

Efficacy of Walking Exercise Program on Serum Interleukin - 2 in Elderly

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ABSTRACT

This study aimed to investigate the effect of walking exercise program on serum interleukin-2 (SIL-2) in elderly, and to find out any relationship between it's blood level and upper respiratory tract infection (URTI). Forty volunteer healthy elderly subjects of both sexes, signed consent form, participated in this study. Their ages ranged from 55 to 68 years. They were divided equally in number and sex into exercise and control group. The exercise group performed symptom limited modified Bruce protocol (first 3 grades), with 60-80% of their predicted maximum heart rate. This program done 3 times/week for 4 weeks, in addition to practice their normal daily community activity hours (DCAHs). While the control group instructed to practice DCAHs only. Blood samples were collected from each subject of both groups before the trial and after completion of 2 and 4 weeks of the trial. The results of this study indicated a highly significant increased difference ($P < 0.001$), in SIL-2 between the two groups, with 5% to 20% of URTI, in exercise and control group respectively. Conclusion: walking exercise program has a significant effect on SIL-2 in elderly subjects, and decreases susceptibility to URTI.

INTRODUCTION

The immune system is a highly complex and well regulated grouping cells, hormones, and interactive modulators that defend the body from invasion from outside microbes (bacterial, viral and fungal) or any foreign macromolecules and from abnormal cells such as cancer cells. Human immune function undergoes adverse changes with aging⁴, including development of a relative immune deficiency and an immune dysregulated state⁴¹. The age-related alterations in the immune system may account for the increased susceptibility to and the increased severity of infections in the elderly. It should be noted,

however that the opportunistic infections commonly associated with immunodeficiency are common in the elderly patient populations²⁶.

Recent studies suggested that a complex reshaping or continuous remodeling of the immune system rather than immune deterioration occurs with age, a situation where some immune parameters increase, other decrease and still others remain unchanged⁴⁵.

Interleukines were originally defined as proteins secreted by certain leukocytes, which regulated leucocyte growth and activity, hence, the name inter-leukin (IL)¹. They are members of the big family cytokines, which include a long-list of mediators: interleukines

from (IL-1 to IL-13), interferons (IFNs), colony stimulating factors (CSFs), growth factors and tumor necrosis factors (TNFs)³. Interleukine-2 (IL-2) is a sigle glycoprotein, produced by activated T-cells²⁰. Activated B cells, natural killer (NK) cells and large granular lymphocyte (LGLs) may also share the ability to produce IL-2²⁴.

IL-2 production can be inhibited by human suppressor T cells. In addition, a number of immunosuppressive agents exert their effects primary by inhibiting IL-2 production, such as glucocorticosteroids, cyclosporine and prostaglandin. Also, there are physiological and non physiological agents, which augment IL-2 production, These include vasopressin, hydroxyurea and numerous all surface-active compounds¹³. IL-2 promotes lymphocyte function³⁸, and it is an autocrine growth factor for T-helper 1 cells²¹, and may induce maturation of resting murine B lymphocytes and may propagate proliferation of activated B cell blasts¹⁹. IL-2 activated T cells, also can exhibit enhanced cytotoxicity³⁵, and it has a major activator of T and NK cell function⁶.

Production of IL-2, tend to be decreased in elderly sedentary subjects^{35,42}. Recently, the relationship between exercise and immunity had drawn attention. An appropriate regular regimen of endurance exercises might help elderly to lead a quality of life by preserving immune function⁴³. So, the purposes of this initial investigation were, to determine the effect of walking as a moderate type of exercise on the serum interleukine-2 (SIL-2) level, and to may clarify any relationship between upper respiratory tract infection (URTI) and IL-2 blood level in elderly subjects.

METHODS

Subjects

The study protocol, approved by the Department of Internal Medicine and Geriatrics- Faculty of Physical Therapy- Cairo University. Forty volunteers healthy elderly, from Kasr Al Aini out clinic, were classified equally into a control and exercise group, each included (10 males, 10 females). The mean ages were (58.15 ± 0.93) and (57.45 ± 0.76) for the control and exercise group respectively. All subjects were normotensive, nonsmokers, nondiabetics and cardiorespiratory free. They informed to stop receiving anti-inflammatory or corticosteroid and hormonal drugs one week before starting the trial. Also, they gave informed, written consent before participating. Baseline characteristics of both groups were shown in table (1). Clinical examination, and resting 12 leads EKG were done for all participants by the staffs in the critical care unit-Cairo university Hospital.

