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Effect of an advanced glycation end product-restricted diet and exercise on metabolic parameters in adult overweight men

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ABSTRACT

Objectives: The aim of this study was to review the effect of a low advanced glycation end product (AGEs) diet, exercise, and a combination of both on circulating AGE levels as well as on plasma lipids and anthropometric parameters.
Methods: Forty-three overweight or obese men (body mass index [BMI] >25 kg/m^2), 30 to 55 y, participated in a 12-wk study and were randomly assigned to one of three groups: low AGE diet, exercise with habitual food intake, or exercise plus low AGE diet. Exercise was for 45 min at 65% to 75% of their maximum heart rate three times a week. We measured somatometric variables (BMI and waist circumference), blood glucose, lipids, and serum AGEs (N^e-[Carboxymethyl]Lysine [CML] and methylglyoxal [MG]) at baseline and at 12 wk.
Results: Exercise alone was associated with decreased somatometric variables; the low AGE diet had the same effects and decreased serum CML and MG and when combined with exercise reproduced all these effects, but also decreased triacylglycerols and increased high-density lipoprotein. Correlation analysis showed that both changes of CML and MG correlated with changes in dietary AGEs ($P < 0.020$ and $P < 0.038$, respectively); change in maximum oxygen consumption correlated inversely with change in weight and triacylglycerols. Regression analyses, including change in dietary AGEs and in dietary calories, showed that change in dietary AGEs was the independent determinant of change in CML ($P < 0.020$) and MG ($P < 0.038$).
Conclusions: An AGE-restricted diet reduces serum AGE and indices of body fat. The addition of exercise to the restricted diet has the same effects but also improves lipid profile.

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Introduction

The epidemic of overweight and obesity and their complications, including insulin resistance (IR) and type 2 diabetes mellitus (T2DM), is rising worldwide both in developed and in developing countries [1], and in all age groups [2]. It is also an important health problem in Mexico where there is a high prevalence of overweight and obesity [3]. Both dietary caloric restriction and exercise have been reported to reduce obesity [4, 5]. A study in young, healthy, nonsmoking women during 2-mo of aerobic cycling training with 60-min duration, three times a week induced significant changes in the parameters of body

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composition, increased levels of high-density lipoprotein (HDL) and low-density lipoprotein (LDL) and increased maximum oxygen consumption (VO_2 max) [6]. Exercise training also has been shown to improve lipid profile in adolescent males [7]. Additionally, regular exercise may cause a gradual reduction of serum triacylglycerols (TGs), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), body mass index (BMI) and body fat, and an increase of HDL cholesterol (HDL-C). Aerobic exercise seems more effective than other forms of exercise in reducing body fat [8]. A calorie-restricted diet has been shown to improve serum lipid profile, which if combined with exercise, is targeted at improving body composition [4]. The effectiveness of both aerobic exercise and resistance training in controlling and improving cholesterol levels through various modalities, frequency, intensity, and duration of exercise has been demonstrated in different populations [9]. Genetic factors may be important in terms of the response to diet; for example it has been reported that Thr54 allele carriers responded better to a moderate fat diet decreasing somatometric variables and C-reactive protein [10].

Exercise also has been shown to diminish levels of circulating advanced glycation end products (AGEs). AGEs are a heterogeneous group of compounds created through nonenzymatic reactions between reducing sugars and free amino groups of proteins, lipids, or nucleic acids [11,12], Their pathologic effects in diabetes [13] and in the development of complications of obesity such as metabolic syndrome (MetS) and IR [14], are related to the ability of these compounds to promote oxidative stress and inflammation by binding with cell surface receptors or cross-linking with body proteins, altering their structure and function [15]. It has been demonstrated that a program of tai chi performed twice per week for 12 mo decreased serum AGE concentrations in 60 healthy overweight patients, aged 49 to 53 y [16].

