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Impact of Aerobic Versus Anaerobic Exercise Programs on Cardiopulmonary and Platelets Functions in Obese Adult Subjects

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ABSTRACT

This piece of work investigated the effect of aerobic and anaerobic exercise programs on cardiopulmonary and platelets function in obese subjects. Platelet activation in 40 volunteers with normal blood pressure has been studied. Blood was drawn before and after the exercise program. Antibody-staining for platelet activation markers P-selectin and fibrinogen receptors was done without any stimulation in platelets rich-plasma for flow cytometric analyses. All subjects were included in exercise programs for three successive months, three times per week. At the end of the program, it has been shown that exercises led to increases in percentage aggregated platelets and percentage of platelets expressing P-selectin or CD62p binding and improved parameters of cardiopulmonary functions ($p < 0.05$). This increase in percentage of platelets that expressing P-selectin continued even with anaerobic exercises; and was accompanied by an increase in percentage aggregated platelets ($p < 0.05$).

KEY WORDS: Blood pressure, Physical stress, Platelets, Flow cytometry, P-selectin, Aerobic, Anaerobic exercises.

INTRODUCTION

Obesity is a complex pathology with interacting and confounding causes proposed from the environment, hormonal signaling patterns, adipogenic pathogens, genetic predispositions, adipokine receptor defects [1,2] and numerous behavioral aspects such as eating disorders, inadequate portion control and decreased physical activity. Although the etiology of obesity may be extremely complicated; a central imbalance in caloric homeostasis is the primary contributing factor to this condition [3, 4]

The progression of obesity has been associated with an increased predisposition for the development of additional pathological conditions [5]. These include a wide array of cardiovascular disease risk factors (e.g., diabetes, hypertension, dys-lipidemia, prothrombotic and pro-inflammatory environments) [6, 7], as well as the development of respiratory dysfunction (obstructive sleep apnea), arthritic disorders and a wide array of adverse psychological conditions [8]. When other multiple cardiovascular disease risk factors in addition to the progression of obesity are present, this combination leads to the creation of a condition termed “metabolic syndrome”, which can dramatically increase the likelihood of negative health outcomes in the afflicted individuals [9, 10].

Platelets are involved in both the mechanisms of atherogenesis and in the thrombotic complications of atherosclerosis [11]. Several previous studies assessed the effects of lifestyle factors on platelet function. The effects of exercise, in particular, have been extensively studied but the results are controversial [12, 13]. This may be attributed to multiple factors such as differences in patient selection, drug therapy and techniques used for the assessment of platelet function and reactivity, either in vitro or in vivo, were often associated with considerable methodological difficulties, which might also account, at least in part, for the discrepancies reported in earlier studies [14].

Regular aerobic training induces significant adaptations both at rest and during exercise in a variety of dimensional and functional capacities related to the cardiovascular and respiratory regulation system [15]. However, High-intensity exercise (anaerobic) training has the added benefit of improving fitness, thus making low-intensity exercise less difficult and more easily tolerated, although continuous intense exercise is difficult to maintain for extended periods of time [16].

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To address this issue, flow cytometric analysis was performed to study the effect of exercise that may induce changes of platelet reactivity by assessment of the platelet surface receptors expression, in a group of normal healthy obese students.

MATERIALS AND METHODS

Subjects

Forty healthy obese untrained non-smoking males from King Abdul-Aziz University, Jeddah, Saudi Arabia, who did their training in fitness time health club, Jeddah, Saudi Arabia, were included in the study. Their ages ranged from 18 to 20 years old, while their body mass index ranged from 30 to 35 kg/m2. Initially, each subject was examined medically by a physician at King Abdulaziz University Out-patient Clinics in order to exclude any abnormal medical problems. Subsequently, their medical history was taken to collect information about general condition, physical activity and current medications if any. All subjects with any cardiovascular conditions (those with a known history of uncontrolled hypertension, congenital and rheumatic heart diseases), any pulmonary disease (obstructive or restrictive lung diseases), orthopedic or neurological abnormality were excluded from the study. Subjects had neither used any medication 6 weeks prior to the study till the end nor participated in any regular physical exercise. Procedures used in this study were approved by the Ethics Committee of the Faculty of Applied Medical Sciences, King Abdulaziz University. Written informed consent was obtained from each subject, prior to the start of the study. The subjects were divided randomly into two equal groups (A and B), each comprised 20 subjects. Subjects belonging to the first group (A) participated in an aerobic exercise program, while those belonging to the second one (B) participated in an anaerobic exercise program. Both programs continued for three successive months, three times per week.