PROCEDURES

Each subject of both groups was allowed to rest comfortably in supine posture in a quite room for 15 minutes, then a first venous blood sample was taken and considered as baseline level, then another two samples were taken similarly post 2 and 4 weeks from the first one during the testing period. The collected three blood samples, then chemically analyzed, using ELISA technique, with human IL-2 EIA Kits, in the Medical Biochemistry Department- Faculty of Medicine-Cairo University, to estimate the serum IL-2 level.

Control group: The subjects of this group instructed to practice their normal community daily activities, and to come back after 2 and 4 weeks for another clinical

examinations and at any time he/or she has any cardiorespiratory problem within these periods.

Exercise group: Each subject of this group was trained individually on the computerized stress test treadmill, using symptom limited modified Bruce protocol (first 3 grades) as 1.2 mph with 0° for one minute, 1.7 mph with 5° elevation for 3 minutes, 1.7 mph with 10° elevation for 3 minutes and 1.2 mph with 0° for one minute, with 60-80% of the predicted maximum heart rate. This program was done 3 times/week for 4 weeks as a total testing period. Also, the subject was instructed to terminate the exercise

if he/or she feels chest pain, discomfort, leg pain or claudication, dizziness and fatigue. In addition all subjects of both groups had been instructed to practice their daily community activity hours (DCAHs). A questionnaire was used to record (DCAHs). Statistical analysis was performed with paired t- test to deal with changes in the same group and unpaired t-test to deal with changes occurring in different groups also correlation coefficient also was used to clarify if there is any relation between changes in SIL-2 levels, DCAHs and chest infection. All data presented are mean \pm standard error of the mean (mean \pm SEM).

Table (1) Characteristic features of the all subjects in both groups.

	Age (year) (Mean \pm SEM)	Weight(kg) (Mean \pm SEM)	Height(Cm) (Mean \pm SEM)	BMI (Kg/m ²) (Mean \pm SEM)
Exercise Group (n=20)	(r=55-68) 57.45 \pm 0.76	(r=44-84) 64.5 \pm 3.00	(r=150-180) 164.05 \pm 2.44	(r=19.56-27.30) 23.84 \pm 0.16
Control Group (n=20)	(r=55-64) 58.15 \pm 0.93	(r=50-85) 65.5 \pm 2.88	(r=130-175) 161.25 \pm 3.10	(r=19.35-31.95) 25.08 \pm 1.02
P value	< 0.10*	< 0.10*	< 0.10*	< 0.10*

The values are mean \pm SEM, *: No significant difference, r: Range, n: Number of subjects, BMI: Body mass index.

RESULTS

No significant differences had been resulted in age, weight, height and body mass index between the two groups table (1).

The means of serum interleukine-2 (SIL-2), after 2 weeks in the exercise group, were 5.539 \pm 0.32 and 6.085 \pm 0.5 ng/ml, in both males and females respectively. This increased values was being statistically insignificant. While after 4 weeks the mean increased values were 6.166 \pm 0.31 and 6.542 \pm 0.52 ng/ml, in males and females respectively, and

statistically considered significant in the males (P= 0.02), and not significant in the females (P= 0.10), table (2).

In the control group the means of SIL-2, after 2 weeks were 5.186 \pm 0.3 and 5.488 \pm 0.32 ng/ml, in the males and females respectively. This increased values were statistically considered insignificant. While after 4 weeks the mean value of SIL-2 in the males decreased to 5.148 \pm 0.3 ng/ml. But in the females it was increased to be 5.940 \pm 0.33 ng/ml, and it considered statistically insignificant (P = 0.10), table (2), Fig (1).

Table (2): Changes in SIL-2 ng/ml, two and four weeks post trial of all subjects in both groups.

	Exercise Group		Control Group	
	Males (n=10) (Mean \pm SEM)	Females (n=10) (Mean \pm SEM)	Males (n=10) (Mean \pm SEM)	Females (n=10) (Mean \pm SEM)
Pre	4.874 \pm 0.38	5.627 \pm 0.5	5.175 \pm 0.3	5.479 \pm 0.32
2 Weeks Post	5.539 \pm 0.32	6.085 \pm 0.5	5.186 \pm 0.3	5.488 \pm 0.32
4 Weeks Post	6.166 \pm 0.31	6.542 \pm 0.52	5.148 \pm 0.3	5.490 \pm 0.33
P value	< 0.02		NS	
	< 0.10*		< 0.10*	

