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Osteocalcin and glucose metabolism in postmenopausal women subjected to aerobic training program for 8 weeks

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ARTICLE INFO

Article history:
Received 20 December 2010
Accepted 26 August 2011

ABSTRACT

Results of animal studies suggest that osteocalcin (OC) plays an important role in the regulation of carbohydrate metabolism. The aim of the present study was to assess the relationship between biochemical indices of bone turnover and carbohydrate metabolism in postmenopausal women subjected to aerobic training for 8 weeks. The study was conducted on 44 postmenopausal women: 27 of them participated in the training program, and 17 did not undertake any additional physical activity during the study period (control group). Subjects performed a cycle-ergometer physical workout at a level of 70% to 80% of ventilatory threshold intensity for 8 weeks (40-minute sessions, 3 times per week). Serum concentrations of OC, C-terminal telopeptide of type I collagen, osteoprotegerin (OPG), insulin, and glucose were measured; and the homeostasis model assessment of insulin resistance index (HOMA-IR) was calculated before and after the 8-week training program. The training program caused significant decrease in levels of OC ($P < .05$), HOMA-IR ($P < .05$), and waist-to-hip ratio ($P < .05$). No significant changes were observed in C-terminal telopeptide of type I collagen, OPG, insulin, and glucose concentrations. Pretraining OC levels inversely correlated with concentrations of OPG ($P < .05$), glucose ($P < .05$), and insulin ($P < .05$) and with HOMA-IR values ($P < .05$). Our study revealed an association between serum OC concentrations and metabolic markers in postmenopausal women. Regular physical activity was associated with decrease in central adiposity and OC levels and slight reduction of insulin resistance. However, no direct relationships between training-related changes in OC concentrations and metabolic markers were observed.

1. Introduction

Lifestyle modification plays an important role in the prevention and management of metabolic disturbances related to menopause. It is well established that endurance training improves glucose tolerance and decreases insulinemia [1,2]. On the other hand, insulin participates in the homeostasis of skeletal tissue [3]. Insulin sensitivity has been accepted as a significant predictor of bone mineral density, even after correction for weight and age [4]. Strong relationships between total body or femoral neck bone mineral density and blood insulin concentrations have been observed in postmenopausal women, which may explain the protective effects of hyperinsulinemia against bone loss related to decreased estrogen levels during menopause [5].

Animal studies have confirmed the mutual association between carbohydrate and bone metabolism, demonstrating

Author contributions: Anna Wieczorek-Baranowska: conduction of the study, data collection, biochemical analysis, manuscript writing, data discussion; Alicja Nowak: project of the study, data analysis and discussion; Łucja Pilaczyńska-Szcześniak: data interpretation.

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0026-0495/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2011.08.011

the contribution of uncarboxylated osteocalcin (OC), released from bone, to the stimulation of insulin secretion and to the regulation of energy metabolism [6]. Therefore, the aim of the study was to examine the relationship between biochemical bone turnover markers and measures of carbohydrate metabolism in postmenopausal women subjected to aerobic exercise.

2. Methods

2.1. Subjects

The study was conducted on 44 postmenopausal women without diabetes, inflammatory disorders, and recent infections who were not undergoing hormonal replacement therapy. Subjects were assigned to 1 of 2 groups: the training group (T), consisting of 27 volunteers who participated in the training program (64 ± 6.13 years old), and the control group (C), consisting of 17 women who did not undertake any additional physical activity during the study period (65 ± 7.43 years old). The participants were matched, as closely as possible, with respect to age, body mass, and body mass index (BMI). The absence of contraindications to moderate-intensity physical exercise for subjects was confirmed by physicians. All participants were informed and provided their consent to participate in the study. The study protocol was approved by the Local Ethics Committee at the University of Medical Sciences in Poznań.

2.2. Training program

Before the study, and after 4 and 8 weeks of the training period, subjects from the T group underwent ventilatory threshold estimation during the ergometric exercise test (model Ergo Metrics 900; Ergoline, Germany). Respiratory parameters were continuously assessed with the Cardi O_2 computer system (Medical Graphics). The initial workload (25 W) was increased by 25 W every 3 minutes, up to the ventilatory threshold. Maximal oxygen uptake was measured using the indirect method [7].