Recently, it has been recognized that AGEs of dietary origin are an important determinant of the body AGE pool [17] and an AGE-restricted diet has been shown to have a significant effect in improving IR in patients with T2DM [18]. Moreover, many of the beneficial effects of reduced caloric intake have been associated with reduced AGE intake, at least in mice [19].

The aim of the present study was to investigate the effect of a 12-wk intervention with a low AGE diet, exercise, or a combination of both on circulating AGE levels as well as on plasma lipid profile and anthropometric parameters in a group of overweight or obese men. Our hypothesis was that aerobic exercise and a low AGE diet would have a synergistic effect, diminishing serum AGEs and improving metabolic parameters compared with the effect of each intervention alone.

Material and methods

Seventy-five overweight or obese men (BMI >25 kg/m^2), aged 30 to 55 y, were invited to participate in the study (43 completed the study and 32 dropped out for personal reasons) from the community served by the Department of Medical Sciences of The University of Guanajuato (León, México) using advertisement in local newspapers and on the radio. Interested individuals were screened by personal interview with a member of the research team. Participants were required to be sedentary or relatively inactive; involved in less than three sessions of 30 min each per week of physical activity; nonsmokers; and free of known chronic diseases including diabetes, renal, or cardiovascular disease. Participants were randomly assigned to one of three groups: a low AGE diet (group 1), an exercise with habitual food intake (group 2), or an exercise plus low AGE diet group (group 3). Randomization was done according to aleatory numbers generated by computer and were kept in consecutively numbered envelopes opened at the moment of participant enrollment into the study. All participants signed an informed consent approved by the Institutional Review Board at the Department of Medical Sciences. Universidad de Guanajuato, Guanajuato, México.

Anthropometric parameters

Weight and height were measured with a stadiometer (Seca, Germany). Participants were barefoot and wearing light clothing; waist circumference (WC) was measured as previously described [20].

Aerobic exercise

All participants were initially evaluated with a resting electrocardiogram and then started on an incremental treadmill exercise test according to an earlier developed protocol [21]. Heart rate was measured every 60 sec using a portable heart rate monitor (Polar RS400, Finland). At the end of the test, VO_2 max (expressed in mL·kg·min^{-1}) and maximum heart rate (HR max) of training were calculated. The VO_2 max was calculated using the following equation: VO_2 max (mL·kg·min^{-1}) = 0.2 (speed) + 0.9 (speed) (% inclination) speed + 3.5 [22]. VO_2 peak was used as an index of cardiorespiratory fitness.

Exercise training and nutritional intervention

All participants in the exercise groups underwent a 12-wk supervised aerobic exercise program three times per week, lasting 45 min each time according to pre-established heart rate (65%–75% of their HR max). Each session was supervised by one researcher in a municipal sport center. The participants wore a portable heart rate monitor (Polar RS400, Finland) and heart rate was recorded every 5 min to check exercise intensity. Each session consisted of 5-min warm-up and stretching, followed by 45 min of aerobic running and finally 5 min at the end for stretching.

Groups 1 and 3 were given precise instructions on how to follow a diet that maintained their caloric and nutrient intakes but significantly reduced AGE content; the latter was achieved mostly by changing cooking methods in food preparation to avoid exposure to dry heat such as frying, broiling, grilling, and roasting and to favor cooking with lower temperatures and high-water, content as in stewing and poaching, as previously described [22]. The second group continued consuming their habitual meals. The energy and nutrient consumption was calculated with the program Nutrikcal (University of Monterrey, México) and AGE intake was calculated from a database of ~560 foods that listed AGE values and expressed as AGE kU/d [23].

Of the initial 75 participants, only 43 completed the intervention (15 in the diet plus exercise group, 14 in the exercise group, and 14 in the diet group). The remainder of the participants were excluded because of lack of adherence with the diet or exercise (attendance to <80% of the exercise sessions), or both. The sample size was calculated according to expected changes in serum AGEs, as previously reported [24] and considering $\alpha = 0.05$ and $\beta = 0.20$ and power of 80%.

