Responses of Blood Lipids and Lipoproteins to Extended-Release Niacin and Exercise in Sedentary Postmenopausal Women

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Niacin and exercise positively alter blood lipids and lipoproteins via different mechanisms. However, the effects of niacin combined with exercise on blood lipid and lipoprotein profiles have not been investigated in sedentary postmenopausal women. The current study examined the responses of blood lipids and lipoproteins to niacin and exercise in 18 sedentary postmenopausal women, who underwent four conditions: no-niacin rest, no-niacin exercise, niacin rest, and niacin exercise. Participants ingested 1,000 mg/day of extended-release niacin for 4 weeks during the niacin condition. As an exercise treatment, participants performed a single bout of exercise on a treadmill at 60% heart rate reserve until 400 kcal were expended. Extended-release niacin without the exercise intervention significantly (p < .001) increased high-density lipoprotein cholesterol and high-density lipoprotein-2 cholesterol by 12.4% and 33.3%, respectively, and decreased the total cholesterol to high-density lipoprotein cholesterol ratio by 14.8%. Thus, 4 weeks of 1,000 mg/day of extended-release niacin can improve the blood lipid and lipoprotein profiles in sedentary postmenopausal women.

Key Words: Blood lipids and lipoproteins—Postmenopausal women—Exercise—Niaspan.

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CARDIOVASCULAR disease (CVD) is the number one leading cause of death in the United States, and nearly 2,400 Americans die of CVD every day. Approximately 80 million American adults have CVD, and 47% of these individuals are older than 60 years. The lifetime risk for CVD is more than one in two for women at age 40 (1). Menopause usually occurs at the average age of 50 years in American and European women and is associated with progressive reductions in reproductive hormones such as estradiol, progesterone, and 17-hydroxyprogesterone (2). Changes in these hormones, particularly a reduction of estrogen, are associated with negative alterations of blood lipids and lipoproteins (2,3). Atherogenic dyslipidemia is one of the primary risk factors for CVD and is characterized by elevated triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) and lowered high-density lipoprotein cholesterol (HDL-C) (4). Postmenopausal women are more likely to have elevated TC, TG, and very low-density lipoprotein cholesterol (VLDL-C) than men (5) or premenopausal women (6). In addition, the incidence of chronic diseases such as CVD, type 2 diabetes, and osteoporotic fractures in women significantly increases after menopause (2,7,8). Sedentary lifestyle, particularly in postmenopausal women, is also one of the key risk factors that negatively influences blood lipid and lipoprotein profiles, cardiovascular fitness, and bone mineral density (8).

Both chronic and acute bouts of exercise can improve CVD risk factors and other health problems by positively modifying blood lipids and lipoproteins (9,10). Despite the beneficial effects of exercise, only 25% of publications have reported a positive effect of exercise on TC, VLDL-C, or LDL-C (9). Exercise alone may not significantly influence TC, VLDL-C, or LDL-C in either healthy individuals or patients with CVD (10), but exercise leading to weight loss or combined with the diet intervention may reduce TC, VLDL-C, or LDL-C. In contrast, decreased TG and increased HDL-C have been often observed following chronic (11,12) and a single bout of exercise in both men and women (13–15). Although some studies have suggested that HDL-C and TG in women may be more resistant to exercise-induced alterations than men (16,17), beneficial changes in blood lipids and lipoproteins in response to exercise are similar between men and women (9,18).

Niacin, also known as pyridine-3-carboxylic acid or nicotinic acid, is a water-soluble B complex vitamin (19). Niacin has been widely used for patients with dyslipidemia to improve their lipid and lipoprotein profiles (19–21) since Altschul and colleagues (22) first reported its antilipidemic effects. Numerous clinical studies have reported that niacin significantly increased HDL-C and high-density lipoprotein-2 cholesterol (HDL2-C) and reduced TC, VLDL-C, LDL-C, TG, and the TC/HDL-C ratio (20,23–27). Although
that (a) both niacin and exercise independently improve blood lipids and lipoproteins with minimum adverse effects, such as flushing, itching, redness, or hepatotoxicity (20,23,29).

