Iranian Journal of Health and Physical Activity (2014) 5 (1), (43-49)

Effects of Regular Aerobic Exercise Combined with Milk Consumption on Angiotensin II, ACE and AT1 levels in Obese Prepubertal Boys

Parvin Farzanegi[1*], Mohammadali Azarbaijani [2], Kasra Manouchehri[3]

[1] *Department of Exercise Physiology,Faculty of Humaneties, Sari Branch, Islamic Azad University, Sari,Iran*
[2] *Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences, Central Tehran Branch, Islamic Azad University,Iran*
[3]*Mazandaran science and Research Branch,Islamic Azad University,Mazandaran,Iran*

Received 2 December 2013 Accepted 23 February 2014

Abstract

Purpose: This study aimed to investigate the effects of eight weeks of regular aerobic exercise combined with milk consumption on angiotensin II, ACE and AT1 levels in obese prepubertal boys.

Material and Methods: 28 healthy obese prepubertal boys, 9 to 11 years old, were selected and randomly divided into four groups: exercise (Exe), exercise-supplement (Exe-Sup), control (Con) and supplement (Sup). Exercise program included three sessions of aerobic exercise (60% - 75% of maximum heart rate). Milk consumer groups received 300 ml of low-fat cow milk every day. Blood samples were collected before and after the eight weeks.

Results: After eight weeks, a significant reduction was observed in angiotensin II, AT1, and ACE levels in the Exe (p= 0.000, p=0.000, p= 0.000 respectively), Exe-Sup (p= 0.000, p=0.000, p=0.002 respectively) and Sup group (p= 0.000, p=0.001, p=0.000 respectively).

Discussion and Conclusion: The results showed that regular aerobic exercise may decreased angiotensin II, AT1 and ACE indices and that, this effect was highly intensified when exercise was combined with milk consumption. However, further study is required for more accurate results.

Key words: Angiotensin II, Angiotensin II Receptor, Angiotensin-Converting-Enzyme, Obese prepubertal boys, Aerobic exercise, Milk supplement

Introduction

Epidemiological studies show that obesity is a common disease in the present era that has become a problem of global concern [1,2]. Many internal and environmental factors play a role in formation and prevalence of obesity such as cultural, social, economic, and genetic factors, as well as lifestyle and diet [3]. Obesity paves the ground for cardiovascular diseases and hypertension, which are the main causes of death in the world [4]. Studies show that many adulthood diseases are rooted in childhood, including cardiovascular disease, hypertension, atherosclerosis, and renal failure, which in turn, pave the way for non-communicable diseases [5]. Previous studies have shown that chronic hypertension leads to disturbance in fluid balance and homeostasis of the body by damaging various body tissues, including the heart and blood vessels [6]. On the other hand, the mentioned non-communicable diseases, in turn, restrict mobility and intensify this closed cycle [7]. Available evidence indicates widespread prevalence of hypertension worldwide, and children and adolescents are not excluded [8]. Treatment of childhood obesity requires a long-term process, contrary to the prevention and treatment of its related diseases including hypertension, especially in the critical period of puberty. Therefore, taking advantage of preventive intervention programs, such as exercise and nutritional programs seem logical [9]. Angiotensin II, Angiotensin-Converting-Enzyme (ACE) and Angiotensin II Receptor (AT1) are biomarkers with peptide chemical structure, which have a powerful function in the renin-angiotensin system in increasing blood pressure and are considered as an index of inflammation in the target tissue [10]. Exercise and nutrition affect the mentioned biomarkers. It has been found that good physical activity has a positive effect on health levels [11]. In a study on obese