Methods

1. Exercise

The purpose of the training program was explained for each subject. Blood pressure (BP) was recorded in the relaxed sitting position after giving the subject rest for at least 30 minutes and repeated for 3 times. Arterial oxygen saturation (SaO_2) was measured using pulse oximeter (Handy pulse oximetry, Oxy 9, Korea), with a special sensor to measure SaO2. The body mass index (BMI) was calculated and the cardio-pulmonary fitness was evaluated for all subjects from both groups as a pre-test.

a) Aerobic exercise program:

The first group of aerobic exercise program (A) had their exercise training as following: warming up before the exercise program, included walking on the treadmill for 5 minutes at speed 1.5 km / h, with zero inclination. Duration was gradually increased from 20 to 40 minutes. Mode of walk / run on the electronic treadmill was with zero inclination, the frequency was three times weekly; for three successive months. The intensity was increased gradually to 60 - 80 % of maximum heart rate [17].

b) Anaerobic exercise program:

The second group of anaerobic exercise program had exercise for two months as follow: warming up was done before the exercise program, including walking on the treadmill for 5 minutes at speed 1.5 km / h with zero inclination. The duration was a short period of high-intensity anaerobic exercise, started with 2 minutes and the was gradually increased up to 10 seconds each session until reaching 3 minutes. Then, there was a break for 2 minutes; this procedure was repeated 5 times in each session. The mode was run on electronic treadmill with inclination. The frequency was three times per week; for three months. Intensity was gradually increased from 85 % to 93 % of maximum heart rate [18].

Finally, cooling down procedure for all subjects after the exercise program included walking on the treadmill for 5 minutes at speed of 1 km / h, with zero inclination and gradually decreasing speed until reaching zero.

2. Analytical methods:

a) Blood sampling and laboratory methods:

Blood samples were taken at the exercise days after at least a 10-hour overnight fasting and a small standardized breakfast by a clean vein-puncture (20 gauge needle) from an ante-cubital vein under controlled venous stasis (< 30 s) of 40 Torr after 30 minutes rest and immediately after exercise. All vein-punctures were taken from the subjects in reclined position. Whole blood was drawn and collected in three different test tubes; one containing no anticoagulant for the study of lipid profile, while the other two tubes contained ethylenediaminetetraacetic acid–treated (EDTA) for complete blood count (CBC) and platelet activation study by flow cytometry.

b) Complete Blood Count (CBC):

Complete blood count was performed on the ethylenediaminetetraacetic acid-treated blood sample using a Beckman Coulter AC-T (Beckman Coulter, Fullerton, CA, USA) at king Abdulaziz University Hospital. Complete blood count provided red blood cell, white blood cells (WBC), platelet (Plt) numbers and measurement of hematocrit (Hct) and hemoglobin (Hgb).

c) Biochemical Parameters:

Biochemical parameters including serum for total Cholesterol (Chol), Triglycerides (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL) were measured at the same time when the medical pre-check up was performed. All the biochemical assessments were performed using a fully automated analyzer (Dimenition RxL, Diagnostics) machine at king Abdulaziz University Hospital.

d) Flow cytometric analysis:

Direct immuno-fluorescence technique was used for the determination of changes in platelet activity and response to exercise. Fluorescein-isothiocyanat (FITC), anti-CD62P-FITC, and Phycoerythrin (PE)-conjugated anti-CD42b-PE (Becton-Dickinson, San Jose, CA, USA), were used in this study. Platelet rich plasma (PRP) was prepared by centrifugation of whole blood at 900 rpm for 10 minutes. An aliquot of 100 µl platelet-rich-plasma was directly labeled with monoclonal antibodies. For analyses of CD42b, CD62p (P-selectin) and IgG isotype controls were applied to detect non-specific staining (Becton Dickinson, Mountain View, USA). After incubation (30 minutes at 20 ± 2°C) in a dark place, the samples were re-suspended in 1 ml of PBS and stored at + 4°C for a maximum of 120 minutes prior to flow cytometric analysis. CD41a was used as tagging antibody to detect CD62P positive platelets. Samples were analyzed on a FACScan® cytometer (Becton Dickinson). Fluorescent beads were applied daily to ensure the stability of the system (CaliBRITE™, Becton Dickinson). Following the setting of the appropriate threshold in the FSC, 10,000 events were acquired in a life-gate. List mode data were acquired and analyzed using CELLQuest® software (Becton Dickinson). The results were expressed percentage of antibody-positive cells. Percentage of antibody-positive cells was defined as cells with specific fluorescence higher than the isotype and autofluorescence samples.

