CHAPTER IV

DISCUSSION

This is the first study in Thailand to report that moderate intensity exercise can reduce oxidative stress by stimulating antioxidant defense system and can improve lipid profile in elderly Thai men. It is widely accepted that free radicals generation is enhanced during strenuous exercise (8,11,12,97). Aerobic exercise has been reported to increase the production of oxygen free radicals and oxidative stress, because of electron leakage at intermediary steps in the mitochondrial electron transport chain (46,57). However, regular exercise has been claimed to reduce lipid peroxidation by inducing antioxidant or by scavenging enzyme activities (70,92,93). The results of this investigation demonstrate that moderate intensity exercise of 30 minutes duration, 3 days per week for 12 weeks in elderly men can be an oxidative stressor which alter antioxidant capacity and lipid profile whereas vitamin E supplementation does not show additional effect over exercise only.

Subjects

The volunteers of this study are aging population in Chiang Mai province. All subjects were healthy, non-smokers with normal medical history and had not been engaged in regular aerobic exercise. A face to face interview about food consumption was conducted with every participant and details of frequency questionnaire was completed in order to obtain information about their dietary habit one week before the experiment began and throughout the project. It was found that there were no significantly difference in dietary intake among the volunteer. In addition, the propose of choosing sedentary subject from the same province was to minimize the differences in environment and life style. Thus, these elderly men in this study were good models for the experiments of the intensive exercise training and vitamin E supplement program.

Effect of exercise training and exercise training plus vitamin E supplement on physical fitness

Exercise of a sufficient intensity and duration has been shown to increase some indicators of oxidative stress (102). In this study, exercise training program was cycling at 70%, 30 minutes per day, 3 days per week for 12 weeks which is a hard exercise for aging. According to the guideline for aerobic exercise prescription for healthy adults recommended by the American College of Sports Medicine (76), an intensity of 60% to 75% of HRmax, 3 days per week for at least 6 weeks is proper in developing and maintained cardiorespiratory and muscle fitness in older persons. It is well accepted that aerobic capacity will be improved if exercise is done at sufficient intensity to increase heart rate to about 70% of HRmax so it is likely that our exercise protocol was vigorous enough to induce the oxidative stress (103).

In this study we have demonstrated that aerobic capacity was improved significantly in both groups of subject under 12-weeks receving moderate intensity exercise program. All of subjects had no change in resting heart rate after 12-weeks training (Table 4). It was similar to previous reported by Merdith, C.N. et. al. (104). After training the systolic blood pressure was significantly lowered and diastolic blood pressure has attendency to decline comparing with those before the exercise training. It has generally been thought that training apparently increases parasympathetic activity to the heart with a reduction in resting sympathetic activity. It is possible that decreasing in sympathetic tone might reduced total peripheral resistance (100). The peripheral adaptation is an important factor in the response to exercise training in aging (104,105) and peripheral resistance is possibly reduced. Furthermore, the VO_2max after exercise training in both groups of subject was significantly higher than that before exercise training found in this study. This result is in agreement with other studies reported that VO_2max in trained subjects was significantly higher than in sedentary subjects (29,79,80,106). The exercise training-related increase in VO_2max in the elderly has been ascribed a combination of an increase blood volume, cardiac output (CO) and better ability of skeletal muscles to extract O_2 (107) to the same extent as in young adult subjects (78).

Both groups of subject were of the same range of body weight, body height, lean body mass and body fat, (Table 2). After 12 weeks of exercise training, the percent body fat was decreased and lean body mass was increased in both groups of subject. Kohrt, W.M., et al. (83) reported that exercise training caused a reduction in total body fat content with a preferential loss of fat from the central regions of the body, and the magnitude and the pattern of fat loss were similar in both men and women aged 60 to 70 years. The fat loss normally found with training is due to the increased activities of enzymes involved in the activation, transport and the oxidation of fatty acid (100,101).

