The Effects of Endurance Exercise and Vitamin E on Oxidative Stress in the Elderly

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To examine the effects of exercise and vitamin E supplementation on oxidative stress in older adults, 59 participants, age 76.3 ± 4.2 years, were randomly assigned to 1 of 4 groups: an exercise group taking placebos (EGP) or vitamin E (EGE) or a sedentary group taking placebos (SGP) or vitamin E (SGE). Measures included weight, VO_2max, blood pressure (BP), and serum concentrations of vitamin E and lipid hydroperoxide (LOOH). At the end of the 16-week trial, the EGP and EGE had significant increases in VO_2max and significant decreases in resting BP, weight, and LOOH concentrations ($P < 0.05$). The SGE had significant decreases in LOOH and BP ($P < 0.05$). There were no significant changes in the SGP ($P > 0.05$). The results suggest that endurance exercise in combination with vitamin E reduces oxidative stress, improves aerobic fitness, and reduces BP and weight in older adults. Even sedentary participants who take vitamin E may reduce oxidative stress and lower BP.

Key words: *exercise, vitamin E, oxidative stress, blood pressure, lipid hydroperoxide, aging*

Regular exercise is especially important for older adults as there is substantial evidence linking many age-related biologic declines with sedentary living (Blumenthal and others 1989; Cress and others 1991; Pollock and Wilmore 1995; Jessup and others 1998). There is a significant gap, however, in our knowledge of the effects of exercise on human aging. Animal studies have shown that both a sudden increase in physical activity and aging are associated with an increase in oxygen radical generation (Kanter 1995; Ji 2002). Many studies have also shown an age-related decline in the production of endogenous antioxidants, the body's protection against oxidative damage (Ji 1995; Hu and others 2000; Arivazhagan and others 2001). In contrast, other studies have found that increased oxidative damage in aged animals was not consistently accompanied by a decline in endogenous antioxidants (Vohra and others 2001).

An increased flux of oxidants not only damages the mitochondria but also damages lipids, proteins, carbohydrates, and DNA. To date, oxidative damage has been implicated in the etiology of more than 200 human pathologic conditions, including many of the degenerative changes associated with aging (Packer 1984; Kanter 1995; Baskin and Salem 1997; Ji 2002). Although the exact mechanisms responsible for increased oxidative damage in human aging are not clearly understood, numerous animal studies have demonstrated that mitochondria in aged muscles use

BIOLOGICAL RESEARCH FOR NURSING
Vol. 5, No. 1, July 2003, 47-55
DOI: 10.1177/1099800403255378

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This study was funded by NIH/NINR grant R15, NR05181.

oxygen inefficiently (Barja 2002). This impairs ATP synthesis and results in increased oxidant production.

Aerobic organisms produce endogenous antioxidants, which provide defense against oxidative damage. They include the enzymes superoxide dismutase, catalase, glutathione, peroxidase, and sulfhydryls and a number of other reducing enzymes (Kanter 1995). Regular (chronic) exercise has been shown to improve the intracellular antioxidant/pro-oxidant ratio (Lawler and others 1993; Powers and others 1993; Leeuwenburgh and others 1994; Ji 1995; Demirel and others 1998; Ji 2002): Endogenous antioxidant production increases in response to an exercise-induced increase in oxidants. In addition, there are many nutritional antioxidants, such as vitamins E, C, β-carotene, selenium, and others (Ji 1995; Kanter 1995). Vitamin E (α-tocopherol), a lipid-soluble vitamin, is perhaps the most important chain-breaking antioxidant (Haramaki and others 1995; Ji 1995). Tocopherols protect cell membranes by quenching, or reducing, an electron from a free oxygen radical, thus preventing or limiting peroxidation of lipids in the membrane. This reduction process produces LOOH as a by-product (Haramaki and others 1995) (see Fig. 1).