Statistical analysis

Paired -*t*-test was used to compare between pre-test and post-test values of the investigated parameters in both groups. On the other hand, the unpaired -*t*-test was used to compare between results of both groups ($p < 0.05$).

RESULTS

As shown in table (1), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and arterial oxygen saturation (SaO_2) for patients belonging to the aerobic group (A) are shown. These data have demonstrated a significant difference in all parameters that have been measured before and after two successive months of aerobic exercises.

Table (1): Mean values of measured parameters before and after exercise in anaerobic exercise group (A).

Item		BMI (Kg/m^2)	SBP (mmHg)	DBP (mmHg)	HR (Beat/min.)	SaO_2 (%)
Mean ± SD	Before	36.45 ± 3.36	136.0 ± 5.90	87.5 ± 4.40	82.1 ± 2.7	93.34 ± 3.76
	After	30.01 ± 2.56	124.5 ± 6.80	80.1 ± 5.02	74.3 ± 3.8	98.56 ± 3.18
MD		- 6.44	- 11.50	- 7.40	- 7.80	5.22
% of Change		17.7	8.5	8.5	9.5	5.6
p value		P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**

However, there were no significant differences between the mean values of the same investigated parameters in the anaerobic group (B), as illustrated in Table (2).

Table (2): Mean values of measured parameters before and after exercise in anaerobic exercise group (B).

Item		BMI (Kg/m^2)	SBP (mmHg)	DBP (mmHg)	HR (beat/min.)	SaO_2 (%)
Mean ± SD	Before	35.95 ± 3.72	136.5 ± 4.8	88 ± 4.1	81.6 ± 3.6	93.80 ± 3.71
	After	33.54 ± 2.26	136.4 ± 5.8	88.5 ± 3.6	82.0 ± 4.6	95.51 ± 3.88
MD		- 2.41	- 0.10	0.50	0.40	1.71
% of Change		6.7	0.7	0.6	0.5	1.8
p value		> 0.05 **(N.S.)**	> 0.05 **(N.S.)**	> 0.05 **(N.S.)**	> 0.05 **(N.S.)**	> 0.05 **(N.S.)**

The physiologic impact of exercise at various durations and intensities, including measurements of lipid profile "cholesterol (Chol), triglyceride (TG), low-density lipo-protein (LDL) and high-density lipo-protein (HDL)" has been investigated. Exercises were associated with changes in the lipid profile, as has been illustrated in table (3). There was a significant decrease in the concentration of Chol, LDL and HDL. Meanwhile, there was no significant difference in the concentration of TG, with the aerobic exercise group. Conversely, there was no significant difference in these parameters in the anaerobic exercise group, except in the cholesterol concentration, which demonstrated a significant reduction, as shown in table (4).

Table (3): Mean values of measured parameters before and after exercise in anaerobic exercise group (A).

Item		Chol (mmol/L)	TG (mmol/L	LDL (mmol/Ll)	HDL (mmol/L)
Mean ± SD	Before	5.1 ± 0.3	1.0 ± 0.5	2.5 ± 0.4	1.5 ± 0.2
	After	4.6 ± 0.4	0.8 ± 0.3	2.2 ± 0.2	1.2 ± 0.2
MD		- 0.5	- 0.2	- 0.3	- 0.3
% of Change		9.8	20.0	12.0	20.0
p value		< 0.05 **(S.)**	> 0.05 **(N.S.)**	< 0.05 **(S.)**	< 0.05 **(S.)**

Table (4): Mean values of measured parameters before and after exercise in anaerobic exercise group (B).