This study shows no significant difference in physical fitness between exercise training and exercise training plus vitamin E supplementation. This finding indicated that vitamin E supplementation has no beneficial effects on the physical fitness. The improvement in physical fitness of subjects appears to reflect exercise training rather than vitamin E supplement. Lawrence, J.D., et al. (132) have studied in the trained swimmer and the trained swimmer plus 900 IU vitamin E supplement and they found no difference in endurance and post-exercise serum lactic acid levels between the two groups during the 6-months period. In agreement with many studies, vitamin E supplementation were not effect on exercise performance and the changes in VO_2max, marker of aerobic capacity in human (113,134). Witt, T. et al. (133) suggested that vitamin E supplementation has not beneficial effect in improving the oxygen transports system.

Effect of exercise training and exercise training plus vitamin E supplement on lipid profile

Few studies have evaluated the lipid and lipoprotein differences in physically active elderly men (127). This study found that a serum cholesterol levels was significant reduced from the resting levels in both groups of subject, which correlated positively with the moderate-intensity exercise training. Serum LDL-C levels was significantly reduced in exercise training subjects whereas there was a tendency to decrease the serum LDL-C levels in exercise training plus vitamin E supplement subjects. These results are in agreement with various studies (128-131). In both groups, the serum triglyceride levels had attendency to decline whereas HDL-C levels were unchanged, resulted in a significantly lower TC/HDL-C ratio. It was similar to previous study which reported by Seals. D.R. et al (129), they found that exercise training in older men and women resulted in a reduced TC/HDL-C ratio after 24 weeks of exercise. In agreement with Wei, M.

et al (130) who suggested that regular exercise had significant decreased in the ratio of TC/HDL-C in elderly men. In addition, HDL-C/LDL-C ratio was significantly increased in exercise training subjects. It was supported by Brownell, K.D. et al (67), their work showed that 10 weeks exercise program can increased in HDL-C/LDL-C ratio 12.4% in healthy men. Exercise training can improved cardiovascular risk factors by the reduction of LDL level, which is the source of the lipid that accumulates in the atherosclerotic lesion, or at least maintains the favorable lipid profile (130). The mechanisms responsible for these modifications are related to the increase in lipoprotein lipase (LPL) and lecithin cholesterol acyltranferase (LCAT) enzyme activity. These enzymes enhance the reverse transport of cholesterol. The processes for the removal of cholesterol from HDL are not clear, but most likely related to alteration of cholesteryl ester transfer protein (CEPT) and hepatic lipase (HL) enzyme activity and /or an increase hapatic apo E receptor-mediated pathway (127).

In this study there are no significant differences in serum lipid profile levels between the two groups. In agreement with Meydani, M., et al. (136) who found that vitamin E supplementation (800 IU per day for 30 days) had no effects on plasma total cholesterol and triglyceride. Meydani, S.N., et al. (22) also showed that vitamin E supplementation had no significant effects on plasma antioxidant, lipid, and lipoprotein profile. Thus, exercise plus vitamin E supplement does not show more effect on serum lipid profile and can not improve cardiovascular risk factors.

Effect of exercise training and exercise training plus vitamin E supplement on antioxidant and lipid peroxidation

The major antioxidant defense in plasma involves a series of inter-relating component i.e., ascorbate, alpha tochopherol, bilirubin, urate and protein thiols (108). Thus, total antioxidant capacity (TAC) is a composite value based on different contributions from a number of different components. It has been designed to evaluate the overall performance of the plasma antioxidant system (109). In this study, 12 weeks of exercise training produce a significant increase in TAC level in all subjects (Figure 20). Exercise training induces oxidative stress in muscles and enhances antioxidant enzymes activity in rodents (56,110-113). In human, there were some studies that exercise training can increase antioxidant defense system (114-116). Robertson, J.D., et al.(117) examined the antioxidant status of high intensity trained runners, low-moderate intensity trained runners and sedentary subjects and found that the antioxidant capacity was enhanced in both high and low-moderate intensity runners. However, there are some studies suggested that exercise training could not increase capacity for enzymatic scavenging activity against free radical damage (92,90,118,119).