∗ Corresponding author E-mail:
parvin.farzanegi@gmail.com

people with hypertension, Schoenenberger et al. (2007) showed that weight loss through diet intervention resulted in a significant decrease in blood pressure at rest and exercise modes, along with improved cardiac output status [12]. Habibzadeh et al. (2010) reported that regular exercise reduced cardiovascular risk factors by changing lipoprotein metabolism [13]. About the role of nutrition, milk is a perfect food with a high value in growth, metabolism, and the immune system. Unfortunately consumption of milk as compared to other sweetened beverages, has decreased among children and adolescents during the past ten years and it is likely to be an important factor in the prevalence of obesity and hypertension [14]. It has been shown that the consumption of milk and dairy products balances metabolism and reduces some inflammatory indicators [15]. The study by St-Onge et al.(2009) revealed that very low-fat milk consumption by children improves their insulin levels [16]. Having too much calcium and peptides bondable with peptide ligands of biomarkers of angiotensin II, AT1 and ACE, milk inhibits these inflammatory indicators in the renin-angiotensin system and decreases blood pressure [17]. There are quantitative studies on the effect of exercise combined with milk consumption in childhood before the age of puberty, but most previous studies had a therapeutic approach and were associated with adults and animal specimens suffering from hypertension [18, 19]. The present study examined the effects of regular aerobic exercise combined with milk consumption on angiotensin II, AT1 and ACE levels in obese prepubertal boys.

Material and Methods

Subjects

This study was a quasi-experimental, clinical trial with a control group and a pre-test, post-test design. The study population consisted of obese boys in A zadshahr City, in 2012. For the purposes of this study, 28 healthy, obese children 9 to 11 years old with, a BMI above the 95th percentile of the standard for sex and age, without athletic background, disease and lactose allergy, who could stand the daily consumption of 300 mL of low-fat cow milk , provided that their parents were not suffering from non-communicable diseases of diabetes, cardiovascular and hypertension volunteered to take part in the study. (Table 1 shows the subjects' characteristics). Subjects were then divided into four groups: exercise (Exe), exercise-supplement (Exe-Sup), control (Con) and supplement (Sup). Before the exercise protocol, all subjects completed a consent form and a sports-medical record questionnaire. Height and weight of subjects were measured using a standard digital scale and diometer with a precision of 0.1 kg and 0.1 cm respectively.

Exercise protocol included doing aerobic exercises for 8 weeks, three 90-minute sessions per week. Each exercise session included 10 minutes of general warm-up, 10 minutes of specific warm-up, 60 minutes of aerobic exercise and doing basic and exclusive techniques of karate within the desired heart rate range, and 10 minutes of cool-down. Using Polar) chest belts (f-11, Germany, the intensity of exercises for the first week was determined 60% of maximum heart rate to which 5% was added progressively every two weeks so that in the last week, 75% of maximum heart rate was considered for the subjects' exercises [17].

Diet and supplements

According to the nutritional protocol used in the study by St-Onge et al. (2009), foods were divided into three main categories [16]. The first category included foods without restrictions on the amount and timing of consumption, such as low-fat fruits and vegetables. The second category was composed of low-fat protein (fat <9%), low-fat dairy products (fat <5%), low-fat grains (fat <3%), starchy grains and vegetables (fat <3%) with restrictions on energy production; they were consumed five times a week (three main meals a day and 3 to 8 Snack). The third category included fatty proteins (fat >9%), fats, vegetables and grains (fat >3%) and other similar high energy foods, with this restriction: they were consumed as a meal only one day in a week, or the same meal was split in the same day or some consecutive days within a week. One week before the start of the study, all subjects were instructed to identify foods and how to read food labels and consume foods in a training/justification session; and at least one parent attended the training and justification programs. To complete the present plan, the program was set up separately for each group to use drinking supplements combined with their basic daily diet in such a way that the supplement groups received 300 ml of natural low-fat cow milk (1% fat) every day. On the contrary, the control and exercise groups received 200 ml of other sugar drinks, twice a day, with the same amount of energy produced during a week. During the research program, all groups were monitored and consulted by a physician and nutritionist. 24 hours before the start of the first session and 48 hours after the end of the last exercise session, 7 cc blood samples were taken from the brachial vein after 12 to 14 hours of fasting, and between 8 and 10 o'clock in the morning. Once serum was obtained from heparinized blood using floating centrifuge vessel (3000 rpm) for 10 minutes, the measurement of angiotensin II and AT1 was done by the ELISA method using specific kits (Cusabio company, China) with sensitivity 0.04 ng/m. Moreover, ACE was measured by the uv/fixed method using ACE kit (Ziestchem Diagnostice Tehran Company, Iran) with a sensitivity range of 3-150 U/L. For the assessment of inter-group variations, paired t-test was used. To determine the differences between groups, one-way analysis of variances (ANOVA) with the post hoc Tukey test was used. The Shapiro Wilkie test was used to assess normality of the variables distribution . P-values <0.05 were considered statically Significant.