Exercise and niacin positively alter blood lipids and lipoproteins via different mechanisms (9,19,30–37). An exercise-induced reduction of TG results from increased lipoprotein lipase (LPL) activity, a principal enzyme for TG hydrolysis in lipoprotein lipase (9,30,32). Exercise also increases lecithin cholesterol acyltransferase (LCAT) activity, which consequently promotes conversion of high-density lipoprotein-3 cholesterol (HDL₃-C) to HDL₂-C and the reverse cholesterol transport pathway (9,30). Exercise may reduce cholesterylester transfer protein activity, which decreases the rate of cholesterol transfer from HDL-C to LDL-C or VLDL-C, leading to an increase in the cholesterol carrying capacity of HDL-C (30). Niacin decreases adipose lipolysis by inhibiting cyclic adenosine monophosphate, resulting in a decrease in mobilization of plasma free fatty acids (33). A niacin-induced decrease in mobilization of plasma free fatty acids contributes to a decrease in uptake of free fatty acids by the liver and, consequently, reduces the synthesis of TG and very low–density lipoprotein in the liver (34). Niacin also directly decreases the hepatic synthases of TG and fatty acyl CoA by inhibiting diacylglycerol acyltransferase 2 and acetyl CoA, respectively (31). A niacin-induced reduction in hepatic TG synthesis leads to the secretion of a fewer number of very low–density lipoprotein and smaller very low–density lipoprotein particles, which contain less TG. Thus, a reduction in the number of very low–density lipoprotein particles available for catabolism leads to a reduction in low-density lipoprotein particles in the blood stream (31,34,35). Although not clearly understood, one of the proposed mechanisms by which niacin increases HDL-C may result from the increased activity of selective cholesterol uptake, which selectively removes cholesterol from HDL-C and blocks hepatic catabolism of high-density lipoprotein particles containing apo A-I (35–37). Thus, the increased activity of selective cholesterol uptake augments the reverse cholesterol transport pathway (38).

Exercise and niacin are often suggested for sedentary postmenopausal women to improve their health (2–4,35). Despite its known positive effects of exercise or niacin on blood lipid and lipoprotein profiles, no research has yet examined the combination of niacin and exercise intervention in sedentary postmenopausal women. Thus, the current study examined the independent and combined effects of niacin (1,000 mg/d for 4 weeks) and a single bout of aerobic exercise (400 kcal) on blood lipid and lipoprotein profiles in sedentary postmenopausal women. Because exercise and niacin independently ameliorate blood lipids and lipoproteins via different mechanisms, the current study hypothesized that (a) both niacin and exercise independently improve blood lipid and lipoprotein profiles and (b) the combination of niacin and exercise interventions improve blood lipids and lipoproteins significantly more than either niacin or exercise alone. Additionally, the results of the current study will provide insight into the development of future research that involves effective dosing of both niacin and exercise on improvement in blood lipids and lipoproteins in sedentary postmenopausal women.

Methods

Participants

Eighteen sedentary postmenopausal women between 40 and 80 years of age were recruited. All participants met the following criteria to participate in the study: (a) had been postmenopausal at least 1 year (naturally or surgically); (b) not engaged in any exercise program defined as any physical activity accumulating more than 20 minutes per session at least 2 days per week for the previous 6 months; (c) not taking any medication known to alter blood lipids and lipoproteins; (d) nonsmokers or had quit smoking for at least the past 6 months; and (e) no self-reported diagnoses of CVDs, type 1 or 2 diabetes mellitus, or any known metabolic disorder. All study methods and procedures were reviewed and approved by the Institutional Review Board of Texas Woman’s University. Participants who agreed to volunteer for the study provided written informed consent and completed medical history forms. Before performing any study procedures, all participants were requested to provide a written permission letter from the primary care physician to participate in the study. All participants agreed to refrain from exercise training during the study period.

Study Design

There was no randomization in the order of niacin conditions due to its known potential flushing side-effect. Thus, all participants were first assigned to the no-niacin condition followed by the niacin condition for 4 weeks. During the no-niacin and niacin conditions, both rest and exercise trials were randomly assigned to each condition, and venous blood samples were collected immediately before (0 hour) and at 24 and 48 hours after each condition (R, no-niacin rest; EX, no-niacin exercise; NR, niacin rest; and NEX, niacin exercise).