Item		Chol (mmol/L)	TG (mmol/L	LDL (mmol/Ll)	HDL (mmol/L)
Mean ± SD	Before	5.6 ± 0.7	1.9 ± 1.3	3.4 ± 1.1	1.7 ± 0.4
	After	4.9 ± 0.5	1.3 ± 0.7	2.9 ± 1.5	1.5 ± 0.4
MD		- 0.7	- 0.6	- 0.5	- 0.2
% of Change		12.5	31.6	14.7	11.8
p value		< 0.05 **(S.)**	P > 0.05 **(N.S.)**	P > 0.05 **(N.S.)**	P > 0.05 **(N.S.)**

Another physiological impact of exercise at various durations and intensities has been measured in this study; including measurements of hemoglobin concentration, platelet count, leukocyte counts and hematocrit percentage, as demonstrated in table (5). Hemoglobin has been shown to increase after exercise; moreover there was an increase in the number of circulating platelet and in hematocrit and leukocyte counts ($P < 0.05$). There was no significant difference between aerobic and anaerobic exercise groups in the hematological parameters because both types of exercise led to an increase in hematocrit, Hgb, platelet and leukocyte counts, as seen in table (6).

Table (5): Mean values of measured hematological parameters before and after exercise in group (A).

Item		WBCs ($x10^9/L$)	Plt Count ($x10^9/L$)	Hgb Conc. (g/dl)	Hct (%)
Mean ± SD	Before	5.9 ± 0.3	225 ± 10.2	14.3 ± 0.3	39.8 ± 5.9
	After	6.5 ± 0.4	263 ± 11.8	15.5 ± 0.4	43.8 ± 4.8
MD		0.6	38.0	1.2	4.0
% of Change		10.2	16.9	8.4	10.1
p value		P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**

Table (6): Mean values of measured hematological parameters before and after exercise in group (B).

Item		WBCs ($x10^9$/L)	Plt Count ($x10^9$/L)	Hgb Conc. (g/dl)	Hct (%)
Mean ± SD	Before	6.7 ± 0.3	275 ± 13.2	13.6 ± 2.1	40.8 ± 5.9
	After	7.3 ± 0.6	290 ± 29.8	14.9 ± 1.6	42.9 ± 4.8
MD		0.6	15.0	1.3	2.1
% of Change		9.0	5.5	9.6	5.1
p value		P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**	P < 0.05 **(S.)**

The expression of platelet P-selectin is an excellent indicator of platelet α granule release and thus a direct measure of platelets activation. The P-selectin expression on platelet surface increased significantly after aerobic exercise (10.5 % vs. 15.4 %, $p < 0.05$) and more pronounced after anaerobic exercise (9.7 %, vs. 20.9, $p < 0.05$). Individual values are given as percent of platelets with P-selectin expression, as seen in table 7.

Table (7): Mean values of platelets CD markers before and after exercise in both groups.

Item		Aerobic exercise group (A)		Anaerobic exercise group (B)	
		CD42 (%)	CD62 (%)	CD42 (%)	CD62 (%)
Mean ± SD	Before	81.7 ± 8.3	10.5 ± 4.2	92.7 ± 9.3	09.7 ± 5.3
	After	88.2 ± 6.6	15.4 ± 3.2	88.9 ± 4.6	20.9 ± 6.3
MD		6.5	4.9	- 3.8	11.2
p value		< 0.05 **(S.)**	< 0.05 **(S.)**	> 0.05 **(N.S.)**	< 0.05 **(S.)**

DISCUSSION

Physical activity, particularly endurance type exercise of sufficient intensity, duration, and frequency, definitely affects weight loss, total fat content and body fat distribution. However, data comparing diet, exercise or a combination suggest that diet is more effective than exercise in causing initial weight loss [19].

Regular aerobic training induces significant adaptations both at rest and during exercise in a variety of dimensional and functional capacities related to the cardiovascular and respiratory regulation system, enhancing the delivery of oxygen into active muscles. These changes include decreases in resting and sub-maximal exercise HR, enhanced stroke volume and cardiac output, an increasing arterio-venous oxygen difference and reduction in VE during sub-maximal exercise. With an adequate training stimulus, most of these responses are independent of race, gender and age [20].

Regular aerobic training at moderate intensity levels elicits significant reductions in systolic and diastolic BP. The average training-induced reductions in SBP and DBP have varied from 2 to 11 mmHg and from 1 to 8 mmHg, respectively. Aerobic training stimulates adaptations in pulmonary ventilation during sub-maximal and maximal exercise. During maximal exercise, VE increases as VO_2 max increases. The increase in VO_2 max increases both the O_2 requirement and the corresponding need to eliminate CO_2 via alveolar ventilation [21].