Subjects performed an 8-week cycle-ergometer physical workout at the level of 70% to 80% of a ventilatory threshold intensity (40-minute sessions: 5-minute warm-up, 30-minute cycling with an individual load, and 5-minute cycling without load), which was repeated 3 times a week.

2.3. Anthropometric and biochemical measurements

Body mass (WPT 60/150.O; Radwag, Radom, Poland) and waist and hip circumferences were measured before and after the training program. Fasting blood samples were taken from the antecubital vein. Serum was separated and stored at −70°C. The immunoenzymatic enzyme-linked immunosorbent assay (ELISA) methods were used to determine serum concentrations of OC (human Osteocalcin Instant ELISA kit; Bender MedSystems, Austria; sensitivity, 0.2 ng/mL; intra-and inter-assay coefficient of variation [CV] of 8.1% and 8.3%, respectively), C-terminal telopeptide of type I collagen (CTX) (CrossLaps ELISA kit; Nordic Bioscience Diagnostics, Denmark; sensitivity, 0.02 ng/mL; CV of 5.2% and 6.7%), and osteoprotegerin (OPG) (human Osteoprotegerin ELISA kit; Biomedica, Austria; sensitivity, 0.14 pmol/L; CV of 7.0% and 7.5%). The concentration of insulin was analyzed using a radioimmunologic assay (BioSource Europe, Belgium; sensitivity, 1 μIU/mL; CV of 1.9% and 6.3%). Glucose concentrations were measured with a commercially available assay (Cormay, Poland), and the homeostasis model assessment of insulin resistance index (HOMA-IR) was calculated [8].

2.4. Statistical methods

The normality of the data distribution was verified using the Shapiro-Wilk test. The *t* test and Mann-Whitney test were used to evaluate the significance of differences between the groups. The differences between paired normally and non-normally distributed variables were evaluated by the *t* test and the Wilcoxon test, respectively. Analysis of covariance was used to calculate the differences between the T and C groups after the intervention. Spearman rank analysis was used to calculate correlation coefficients. P value < .05 was considered significant. The Statistica 8.0 software package was used for statistical analyses.

3. Results

At the beginning of the study, a significant positive correlation between OC and CTX ($P \leq .01$) and inverse correlations between OC and insulin, glucose, HOMA-IR, and OPG ($P < .05$) were found in all participants (Table 1).

The training caused significant decreases in mean levels of OC, waist-to-hip ratio (WHR), and HOMA-IR in the T group (Table 2). Comparative analysis did not reveal any significant time-related changes in other anthropometric and biochemical variables in the T group or in any studied parameters in the C group.

Significant differences between the T and C groups were found with respect to WHR values ($P = .0382$ after the intervention) and glucose concentrations ($P = .0053$ and $P = .0045$, before and after the intervention, respectively). A tendency to between-groups differences in levels of OC and CTX ($P = .0955$, $P = .0809$, respectively) was observed after the intervention; but after adjustment for BMI values, these differences were significant (OC, $P = .0301$; CTX, $P = .0113$).

No significant correlations between training-related changes (differences between the value at baseline and the

Table 1 – Correlations between OC concentrations and biochemical indices in all investigated participants (N = 44) at the beginning of study

OC	Correlation coefficient (*r*)	*P* value
CTX (ng/mL)	0.65	.0001
OPG (pmol/L)	−0.38	.0183
Glucose (mmol/L)	−0.38	.0120
Insulin (μIU/mL)	−0.38	.0106
HOMA-IR	−0.34	.0261

Table 2 – Anthropometric and biochemical indices before and after the intervention in the training (n = 27) and control (n = 17) groups