Several well-designed studies have reported reduced oxidative stress and skeletal muscle damage in animals receiving nutritional supplements of vitamin E (Gohil and others 1986; Takasaki and others 2002). Similar studies in humans, however, have been equivocal. Cannon and others (1990) and Meydani and Evans (1993) reported that 800 IU/d of vitamin E for 48 days diminished exercise-induced lipid peroxidation in active older participants. Conversely, other studies have failed to show any protective effects of dietary antioxidant supplementation against peroxidation (Helgheim and others 1979; Warren and others 1992; Kanter 1995).

Exercise may increase the requirements for dietary antioxidants. Kumar and others (1992) and Packer (1984) reported a decrease in serum vitamin E concentration following acute exercise in rats. These findings support other studies that measured lipid peroxidation in vitamin E–depleted animals following exercise.

Although findings from both animal and human studies support the hypotheses that both regular (chronic) exercise and vitamin E supplementation are efficacious in reducing oxidative stress, there have been no well-designed studies that have investigated

α-tocopherol + peroxyl radical → tocopheroxyl radical + ascorbate and/or glutathione
↓
α-tocopherol and LOOH

Figure 1. Vitamin E (α-tocopherol) converting a peroxyl radical to a tocopheroxyl radical and simultaneously being converted back to α-tocopherol and lipid hydroperoxide (LOOH) by vitamin C (ascorbate) and/or glutathione (an endogenous antioxidant).

the effects of these 2 therapies in aging humans. Interpretation of previous results regarding the effects of dietary antioxidant supplementation and exercise on oxidative stress in humans is difficult due to various methodological inconsistencies. Many researchers have utilized dietary antioxidant supplementation and exercise for relatively short periods of time (ranging from a few days to a few weeks), and many have used only young, healthy, well-nourished adults or endurance athletes as participants.

This study, therefore, was designed to evaluate the effects of exercise training and dietary supplementation with vitamin E on oxidative stress in older humans, as well as to circumvent some of the methodological inconsistencies of previous studies. Specifically, we tested the hypotheses that 1) 16 weeks of dietary supplementation with 800 IU of dl-α-tocopherol daily will reduce serum LOOH concentrations in nonexercising older adults, 2) 16 weeks of moderate-intensity endurance exercise training without dl-α-tocopherol supplementation will reduce serum LOOH concentrations in sedentary older adults, 3) 16 weeks of moderate-intensity endurance exercise training plus 800 IU of dl-α-tocopherol daily will produce greater reductions in free radical–induced oxidative stress (as measured by serum concentrations of LOOH) in older men and women than exercise or dl-α-tocopherol alone.

Method

Sample and Setting

We recruited 74 men and women, age 70 to 85 years, by word of mouth from a retirement community in north central Florida. Sixty of these met the inclusion criteria and were enrolled in the study. All partici-

pants signed an informed consent document approved by the University of Florida Institutional Review Board and completed demographic and health history questionnaires. Participants selected were healthy, nonsmoking individuals free from overt cardiovascular diseases or other chronic or acute medical or psychiatric disorders that would prevent safe participation in the study. In addition, all participants selected were sedentary (i.e., were not currently participating in regular endurance exercises such as walking, jogging, cycling, dance aerobics, swimming, etc., and had not done so for the previous 12 months). The principal investigator performed all baseline and posttest measurements. Baseline screening and testing included 1) a physical examination; 2) measurements of resting blood pressure (BP) and heart rate, height, and weight; 3) a 12-lead ECG; and 4) a submaximal graded exercise test (GXT) on a treadmill with ECG and BP monitoring. In addition, venous blood was obtained for measuring serum concentrations of LOOH and α-tocopherol. Exclusion criteria included resting systolic BP >140 mm Hg and/or diastolic BP >90 mm Hg. Resting electrocardiographic exclusion criteria included heart rate >100 or <50 at rest, ST-segment elevation or depression at rest >1 mm, abnormal Q waves at rest, premature ventricular contractions (PVCs) >2 per minute, atrial fibrillation, or AV blocks >first degree. The GXT was terminated and the participant excluded from the study if 1) the participant requested that the test be stopped; 2) the ECG recorded cardiac dysrhythmias including single PVCs >6/min, couplets, salvos, or runs of ventricular tachycardia, atrial fibrillation or flutter, the onset of 2nd- or 3rd-degree AV block, or bundle branch block; 3) BP increased to > 190 mm Hg systolic and/or 110 mm Hg diastolic; or 4) the participant exhibited or complained of dizziness, severe dyspnea, chest pain, or loss of balance.

