test phase was respectively 14.1 and 19.5 higher than the control group.

These results show that taking moderate aerobic exercise for 3 and 6 months increases the elderly's aerobic power. Based on evidences (6, 18) increased aerobic power in the first 3 months of aerobic exercise in aerobic group may reflect the fact that taking 8-12 week exercise lead to improved cardiovascular function and taking more exercise than this will gradually improve aerobic power. Those findings are aligned to Spirduse, Bream and Yamamoto's results (8, 13, 19), increased aerobic power can be due to increased beating volume or increased oxygen up taking and absorption by the cells, increased mitochondria's number and volume, improvement of capillary networks and increased blood hemoglobin concentration and pulmonary changes. Therefore based on exercise principle, taking aerobic exercises will increase aerobic power and enhance cardiovascular function in all ages as was proved in this research i.e. increased aerobic power in the elderly after 3-6 months of aerobic training (3). Statistical analysis showed that there are significant differences in the subjects CD25 cells count and Interleukin-2 and salivary IgA concentration between control and aerobic groups in post-test phase. In other words, after 6 months exercise, there were significant differences between both groups in the CD25 cells count and interleukin-2 and salivary IgA concentration after 6 months of exercise. These results show that although the CD25 cells count and Interleukin-2 and salivary IgA concentration decreases with aging but taking moderate aerobic exercises for 6 months may cause significant increase ($p<0.05$) while after 3 months of exercise, we find no significant increase in the CD25 cells count and Interleukin-2 concentration in both group and only significant increase in salivary IgA concentration can be seen.

So we conclude that to increase the CD25 cells count and Interleukin-2, we must exercise for more than 3 months (6).

These findings are aligned to the findings of Shinkai et al (1995), Susan Louise et al (1998), Drela et al (2004), Milton et al and Broadbent et al (11, 16-18). However, these findings contradicts with Bream's , et al findings (13). Such contradiction is probably due to aerobic fitness level, the subjects age and exercise intensity so that several research groups have announced that the effect of exercise training on people's immune system relies on the fitness level, intensity and duration (6, 9, 17). So present study refers to this point that taking aerobic exercises with desirable intensity and duration lead to increased CD25 cells count, increased Interleukin-2 and salivary IgA concentration (5, 16-18). Therefore because the expression of Interleukin-2 Receptor (Il-2R) (the CD25 cells count) and Interleukin-2 production and some of the specific intracellular mechanisms that enhance the people's lymphocyte reproduction ability (6, 10) , so we can claim that the proliferation rate of T help cells increases and actions of other immune cells and immune responses will be better regulated due to increased IgA concentration, the performance of mucosal immune system will enhance. At present, the mechanism that increases immune function in elderly subjects after 6 month aerobic training is not known. But increased cell breath due to aerobic exercise is possible, therefore this was free radicals will be produced (1, 2). Sport exercises will increase oxygen consumption in active muscles to times more than resting position. Therefore, due to increased consumed oxygen during sport activities, more oxygen will be changed to free radicals and then the amount of reactive oxygen species will increase. In order to defend against free radicals, body responses through antioxidant enzymes like super oxide dismutase, catalase, peroxidase Glotatyn and due to exercise continuation, we see body adaptation and the amount and performance of antioxidant enzymes will increase and due to this reaction an oxygen- antioxidant balance named Antioxidant Position has been created and this balance is a significant parameter of immune function which not only causes maintenance, integrity and function of fats. Proteins and nucleic acids of immune cell membrane, but also plays an important role in the control of message transmission and genetic expression of immune cell, so it is probable to enhance the immune cells poor performance, amount and concentration in aged people in aged people by adapting in Antioxidant enzymes performance (1, 2). And also based on this probability that along with aging T helper cell 1 (Th1) will change more than T helper cell 2 (Th2), it is possible that sport activities lead to more balance between Th1 and Th2 cells and this will finally cause better immune function in the elderly (7).

## CONCLUSION

This study results showed that 6 months of moderate aerobic exercises will cause increased CD25 cells count, increased Interleukin-2 and salivary IgA concentration. There fore, 6 month moderate aerobic exercise can be very effective to delay immune system aging. Increased Interleukin-2 production and increased CD25 cells count can be either the reason or the result of increased T-cells proliferation response which ultimately lead to improved T-cells performance and better cellular system performance. Also, increased salivary IgA concentration can lead to enhanced mucosal immune system performance and reduced probability of upper respiratory tract infection (2, 3, 6). Also the study results showed that increased CD25 cells count cells, Interleukin 2 concentration fake place in a delay process so that the CD25 cells count and Interleukin-2 concentration will not show a meaningful increase after 3 months of aerobic exercise and with 6 months of aerobic exercise we'll find a significant increase. Therefore it is probable that increased CD25 cells count and Interleukin-2 concentration in the elderly is a function at time. So to enhance cellular immune system performance in the elderly it is advised

to take moderate aerobic exercise for a period of more than 3 months so that the aged people have better immune performance and finally increased quality of life.

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