

# Impact of exercise training program on markers of Atherosclerosis in hypertensive patients with blood group A

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## ABSTRACT

**Background:** It was found that blood pressure, p-selectin, and ICAM -1 reduced and six-minute walk distance increased by concurrent training in hypertension, but research covering this area in blood group A is limited. **Objective:** The current study aimed to evaluate the efficacy of exercise training program on p-selectin and ICAM -1 in hypertensive patients with blood group A. **Patients and methods:** The study was performed on twenty patients from both sexes with the age ranged from 40 to 55 years who performed concurrent training for ~45–60 min per session involving 20–40 min of aerobic and 15–40 min of resistance exercise, 3 session per week for 10 weeks in addition to their traditional medications. Blood pressure, p-selectin, ICAM-1, and six-minute walk distance were measured before and after the study. **Results:** Statistical analysis revealed that the blood group A positively responded to concurrent training by decreasing systolic, diastolic, p-selectin, and ICAM-1 by 9.54%, 11.34%, 42.42%, and 36.03%, respectively and increasing six-minute walk distance by 24.83%. **Conclusion:** It was recommended to hypertensive patients with blood group A to practice concurrent training to decrease the risk of cardiovascular complications.

**Keywords:** exercise training, atherosclerosis, hypertension, blood group A

## Introduction

Hypertension is a major risk factor for chronic diseases, which has many effects on health and even can lead to death because of its relation to cardiovascular disease<sup>[1, 2]</sup>.

Soluble p-selectin (sP-selectin) is a biomarker for

atherosclerosis and inflammation and helps to identify patients with cardiovascular risk. It gives prognostic information about cardiovascular events<sup>[3]</sup>.

Intracellular cellular adhesion molecule-1 (ICAM-1) is also used as a new and effective tool for the diagnosis of vascular disorders and inflammatory conditions in humans<sup>[4]</sup>.

Soluble forms of cellular adhesion molecule (CAMs), E-selectin (sE-Selectin), P-selectin (sP-selectin) and ICAM-1 (sICAM-1) are indicators of inflammation and increased circulation of one or more of these markers is related to coronary artery disease, myocardial infarction, and atherosclerosis<sup>[5]</sup>.

Subjects with blood group (A) are exposed to increased incidence of high blood pressure, which may lead to risk of other cardiovascular diseases i.e. stroke, myocardial infarction, CHD etc. than people with blood groups AB, B, and O, people with type A blood group are recommended to avoid eating fatty foods, apply regular exercise, and stop smoking<sup>[6]</sup>.

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Aerobic and resistance exercise (concurrent training) are recommended as nonpharmacological treatment of hypertension due to improve systolic and diastolic blood pressure in hypertensive women and improve anthropometric, biochemical, and functional variables related to health<sup>[7-9]</sup>.

Aerobic performance increases the walking distance during the 6-minute walk test and concurrent training increases muscle strength<sup>[10]</sup>.

The beneficial effects of physical activity could be expressed by improved markers of endothelial dysfunction, including adhesion molecules<sup>[11]</sup>.

Performing concurrent training is better than aerobic or dynamic resistance training alone because of improving cardiorespiratory fitness, muscle strength, and other cardiometabolic health biomarkers simultaneously e.g sP-selectin) and ICAM-1<sup>[12]</sup>.

## Materials and Method

### Subjects

Twenty Egyptian patients from both sexes (11 males, 9 females) were recruited from the outpatient clinic of faculty of physical therapy, Cairo University; their ages ranged from 40 to 55 years old with the mean $\pm$ SD of 49.85 $\pm$ 4.32. Patients with a mild degree of hypertension with SBP ranged 140-159 mmHg and DBP 90-99 mmHg were included in the study. This investigation was done in the outpatient clinic in the Faculty of Physical Therapy, Cairo University, from December 2016 to May 2018.

All patients received a thorough explanation of the objectives and procedures of the study and written informed consent was signed by each patient before participation in the study. Before starting the program, a complete history and physical examination were taken for all patients with particular attention to identifying any long-term complications of hypertension. This study was reviewed and approved by the Ethics Committee for Scientific Researches of Faculty of Physical therapy.