Following baseline testing, participants were randomly assigned, utilizing a random number table described by Burns and Grove (1997), to the exercise group (EG) or the sedentary group (SG). Participants were also randomly assigned to take 800 IU of vitamin E or placebos daily. Thus, the study had 4 arms: 1) exercise group taking placebos (EGP), 2) exercise group taking vitamin E (EGE), 3) sedentary group taking placebos (SGP), and 4) sedentary group taking vitamin E (SGE).

Measures

All measures were performed at baseline and after the 16-week study period.

Maximum oxygen uptake (VO_2max, ml/kg/min). The maximum oxygen uptake, a measure of cardiorespiratory fitness and endurance, was estimated from the results of the GXT. The target heart rate (THR) was established for each participant as 75% of their maximum heart rate (HRmax) calculated by the formula HRmax = 0.75 (220 – age [years]). A continuous 12-lead ECG strip was recorded during the test. Participants selected a comfortable speed and walked on the treadmill at an elevation of 5% until their heart rate reached THR and then continued to walk for 60 s after reaching THR. VO_2max was calculated for each participant using the following formula published by the American College of Sports Medicine (2001):

$$VO_2max\ (ml/kg/min) = 3.5\ ml/kg/min + (m/min \times 0.1) + (grade \times m/min) \times 1.8,$$

where 3.5 ml/kg/min is the participant's resting oxygen uptake; m/min is the speed of the treadmill belt in meters per minute; 0.1 is the regression constant for converting treadmill speed in m/min to ml/kg/min; grade is the elevation of the bed of the treadmill in percentage, written as a decimal (e.g., 5% is written 0.05); and 1.8 is the constant for converting treadmill speed and elevation into ml/kg/min.

BP. BPs were measured using an electronic pulse oscillometric sphygmomanometer (Dynapulse model 200M). All BPs were measured between 8 AM and 10 AM, and participants were instructed not to take any scheduled prescription vasoactive or diuretic medications prior to the measurements. After resting (sitting) for 10 to 15 minutes, the participant's left arm was placed on a padded table at heart level, and a cuff of the proper size, as determined by the circumference of the participant's left upper arm, was placed 2 inches above the bend of the elbow. BP and heart rate were recorded.

Serum concentrations of vitamin E (dl-α-tocopherol). Serum vitamin E was analyzed to control