Measurement of biochemical markers

All participants underwent a complete physical examination and provided fasting blood samples at baseline and at the completion of 12 wk of intervention for measurement of several parameters.

Serum TG, TC, and HDL-C levels were measured by enzymatic colorimetric kits (Spinreact, Spain). Plasma glucose was measured using glucose oxidase/peroxidase (Lakeside, Mexico City). N^{ε}-(Carboxymethyl)Lysine (CML) and methylglyoxal (MG) derivatives in serum were quantified by enzyme-linked immunosorbent assays (ELISAs), using two non–cross-reactive monoclonal antibodies (mAbs; 4 G9 and MG3 D11 mAbs) raised against synthetic standards, CML-bovine serum albumin (BSA) and MG-BSA, respectively. CML and MG were measured by ELISA as previously described [25]. Test sensitivity for CML and MG was 0.1 U/mL and 0.004 nmol/mL, respectively; the intra-assay variation was ±2.6% (for CML) and ±2.8% (for MG), and the inter-assay variation was ±4.1% (CML) and ±5.2% (MG).

The researchers involved in the assessment of metabolic parameters and biochemical determinations were unaware of the group assignment of participants.

Statistical analysis

All values are expressed as mean ± SD. Difference of means between groups were analyzed by Student's *t* test or analysis of variance (ANOVA), followed by the Bonferroni collection for multiple comparisons, depending on the number of groups. We performed correlation analyses between changes in different parameters during the intervention using Spearman's coefficients. There were only two visits for blood tests: at baseline and at the end of 3 mo. Significance of changes during the intervention was determined by comparing the changes between baseline and end of study within each group by paired *t* test, and by comparing the differences among means of the three groups at the end of the

study by ANOVA. We also performed a two-way ANOVA with factors for group and time. Linear regression analysis was used to examine the effect of dietary AGE intake on several parameters in a model including weight change. First, we determined the association between study group and each one of the other biochemical/metabolic parameters (CML, MG); then we added weight change to the model and determined the effect on the association.

All analyses were performed using SPSS 20.0 software (SPSS, Chicago, IL, USA). Significance was defined as a value of $P < 0.05$ and based on two-sided tests.

Results

At baseline there were no differences among the three groups, except for weight and HDL-C, suggesting adequate randomization (Table 1).

Tables 2–4 describe the effect of the respective intervention on anthropometric parameters, lipid profile, and serum AGE levels. Table 2 demonstrates that a low AGE diet alone significantly diminished weight, BMI, WC, and serum AGEs (both CML and MG). Table 3 shows that exercise with habitual diet only diminished weight, BMI, and WC. The combination of a low AGE diet plus exercise demonstrated significant decrease of weight, BMI, WC, Tgs, and serum AGEs (CML and MG), while increasing HDL-C (Table 4).

As expected, both dietary intervention groups showed significant decreases in dietary AGE intake, expressed in absolute terms and as a fraction of dietary caloric intake. Both exercise intervention groups with showed improvement of VO_2 max, suggesting aerobic conditioning (Tables 2–4). No adverse events attributable to the intervention were reported during the duration of the study. Both changes of CML and MG correlated with changes in dietary AGEs ($r = 0.353$, $P < 0.020$; $r = 0.317$, $P < 0.038$, respectively) and changes in dietary kcal ($r = 0.305$, $P < 0.047$; $r = 0.287$, $P < 0.062$, respectively). Regression analyses including changes in dietary AGEs and changes in dietary energy intakes showed that changes in dietary AGEs were the independent determinants of changes in CML ($P < 0.020$) and in MG ($P < 0.038$). Change in VO_2 max correlated inversely with changes in weight and changes in TGs ($r = -0.464$, $P < 0.002$; $r = -0.424$, $P < 0.005$, respectively). Change in VO_2 max was the independent determinant of changes in TGs ($P < 0.026$) in a model including changes in dietary AGEs, changes in dietary kcal, and changes in weight. Change in VO_2 max also was the independent determinant of changes in weight ($P < 0.008$) in a model including changes in dietary kcals and changes in dietary AGEs.