High-intensity exercise (anaerobic) training has the added benefit of improving fitness, thus making low-intensity exercise less difficult and more easily tolerated. Although continuous intense exercise is difficult to maintain for extended periods of time, intense interval exercise can be easily tolerated and may be an important adjunct to lifestyle modifications for body weight control [22].

The results also indicated that there was a significant increase in SaO_2 in both aerobic exercise group and anaerobic exercise group. Where, aerobic exercise group obtained a greater increase in SaO_2 than anaerobic exercise program. This result is supported by a study reported that aerobic training induces significant physiological adaptations in the cardio-respiratory system of middle-aged men. The best markers of these adaptations were the smaller sympathetic tachycardia at comparable workloads and the improvement of oxygen transport, as documented by the increase in the anaerobic threshold and VO_2 peak during dynamic exercise [23]. The results also indicated that there was a significant reduction in HR, SBP and DBP in the aerobic exercise group at the end of aerobic exercise program.

The results of this study also indicated that there were no significant changes in HR, SBP and DBP in the anaerobic exercise group after finishing the program of anaerobic exercise. But there was significant reduction after aerobic exercise program. This reflects an increased cardio respiratory load related to the prolonged duration of training session from 20 to 30 minutes. However, the greater blood flow under the influence of the rise in heart rate and systolic blood pressure doesn't satisfy the increased oxygen requirements during anaerobic exercise. This explains the significant augmentation of pulmonary ventilation and ventilation capacity in a trial to satisfy the expanding oxygen transport requirements during maximal exercise [24].

The results concerning myocardial oxygen consumption in our study indicated that there were no significant changes after finishing the program of anaerobic exercise in myocardial oxygen consumption. But there was significant reduction after aerobic exercise program. The improvement of resting heart rate and systolic blood pressure are reflected on myocardial oxygen consumption in this study. This improvement of myocardial oxygen consumption might be due to improvement in endothelium–dependant vasodilatation both in epicardial coronary vessels. It might also be due to recruitment of coronary collateral vessels and enhanced blood flow with regulation of vasomotor tone toward vagal modulation. The myocardial oxygen consumption was lowered after eight weeks training program at 60 to 80 % of maximum HR. this improvements might be due to increased peripheral vasodilatation and, consequently, decreased after load following exercise and a reduction in adrenergic efferent stimuli [25].

Platelets are important in normal hemostasis; recent evidence emphasizes the underlying role of abnormal platelet function in acute coronary artery diseases, myocardial infarction, unstable angina and stroke. Recently there is an enormous progress has been made to understand the interaction between exercise and platelets in health and disease. The association between exercise and platelet aggregation and function, in normal healthy subjects has been extensively examined. Few studies are available on the effect of training on blood platelets and the exact effects of exercise training on platelet activation and function is not as yet known [26]. The effects concerning moderate exercise (aerobic and anaerobic) were measured using treadmill exercise on platelet function, including activation and aggregation in normal healthy individuals.

The physiologic impact of exercise at different durations and intensities, including measurements of hematological parameters, lipid profile and platelets activation was performed. Exercise was associated with changes in hematological parameters (Hgb, Hct, Plt and white blood cells count). These changes occurred in both individuals using aerobic and individuals using anaerobic kind of exercise suggesting that exercise, has a direct effect on hematopoietic indices. The hematologic data in this study were consistent with previous studies [27].

Platelet function can be assessed in several different ways. Platelet aggregometry indicates that a condition causes a change in platelet reactivity, but cannot determine if the condition directly activates platelets. On the contrary, plasma assays, such as platelet factor 4 and β-thromboglobulin, may indirectly indicate that a condition activates platelets, but cannot measure changes in cell reactivity. To address this issue, in this study flow cytometric analysis (FACS) was performed to study the effect of exercise that may induce changes of platelet reactivity by assessment of the platelet surface receptors expression, in a group of normal healthy obese students. Immunolabeling of platelet surface proteins along with (FACS) analysis allows the measurements of both the state of platelet activation and platelet reactivity.

Flow cytometry is a sensitive and reliable method to directly measure expression of these activation-dependent surface markers on platelets in whole blood with minimal handling, greatly reducing the chances of *in vitro* platelet activation. FACS analysis was used to specifically determine the expression of platelet P-selectin and the activated form of the GPIb receptor for several reasons. First, these membrane surface proteins are sensitive indicators of platelet function. P-selectin is a key adhesion molecule, expressed by both platelets and endothelial cells upon activation [28].