### Inclusion criteria:

to 55 years old from both sexes, their body mass index (BMI) ranged from 25 to 29.9 kg/m<sup>2</sup> (overweight). They had a mild degree of hypertension for a maximum of five years with SBP ranges from 140 to 159 mm Hg, DBP from 90 to 99 mm Hg, blood group A, and medically controlled for hypertension.

### Exclusion criteria:

Patients with one of the following criteria were excluded from the study; cardiac disorders as ischemic heart disease or heart failure, pulmonary disorders, chronic renal impairments, previous stroke, use of oral contraceptive, musculoskeletal disorders that interfere with the ability to exercise, and auditory and visual problems.

## Instrumentation

### 1) Evaluation tools and equipment:

A mercury Sphygmomanometer and Stethoscope (Model no 300, Made in China ) were used for measuring BP for all patients, weight and height scale was used for measuring the weight and height of each patient to calculate the BMI for everyone to exclude subjects with BMI less than 30 kg/m<sup>2</sup>, Enzyme-linked immunosorbent assay (ELISA) reader (stat fax - 2100) for estimation of serum level of p-selectin and intercellular adhesion molecule-1 (ICAM-1).

### 2) Training equipment

Treadmill: Electronic treadmill (JS .1688 electrical treadmill, made in China ) was used to perform aerobic exercises.

sSandbags: (e.g .0.5 -1 or 3 Kg ) with the weight ranged from 0.5 -3 kg were used to apply resistance exercise.

## Procedure

### Evaluation procedure:

1. The patients' blood pressure was measured to fulfill the inclusion criteria. The recommended protocol for measuring blood pressure was as follows:<sup>[13]</sup>

Measurements were taken with a calibrated mercury sphygmomanometer by auscultatory methods, the constricting clothes were removed from the selected arm and the arm was placed at heart level. The patient should comfortably rest in the seated position with back support for 5 min, should no talk, and his/her legs should not be crossed. The cuff was wrapped approximately 2 cm above the elbow bend (antecubital fossa) over the brachial artery. The diaphragm of the stethoscope was gently placed and steadily over the brachial artery, the cuff was inflated until brachial pulse disappeared then slowly deflated. The systolic and diastolic levels i.e. the first appearance of a clear tapping sound and the point at which the sounds disappeared, were read respectively. The second measurement was taken on the same arm after waiting for 30s.

2. (BMI) is a measure of body fat based on the person's height and weight. It is calculated by dividing an individual's weight in kilograms by his height in meters squared (to fulfill the inclusion criteria)<sup>[14]</sup>:

$$\text{BMI (kg/m}^2\text{)} = \text{body weight (kg)/height (m}^2\text{)}$$

3. Blood The blood sampling to measure P-selectin and intercellular adhesion molecule-1 (ICAM-1):

Taking blood sampling to evaluate the amount of adhesive molecules before the study and 10 weeks later. The blood sampling site was cleaned with antiseptic, an elastic band was wrapped around the upper arm where the blood would be drawn. 10 cc of venous blood was taken from the right hand of the

subjects under laboratory conditions, after 5 minutes of complete rest, using sterile Venojack needles. Blood sample was collected in an anticoagulant tube (EDTA). Then samples were put into ice, serum was gained using a 1500 g centrifuge for 15 minutes and then it was stored at -70 °C for the next analyses. P-selectin and ICAM-1 were measured using the immunosorbent method by Elisa Stat Fax2100 [11].

4. Six-minute walk test carried out before and after interventions to determine the patient functional capacity, according to [15].

**Patient preparation:**

Patients wore comfortable clothing and appropriate shoes for walking, ate a light meal before early morning or early afternoon tests and should not apply vigorous exercise within 2 hours of beginning the test.

**Steps of application:**

The test was performed indoors, in along, flat, straight, and enclosed corridor with about 20 meters in length. The turn round points were marked with a cone, the starting line, that marks the beginning and the end was marked on the floor using brightly colored tape. At least 10 min before the test started, the patient sat at rest on a chair, located near the starting point. During this time, any contraindications were checked.

Absolute contraindications for the 6MWT included: myocardial infarction and unstable angina during the previous month. Relative contraindications included a systolic blood pressure of more than 180 mm Hg, a diastolic blood pressure of more than 100 mm Hg, and a resting heart rate of more than 120.