for participants' dietary intake of nutrients containing vitamin E and to determine if the participants were taking their vitamin E or placebos as instructed. Following a 4-week vitamin E washout period (natural and synthetic α-tocopherol has a terminal phase half-life of approximately 8 days), two 15-ml tubes of blood were obtained, following a 10-h fast, from each participant via venipuncture from an antecubital vein. (One tube was used for the tocopherol analyses, the other was used to assay LOOH.) The tubes were centrifuged at 8000× *g* for 15 min. The serum was then piped into 1.5-ml cryogenic tubes and frozen at –80 °C until analysis. Vitamin E was extracted and analyzed from human serum using a modification of the procedure used by Talwar and others (1998). To a measured volume of sample (maximum of 1000 µL), 100 µL of 100 µg/mL × α-tocopherol acetate in ethanol was added and mixed. In order, 2 mL of ethanol and 3 mL of cyclohexane were added and vortex mixed. Centrifuging at 4000 rpm for 2 min separated the organic layer from the residue, which was then transferred via pipette to a clean tube. The extraction step was repeated with the extracts collected together. The combined extract was taken to dryness under a stream of dry nitrogen, reconstituted in 100 µL of ethanol, and transferred to an amber autosampler vial for analysis. The extraction procedure was conducted under reduced lighting. Vitamin E content was determined in serum extracts using a Hewlett-Packard HP1100 high-performance liquid chromatography (HPLC) system (Hewlett-Packard Company, Wilmington, DE) with autosampler, degasser, binary pump modules, and variable wavelength UV detector. Fifty microliters of each extract were injected onto an Adsorbosphere C18 column (5 m; 250 × 4.6 mm; Alltech, Deerfield, IL) held at 25 °C. Separation was isocratic at 2 mL/min in methanol (modified from Choi and others 1999). The analyte was detected at 294 nm with quantitation against a 5-point standard curve ($R^2 \geq 0.997$) composed of α-tocopherol (Sigma Chemical, St. Louis, MO) diluted in ethanol to concentrations ranging from 25 to 250 µg/mL and α-tocopherol acetate (Sigma Chemical), as the internal standard, present at 100 µg/mL in each standard. Quality control standards (100 µg/mL) prepared from independent stocks of α-tocopherol showed an average relative error of 1.49% (n = 8; 3.46% coefficient of variation [CV]). Sample recoveries based on the recovery of the internal standard (α-tocopherol acetate at 100 µg/mL) averaged 80.93% (n = 122; 6.42% CV). Due to limitations in sample volume, duplicate analyses could not be performed. All solvents used during extraction and analyses were of HPLC grade.

Serum concentrations of LOOH. Serum concentrations of LOOH, as a biochemical marker of lipid peroxidation, were analyzed by the method of Nourooz-Zadeh (FOX). This method was chosen over other lipid peroxidation assays (such as F_2-isoprostanes) for its accuracy, applicability to serum samples, and cost-effectiveness. The FOX method uses a work solution that includes ferrous ammonium sulfate and xylenol orange. In short, a stable chromophore that absorbs light at 560 nm is formed from the reaction of xylenol orange and ferric ions, which are oxidized from the ferrous form in proportion to the amount of LOOHs present. Using heparin as the anticoagulant, samples were combined with 10 µl catalase and either 10 µl distilled H_2O or 10 µl tris (2-carboxyethyl) phosphine HCl (TCEP). Catalase was added to prevent H_2O_2 interference, whereas TCEP was used to reduce LOOHs present within the sample. Following incubation at room temperature, a solution containing ferrous chloride and xylenol orange was added. After a second incubation, samples were centrifuged for 20 min at 17× *g* to obtain supernatant. Supernatant absorbance was then read in a Milton Roy Spectronic array 3000 spectrophotometer (Rochester, NY) at 560 nm with the distilled H_2O sample absorbances being subtracted from the TCEP sample. All samples were performed in triplicate, with the 2 closest measures within 0.005 absorbance units being used in the final LPO calculation. Final LPO levels were calculated using a cumene hydroperoxide standard curve (r = 0.986) and reported in units of µM. For assay, the difference between aliquots incubated with and without a reducing agent (tris[2-carboxyethyl] phosphine HCl) represented LOOHs present within a given sample. Final concentrations were determined according to a cumin hydroperoxide standard curve (r = 0.998). Percentage CV between and within days was 3.9% and 2.6%, respectively.

Height and weight. Height and weight were measured on a standard balance-beam scale equipped with a height stadiometer.

EG Protocol

Participants in the EGP and EGE completed 16 weeks (two 1-h bouts/week) of supervised endurance exercise on treadmill, cycle, and stairclimber ergometers. Participants were free to select any 2 nonconsecutive days each week to exercise (e.g., Mondays and Wednesdays, Tuesdays and Thursdays, or Wednesdays and Fridays). Each exercise session began with 5 to 10 min of stretching and warm-up calisthenics and ended with 5 to 10 min of cool-down walking and stretching. During the initial 2 to 3 weeks, participants exercised at 50% of their predicted maximum heart rate for 15 to 20 min per session. Intensity and duration were increased during weeks 4 and 5 to 75% of predicted maximum heart rate for a minimum of 30 min during each session. Participants' heart rates were monitored by the investigators prior to each session, during peak exertion, and at the end of a 5- to 10-min stretching and cool-down period.