Parameters		Assessment at baseline	Assessment at 8 wk	P value
Body mass (kg)	T	69.4 ± 9.12	69.2 ± 9.14	.2158
	C	72.8 ± 8.76	72.5 ± 8.64	.1914
BMI (kg/m^2)	T	27.2 ± 3.30	27.2 ± 3.30	.2758
	C	28.8 ± 3.13	28.6 ± 3.07	.3259
WHR	T	0.83 ± 0.05	0.81 ± 0.06*	.0124
	C	0.84 ± 0.07	0.84 ± 0.05	.7897
OC (ng/mL)	T	3.02 ± 2.085	2.54 ± 1.660	.0225
	C	3.19 ± 1.759	3.62 ± 2.445	.7764
CTX (ng/mL)	T	0.38 ± 0.219	0.35 ± 0.227	.1864
	C	0.47 ± 0.250	0.49 ± 0.295	.4265
OPG (pmol/L)	T	7.22 ± 3.273	7.03 ± 2.582	.6849
	C	6.40 ± 1.987	6.31 ± 1.538	.9434
Insulin (μIU/mL)	T	12.73 ± 5.520	10.88 ± 2.956	.0775
	C	11.87 ± 4.116	12.22 ± 5.653	.8361
Glucose (mmol/L)	T	5.64 ± 1.115†	5.37 ± 0.929†	.1075
	C	4.67 ± 0.942	4.58 ± 0.631	.6603
HOMA-IR	T	3.31 ± 1.809	2.64 ± 0.987	.0325
	C	2.52 ± 1.066	2.53 ± 0.963	1.000

Data are expressed as means ± SD. P value among variables at baseline and at 8 weeks.
* $P < .05$ vs control group.
† $P \leq .01$ vs control group.

value after 8 weeks) in levels of OC and HOMA-IR or other variables were found in the T group.

4. Discussion

In the present study, we observed a decrease in OC concentrations and a slight reduction in WHR and HOMA-IR levels after the 8-week aerobic training program; however, changes in these variables were not directly associated. The lack of significant differences between the T and C groups with respect to posttraining values of HOMA-IR probably resulted from the absence of marked disturbances in carbohydrate metabolism and proper body mass in several women recruited for this study (mean BMI in T group = 27.2 kg/m^2). Previous studies have revealed the positive influence of training programs, similar in duration and training regimen to the program applied in the present study, on carbohydrate metabolism [9,10].

The positive correlation between circulating OC (bone formation marker) and CTX (a marker of bone resorption) and the negative relationship between OC and OPG (a marker of osteoclastogenesis inhibition) in all participants at the beginning of the study suggest the coexistence of both of these bone turnover processes. The training-related change in OC and the same tendency in CTX concentrations in the T group (by approximately 16% and 8%, respectively) indicate a decrease in the bone turnover rate after the intervention, which may be favorable for bone mass. Systematic exercises that provide skeletal loading appear to be effective in reducing postmenopausal bone loss [11]. However, OC may have a protective effect on carbohydrate homeostasis, which has been suggested by several authors in the context of obesity or aging [12,13]. Thus, it cannot be excluded that the decrease in OC levels after the training program was the consequence of an improvement in insulin sensitivity. Ferron et al [14] suggested that a positive feedback loop exists between insulin signaling in osteoblasts and OC functions.

In our study, the association between OC and carbohydrate metabolism is confirmed by inverse correlations between serum OC levels and metabolic markers in all participants before the intervention, findings that are consistent with previous studies in postmenopausal women and older individuals [15-19]. The lack of significant associations between changes in OC and HOMA-IR levels during the training program could be due to the influence of several confounders with respect to OC levels. The determination of 25-hydroxy vitamin D serum levels could exclude the contribution of environmental factors to OC levels, but it has been omitted in our study.

The limitation of the present study is the small number of participants. In addition, we did not measure the carboxylated form of OC, which in a study by Shea et al [13] was inversely associated with a 3-year change in HOMA-IR in older adults; this trend was not observed for total OC. Therefore, our results regarding the effects of training on the relationships between OC and metabolic markers should be interpreted with caution. However, correlations between serum levels of OC and CTX, OPG, insulin, glucose, and HOMA-IR in this study may support recently proposed interactions between the bone remodeling and energy metabolism [20].

In conclusion, regular physical activity decreased central adiposity and OC levels and slightly reduced insulin resistance in postmenopausal women. However, no direct associations between training-related changes in OC concentrations and metabolic markers were observed, in spite of their relationships at the beginning of study. Further studies on the various types of exercises and various populations are necessary to reveal the training effects on OC and the metabolic response.

Funding

Authors state no funding.

Conflict of Interest

Authors state no conflicts of interest.

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