Results

The general characteristics of the participants are presented in table 1. After 8 weeks, a significant reduction was observed in angiotensin II levels in Exe-Sup (P=0.000), Sup (P=0.000) and Exe groups (P=0.000) groups. A significant reduction was also observed in AT1 levels in Exe-Sup (P=0.000), Exe (P=0.001), Sup groups (P=0.001). Assessment of other data revealed a significant reduction in ACE levels in Exe-Sup (P=0.002), Exe (P=0.000) and Sup groups (P=0.000). tukey test results also showed that there was a significant difference in ACE levels between the Exe and the Exe-Sup groups (p=0.027), between the Con and Sup groups (p=0.042) and in AT1 levels between the Exe and Exe-Sup groups (p=0.003) (Figure 1).

Table 1: Clinical characteristics of study subjects at baseline

Variables	EG(n=8)	E-SG (n=8)	SG (n=8)	CG(n=8)	P value
Age, yr	11.83 ± 6. 9	11.17±4.8	11.33±5.08	10.17 ± 6.34	0.466
Weight, kg	59.5 ± 4.96	58.83±7.88	59.5 ± 6.89	58.67 ± 6.44	0.775
Height, cm	143.5 ± 6.53	145.5 ± 6.5	146.17 ± 3. 5	147.4 ± 3.54	0.602
BMI, Kg/m^2	29. 1 ± 5. 4	28.01 ±5.35	27.93 ± 4.13	27.16 ± 4. 5	0.550

Values are presented as mean ± standard deviation. EG, exercise group; E-SG, exercise-supplement group; SG, supplement group CG, control group; BMI, body mass index.

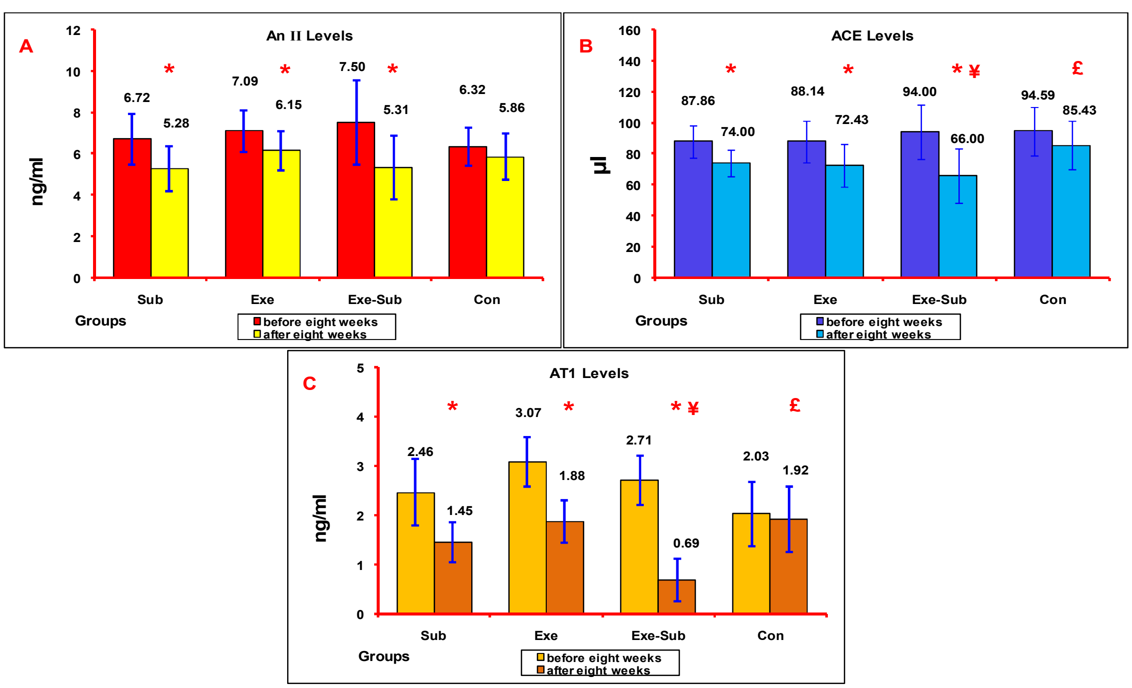

Figure 1: Changes in the measured variables in the 4 study groups before and after 8 weeks. EG, exercise group; E-SG, exercise-supplement group; SG, supplement group; CG, control group; An II, angiotensin II; AT1, Angiotensin II Receptor; ACE, Angiotensin-Converting-Enzyme; * changes of variables within groups; ¥ significant difference between EG and E- SG groups; £ significant difference between CG and SG groups.