Values are mean \pm SEM, n ; Numbers of subjects

* ; increased but not significant NS ; not significant but decreased

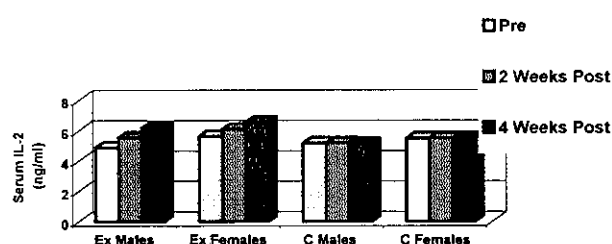


Fig (1) Changes in the means of serum IL-2 In all subjects pre and 2 weeks, 4 weeks post trials

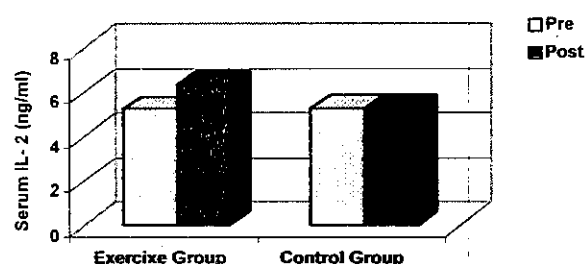


Fig (2) Changes in SIL- 2 In both groups pre and 4 weeks post trials.

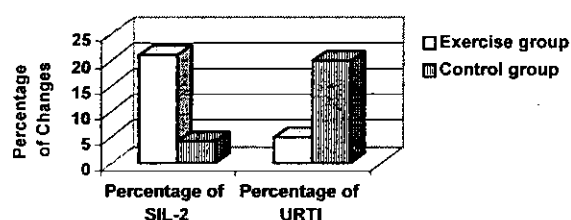


Fig (3) Relation between increased percentages in SIL- 2 and upper respiratory tract infection (URTI) in both groups over 4 weeks

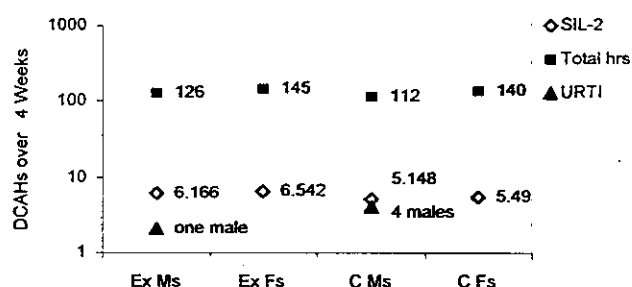


Fig (4) Relation between total daily(DCAHs) community activities hours,SIL- 2 and upper respiratory tract infections (URTI) in all subjects over 4 weeks. (Ex; Exercise, C;Control, Ms; Males, Fs;Females)

Table (3): Changes in SIL-2 post 4 weeks for each group and between the two groups.

	Exercise Group (n=20) (mean \pm SEM)	Control Group (n=20) (mean \pm SEM)	P value between groups
Pre	5.251 \pm 0.32	5.327 \pm 0.22	< 0.10*
Post	6.354 \pm 0.30	5.328 \pm 0.22	< 0.001***
% of Changes	21	4.3	
P value	< 0.02**	< 0.10	

Values are mean \pm SEM, n; Numbers of subjects

*; no significant difference, **; Significant increase

***; Highly significant increase ; Not significant increase

In table (3), there was no significant difference between the exercise and the control groups in SIL-2, before starting the trial. But after 4 weeks, SIL-2 increased significantly ($P = 0.02$), with 21% of change in the exercise group ($n=20$). While in the control group ($n=20$) it was being insignificantly increased ($P = 0.10$), with only 4.3% change.

When a comparison had been done to clarify the effect of 4 weeks exercise program on the SIL-2 blood level, the data indicated a highly significant difference ($P = 0.001$), table (3).

The mean DCAHs of the exercised females was more than exercised males 145 ± 10.89 hr and 126 ± 11.25 hr respectively, but no significant difference had been resulted between them, table (4). Concerning the mean DCAHs in the controlled females it was more

than the matching controlled male hr and 112 ± 7.24 hr, respectively and it was being statistically highly significant difference ($P = 0.001$), table (4).

Concerning the upper respiratory tract infection ranged from simple influenza to acute bronchitis, in both groups the data indicated a ratio of 1 to 4, with 5% to 20% in the males subjects of the exercise and control group respectively, table (4).

Also, we noticed that both increased mean values in SIL-2 and DCAHs of the exercised females were being associated with non of URTI. In the controlled females both highly significant increase in DCAHs and the insignificant increase in SIL-2, were being also associated with non of URTI cases (Fig: 3).