ANOVA comparison of the means of the three groups at the end of the study demonstrated significant changes in means for dietary AGEs, serum CML, and serum MG in both, dietary intervention groups compared with exercise alone and for VO_2 max in both exercise groups compared with diet alone.

Table 1
Baseline characteristics of study population

Parameters	Diet* + exercise	Diet* alone	Exercise alone	*P*-value†
n	15	14	14	
Age (y)	44.3 ± 5.3	40. ± 4.8	43.5 ± 7.1	0.139
Weight (kg)	82.7 ± 9.6	88.2 ± 8.9	80.3 ± 5.8	0.046
BMI (kg/m^2)	28.9 ± 2.2	29.4 ± 2.2	28.3 ± 1.7	0.352
Waist (cm)	102.2 ± 5.1	103.4 ± 7.0	100.2 ± 6.4	0.382
SBP (mm Hg)	125.1 ± 12.5	128.2 ± 15.3	126.7 ± 10.4	0.814
DBP (mm Hg)	82.2 ± 13.3	81.1 ± 12.4	81.7 ± 8.5	0.967
FBG* (mmol/L)	4.99 ± 0.78	5.08 ± 0.46	5.30 ± 0.72	0.462
TG (mmol/L)	2.2 ± 1.32	2.0 ± 0.78	2.31 ± 0.91	0.734
HDL-C (mmol/L)	1.27 ± 0.16	1.45 ± 0.22	1.28 ± 0.16	0.022
LDL-C (mmol/L)	2.37 ± 0.59	2.30 ± 0.77	2.66 ± 0.47	0.281
sCML (U/mL)	10.1 ± 1.5	10.8 ± 1.7	10.3 ± 2.1	0.599
sMG (nmol/mL)	2.1 ± 0.29	2.0 ± 0.40	2.0 ± 0.27	0.770
Diet-Cal (kcal/d)	2471 ± 595	2635 ± 572	2353.0 ± 604	0.453
Diet-AGE (kU/d)	13 019 ± 4526	14 311 ± 5818	13 284 ± 4983	0.777
Diet-AGE density*	5.3 ± 1.4	5.5 ± 2.0	5.8 ± 1.9	0.781
Heart rate max (bpm)	174.9 ± 10.3	180.6 ± 9.0	178.2 ± 14.5	0.413
VO_2 max (mL·kg·min^{-1})	36.5 ± 4.1	33.8 ± 2.3	35.6 ± 2.8	0.075

AGE, advanced glycation end product; BMI, body mass index; DBP, diastolic blood pressure; bpm, beats per minute; Diet-Cal, low AGE diet; Diet-AGE density, daily AGE intake/daily caloric intake; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HR, heart rate; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; sCML, N^{ε}-(Carboxymethyl)Lysine; sMG, methylglyoxal; TG, triacylglycerol; VO_2, oxygen consumption

* All values are expressed in means ± SD.

† *P*-value, statistically significant differences among means by analysis of variance.

Table 2
Changes in men on a low AGE diet intervention

Parameters	Baseline*	3-mo follow-up*	*P*-value
Weight (kg)	88.2 ± 8.9	85.1 ± 8.8	0.009
BMI (kg/m^2)	29.4 ± 2.23	28.3 ± 1.9	0.010
Waist (cm)	103.4 ± 7.0	99.1 ± 6.6	0.008
SBP (mm Hg)	128.2 ± 15.3	123.3 ± 12.5	0.073
DBP (mm Hg)	81.1 ± 12.4	78.8 ± 10.21	0.284
FBG* (mmol/L)	5.08 ± 0.46	4.89 ± 0.36	0.080
TG (mmol/L)	2.00 ± 0.79	1.79 ± 0.85	0.165
HDL-C (mmol/L)	1.45 ± 0.22	1.34 ± 0.19	0.075
LDL-C (mmol/L)	2.30 ± 0.77	2.30 ± 0.72	0.970
sCML (U/mL)	10.8 ± 1.7	9.4 ± 2.0	0.012
sMG (nmol/mL)	2.0 ± 0.40	1.7 ± 0.34	0.013
Diet-Cal (kcal/d)	2635 ± 572	1940 ± 301	0.000
Diet-AGE (kU/d)	14 311 ± 5818	6389 ± 2501	0.000
Diet-AGE density*	5.5 ± 2.0	3.3 ± 1.1	0.003
HR max (bpm)	180.6 ± 9.0	178.6 ± 11.5	0.322
VO_2 max (mL·kg·min^{-1})	33.8 ± 2.3	34.9 ± 3.2	0.202