Discussion and Conclusion

Exercise and nutrition play an important role in reducing obesity. However, obesity gives a lower response to treatment as compared to other non-communicable diseases associated with it, and it requires longer treatment period. Therefore, it is imperative to identify and control effective factors in negative side-effects of obesity, such as hypertension [20,21].

The results of this study showed a significant reduction in angiotensin II levels as a powerful constrictor of blood vessels and multiplier of blood pressure in the Exe-Sup, Exe and Sup groups tested (figure 1 A). The greatest decrease was associated with the Exe-Sup (29.2%), Sup(21.43%) and Exe(13.26%) groups. These figures indicate that milk consumption led to more reduction in angiotensin II levels.

Previous studies in this regard were mostly associated with patients, adults and animal specimens [22]. Richard et al. (2000) reported that due to containing LPP[1] and VPP[2] tripeptides, sour milk reduced blood pressure in patient mice by adjusting the RAS[3] function and reducing angiotensin [23]. Some other studies have reached contradicting results. Karandish et al. (2009) did not positively evaluate the effect of consuming the Whey protein supplement (available in cheese-water) combined with exercise on hematologic changes. It could be due to the type of subjects and the level of physical activity [24]. However, our data suggests that the reduction level observed in the Exe group represented the lower efficacy of exercise as compared to milk in this regards. Due to different mechanisms of exercise in reducing blood pressure, such as reducing sympathetic activity combined with reducing vascular resistance, insulin resistance, and stress, as well as greater synthesis of nitric oxide (NO) and the production of bradykinin, the observed reduction in angiotensin II levels in the Exe group may be due to this mechanism [25]. In this regard, a study by Fernandez et al. (2012) showed that 10 weeks of aerobic swimming exercise led to higher concentrations of nitrite in blood, endothelial growth, higher absorbance of oxygen and citrate synthase, synthesis of NO, lower resting heart rate and blood pressure in mice with hypertension [26]. Zamo et al. (2011) observed a positive impact of exercise on reducing angiotensin II levels of blood pressure in rat, which is consistent with the present study. Moreover, the results obtained in the Sup group can be attributed to the metabolic role of milk in better balancing metabolism, which indeed led to higher effectiveness of exercise in the subjects [27].

Martinelli et al. (2010) reported that aerobic exercise reduced plasma renin activity in patients with overweight and hypertension [28]. Dengel et al. (1998) positively evaluated the separate effects of exercise and a calorie-restricted diet in reducing overweight and hypertension, but they did not observe higher effects in the combined program, which is not consistent with the present study and may be due to the amount of exercise, subjects' differences or the lack of milk consumption [29]. In general, given that angiotensin is the product of the renin-angiotensin system, most studies point to the role of ACE and AT1 enzymes active in this system for producing and absorbing angiotensin II, which is also addressed in this study.

Other result from this study show a significant reduction in the ACE levels of the Exe-Sup (29.78%), Sup (15.77%) and Exe (17.8%) groups, (figure 1 B). So aerobic exercise and milk consumption alone are effective in reducing serum ACE but this effect is far more in a combined program. Our results also show that the reducing effect of milk was a little higher while the effect of the combined program was considerably higher. Seppo et al. (2003) reported that daily consumption of 150 ml of milk fermented by lactobacillus helveticus bacteria reduced ACE levels and therefore, systolic and diastolic blood pressures in patients with hypertension, but it did not have any significant effect on healthy individuals. Among possible reasons for this result, one can point to the different proteins in normal milk (casein) and fermented milk (tripeptide) and also the lack of physical activity [30]. In this regard, Athithan et al. (2009) showed that prolong consumption of both proteins of casein in normal milk and tripeptide of fermented milk decreased ACE, total cholestrol (TC) and Triglyceride (TG) levels in the rats [31].