Table (4): Means of daily community activity hours, increased SIL-2, and their relation to URTI in all subjects over 4 weeks.

	Exercise Group		P value between males and Females (Exercise Group)	Control Group		P value between males and Females (Control Group)
	Males (n=10)	Females (n=10)		Males (n=10)	Females (n=10)	
SIL-2 (ng/ml)	(mean \pm SEM) 6.166 \pm 0.31	(mean \pm SEM) 6.542 \pm 0.52	NS	(mean \pm SEM) 5.148 \pm 0.3	(mean \pm SEM) 5.490 \pm 0.33	NS
DCAHs	(mean \pm SEM) 126 \pm 11.25	(mean \pm SEM) 145 \pm 10.89	NS	(mean \pm SEM) 112 \pm 7.24	(mean \pm SEM) 140 \pm 5.91	HS
Cases of URTI	1	-		4	-	
% of URTI	5 %			20 %		

NS ; No significant difference, HS ; Highly significant difference

URT I ; Upper respiratory tract infection, DCAHs ; Daily community activity hours.

DISCUSSION

Little is known regarding the effect of exercise on the senescent immune system⁸. So, the primary purpose of this study was to determine the influence of walking exercise program on serum interleukine-2 (SIL-2) in healthy elderly. An additional purpose was to find out any possible relationship between the level of SIL-2 and chest infection among participating subjects. The immunological changes observed during aging are consistent with a reshaping rather than a generalized deterioration of the main immune functions¹⁵.

In the present study SIL-2 increased significantly with 21% in the healthy elderly exercised group (n=20), after 4 weeks of practicing walking exercise program. This result considered as reshaping in the SIL-2 and it was in agreement with that study mentioned above. Also, a 13% increase in the lymphocyte sub-population observed after prolonged exercise³⁷. In contrast no change had been reported in lymphocyte sub-population, in a study used a similar protocol⁴³. Moderate exercise has a favorable effect upon specific and non specific immune functions³⁹, and may has a predominantly immuno enhancing effect³⁶. An increased activity rather than the percentage of T-lymphocyte post acute submaximal exercise had been reported¹⁰. Concomitant studies to our result, stated that during exercise the augmented secretion of the cytokine IL-1 by macrophages in turn, stimulated the production of the IL-2 by T-helper (CD4⁺), the IL-2 thus produced can stimulate growth-activated T-cells to produce more IL-2⁴⁰. Many supporting studies stated that activity and exercise in elderly individuals had a higher production of IL-2²². Also, moderate training program could enhance the resting natural killing cell (NK)

function of the elderly subjects⁴⁵, and the IL-2 proliferative response increased due to increased sensitivity of NK cells⁴⁴. In addition the post exercised value of IL-2 in present study, may be related to some of mechanisms reported by many authors. The first is that the decrease in plasma volume appear to explain the acute increase seen in immunoglobulins following graded exercises³². The second is the increased flow of lymph during exercise³¹. While the third was regarded to be due contribution from extravascular pools or non specific stimulation of memory B-cells²⁸. The fourth mechanism may be referred to the increased influx of extra-vascular proteins into the intra-vascular pool³¹. The last mechanism is that exercise increases cytokine IL-1, which in turn stimulates production of IL-2, through T-helper cells⁴⁰.

The SIL-2, in the females exercised group was insignificantly increased in our study. This result is being consistent with a study stated that moderate exercise training for 12 weeks failed to alter T-cell function in elderly women^{14,33}. Another documentation found that no significant change in SIL-2 concentration of 3 women, following running exercise¹⁶.

In spite of the significant and insignificant increased values of SIL-2 in the male and female subjects in the present study, no statistical difference had been found between them. This insignificant difference was being supported by study stated that, after a bout of moderate exercise no significant difference in serum immunoglobulin between males and females had been found^{17,34}. The result of this study concerning changes of SIL-2 in the control group, showed both insignificant increase in the female subjects and a decreased level than the baseline in the male subjects as follow up over 4 weeks. The

decreased value in the males may be related to lowering of the total daily community activity hours (DCAHs). While the insignificant increased value in females may be attributed to the highly significant increase in the total DCAHs. Also, no significant difference in DCAHs between both the exercise and control group occurred. But the insignificant increase of the SIL-2 in the control group may be attributed to the consideration that the amount of activities was not enough to stimulate the immune system, as being reported in a study stated that moderate exercise failed to alter T-cell function in elderly women, indicating that an unusual commitment to vigorous exercise may be necessary before an effect on T-cell function can be measured in the elderly³⁰. This study documents our hypothesis, because when the exercise walking program added to the same amount of DCAHs as in the exercise elderly group, The SIL-2 was significantly increased.