The patient encouraged to walk for 6 minutes as far as possible and allowed to slow down to stop and to rest as needed but resume walking as soon as he was able, as the patient started walking, the numbers of laps were recorded until he finished the test. Finally, the distance walked by the patient was calculated and recorded.

**Training procedure:**

All patients were individually instructed at first training session about signs and symptoms that when occurred he/she should stop the exercise or decrease the intensity of it, which were chest pain, dizziness, headache, confusion, severe and fatigue. They were also instructed how to work on the treadmill and how to stop it.

**Concurrent training protocol:**

All patients were performed concurrent training (Combinations of low to moderate-intensity aerobic exercise at 40– 60 % oxygen consumption reserve [VO2R] and five resistance exercises (in the form of circuit weight training) that targeted the major muscle groups of the upper and lower body consisted of the following exercises: biceps curl, shoulder flexion, hip flexion, hip abduction, and knee extension using low (40–50% 1-RM) to moderately heavy resistance training loads (60–80% 1-RM) for 2-3 sets of 10-20 repetitions with ~1 min rest intervals between sets. The training was performed for ~45-60 min per session involving 20–40 min of aerobic and 15-40 min of resistance and 5-minute rest between aerobic and resisted exercise), the exercises were performed 3 sessions per week for 10 weeks in addition to their traditional medications [12].

**Statistical analysis:**

The statistical analysis was performed using SPSS software. The data obtained were statistically analyzed to compare the difference before and after the treatment.

**Results**

The main purpose of this study was to find out the efficacy of concurrent training on p-Selectin, sICAM, and 6 minutes walk distance in hypertensive patients with blood group A. Blood pressure, p-selectin, ICAM-1, and six-minute walk distance were measured before and after the study (10 weeks).

The results revealed statistically significant improvement (decrease) in systolic and diastolic blood pressure, p-Selectin, sICAM, and increase in six-minute walk distance, which is represented in Table (1).

**Table 1: Analytic statistics for -SBP, DBP, p-Selectin, sICAM, and 6 minutes walk test.**

Items	SBP	DBP	p-Selectin (ng/ml)	sICAM-1 (pg/ml)	6 minutes walk test (meter)
<b>Pre-treatment (Mean ±SD)</b>	151.50 ±6.70	91.00 ±4.47	6.27 ±2.12	223.82 ±40.65	249.50 ±48.90
<b>Post-treatment (Mean ±SD)</b>	137.04 ±9.01	80.68 ±4.59	3.61 ±1.54	143.18 ±51.72	311.45 ±66.10
<b>Mean difference</b>	14.46	10.32	2.66	80.64	61.95
<b>%of improvement</b>	9.54%	11.34%	42.42%	36.03%	24.83%
<b>P-value</b>	0.0001	0.0001	0.0001	0.0001	0.0001
<b>Significance (P&lt;0.05)</b>	S	S	S	S	S

SD: standard deviation P-value: probability S: significant

**Discussion:**

Hypertension is an independent risk factor for the development of CVD.[16] The effect of increasing BP >115/75 mm Hg is consistent and exponential, where each 20 mm Hg increase in

systolic blood pressure (SBP) or a 10 mm Hg increase in diastolic BP doubles the risk of a cardiovascular event [17].

Various studies have showed that ABO especially non-O blood groups are associated with the higher risk of cardiovascular disease and CAD due to increased level of VWF[18].

The addition to resistance training, aerobic training can now be considered as an effective and alternative treatment to decrease the prevalence and risk of CHD. Participation in activities that need both resistance and aerobic exercises should be considered as a tool to reduce the absolute risk of CHD since each mode of exercise has unique benefits<sup>[19]</sup>.

The purpose of this study was to find out the impact of concurrent training on blood pressure, p-Selectin, sICAM, and 6 minutes walk distance among hypertensive patients with blood group A.

The current study was conducted on twenty patients with a mild degree of hypertension, performed concurrent training for ~45-60 min per session involving 20-40 min of aerobic and 15-40 min of resistance exercise, 3 sessions per week for 10 weeks. The results of this study revealed a significant improvement (decrease) in systolic and diastolic pressure, as well as in p-selectin, ICAM-1, and increase in six-minute walk distance in blood group (A), that were 9.54%, 11.34%, 42.42%, 36.03%, and 24.83%, respectively.