AGE, advanced glycation end product; BMI, body mass index; DBP, diastolic blood pressure; bpm, beats per minute; Diet-Cal, low AGE diet; Diet-AGE density, daily AGE intake/daily caloric intake; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HR, heart rate; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; sCML, N^{ε}-(Carboxymethyl)Lysine; sMG, methylglyoxal; TG, triacylglycerol; VO_2, oxygen consumption

* All values are expressed in means ± SD.

Table 3
Changes in men on the habitual diet + exercise intervention

Parameters	Baseline*	3-mo follow-up*	*P*-value
Weight (kg)	80.3 ± 5.8	78.5 ± 6.3	0.022
BMI (kg/m^2)	28.3 ± 1.7	27.7 ± 1.72	0.042
Waist (cm)	100.2 ± 6.4	97.3 ± 5.1	0.012
SBP (mm Hg)	126.7 ± 10.4	122.8 ± 13.4	0.063
DBP (mm Hg)	81.7 ± 8.5	80.6 ± 9.0	0.500
FBG* (mmol/L)	5.30 ± 0.72	5.18 ± 0.50	0.456
TG (mmol/L)	2.31 ± 0.91	1.89 ± 1.03	0.084
HDL-C (mmol/L)	1.28 ± 0.16	1.37 ± 0.19	0.074
LDL-C (mmol/L)	2.66 ± 0.47	2.72 ± 0.63	0.753
sCML (U/mL)	10.3 ± 2.1	10.7 ± 2.8	0.646
sMG (nmol/mL)	2.0 ± 0.27	1.9 ± 0.6	0.336
Diet-Cal (kcal/d)	2353 ± 603	2310 ± 757	0.737
Diet-AGE (kU/d)	13284 ± 4983	11223 ± 4147	0.052
Diet-AGE density*	5.8 ± 2	5.1 ± 2	0.114
HR max (bpm)	178.2 ± 14.5	173.6 ± 11.5	0.012
VO_2 max (mL·kg·min^{-1})	35.6 ± 2.8	37.5 ± 2.93	0.001

AGE, advanced glycation end product; BMI, body mass index; DBP, diastolic blood pressure; bpm, beats per minute; Diet-Cal, low AGE diet; Diet-AGE density, daily AGE intake/daily caloric intake; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HR, heart rate; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; sCML, N^{ε}-(Carboxymethyl)Lysine; sMG, methylglyoxal; TG, triacylglycerol; VO_2, oxygen consumption

* All values are expressed in means ± SD.