SG Protocol

Participants in the SGP and SGE were asked to not change their usual daily activities or to begin an exercise program during the 16-week study period. Participants in the SGs were contacted weekly by the investigators or research assistants to record their progress taking the study drugs (either vitamin E or placebos) and to resupply the study drugs. The nonexercising participants were offered a supervised exercise program following their participation in the study. Participants in both the exercise and sedentary groups were asked to not change their usual diets during the study period.

Vitamin E or Placebo Study Drugs

All participants were issued a numbered package containing a 30-day supply (60 doses) of capsules containing either 400 IU vitamin E (dl-α-tocopherol) or a placebo (lactose) and instructed to take 1 capsule twice a day. The investigators issued the study drugs and accounted for the empty drug packages returned by participants. The study drugs were formulated and supplied by a research pharmacy and labeled "antioxidant protocol drug A or B." Neither the investigators nor the participants knew which drugs were vitamin E and which were placebos until the study period ended and the initial data analyses were completed. Participants were instructed to take 1 capsule with their morning and evening meals.

Analyses of Data

The Statistical Analysis System (SAS Institute, Cary, NC, Version 8.2) was used for data analysis. The significance level of 0.05 for rejecting the null hypotheses was chosen. For simultaneous testing of hypotheses, the Bonferroni method for controlling the experimentwise (or overall) error rate was used. Descriptive statistics were used to describe the demographic characteristics of the sample. Repeated measures analysis of variance (ANOVA) using the generalized linear model (GLM) was used to examine pretest to posttest changes in response variables within subjects, between groups, and within-subjects-by-between-group interactions.

Results

Of the initial 60 participants, 59 completed the study: 37 women and 22 men, with a mean age of 76.3 ± 4.2 (*SD*) years. One participant in the exercise group was removed from the study during the 4th week of training due to an abnormal BP response to training. ANOVA statistics revealed no pretest differences between the 4 groups in age, weight, BP, heart rate, VO_2max, serum α-tocopherol concentrations, or LOOH concentrations ($P > 0.05$; see Table 1).

The 2 groups taking vitamin E (EGE and SGE) had a significant pretest to posttest increase in serum α-tocopherol concentrations ($P < 0.05$), whereas the 2 groups taking placebos (EGP and SGP) had no changes in these concentrations (see Fig. 2).

GLM procedures revealed that the 2 exercise groups (EGP and EGE) had significant decreases in weight and systolic and diastolic BP and a significant improvement in VO_2max ($P < 0.05$). In the SGE, there was a significant decrease in systolic BP ($P < 0.05$) but

Table 1. Baseline Characteristics of the Sample

Variable	Total Sample	EGP	EGE	SGP	SGE	*P*
n	59	15	14	15	15	
Age (years)	76.3 ± 4.2	75.9 ± 3.3	76.1 ± 5.0	76.9 ± 4.5	76.1 ± 4.3	*ns*
Weight (kg)	78.7 ± 15.1	80.7 ± 16.8	84.2 ± 18.1	77.0 ± 9.8	73.2 ± 13.9	*ns*
Systolic blood pressure (mm Hg)	141 ± 15.6	141 ± 14.5	144.8 ± 12.7	140.5 ± 19.2	140.5 ± 16.2	*ns*
Diastolic blood pressure (mm Hg)	76 ± 10.0	79 ± 10.7	79 ± 7.8	71 ± 10.2	74.7 ± 9.5	*ns*
Resting heart rate (beats per minute)	72.9 ± 10.3	73.2 ± 10.2	71.1 ± 9.0	73.1 ± 11.2	74.2 ± 11.3	*ns*
VO_2max (ml/kg/min)	14.5 ± 2.0	15.0 ±1.6	13.8 ± 1.1	14.2 ± 2.8	15.2 ± 2.0	*ns*
α-tocopherol (μg/ml)	12.7 ± 4.0	14.3 ± 3.2	11.5 ± 4.2	13.1 ± 4.4	11.7 ± 4.0	*ns*
Lipid hydroperoxide (μM)	4.28 ± 1.3	4.60 ± 1.3	4.34 ± 1.4	3.81 ± 1.5	4.29 ± 1.1	*ns*