Niacin

During 4 weeks of the niacin condition, participants ingested 1,000 mg of the extended-release form of niacin, Niaskan (Kos Pharmaceuticals, Miami, FL), 1 hour before bedtime. To reach a target dosage of 1,000 mg/day, participants first started with 250 mg/day of Slo-Niacin (Upsher-Smith Laboratory, Minneapolis, MN) during the first week of the niacin condition because the lowest dosage
of Niaspan available was 500 mg. During the second week, participants ingested 500 mg/day of extended-release niacin and thereafter 1,000 mg/day for 4 weeks. This particular dosing schedule was designed to minimize the potential flushing side-effect. At the end of the third week of taking 1,000 mg of extended-release niacin, participants reported to the laboratory for either the rest or exercise trial. Participants continued to take 1,000 mg of extended-release niacin throughout the 4th week for either the rest or exercise trial. If needed, participants were allowed to ingest either a 325 mg dose of aspirin or a 200 mg dose of ibuprofen 30 minutes prior to taking extended-release niacin to minimize the potential for flushing side-effects (39). Two participants reported that they ingested a 325 mg of aspirin for 2 and 3 days, respectively, during a week of 500 mg/day of extended niacin. However, no other participants ingested either aspirin or ibuprofen during 4 weeks of 1,000 mg/day of extended-release niacin.

Exercise Testing
All participants performed exercise testing on a treadmill in order to determine the appropriate exercise intensity of 60% heart rate reserve (HRR) for the exercise trial using the following equation: HRR = [HRmax − resting HR] × target intensity % + resting HR; in this equation, HRmax was estimated using a formula of 220 − age (40). After a 2 minutes of warm-up, the exercise protocol started at 3.0 mph with 0% grade. The speed was held constant at 3.0 mph throughout the test while the grade was elevated by 2.0% every 2 minutes. During the exercise testing, heart rate and 12-lead electrocardiograph recordings were monitored using a Quinton Q4500 ECG (Quinton Inc., Bothell, WA). Blood pressure was measured in the last minute of each stage, and the exercise testing was terminated when participants reached 70% HRR. As the exercise treatment, all participants performed a single bout of aerobic exercise on the treadmill at 60% HRR until 400 kcal were expended. The speed was held constant at 3.0 mph while the grade was adjusted to achieve the appropriate exercise intensity (60% HRR) based on the data obtained from the exercise testing. Blood pressure and heart rate were continuously monitored, and expired respiratory gases were collected and analyzed using a Parvo Medics TrueMax 2400 (Consentius Technologies, Sandy, UT) at the initiation, mid, and last 15 minutes of exercise to determine 400 kcal of energy expenditure. Estimation of 400 kcal of energy expenditure was calculated using the thermal equivalents of O2 for respiratory exchange ratio (41). During the exercise trial, all participants had a 5-minute break at a halfway through the exercise bout. During the rest trial, each participant reported to the laboratory for blood collection only. The rest and exercise trials were conducted at least 1 week apart to prevent any acute influence of exercise on blood lipids and lipoproteins.

Dietary and Physical Activity Considerations
Each participant completed a 3-day diet record from the day preceding the first blood draw to the day before the last blood collection to insure consistency in food intake. Based on the first 3-day diet record provided, each participant was asked to consume the same food the night before each blood collection. All self-reported dietary records were evaluated using Nutritionist Pro software (First Data Bank, Indianapolis, IN). In addition, all participants provided a 5-day physical activity record from 3 days prior to the first blood draw to the day before the last blood collection.

Body Composition Assessment
Body composition was assessed by a Lunar DPX-iQ dual-energy x-ray absorptiometer (Lunar, Madison, WI). During the body composition test, participants lay supine, fully clothed, on a padded table for the scan. All x-ray scans were conducted by a licensed x-ray technician.