Table 4
Changes in men on the low AGE diet + exercise

Parameters	Baseline*	3-mo follow-up*	*P*-value
Weight (kg)	82.7 ± 9.6	79.3 ± 9.3	0.015
BMI (kg/m^2)	28.9 ± 2.2	27.7 ± 2.0	0.000
Waist (cm)	102.2 ± 5.1	97.4 ± 6.6	0.000
SBP (mm Hg)	125.1 ± 12.5	126.3 ± 13.7	0.667
DBP (mm Hg)	82.2 ± 13.3	81.0 ± 9.7	0.475
FBG* (mmol/L)	4.99 ± 0.79	4.86 ± 0.42	0.49
TG (mmol/L)	2.20 ± 1.32	1.49 ± 0.52	0.015
HDL-C (mmol/L)	1.27 ± 0.16	1.44 ± 0.18	0.003
LDL-C (mmol/L)	2.37 ± 0.59	2.69 ± 0.71	0.082
sCML (U/mL)	10.1 ± 1.51	8.6 ± 1.87	0.003
sMG (nmol/mL)	2.12 ± 0.29	1.5 ± 0.57	0.001
Diet-Cal (kcal/d)	2471 ± 595	1826 ± 410	0.000
Diet-AGE (kU/d)	13 019 ± 4526	7306 ± 2811	0.000
Diet-AGE density*	5.3 ± 1.4	4.1 ± 1.4	0.038
HR max (bpm)	174.9 ± 10.3	174.9 ±9.5	0.977
VO_2 max (mL·kg·min^{-1})	36.5 ± 4.1	38.6 ± 4.3	0.000

AGE, advanced glycation end product; BMI, body mass index; DBP, diastolic blood pressure; bpm, beats per minute; Diet-Cal, low AGE diet; Diet-AGE density, daily AGE intake/daily caloric intake; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; HR, heart rate; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; sCML, N^{ε}-(Carboxymethyl)Lysine; sMG, methylglyoxal; TG, triacylglycerol; VO_2, oxygen consumption

* All values are expressed in means ± SD.

Two-way ANOVA factored for group and time showed significant difference for serum CML ($P < 0.038$); diet kcals ($P < 0.003$), and diet AGEs ($P < 0.002$) and marginally significant difference for serum MG ($P = 0.05$) and diet AGE density ($P = 0.06$) (see Table 5).

Discussion

The present study showed that a 3-mo intervention with either moderate aerobic exercise and/or dietary AGE restriction in a group of overweight Mexican men had different effects in metabolic risk factors depending on the specific intervention. Although exercise alone was associated with a decrease in weight, BMI and WC, a low AGE diet had the same effects but also decreased levels of circulating AGEs and when combined with exercise reproduced all these effects together while inducing a healthier lipid profile (lowering TGs and raising HDL-C).

Our findings in the group with exercise and habitual dietary intake were similar to those of a previous study that demonstrated decreased body weight, BMI, body fat, and TG levels together with increased HDL-C concentration in a group of healthy young women, aged 18 to 24 y [6]. In another study with 376 overweight men, aged 30 to 62y, who were subjected to brisk walking lasting ≥10 min every day for 1 y a significant decrease of WC and TG levels and an increase of HDL levels were seen [26]. The sex and age of the latter individuals were similar to our study participants, but although there was a tendency to decrease TGs and increase HDL levels in our participants, the changes did not reach statistical significance.

On study examined the effects of an exercise program conducted daily (1.5 h duration) each week for ≥3 mo up to a maximum of 18 mo in a group of 31 individuals, compared with 36 controls [27]. Weight, %body fat, WC, and levels of TG, TC, HDL-C, and LDL-C improved significantly in the exercise group compared with controls, although no differences were found for BMI and blood glucose levels.

A study in obese men assigned to one of four study groups (diet-induced weight loss, exercise-induced weight loss, exercise without weight loss, and control) for 3 mo demonstrated that VO_2 max improved by approximately 16% in the exercise groups [5]. Weight loss was 1.3 greater in the exercise-induced weight loss group than in the diet-induced weight loss group, raising the importance of the intensity of exercise on the final effects. Blood glucose levels did not change in the treatment groups compared with controls; lipid profiles were not evaluated.

Most previous exercise interventions studied individuals of different ages, lengths of interventions, and types and intensity of exercise than our study. Although most exercise interventions have shown a decrease in body weight and increment of VO_2 max indicating cardiorespiratory conditioning, an effect in improving lipid profile has not been uniform. Our failure to demonstrate enough effect on lipid profile may reflect the mild intensity of exercise in our study as VO_2 max increased only by 5.7%. Recently, it has been reported that a mixed aerobic and resistance training was more effective in the chronic modification of lipid profile in overweight men [28]. Moreover, a meta-analysis suggests that combined training might be the most efficacious exercise modality to improve glycemic control and blood lipids [29]. It is also important to consider the volume of exercise. It has been reported that for most individuals the positive effects of regular exercise on blood lipids at low training volumes may take some time to show up, but noticeable differences frequently occur with energy expenditures of 1200 to 2200 kcals/wk [30,31].