NOTE: EGP = exercise group taking placebos; EGE = exercise group taking vitamin E; SGP = sedentary group taking placebos; SGE = sedentary group taking vitamin E. *ns* = no significant differences between the 4 groups ($P > 0.05$). Values are means ± standard deviations. Repeated measures analysis of variance was used to compare differences in the variables between the 4 groups.

no change in weight, diastolic BP, or VO_2max ($P > 0.05$). In the SGP, there were no significant changes in any of these variables ($P > 0.05$; see Table 2).

The 2 exercise groups (EGP and EGE) and the SGE had significant decreases in LOOH ($P < 0.05$). There were no significant differences, however, in the magnitudes of the decreases in LOOH between the EGP, EGE, and SGE groups ($P > 0.05$). The SGP had no significant changes in LOOH ($P > 0.05$; see Fig. 3).

Discussion

The results of this study suggest that 16 weeks of moderate-intensity endurance exercise and 16 weeks of vitamin E supplementation, either alone or in combination, reduce free radical–induced lipid peroxidation in older men and women. These results support the findings of previous animal studies that reported decreased free radical–induced lipid peroxidation following exercise training (Lawler and others 1993; Powers and others 1993; Leeuwenburgh and others 1994; Ji 1995; Demirel and others 1998; Ji 2002) and those reporting decreased oxidative damage in animals receiving nutritional supplementation with vitamin E (Davies and others 1982; Gohil and others 1986; Demirel and others 1998; Hu and others 2000). These findings also lend support to the hypotheses that regular exercise and dietary antioxidants have a positive influence on the prooxidant/antioxidant balance in aerobic animals.

Serum tocopherol concentrations in humans not taking vitamin E supplements normally range from 8 to 15 μg/ml (Chow 2000). The baseline serum concentration of α-tocopherol for the total sample in this study was 12.7 ± 4.02 μg/ml ($M \pm SD$) indicating that the participants, the majority of whom were previously taking multiple-vitamin supplements containing vitamin E, closely followed the 4-week vitamin E washout protocol. The 2 groups taking vitamin E (EGE and SGE) had statistically significant posttest increases in serum α-tocopherol levels (125% and 144%, respectively), whereas the groups taking placebos (EGP and SGP) had no changes. These findings are significant because they indicate that the participants also com-

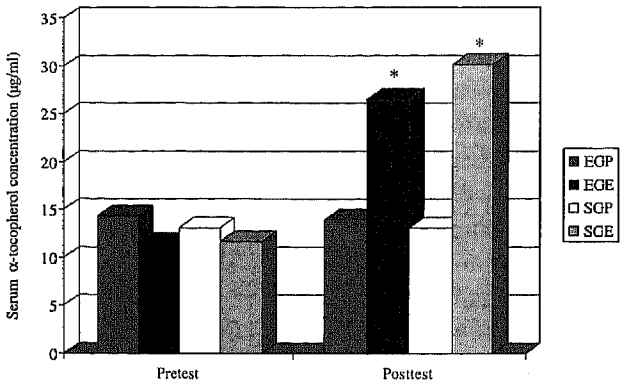

Figure 2. Pretest to posttest changes in serum α-tocopherol (vitamin E) concentrations. EGP = exercise group taking placebos; EGE = exercise group taking vitamin E; SGP = sedentary group taking placebos; SGE = sedentary group taking vitamin E. *$P < 0.05$.