Platelet P-selectin is stored in the α-granules with a low level of surface expression. Following exposure to platelet agonists, such as thrombin, P-selectin is rapidly transported to the cell membrane surface increasing the potential for interactions with other cell types. P-selectin also mediates the adhesion of activated platelets to monocytes and neutrophils. The integrin GPIb receptor is typically expressed on the surface of un-stimulated platelets. However, GPIb is unable to bind its ligands (primarily fibrinogen and von Willenbrand Factor) until activation of the receptor occurs. The expression of platelet P-selectin is an excellent indicator of platelet α granule release and thus a direct measure of platelet activation. In addition, this adhesion protein may enhance coagulation by interacting with monocytes [29].

In this study, platelet activation was investigated in forty normal volunteers who underwent into two different exercise programs, a standardized protocol for quantization of the major platelet surface glycoprotein have been used in this study. In fact, using appropriate standards, Immunolabeling of platelet surface proteins along with flow cytometric (FACS) analysis allows the measurements of both the state of platelet activation and platelet reactivity. FACS analysis was used to specifically determine the expression of platelet P-selectin (CD62P) and the activated form of the GPIIb (CD42) receptor for several reasons. First, these membrane surface proteins are sensitive indicators of platelet function. P-selectin is a key adhesion molecule, expressed by both platelets and endothelial cells upon activation [30].

The finding in this study had demonstrated that, the P-selectin expression on platelet surface (as percent of platelets with positive P-selectin expression) increased significantly after aerobic exercise and more prominent after anaerobic exercise. These findings are in contrast to those results, which indicated exercise-induced platelet activation in sedentary people only [31]. The results of this piece of work confirmed other studies [32], which have been methodologically limited because of in vitro artifacts.

Platelet activation leads to their aggregation and coagulation and thus, is a critical step resulting in thrombus formation and possible subsequent cardiovascular insult. Many studies demonstrate that acute strenuous exercise leads to an increase in platelet activation, adhesiveness and aggregability: bicycle or treadmill exercise until exhaustion or anaerobic threshold was associated with platelet activation [33].

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REFERENCES

[1]. Imig, J.D., 2008. Eicosanoids and renal damage in cardio-metabolic syndrome. Expert Opin Drug Metab Toxicol , **4**: 165-174.

[2]. Druet, C., M. Dabbas and V. Baltakse, 2006. Insulin resistance and the metabolic syndrome in obese French children. Clin Endocrinol (Oxf), 64: 672-678.

[3]. Newbold, R., E. Padilla-Banks, R. Snyder and W. Jefferson, 2007. Perinatal exposure to environmental estrogens and the development of obesity. Mol Nutr Food Res, 51: 912-917.

[4]. Pasarica, M., J. Zachwieja, L. Dejonge, S. Redman and S. Smith, 2007. Effect of growth hormone on body composition and visceral adiposity in middle aged men with visceral obesity. J Clin Endocrinol Metab , 92: 4265-4270.

[5]. Mutch, D. and K. Clement, 2006. Unraveling the genetics of human obesity. PLOS Genet, 2: 188.

[6]. Pasarica, M. and N. Dhurandhar, 2007. Infect-obesity: obesity of infectious origin. Adv Food Nutr Res, 52: 61-102.

[7]. Farooqi, S., 2005. Genetic and hereditary aspects of childhood obesity. Best Pract Res Clin Endocrinol Metab, 19: 359-374.

[8]. Hamilton, M., D. Hamilton and T. Zderic, 2007. The role of low-energy expenditure and sitting on obesity metabolic syndrome, type II diabetes and cardiovascular disease. Diabetes, 56: 2655-2667.

[9]. Poirier, P., T. Giles, G. Bray ,Y. Hong, J. Stern, F. Pi-Sunyer and R. Eckel ,2006. Obesity and cardiovascular disease: Pathophysiology, evaluation and effect of weight loss. Arterioscler Thromb Vasc Biol, 26: 968-976.

[10]. Rubenstein, A., 2005. Obesity: A modern epidemic. Trans Am Clin Climatol Assoc, 116: 103-111.

[11]. Cohen, P., 2007. Obesity in men: The hypogonadal-estrogen receptor relationship and its effect on glucose homeostasis. Med Hypotheses, 70: 358-360.

[12]. Levitsky, D., 2005.The non-regulation of food intake in humans: Hope for reversing the epidemic of obesity. Physiol Behav, 86: 623-632.