This comes in agreement with other previous studies such as Corso *et al.* (2016) who found out that 30 min of moderate-intensity aerobic exercise, preferably all days of the week accompanied with dynamic resistance training 2-3 times/week is recommended as an antihypertensive lifestyle therapy<sup>[20]</sup>.

It was found by the study of Pescatello *et al.* (2015) that aerobic exercise training decreases blood pressure (BP) 5-7 mm Hg, while dynamic resistance training decreases BP 2-3 mmHg in hypertensive patients and lowers CVD risk by 20–30%<sup>[21]</sup>.

This was also supported by Pedralli *et al.* (2016) who showed that regular exercise affects the cardiovascular system through restoring endothelial function even in the presence of cardiovascular disease. Regular exercise makes changes in cholesterol levels and its subfractions, accelerates the removal of chylomicrons and low-density lipoproteins from circulation and increases the release of NO<sup>[22]</sup>.

The mechanisms underlying the beneficial effects of aerobic and resisted exercises that both central and peripheral hemodynamic factors contribute to post-exercise hypotension through a reduction in peripheral resistance during recovery from aerobic activity and resisted exercise. This fall in peripheral resistance may be associated with thermoregulatory vasodilation, suppression in sympathetic nerve activity, or due to the release of vasodilator metabolites from skeletal muscle<sup>[23]</sup>.

The results of this study revealed significant improvement (decrease) in p-selectin and ICAM-1 in the blood group (A), that were 42.42% and 36.03%, respectively

The present study agreed with Koh and Park (2018) who reported that patients with some types of cardiometabolic diseases, such as myocardial infarction, type 2 diabetic mellitus (T2DM), or chronic heart failure (CHF) had reduced sP-selectin, sVCAM-1, and sICAM-1, following moderate-intensity exercise training for 8–12 weeks<sup>[24]</sup>.

In accordance with the current study, Atashak *et al.* (2016) found that soluble intercellular adhesion molecule-1 (sICAM-1) levels are positively associated with high blood pressure and decreased HDL. Eight-week of concurrent exercise training

decreases both circulating concentrations of sICAM-1 and biomarkers of CVD risk<sup>[25]</sup>.

According to Koh and Park (2018) Regarding the mechanisms underlying decline of adhesion molecules as a result of exercise training can be associated with the free oxygen radicals. Investigations have revealed that free oxygen radicals cause the expression of adhesion molecules. It has also been proposed that exercise training enhance the antioxidant defense system. Therefore, the improvement of antioxidant defense system reduces the free oxygen radicals and subsequently the adhesion molecules. Interestingly, sP-selectin was considerably decrease 48h after race, which is probably due to the restoration process of the vascular function and endothelial barrier<sup>[24]</sup>.

Another probable mechanism underlying the adhesion molecules decreased after exercise, that aerobic and endurance training significantly decrease the oxidative stress by increasing the antioxidative capacity. A regular exercise training also inhibits the adipose tissue release of cytokines by reducing sympathetic stimulation, and consequently cell adhesion molecule concentration decrease<sup>[26]</sup>.

In contrast to the current study, Koh and Park (2018) reported that aerobic exercise training increases soluble ICAM-1 following an acute bout of maximal or moderate-intensity exercise<sup>[24]</sup>.

The results of this study revealed a significant improvement (increase) in six-minute walk distance in blood group (A), that was 24.83%.

This was also supported by Ramos *et al.* (2014) who showed an increase of the 6-minute walk distance after a practice period and decrease of BP values as the aerobic training improved hemodynamic and functional parameters<sup>[27]</sup>.

In accordance with the present study, Silveira *et al.* (2018) reported that the main long-term benefits of concurrent training are improvements in glucose control, blood pressure, lipid profile, fat mass, muscle mass strength, and functional or aerobic capacity<sup>[10]</sup>.

### Limitation:

No follow-up

### Conclusion

From the results of the current study, it was concluded that concurrent training has beneficial effects on lowering blood pressure, p-selectin, and ICAM-1, and it also increases six-minute walk distance in mild hypertensive patients with blood group A.

### Conflict of interest:

The authors declare no conflicts of interest.

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