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Communication

Curcumin ingestion and exercise training improve vascular endothelial function in postmenopausal women

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ABSTRACT

Vascular endothelial function is declines with aging and is associated with an increased risk of cardiovascular disease. Lifestyle modification, particularly aerobic exercise and dietary adjustment, has a favorable effect on vascular aging. Curcumin is a major component of turmeric with known anti-inflammatory and anti-oxidative effects. We investigated the effects of curcumin ingestion and aerobic exercise training on flow-mediated dilation as an indicator endothelial function in postmenopausal women. A total of 32 postmenopausal women were assigned to 3 groups: control, exercise, and curcumin groups. The curcumin group ingested curcumin orally for 8 weeks. The exercise group underwent moderate aerobic exercise training for 8 weeks. Before and after each intervention, flow-mediated dilation was measured. No difference in baseline flow-mediated dilation or other key dependent variables were detected among the groups. Flow-mediated dilation increased significantly and equally in the curcumin and exercise groups, whereas no changes were observed in the control group. Our results indicated that curcumin ingestion and aerobic exercise training can increase flow-mediated dilation in postmenopausal women, suggesting that both can potentially improve the age-related decline in endothelial function.

1. Introduction

Arterial endothelial dysfunction has been associated with cardiovascular morbidity and mortality [1]. Flow-mediated dilation (FMD), which is an index of endothelial function [2], is progressively impaired with age [3,4]. In women, the age-associated decline in endothelial function is enhanced during menopause because of the estrogen deficiency [5,6], and postmenopausal women are at a higher risk of cardiovascular disease [7]. Thus, slowing the decline of endothelial function in postmenopausal women could have potential health benefits. We and other groups have reported that aerobic exercise training enhances endothelial function [8–10]. Lifestyle modification is a desirable way to prevent or

Abbreviations: FMD, flow-mediated dilation; VO_{2peak}, peak oxygen consumption; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; TNF-α, tumor necrosis factor-alpha.

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treat endothelial dysfunction without the need for pharmaceutical intervention.

Vascular inflammation and oxidative stress play important roles in development of vascular endothelial dysfunction and cardiovascular disease [11]. Previous studies have demonstrated that increased production of pro-inflammatory cytokines and reactive oxygen species in the aging vessel results in endothelial dysfunction [12,13]. Therefore, following an anti-inflammatory or anti-oxidative diet may help counteract the effects of aging on blood vessel. Curcumin, a polyphenol molecule extracted from turmeric, is a commonly used spice and a yellow pigment. Curcumin regulate biochemical and molecular pathway by modulating several molecular targets including transcription factors, cytokines, enzymes, and genes regulating cell proliferation and apoptosis [14–16]. In addition to the anti-inflammatory and anti-oxidative effects of curcumin [17,18], is has been associated with the protection against cardiovascular disease [19]. However, the effect of curcumin on endothelial function remains unclear.

We hypothesized that, similar to exercise, curcumin ingestion could improve endothelial function. The objective of the present study was to determine the effect of curcumin ingestion and the effect of exercise training on endothelial function. We therefore investigated endothelial function as measured by the FMD in postmenopausal women before and after 8 weeks of curcumin ingestion or exercise training intervention.

2. Methods and materials

2.1. *Subjects*

A total of 32 healthy, sedentary postmenopausal women (amenorrhea for at least 2 years) participated in the study. Subjects were assigned to one of the following intervention groups: control group (n = 10), curcumin group (n = 11), and exercise training group (n = 11).Subjects were nonsmokers, nonobese, and free of cardiovascular disease as assessed by medical history. None of the subjects were taking cardiovascular-acting medications or hormone replacement therapy. All potential risks and associated with the study were explained to the subjects, and they gave their written informed consent for participation in the study. All procedures were reviewed and approved by the ethical committee of the University of Tsukuba.

2.2. *Experimental protocol*

All experiments were performed in the morning after a 12-h overnight fast. Subjects abstained from alcohol and caffeine for at least 12 h and did not exercise for at least 24 h before beginning the experiment to avoid the potential acute effects of exercise. Measurements were taken in a quiet, temperature-controlled room (24–26°C). After a resting period of at least 20 min, FMD, arterial blood pressure, and blood biochemistry were determined. After these measurements, peak oxygen consumption (VO_{2peak}) was measured during incremental cycle ergometer exercise.

2.3. *Curcumin ingestion*

Subjects in the curcumin group ingested 6 pills (150 mg total) of curcumin per day [20,21], which supplies 25 mg of highly absorptive curcumin dispersed with colloidal nanoparticles (Theracurmin; Theravalues Corporation, Tokyo, Japan) [22]. Supplementary curcumin was administered orally for 8 weeks. All subjects were instructed not to alter their dietary habits during the intervention period.

2.4. *Exercise training*

Subjects in the exercise group underwent aerobic exercise training more than 3 days per week (2-3 supervised sessions and additional home-based training) for 8 weeks [23]. Initially, subjects performed cycling and walking 30 min/d at a relatively low intensity (60% of their individually determined maximal heart rate). As their exercise tolerance improved, the intensity and duration of aerobic exercise were increased to 40 to 60 min/d at an intensity of 70% to 75% of the maximal heart rate. Subjects in the control and curcumin groups were instructed not to change their level of physical activity.

2.5. *Measurements*

2.5.1. *FMD*

Brachial artery FMD was assessed noninvasively by using an ultrasound system (UNEXEF18G; Unex, Nagoya, Japan) as previously described [24]. Briefly, high-resolution ultrasound with a 10 MHz linear array transducer was used to obtain a longitudinal image of the right brachial artery in the cubital region at the baseline and then continuously from 30 seconds prior to 2 minutes or more after the release of suprasystolic pressure (50 mm Hg above systolic blood pressure) maintained for 5 minutes of the right forearm. The diameter at the same point of the artery was monitored continuously, and the maximal dilatation after deflation was recorded. FMD was calculated as the percentage change in brachial artery diameter in response to the forearm reactive hyperemic stimulus. FMD was calculated as follows: Maximal diameter-baseline diameter×100/baseline diameter

2.5.2. *Arterial blood pressure*

Arterial blood pressure and heart rate at rest were determined in the supine position using an automated device (form PWV/ABI, Colin Medical Technology, Komaki, Japan)[23].

2.5.3. *Blood chemistry*

A blood sample was collected from the antecubital vein after overnight fasting. Serum of cholesterol and triglyceride and plasma of glucose were determined using standard enzymatic techniques [25].

2.5.4. *Peak oxygen consumption*

VO_{2peak} was measured during incremental cycle ergometer exercise by using online computer-assisted circuit spirometry (AE280, Minato Medical Science, Osaka, Japan) as we previously reported [23]. All subjects underwent an incremental exercise test (2 minutes at 40 W, followed by 20 W increases every 2 minutes) until volitional exhaustion. VO_{2peak} was defined as the highest VO_2 recorded during the test. Heart rate and rating of perceived exertion were recorded throughout the exercise.