Blood Analyses
All participants reported to the laboratory between 06:00 and 08:00 AM with at least 10 hours of fasting. After 20 minutes of resting in a chair, venous blood samples were collected immediately before (0 hour) and at 24 and 48 hours after each condition (R, EX, NR, and NEX). Hematocrit was analyzed immediately after each blood draw using the microhematocrit technique (42). Remaining blood samples were centrifuged at 1,800g for 15 min to separate serum and then immediately frozen at −70°C. Hemoglobin was determined using the Drabkin and Austin cyanmethemoglobin method (43). Serum samples, in duplicate, were used to analyze the concentrations of TG (Kit# 85460; Raichem, Columbia, MD), TC (Kit# 85430; Raichem), HDL-C (Kit# 82051; Raichem), and HDL-C (dextran sulfate precipitation method) using enzymatic measurements. All enzymatic measurements were performed using the PowerWave XS microplate spectrophotometer (BioTek Instruments, Winooski, VT). Plasma volume changes were calculated using the Dill and Costill’s method (44). The with-in samples coefficient of variations for TG, TC, HDL-C, and HDL-C were 2.1%, 1.8%, 0.6%, and 1.5%, respectively. The concentration of HDL-C was calculated from the difference between HDL-C and HDL-C, and the concentration of LDL-C was estimated by the Friedewald formula (45).

Statistical Analysis
All statistical analyses were performed using the Statistical Package for the Social Sciences 15.0 (SPSS Inc., Chicago, IL). All data were reported as mean ± SD. The changes in blood lipids and lipoproteins including TC, TG, LDL-C, HDL-C, HDL-C, LDL-C, and TC/HDL-C ratio were analyzed using a three-way repeated measures analysis of variance for each dependent variable. A repeated measures
analysis of variance was also employed to examine the differences in the average of total caloric intake and macronutrient contents including carbohydrate, fat, and protein for each condition (R, EX, NR, and NEX). When the F ratio was significant, Bonferroni post hoc was applied to determine the significant differences between the conditions. The level of statistical significance was set at \( p < .007 \) to adjust for the multiple analyses of variance. The Mauchly’s test of sphericity for each dependent variable was significant (\( p = .001 \), and the Greenhouse–Geisser adjustment revealed the statistical power for the following dependent variables: TC (df = 2.58, \( F = 3.01 \), \( p = .05 \), observed power = .625), TG (df = 2.45, \( F = 2.15 \), \( p = .12 \), observed power = .460), LDL-C (df = 3.26, \( F = 5.52 \), \( p = .002 \), observed power = .94), HDL-C (df = 2.20, \( F = 16.10 \), \( p = .001 \), observed power = 1.00), HDL_2-C (df = 2.44, \( F = 14.32 \), \( p = .001 \), observed power = 1.00), HDL_3-C (df = 3.05, \( F = 5.20 \), \( p = .003 \), observed power = .909), and TC/HDL-C ratio (df = 1.98, \( F = 18.17 \), \( p = .001 \), observed power = 1.00).

### RESULTS

A total of 45 volunteers initially responded to an advertisement for the study. After the initial screening interview, 25 participants who did not meet the criteria for participation were excluded, and a total of 20 participants signed written informed consent and completed medical history forms. Two of 20 participants dropped out due to the adverse reactions of extended-release niacin such as flushing and swelling at the 1,000 mg/day dosing. The physiological characteristics of the 18 participants who completed the study protocol are presented in Table 1. In regard to CVD risk factors, 3 participants had high blood pressure (systolic blood pressure ≥140 or diastolic blood pressure ≥90 mmHg), 13 participants had TC greater than or equal to 200 mg/dL, 11 participants had HDL-C less than 40 mg/dL, 18 participants had LDL-C greater than or equal to 100 mg/dL, and 8 participants had body mass index greater than or equal to 30.0 kg/m². Every participant had one or more abnormal levels of blood lipids and lipoproteins, and 11 of 18 participants had elevated TC and LDL-C and lowered HDL-C. There was no significant difference in hemocrit or hemoglobin at any time period for any trial. Plasma volumes did not significantly change at any time period compared with baseline. Therefore, the concentrations of blood lipids and lipoproteins in the current study were reported with plasma volume unadjusted values.

Table 2 depicts the mean ± SD values of blood lipids and lipoproteins and the TC/HDL-C ratio for each trial over 48-hour periods. There were no significant three-way interactions between exercise, niacin, and time or two-way interactions between exercise and niacin for any of the blood lipids and lipoproteins. Exercise did not change any blood lipids and lipoproteins over time. However, there was a significant main effect (Table 3) for niacin such that HDL-C and HDL_2-C significantly (\( p = .001 \)) increased by 12.4% (5.4 mg/dL) and 33.3% (3.6 mg/dL), respectively, after 4 weeks of extended-release niacin. In addition, the TC/HDL-C ratio significantly (\( p = .001 \)) decreased by 14.8% (5.4–4.5) with 4 weeks of extended-release niacin. Although the concentrations of TC, LDL-C, and TG tended to decrease with extended-release niacin, the changes were not statistically significant.