Many studies concentrated upon the relationship between aging, immune system and infections. Age related alterations in the immune system may account for the increased susceptibility to and the increased severity of infection in elderly²⁶. Also, older persons show a weaker response to bacterial antigens²⁷, and this is due to the lower levels of immunity at these ages⁷. The most important age related changes that occur is the reduction in the physiologic reserve of the respiratory system, especially the reserve for alveolar gas exchange, thus they are more vulnerable to stress and injuries²⁹. The decreased mobility of the thoracic cage and the decreased efficiency of the resting respiratory muscles alter lung performance and contribute to the decline in pulmonary function with age¹². The percentage of chest diseases among sedentary was 17.6% and 7.4% in males and females respectively as a surveying study². This study documents our

result, which indicated that the percentage of cases of upper respiratory tract infection (URTI), was 20% to 5% in the elderly control and exercise group respectively, and the all affected cases in both groups were males only. This may be related to the total DCAHs, which was being lower in male than female subjects of both groups.

The high rate of URTI in the control group may be due to the lower SIL-2 level. This was in agreement with an observation, concluded that lower IL-2 production in response to influenza viral antigens had been found in elderly sedentary subjects²⁵, and also with a study stated that IL-2 production tend to be decreased in elderly sedentary subjects⁴². During this window of decreased host protection, viruses and bacteria may gain a foothold, increasing the risk of sub-clinical and clinical infection²³.

But the lower rate of the URTI in the exercised group may be attributed to the effect of exercise on the immune system. As being shown in many studies stated that physical movement was recognized as a key factor for the maintenance and improvement of health in the elderly, and might help elderly to lead a quality of life by preserving immune function⁴⁵, and significantly increases the level of IgG, in 33 non smoker healthy subjects, with no URTI⁶. Another study on the influence of moderate exercise training on host protection and immune function has shown that near-daily brisk walking compared with inactivity reduced the number of sickness days by half over a 12-15 week period, and the positive effects on immuno-surveillance and host protection that come with moderate exercise training are probably related to a summation effect from acute positive changes that occur during each exercise bout³⁰. Also, physical exercise was considered as one of the methods needed to restore or reverse

immunological functions in the aged humans¹⁸, and can alter the release of numerous cytokines and modulate their receptor system³⁶. So, in older physically capable men, regular walking is associated with a lower overall mortality rate¹¹, and encouraging elderly people to walk may benefit their health⁵, and that exercise training is a potential avenue for reducing the burden of impairments to pave the road toward improved function in elderly subjects⁹. Now it can be concluded that walking exercise program has a significant effect on the immune system in elderly subjects, and also, decreases susceptibility to URTI among those active elderly.

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الملخص العربي

تأثير برنامج تمرين المشي على مصّل الانترليوكين-٢ في المسنين

تهدف هذه الدراسة على بحث تأثير برنامج تمرين المشي على المصّل الانترليوكين-٢ في المسنين وإيجاد أي علاقة بين مستوى تركيزه في الدم وعدوى الجهاز التنفسي العلوي . وقد شارك في هذه الدراسة أربعون مسناً من الأصحاء من كلا الجنسين ، تراوحت أعمارهم من ٥٥ - ٦٨ سنة وقد قسموا بالتساوي في العدد والجنس إلى مجموعتين متمرنين وحاكمة . وقد أدت المجموعة المتمرنين برنامج بروس المعدل (لأول ثلاث مستويات) من ٦٠ - ٨٠ % من أعلى ضربات القلب المحددة لهم . وهذا بالإضافة إلى أعمالهم ونشاطهم اليومي . بينما أرشدت المجموعة الحاكمة بممارسة أعمالهم اليومية فقط . وقد جمعت عينات الدم من المجموعتين قبل وبعد أسبوعين وأربعة أسابيع من المحاولة . وقد أوضحت نتائج هذه الدراسة فرق ذو دلالة عالية جداً ($P < 0.000$) بين المجموعتين ، ونسبة ٥ % ، ٢٠ % لإصابة الجهاز التنفسي العلوي للمجموعة المتمرنين والحاكمة على التوالي . ويستخلص من هذه الدراسة أن برنامج تمرين المشي له تأثير ذو دلالة معنوية على مستوى الانترليوكين-٢ في الأشخاص المسنين وكذلك يقلل من احتمال إصابة الجهاز التنفسي العلوي .