Thomas et al. (2012) observed that consumption of low-fat milk powder along with high calcium, led to significant reduction in weight, fat mass and biomarkers associated with hypertension, including

1. Leucine-Proline-Proline
2. Valin-Prolin-Prolin
3. Renin Angiotensin System

ACE in rats. They concluded that high calcium consumption along with a good diet was more effective in improving obesity and hypertension [32]. In this regard, Jinaping et al. (2006) found that tripeptide (VPP) and dipeptide (IPP) in fermented milk could be combined with peptide bonds of ACE, which has a key role in the RAS and also bradikinin degradation (vascular dilating substance secreted from endothelial cells), so they could inhibit and reduce blood pressure through reducing angiotensin synthesis and dilating blood vessels. On the other hand, by affecting the synthesis of protein and amino acids, they increase hydrophobic properties of the cell wall and regulate interstitial water [33]. The results of these studies are consistent with the present study that could be due to milk consumption in common. Moreover, the observed reduction of ACE in the Exe group might be caused by various mechanisms. Boix et al. (2004) reported that regular and continuous exercise and captopril medicament consumption, each inhibited and reduced ACE. However, this effect was not intensified in a combined program [34,35].

The other result of this study showed a decrease in AT1 levels in the Exe-Sup (74.53%), Sup (41.05%) and Exe (38.76%) groups (figure 1 C). It indicates the more effective role of milk as compared to aerobic exercise and specifies that either aerobic exercise or milk consumption had a favorable effect on reducing AT1 levels. However this effect was higher in aerobic exercise combined with milk consumption. Some studies consistent with the present study considered a prominent role for exercise and physical activity in AT1 inhibition, and some others for the consumption of milk and dairy products. Sipola et al. (2001) positively evaluated the effect of long term consumption of milk and peptides available in dairy products in the inhibition of ACE and AT1, which has a key role in the RAS, only in rats with hypertension. Inconsistent results might be due to the type of subjects and lack of physical activity [36].

Siampone et al. (2011) observed that swimming training for 6 to 16 weeks significantly reduced AT1 levels and creatinine excretion, increased sodium excretion through kidneys and urine, and reduced blood pressure in rat. Their results are consistent with the present study in terms of reduced AT1 levels and modulated RAS activity, and are inconsistent, in terms of having healthy subjects. This difference could be due to the type of subjects and exercise [37]. Adams et al. (2005) reported that exercise training reduced oxidative agents such as NAD(P)H[1] oxidase and released nitric oxide by reactive oxygen species (ROS) and inhibited AT1 [38]. The reasons for lack of similarity between their results and ours might be due to the different type of exercise applied, milk consumption and/or AT1 inhibitors.

Results from the present study showed that aerobic exercise adjusts the factors affecting the incidence of hypertension in prepubertal obese boys and that milk supplementation may enhance this effect. Therefore, in order to obtain better results, it is recommended to use a combination of the two interventions as a preventive measure for hypertension incidence in prepubertal obese boys.

References

1- Reinher T, Wabisch M (2011). Childhood obesity. Current Opinion in Lipidology 22: 21–25.

2- Mamun AA, O'Callaghan MJ, Cramb SM, Najman JM, Williams GM, Bor W (2009). Childhood behavioral problems predict young adults' BMI and obesity: evidence from a birth cohort study. Obesity (Silver Spring) 17(4):761-766.

3- Mostafavi H, Dabagh Manesh MH, Zare N (2005). Prevalence of obesity and over weight in adolescents and adult population in Shiraz. Iranian Journal of Endocrinology and Metabolsim 7: 57-66.

4- Ahmadi S, Shahsavari S, Ahamdi H, Tabatabaeifar T (2010). Prevalence of Overweight, Obesity and Underweight. Iranian Journal of Endocrinology and Metabolsim 12: 153-159.

5- Cui MJ, Zhang BH, Xiao QF, Zhu FL, Wang HY(2011). The relationship between hyperuricaemia and clinic pathology of IgA nephropathy. Zhonghua Nei Ke Za Zhi 50(8):659-663.

6- Freedman DS, Dietz WH, Srinivasan SR, Berenson GS(1999). The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. Pediatrics 103(6 Pt 1):1175-1182.