The average level of MDA before exercise-training program found in this study was between 35.0-36.6 μmol/L (Table 4). This average level was comparable with those found by the other investigator that used the same thiobarbituric acid reaction (TBARS) method (120). After 12 weeks of intensive training, the level of plasma MDA in both groups of subjects were significant reduced from the resting levels. From this study, it is shown that exercises training may reduce the rate of peroxidation process. This idea was supported by the studies about adaptive reponses of training (69,102,121). Alessio, H.M., et al.

(50) demonstrated that muscle MDA level of the trained rats was not increased after moderate exercise. The mechanism for explaining the effect of exercise training on lipid peroxidation and the induction of antioxidant enzyme activities by free radicals are not proven at the present. However, some mechanisms involved in the defense mechanism are able to reduce some potentially harmful effect of free radicals and lipid peroxidation. These have been shown to increase the activity of antioxidant enzyme (122-124). It is possible that exercise can up–regulate some antioxidant enzymes (105). This mechanism proposed that the exercise induced changes in redox status of tissues might initiate intracellular signal transduction processes that trigger the antioxidant defense (125). Somani, S.M. and Rybak, L.P. (126) found that the changes in the activity of antioxidant enzymes during exercise training was associated with an increased post-translation mRNA of antioxidant enzyme activity rather than an increased transcription in age rats (126).

In addition, the previous studies have reported that vitamin E supplementation can reduce oxidative stress and the rates of lipid peroxidation (19,21,113). Goldfarb, A.H et al. (18) found that vitamin E supplementation can reduced the lipid peroxidation in plasma and all muscle fiber types after exercise. However, few studies have reported that vitamin E supplementation did not prevent injury due to oxidative stress in skeletal muscle of rodents (135). Cannon, J.G., et al. (23) studied in elderly subjects (>55 years) supplemented with 800 IU vitamin E for 48 days and control group. They found that serum creatine kinase (CK) in vitamin E supplement group was significantly higher after exercise when compared with control subjects. Our study found that exercise training plus vitamin E supplement subjects as well as exercise training subjects showed increasing of plasma TAC and reducing of plasma MDA level after exercise for 12 weeks. The data suggested that vitamin E supplementation neither affects the lipid peroxidation nor improved an antioxidant defense system.

However, several studies have demonstrated that the effects of antioxidant nutrient mixtures on exercise-induces lipid peroxidation and the skeletal muscle damage, they found that the combination of vitamin E, vitamin C and β-carotene may be effectively inhibit the oxidative damage (137,138). Kanter, M., et al. (139) studied the effect of ingesting vitamin C (100 mg per day), and β-carotene (300 mg per day) for 6 weeks on the breath pentane and serum MDA and found that the expired pentane and serum MDA levels were reduced. It was possible to explain that ascorbic acid receives unpair electron from α- tocopheroxyl and generate to α-tocopherol and possibly to inhibit oxidation induced by α-tocopheroxyl radical. The β-carotene may exert a cooperative effect by residing and scavenging radicals at different positions in the lipophilic compartment.

In conclusion, this study investigates the effects of exercise training and exercise training plus vitamin E supplementation on the antioxidant capacity and lipid profile. This study has demonstrated three major findings as following: First, moderate intensity exercise training for 12 weeks in the elderly men can reduce malondialdehyde and increase TAC, by enhancing the physiological antioxidant defense system. Second, after exercise training for 12 weeks, serum cholesterol and LDL-C levels were reduced, suggesting that regular exercise can improve serum lipid and lipoprotein levels. Third, exercise training plus vitamin E supplementation 800 IU per day for 12 weeks in elderly men in aspects of affected lipid peroxidation and improve the serum antioxidant capacity and the lipid profile does not show additional benefit over exercise training alone. Thus, this study suggests that habitual physical exercise in aging is very important in maintaining and promoting natural antioxidant capacity defense against the reactive oxygen species, and it is also important for improving blood lipid profile and reducing the risk of cardiovascular diseases.

Future studies need to prolong duration of vitamin E supplementation and compare the effect of exercise training plus vitamin E supplement to that of a mixture of vitamin A, vitamin C and vitamin E supplement. In addition, future study is needed to investigate the mechanism of interaction of vitamin E and exercise on the antioxidant system.