[13]. Singer, G. and N. Granger, 2007. Inflammatory responses underlying the micro-vascular dysfunction associated with obesity and insulin resistance. Microcirculation, 14: 375-387.

[14]. Antic, V., A. Dulloo and J. Montani, 2003. Multiple mechanisms involved in obesity-induced hypertension. Heart Lung Circ, 12: 84-93.

[15]. Skinner, J., A. Jaskolski, A. Jaskolska, J. Krasnoff, J. Gagnon, A. Leon, D. Rao, J. Wilmore and C. Bouchard, 2001. Age, sex, race, initial fitness, and response to training: the heritage Family Study. J Appl Physiol 2001; 90: 1770-1776.

[16]. Hunter, G., M. Weinsier, and D. Larson, 1998. A role for high intensity exercise on energy balance and weight control. International journal of obesity, 22: 489-493.

[17]. El-Sayed, M., 2001. Exercise *and training effects on platelets in health and disease.* Platelets 2002; 13: 261-266.

[18]. Janssen, P., 2001. Training at anaerobic threshold: Lactate threshold training. Patricia, Julie and Myla eds. United States: Human Kinetics, pp: 25-41.

[19]. Saranac, L., B. Bjelakovic, H. Stamenkovic and B. Kamenov, 2007. Orexitropic signaling proteins in obese children. Scientific World J, 7: 1263-1271.

[20]. Oner-Iyidogan, Y., H. Kocak, F. Gurdol, P. Oner, H. Issever and D. Esin, 2007. Circulating ghrelin levels in obese women: a possible association with hypertension. Scand J Clin Lab Invest, 67: 568–576.

[21]. Kuchta, K., 2005. Pathophysiologic changes of obesity. Anesthesiol Clin N Am, 23: 421-429.

[22]. Funahashi, T. and Y. Matsuzawa, 2007. Metabolic syndrome: Clinical concept and molecular basis. Ann Med, 23: 1-13.

[23]. Frisbee, J. and M. Delp, 2006. Vascular function in the metabolic syndrome and the effects on skeletal muscle perfusion: Lessons from the obese Zucker rat. Essays Biochem, 42: 145-161.

[24]. Eckel R., S. Grundy and P. Zimmet, 2005. The metabolic syndrome. Lancet, 365: 1415-1428.

[25]. Gawaz M., H. Langer and A. May, 2005. Platelets in inflammation and atherogenesis. J Clin Invest, 115: 3378-3384.

[26]. Lee K. and G. Lip, 2003. Effect of lifestyle on hemostasis, fibrinolysis and platelet reactivity. Arch Intern Med, 163: 2368-2392.

[27]. Sestito, A., A. Maccallini, G. Sgueglia, F. Infusino, C. Larosa and C. Aurigemma, 2005. Platelet reactivity in response to mental stress in syndrome X and in stable or unstable coronary artery disease. Thromb Res , 116:234-241.

[28]. Carter, J., E. Banister and A. Blaber, 2003. The effect of age and gender on heart rate variability after endurance training. Med Sci Sports Exerc, 35:1333-1340.

[29]. Skinner, J., A. Jaskolski, A. Jaskolska, J. Krasnoff, J. Gagnon, A. Leon, D. Rao, J. Wilmore and C. Bouchard ,2001. Age, sex, race, initial fitness and response to training: the heritage Family Study. J Appl Physiol, 90: 1770-1776.

[30]. Fagard, R., 2001. Exercise characteristics and the blood pressure response to dynamic physical training. Med Sci Sports Exerc, 33 (Suppl 6): 484-494.

[31]. Deschenes, M. and W. Kraemer, 2002.Performance and physiologic adaptations to resistance training. Am J Phys Med Rehabil, 81(Suppl 11): S3-16.

[32]. Juel, C., C. Klarskov, J. Nielsen, P. Krustrup, M. Mohr and J. Bangsbo, 2004. Effect of high-intensity intermittent training on lactate and H+ release from human skeletal muscle. Am J Physiol Endocrinol Metab, 286: 245-251.

[33]. O'Donovan, G., A. Owen, S. Bird, E. Kearney, A. Nevill, D. Jones and K. Woolf-May, 2005. Changes in cardio-respiratory fitness and coronary heart disease risk factors following 24 wk of moderate- or high-intensity exercise of equal energy cost. J Appl Physiol, 98: 1619-1625.