An average of 3-day caloric intake and macronutrient contents including carbohydrate, fat, and protein for each condition are presented in Table 4. All macronutrient contents for each condition were similar, and there were no significant differences in total caloric intake, carbohydrate, fat, and protein contents for each condition. No participant reported any additional physical activity during the study period other than the exercise treatment as part of the investigation.

### DISCUSSION

The present study examined the effects of 1,000 mg/day of extended-release niacin for 4 weeks and a single bout of aerobic exercise expending 400 kcal on blood lipids and lipoproteins in sedentary postmenopausal women. The main research questions were (a) do niacin and exercise independently influence blood lipids and lipoproteins? and (b) does the combination of niacin and exercise intervention improve blood lipids and lipoproteins significantly more than either niacin or exercise alone? In the current study, extended-release niacin significantly increased the concentrations of HDL-C (12.4% or 5.4 mg/dL) and HDL_2-C (33.3% or 3.6 mg/dL) and decreased the TC/HDL-C ratio (14.8%). These changes were similar to the results of Goldberg and colleagues (23) who reported an increase in HDL-C (15% or 6.9 mg/dL) and HDL_2-C (38% or 2.3 mg/dL) and a reduction of the TC/HDL-C ratio (17%) in individuals with
Table 2. Blood Lipids and Lipoproteins and TC/HDL-C Values for Each Trial Over 48-Hour Periods

<table>
<thead>
<tr>
<th></th>
<th>Rest 0 h</th>
<th>Exercise 24 h</th>
<th>Exercise 48 h</th>
<th>Rest 0 h</th>
<th>Exercise 24 h</th>
<th>Exercise 48 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG</td>
<td>96.5±38.0</td>
<td>226.1±31.7</td>
<td>166.3±26.6</td>
<td>101.0±47.8</td>
<td>227.6±31.1</td>
<td>167.4±27.1</td>
</tr>
<tr>
<td>TC</td>
<td>225.0±32.9</td>
<td>221.2±34.5</td>
<td>165.4±28.9</td>
<td>22.2±5.2</td>
<td>11.5±4.8</td>
<td>4.6±1.0</td>
</tr>
<tr>
<td>HDL-C</td>
<td>43.3±8.6</td>
<td>10.4±4.6</td>
<td>16.3±5.8</td>
<td>43.7±9.2</td>
<td>11.1±5.4</td>
<td>4.6±1.0</td>
</tr>
<tr>
<td>LDL-C</td>
<td>32.5±6.2</td>
<td>32.6±6.0</td>
<td>32.6±6.0</td>
<td>11.1±4.9</td>
<td>11.1±4.9</td>
<td>4.6±1.0</td>
</tr>
<tr>
<td>TCHDL-C</td>
<td>5.4±1.3</td>
<td>5.4±1.4</td>
<td>5.4±1.4</td>
<td>5.4±1.4</td>
<td>5.4±1.4</td>
<td>4.6±1.0</td>
</tr>
</tbody>
</table>

Note: All values are means ± SD. HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride.
performing a single bout of exercise at 70% VO2 peak until 400 kcal were expended, whereas TG was reduced to 8.5% (9.0 mg/dL) at 24 hours post-exercise. Although Weise and colleagues (15) and the current study used similar exercise intensity and volume, TG in the current study did not change after a single bout of exercise. One of the main differences between the current study and Weise and colleagues (15) was a different concentration of TG at baseline. The concentration of TG in the current study before exercise was 88.8 mg/dL, whereas the initial concentration of TG in the study by Weise and colleagues (15) was 127.0 mg/dL. The magnitude of exercise-induced reduction in TG is dependent upon the baseline level of TG (9,30), suggesting that individuals with elevated initial TG may have a greater reduction following exercise than those with normal TG at baseline. Although the present study did not measure LPL activity, several studies have previously reported that a single bout of exercise may increase LPL activity, which consequently lowers TG (14,32,53). However, this exercise-induced acute response of LPL activity may be gender specific because LPL activity increased only in men but not in premenopausal women after cycling exercise at 85% of lactate threshold for 90 minutes (54). Neither TG concentration nor LPL activity changed after 4 weeks of aerobic exercise (65% VO2 reserve), accumulating a total of 2,000 kcal/week in postmenopausal women (11). Moreover, both LPL activity and TG concentration actually decreased 24 hours following a single bout of exercise (400 kcal) in hypercholesterolemic (TC ≥ 200 mg/dL) postmenopausal women (15). These inconsistent results of LPL responses to exercise in women suggest that TG may be modulated by factors other than LPL (15).