Table 2. Pretest to Posttest Changes within Groups in Weight, Resting Systolic and Diastolic Blood Pressures, and VO_2max

	Group	*n*	Pretest	Posttest	Δ	*F*	*P*
Weight (kg)	EGP	15	80.7 ± 16.8	78.6 ± 16.3	−2.1	8.82	0.01*
	EGE	14	84.2 ± 18.1	82.2 ± 18.2	−2.0	33.1	0.0001*
	SGP	15	77.1 ± 9.8	77.7 ± 9.5	0.7	3.65	0.07
	SGE	15	73.2 ± 13.9	73.5 ± 14.4	0.3	0.71	0.41
Systolic blood pressure (mm Hg)	EGP	15	141.1 ± 14.5	130.8 ± 15.8	−10.3	6.76	0.02*
	EGE	14	144.8 ± 12.7	129.6 ± 14.7	−15.1	28.83	0.0001*
	SGP	15	140.5 ± 19.2	140.5 ± 12.7	0.1	0.004	0.98
	SGE	15	140.5 ± 16.2	133.7 ± 15.7	−6.7	5.11	0.04*
Diastolic blood pressure (mm Hg)	EGP	15	79.3 ± 10.7	73.9 ± 10.2	−5.5	4.93	0.04*
	EGE	14	79.0 ± 7.8	73.9 ± 8.3	−5.1	12.32	0.004*
	SGP	15	71.2 ± 10.2	72.5 ± 8.7	1.3	0.11	0.74
	SGE	15	74.7 ± 9.5	74.9 ± 9.4	0.3	0.02	0.89
VO_2max (ml/kg/min)	EGP	15	15.0 ± 1.6	17.1 ± 1.9	2.11	4.54	0.0006*
	EGE	14	13.8 ± 1.1	16.3 ± 2.2	2.58	6.07	0.0001*
	SGP	15	14.2 ± 2.8	14.3 ± 1.9	0.10	0.32	0.75
	SGE	15	15.2 ± 2.0	15.8 ± 2.7	0.61	1.13	0.28

NOTE: EGP = exercise group taking placebos; EGE = exercise group taking vitamin E; SGP = sedentary group taking placebos; SGE = sedentary group taking vitamin E. Δ = change from pretest to posttest. Values are means ± standard deviations. *significant changes.

plied well with the 16-week vitamin E or placebo study drug protocols.

The mean serum LOOH concentration for the total sample at baseline was 4.28 μM with a range of 1.1 to 7.3 μM. Previous studies have reported serum LOOH values in humans ranging from 0.5 to 19.5 μM depending on age and health status. Using spectrophotometric (FOX) assay techniques, LOOH values are typically in the range of 0.5 to 5.5 μM for healthy individuals (Sodergren and others 1998). LOOH values for participants in this study, therefore, were within normal ranges. LOOH values in the EGP, EGE, and SGE decreased by 68%, 54%, and 56%, respectively, as a result of exercise and/or vitamin E supplementation. The physiological significance of such decreases in LOOH, however, is not clear at this time because there have been no published studies that examined the correlation between reduced lipid peroxidation and the incidence of pathological consequences in humans. It is interesting to note that there were no significant differences in the magnitude of decreases in serum LOOH concentrations among the exercise groups and the control group taking vitamin E as hypothesized. The reasons for this are not apparent. It may be that exercise and/or vitamin E cannot reduce serum LOOH concentrations below a finite, or baseline, level in older people. Future research should examine this anomaly.