We did not find an effect of 3-mo aerobic exercise intervention alone on serum AGE levels. This differs from three previous reported studies looking at the effect of exercise on AGE levels in general. The first studied the effect of tai chi in a healthy Malaysian population matched with sedentary volunteers >45 y [16]. The participants were randomized either to practice tai chi twice per week or to a control group. Plasma malondialdehyde and AGE concentrations decreased significantly after 12 mo only in the tai chi group. The second study recruited 17 healthy women (aged 30–60 y) who participated in a lifestyle modification protocol aimed at increasing physical activity for 3 mo to measure changes in AGEs [24]. Blood levels of CML decreased in the treatment group compared with controls and changes in CML levels correlated with the intensity of exercise. Finally, the third group studied levels of MG in red blood cells during exercise in eight untrained and five trained men [32]. Each man performed runs of short and long duration. MG content of red blood cells decreased markedly after running, especially in the untrained men. After short runs, the MG concentration had dropped to 13% in the untrained men and 30% in the trained men, and after long runs the concentration fell to 41% in the untrained and 60% in the trained men. Our different results likely reflect the different populations studied and, more importantly, the type and intensity of exercise intervention. We should note that our study followed the American College of Sports Medicine Guidelines supporting aerobic exercise performed 3 to 5 d/wk for 20 to 60 continuous minutes at an intensity of 55% to 90% of HR max [33].

The effect of the low AGE diet on reducing serum AGE levels in our study participants agrees with similar findings previously reported in the literature [34]. A significant decrease in circulating AGE levels was found in a previous study when healthy individuals were exposed to a low AGE diet for 4 mo [35]. A randomized, crossover, diet-controlled intervention trial of 62 healthy volunteers compared the effects of two diets, one consisting of mild steam cooking and the other of high-temperature cooking [36]. The latter group consumed a higher AGE diet and had higher levels of serum CML. A significant effect of a low AGE diet, without significantly changing caloric and nutrient intake, in reducing body weight, BMI or WC, however, has not been reported previously.

Food is a major source of AGEs and these exogenous AGEs are an important contributor to the body AGE pool as they have the same pro-oxidative and proinflammatory actions as their endogenous counterparts [17]. Food-derived AGEs are associated with the development of IR, diabetes, renal disease, and atherosclerosis in mice. Emerging data from several clinical trials support an important role for a high intake of exogenous AGEs in generating increased oxidative stress and inflammation. More importantly, these trials have shown that reducing the dietary AGE content decreases the high oxidative stress characteristic of most chronic diseases [37,38]. A group of women with MetS treated with a calorie-restricted diet with moderate carbohydrate restriction showed decreased diastolic blood pressure and lower prevalence of MetS [39].

The most significant effects in our study were in the group of men with combined exercise and dietary intervention. This group not only decreased anthropometric parameters and serum AGEs, but also improved the lipid profile with reduction of TGs and an increase in HDL levels. We do not find any previous reported studies examining the combined effect of exercise and an AGE-restricted diet without caloric restriction; and this significance remained when we evaluated the differences within and between groups. Main limitations of our study were the relatively small number of participants and a significant percent of dropouts who could not be invited for assessment at the end of the intervention as a control. Moreover, all the participants were men, which limits its generalizability, and perhaps more importantly, the intensity of the exercise might have not been sufficient to elicit significant metabolic changes.

Conclusions

We have demonstrated a beneficial effect of an AGE-restricted diet in reducing serum AGE levels and indices of body fat. Although exercise alone did not have significant metabolic effects in our study, this type of moderate exercise appears to have potentiated the effects of a low AGE diet and it should be recommended.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.nut.2014.10.004

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