The concentration of HDL-C in the current study did not change, although other studies have suggested that a single bout of exercise can increase HDL-C up to 34% (13,55,56). Following 15-minute interval arm ergometry exercise at 65%–75% HRmax, HDL-C increased by 9.0% (34.0 to 37.0 mg/dL) in middle-aged cardiac patients (13). The HDL-C concentration increased up to 6.0 mg/dL 48 hours after a single session of moderate intensity exercise in both normocholesterolemic and hypercholesterolemic men (14) and trained women (56). Weise and colleagues reported an increase in HDL-C (3.0 mg/dL or 4.8%) in postmenopausal women 24 hours after a single bout of exercise. However, this exercise-induced increase in HDL-C was not significant anymore at 48 hours post-exercise. It also has to be noted that HDL-C at baseline (65.0 mg/dL) in the study by Weise and colleagues (15) decreased to 62.0 mg/dL immediately following exercise and then increased back to 65.0 mg/dL 24 hours after exercise, which was statistically significant from immediately following exercise. Changes in lipids and lipoproteins including HDL-C immediately after exercise may be associated with a change in plasma volume (9), but Weise and colleagues (15) did not measure or control for the plasma volume change. Therefore, it is difficult to determine if the significant increase in HDL-C immediately following exercise was actually induced by exercise or plasma volume change. Williams and colleagues (17) suggested that the HDL-C response to exercise may be influenced by the preexercise HDL-C concentration. However, given the large differences in initial HDL-C between the current study (43.1 mg/dL) and the study by Weise and colleagues (15) (65.0 mg/dL), baseline HDL-C does not appear to be a significant factor in sedentary postmenopausal women. Alternatively, a minimal exercise threshold may be required to significantly increase HDL-C in different individuals (53,57). Therefore, an energy expenditure greater than 400 kcal may be required to significantly alter HDL-C in sedentary postmenopausal women.

The responses of HDL-C subfractions and the TC/HDL-C ratio to a single bout of exercise are inconsistent (15,16,32,53,58,59). In the current study, HDL2-C, HDL3-C, or the TC/HDL-C ratio was not altered by exercise. Similar to the current study, both HDL2-C and HDL3-C did not change in response to a single bout of exercise in young (16) and postmenopausal (15) women or normolipidemic and hyperlipidemic men (32). In contrast, following a high

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Table 4. Average of 3-Day Dietary Consumption for Each Trial

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Niacin</th>
<th>After Niacin</th>
<th>Before Exercise</th>
<th>After Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Calories (kcal)</td>
<td>1,514.1 ± 399.9</td>
<td>217.4 ± 30.0</td>
<td>223.8 ± 32.6</td>
<td>219.5 ± 29.7</td>
</tr>
<tr>
<td>CHO (%)</td>
<td>47.5 ± 9.2</td>
<td>35.7 ± 8.3</td>
<td>16.8 ± 5.9</td>
<td></td>
</tr>
<tr>
<td>Fat (%)</td>
<td>46.8 ± 6.0</td>
<td>37.8 ± 6.2</td>
<td>15.0 ± 2.5</td>
<td></td>
</tr>
<tr>
<td>Protein (%)</td>
<td>51.2 ± 13.1</td>
<td>36.0 ± 10.6</td>
<td>17.4 ± 5.1</td>
<td></td>
</tr>
</tbody>
</table>