7- Martinelli B, Barrile SR, Arca EA, Franco RJ, Martin LC(2010). Effect of aerobic exercise on plasma renin in overweight patients with hypertension. Arq Bras Cardiol 95(1):91-98.

8- Guinn CH, Baxter SD, Litaker MS, Thompson WO(2007). Prevalence of Overweight and At Risk of Overweight in Fourth-Grade Children across Five School-Based Studies Conducted during Four School

1. Nicotinamide adenine dinucleotide phosphate

Years. J Child Nutr Manag 361(1).

9- Lurbe E, Cifkova R, Cruickshank JK, Dillon MJ, Ferreira I, Invitti C, Kuznetsova T, Laurent S, Mancia G, Morales-Olivas F, Rascher W, Redon J, Schaefer F(2010). Management of high blood pressure in children and adolescents: Recommendations of the European Society of hypertension. An Pediatr (Barc). 73(1):28-51.

10- Kishi T, Hirooka Y, Konno S, Sunagawa K (2012). Angiotensin II receptor blockers improve endothelial dysfunction associated with sympathetic hyperactivity in metabolic syndrome. J Hypertens. 30(8):1646-1655.

11- Zarei M, HamidNia MR, Mhmdnya A, Jaberi M (2010). Fat oxidation and energy consumption of different types of exercise, running and cycling in obese adolescent boys. Iranian Journal of Endocrinology and Metabolism 12 (3): 283 – 293.

12- Schoenenberger AW, Schoenenberger-Berzins R , Suter P M, Zuber M (2007) . Effect of moderate weight reduction on resting and exercise blood pressure in overweight subjects. Journal of Human Hypertension 21:683–685.

13- Habib Zadeh SN, Rahmani Nia F(2010). The effect of two months examine aerobic exercise on serum's lipids and body mass index in obese adolescents, Journal of School, Mashhad University of Medical Sciences 54 (2): 100-104.

14- Rosado JH (2011). Intake of milk with added micronutrients increases the effectiveness of an energy restricted diet to reduce body weight :Randomized controlled clinical trial in mexician women. J Am Diet Assoc 111(10):1507-1516.

15- Minervini F, Bilancia MT, Siragusa S, Gobbetti M, Caponio F (2009). Fermented goats' milk produced with selected multiple starters as a potentially functional food. Food Microbiol. 26(6):559-564.

16- St-Onge MP, Goree LL, Gower B (2009). High-milk supplementation with healthy diet counseling does not affect weight loss but ameliorates insulin action compared with low-milk supplementation in overweight children. J Nutr 139(5):933-938.

17- Nassis GP, Papantakou K, Skenderi K, Triandafillopoulou M, Kavouras SA, Yannakoulia M, Chrousos GP, Sidossis LS(2005). Aerobic exercise training improves insulin sensitivity without changes in body weight, body fat, adiponectin, and inflammatory markers in overweight and obese girls. Metabolism 54:1472 –1479.

18- Steward NF (2009). independent and combined influence of AGTR1 variants and aerobic exercise on oxidative stress in hypertensives. J Blood press 18(4):204-212.

19- Symons JD, Stebbins CL, Musch TI (1999). Interactions between angiotensin II and nitric oxide during exercise in normal and heart failure rats. J Appl Physiol 87(2):574-581.

20- Taguchi K(2012). Angiotensin II type 2 receptor-dependent increase in nitric oxide synthase activity in the endothelium of db/db mice is mediated via a MEK pathway. Pharmacol Res 66(1): 41-50.

21- Troiano RP, Flegal KM, Kuczmarski RJ, Campbell SM, Johnson CL (1995). Overweight prevalence and trends for children and adolescents. The National Health and Nutrition Examination Surveys, 1963 to 1991. Arch Pediatr Adolesc Med 149(10):1085-1091.

22- Baños M, Arellano-Mendoza MG, Vargas-Robles H, Avila-Casado MC, Soto V, Romo E, Rios A, Hernandez-Zavala A, de la Peña-Diaz A, Escalante B (2011).Relationship between angiotensin II receptor expression and cardiovascular risk factors in Mexican patients with coronary occlusive disease. Exp Mol Pathol 91(1):478-483.