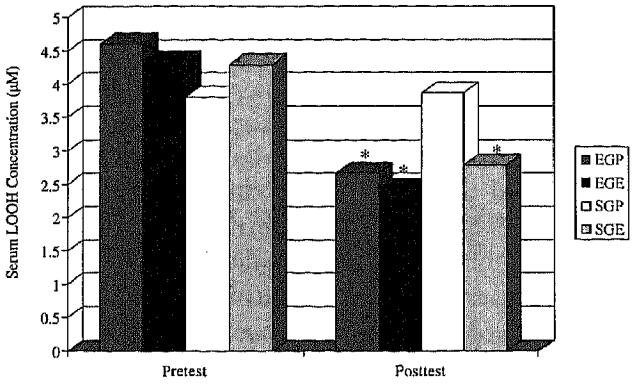

Figure 3. Pretest to posttest changes in serum lipid hydroperoxide concentrations. EGP = exercise group taking placebos; EGE = exercise group taking vitamin E; SGP = sedentary group taking placebos; SGE = sedentary group taking vitamin E. *$P < 0.05$.

Participants in the exercise groups also demonstrated significant decreases in weight and BP as well as increases in VO_2max, an indicator of cardio-

respiratory fitness and endurance. These findings were consistent with previous studies (Pollock and Wilmore 1995; Jessup and others 1998). An additional finding was that the SGE demonstrated a significant reduction in systolic BP (from 140.5 ± 16.2 mm Hg to 133.7 ± 15.7 mm Hg, $P < 0.05$). This is consistent with findings from recent studies (Noguchi and others 2001; Varziri and others 2002) that reported a reduction in BP in hypertensive patients as a result of vitamin E supplementation. Researchers have postulated that vitamin E inhibits the superoxide anion radical from degrading vascular endothelial-produced nitric oxide, a vascular smooth muscle relaxant.

An obvious weakness of this study was the relatively small sample, considering that 4 treatment groups were involved. With only 15 participants in each of the 4 groups, caution must be used when generalizing findings from this study to other populations. In addition, the sample was relatively homogeneous, with the majority of the participants being middle-class Caucasians living in a very structured, rural retirement community. Another weakness of this study was the fact that only a single measure of lipid peroxidation (serum concentrations of LOOH) was used to quantify changes in oxidative stress as a result of exercise and/or vitamin E supplementation. Other measures, such as serum concentrations of F2-isoprostanes, would have added strength to the findings. A 3rd weakness of this study was the use of submaximal exercise testing to estimate VO_2 as a measure of aerobic fitness. Such testing leads to an inherent standard error of the estimate of 4 to 5 ml/kg/min of O_2 uptake (American College of Sports Medicine 2001). Since the pretest VO_2 of this study cohort was only 15.9 ml/kg/min of O_2, a standard error of the estimate of 4 to 5 ml/kg/min represents a significant error. The criterion measurement of aerobic fitness is the graded exercise test to maximum effort with direct inspiratory and expiratory gas analyses. Due to the age and sedentary nature of this study cohort, it was decided that such testing could be unsafe and not in the participants' best interest. In addition, the goal of exercise testing in this study was not to establish an absolute level of aerobic fitness for the sample but simply to quantify that a training response had occurred. From this evidence, it can be concluded that the exercise intervention did in fact influence the favorable changes seen in the response variables.

Implications for Nursing Practice and Research

A large body of literature strongly suggests that free radical–mediated reactions increase in senescence and play a major role in the pathogenesis of cardiovascular disease, certain forms of cancer, diabetes, cataracts, and other diseases associated with aging (Baskin and Salem 1997; De Zwart and others 1999). Numerous investigations have suggested that older adults could benefit from regular, moderate-intensity aerobic exercise and daily supplementation of vitamin E. It had not been clearly determined, however, whether exercise alone, vitamin E alone, or a combination of exercise plus vitamin E was the best recommendation for the older population. The results of this study suggest that both exercise and vitamin E supplementation can reduce oxidative stress in the elderly. The combination of exercise and vitamin E supplementation, however, offers additional health benefits such as weight control and improved overall physical function. Future research that examines more demographically and ethnically diverse populations of older adults and that uses various combinations of dietary antioxidants and exercise modalities could build on these findings. Multiple biochemical markers of oxidative stress should also be measured to lend validity to the findings. This knowledge will enhance our development of therapeutic nursing interventions aimed at health promotion and illness prevention in the growing geriatric population.

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