*Note: All values are mean ± SD. CHO = carbohydrate; EX = no-niacin exercise; NR = niacin rest; NEX = niacin exercise; R = no-niacin rest.*
volume (1,500 kcal) single bout of exercise, trained men increased HDL₂-C and HDL₃-C by 43.0% (6.0 mg/dL) and 25.0% (7.0 mg/dL), respectively (53). The high-density lipoprotein subfraction metabolism is associated with LCAT activity (38). Increased LCAT activity promotes conversion of small dense HDL₂-C to large less dense HDL₂-C by progressively converting and storing cholesterol esters in the core of HDL₂-C particles (38,60,61). The LCAT activity plays an important role in the maturation of pre-β-1 HDL (38), which consequently promotes the initiation of the reverse cholesterol transport pathway (38,58). The activity of LCAT 24 hours following a single bout of exercise (400 kcal) significantly increased from 4.78 to 5.12 μmol cholesterol ester L/h (liters per hour) only in normocholesterolemic (mean TC = 172.0 mg/dL) but not in hypercholesterolemic postmenopausal women (mean TC = 228.0 mg/dL) (15). In contrast, the LCAT activity in both normocholesterolemic and hypercholesterolemic men did not change following a single bout of exercise at 70% VO₂max requiring 500 kcal (14). Therefore, it is difficult to conclude how a single bout of exercise affects LCAT activity in different populations. It may be speculated, based on the study by Weise and colleagues (15), that LCAT activity in sedentary postmenopausal women with elevated TC levels (TC = 226.0 mg/dL) in the current study may not be influenced by a single bout of exercise.

Because niacin and exercise ameliorate blood lipids and lipoproteins via different mechanisms, the current study expected an additive effect of a single bout of exercise when combined with extended-release niacin on blood lipids and lipoproteins. Although extended-release niacin alone improved HDL-C, HDL₂-C, and the TC/HDL-C ratio, these niacin-induced changes were not significant anymore when combined with a single bout of exercise. There was no synergistic effect of the combination of a single bout of exercise and extended niacin on TC, LDL-C, TG, or HDL₃-C. Thus, the current study suggests that a minimal dosage (>1,000 mg/d) and duration (>4 weeks) of extended-release niacin may be required to significantly decrease TC, LDL-C, and TG in sedentary postmenopausal women who have initially elevated TC and LDL-C but normal TG. In addition, a single bout of exercise that requires an energy expenditure greater than 400 kcal may be necessary to significantly improve blood lipid and lipoprotein profiles in sedentary postmenopausal women. Although the current study did not examine any biochemical events related to exercise or niacin metabolism, some of the proteins or enzymes associated with lipid and lipoprotein metabolism may interfere with each other when the exercise intervention was added to extended-release niacin. Due to the lack of information available, it is difficult to mechanistically explain why a single bout of exercise when combined with extended-release niacin could not further improve blood lipids and lipoproteins more than extended-release niacin or exercise alone in sedentary postmenopausal women. Further research investigating the biochemical mechanism of the niacin and exercise interventions and targeting on different population with the different doses of niacin and exercise is warranted. Clinicians and health providers have often recommended hormone replacement therapy for postmenopausal women to improve their CVD risk factors because hormone replacement therapy can positively alter blood lipids and lipoproteins by increasing HDL-C and decreasing LDL-C (3). Thus, additional studies examining the biochemical events of the niacin, hormone replacement therapy, and exercise interventions in healthy or dyslipidemic postmenopausal women are necessary to provide clinicians and researchers with a clear understanding of blood lipid and lipoprotein metabolism associated with these interventions and an appropriate and effective dose of these interventions.

Conclusion

The concentration of TC, LDL-C, or TG did not significantly change after 4 weeks of 1,000 mg/d extended-release niacin, whereas HDL-C and HDL₂-C increased and the TC/HDL-C ratio decreased following extended-release niacin without the exercise intervention. Therefore, 1,000 mg/d of extended-release niacin for 4 weeks favorably increases HDL-C, predominantly HDL₂-C, and decrease the TC/HDL-C ratio in sedentary postmenopausal women, who are generally at greater risk for developing CVD. Despite its known positive effect, a single bout of aerobic exercise requiring 400 kcal in the current study did not provide lipid or lipoprotein altering effects. The combined effects of extended-release niacin and a single bout of exercise did not provide a synergistic effect on blood lipids and lipoproteins in sedentary postmenopausal women.

References