23- Richard J, Meisel H(2000). Milk's protein derived peptide inhibitors of angiotensinI converting Enzyme. J Bri Nutr. 84(1):33-37.

24- Karandish M (2008). Effects of Whey protein supplementation on blood parameters after resistance exercise in healthy young athletes. Iranian Journal of Endocrinology and Metabolism 10 (4): 373-379.

25- Nassi GP, Papantakou K, Skenderi K, Triandafillopoulou M, Kavouras SA, Yannakoulia M, Chrousos GP, Sidossis LS(2005). Aerobic exercise training improves insulin sensitivity without changes in body weight, body fat, adiponectin and inflammatory markers in overweight and obese girls. J Metabolism 54(11):1472-1479 .

26- Fernandes T, Nakamuta JS, Magalhães FC, Roque FR, Lavini-Ramos C, Schettert IT, Coelho V, Krieger JE, Oliveira EM (2012). Exercise training restores the endothelial progenitor cells number and function in hypertension: implications for angiogenesis. J Hypertens 30(11):2133-2143.

27- Zamo FS, Barauna VG, Chiavegatto S, Irigoyen MC, Oliveira EM (2011). The rennin angiotensin system is modulated by swimming training depending on the age of spontaneously hypertensive rats. Life Sci 89(3-4):93-99.

28- Martinelli B, Barrile SR, Arca EA, Franco RJ, Martin LC(2010). Effect of aerobic exercise on plasma renin in overweight patients with hypertension. Arq Bras Cardiol 95(1):91-98.

29- Dengel DR, Galecki AT, Hagberg JM, Pratley RE(1998). The independent and combined effects of weight loss and aerobic exercise on blood pressure and oral glucose tolerance in older men. Am J Hypertens 11(12):1405-1412.

30- Seppo L, Jauhiainen T, Poussa T, Korpela R (2003). A fermented milk high in bioactive peptides has a blood pressure–lowering effect in hypertensive subjects. Am J Clin Nutr 77:326–330.

31- Athithan LV, Jayaratne SD, Peiri s H, Jayesekera S (2009).The effect of milk proteins and curd on serum

Angiotensin Converting Enzyme activity and lipid profile in Wistar rats. J.Natn.Sci.Foundation Sri Lanka 37 (3):209-214

32- Thomas AP, Dunn TN, Drayton JB, Oort PJ, Adams SH (2012). A high calcium diet containing nonfat dry milk reduces weight gain and associated adipose tissue inflammation in diet-induced obese mice when compared to high calcium alone. Nutr Metab (Lond) 23;9(1):3.

33- Jinaping WU, Rotimi E, Nakai S(2006). Structural Requirements of Angiotensin I-Converting Enzyme Inhibitory Peptides: Quantitative Structure-Activity Relationship Study of Di- and Tripeptides. J Agric(Food Chem) 54:732-738.

34- Boix F, Røe C, Rosenborg L, Knardahl S(2004). Effect of chronic exercise and Angiotensin-converting enzyme inhibition on rodent thoracic aorta. J Cardiovasc Pharmacol 44(5):582-590 .

35- Westerkamp CM, Gordon SE (2004). Angiotensin-converting enzyme inhibition attenuates myonuclear addition in overloaded slow-twitch skeletal muscle. J Cardiovasc Pharmacol 44(5):582-590.

36- Sipola M, Finckenberg P, Santisteban J, Korpela R, Vapaatalo H, Nurminen ML (2001). Long term intak of milk peptides attenuates development of hypertension in spontaneously physiology and hypertension Rats. J physiology and pharmacology 52(4):745-754.

37- Ciampone R, Borges IP, de Lima FF, Mesquita EC, Cambiucci JA(2011). Long-term exercise attenuates blood pressure responsiveness and modulates kidney angiotensin II signalling and urinary sodium excretion in HSR. J Renin Angiotensin Aldosterone Syst 12(4): 394 - 403.

38- Adams V, Linke A, Kränkel N, Erbs S, Gielen S, Möbius-Winkler S, Gummert JF, Mohr FW, Schuler G, Hambrecht R(2005). Impact of regular physical activity on the NAD(P)H oxidase and angiotensin receptor system in patients with coronary artery disease. Circulation 8;111(5):555-562.