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Effects of High Protein and Balanced Diets on Lipid Profiles and Inflammation Biomarkers in Obese and Overweight Women at Aerobic Clubs: A Randomized Clinical Trial

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ABSTRACT

Background: We studied the effects of high protein (HP) and balanced diets (BDs) on lipid profiles, and high-sensitive C-reactive protein (hs-CRP) levels in obese and overweight women.

Methods: In a parallel designed randomized controlled clinical trial, 60 healthy women with body mass index ≥25 kg/m^2, aged 20–46 years, enrolled in an 8-week investigation at aerobic clubs. They were categorized into two groups (HP and BDs), randomly. Fasting lipid profile and hs-CRP levels were evaluated at the beginning and end of the trial. We assessed dietary intake by 3-day records and also used SPSS (version 18; SPSS Inc., Chicago, IL, USA) for data analyzing.

Results: Fifty-six participants completed the intervention. Concentrations of low-density lipoprotein cholesterol ($P < 0.001$ in BD group vs. $P = 0.023$ in HP group) and high-density lipoprotein cholesterol ($P < 0.001$ in BD group vs. $P = 0.002$ in HP group) increased significantly in both groups. Circulating triglycerides levels increased in both intervention grows, but the change in the HP group was not significant compared with the other group ($P = 0.007$ in BD group vs. $P = 0.099$ in HP group). Whereas total cholesterol concentration decreased but not significantly so ($P = 0.53$ in BD group vs. $P = 0.73$ in HP group). There were marginally significant decreases in the hs-CRP levels due to both diets ($P = 0.057$ in BD group vs. $P = 0.086$ in HP group); however, there were no significant differences between the groups.

Conclusions: Administration of HP and BD in overweight and obese women with regular aerobic exercise showed improvement in lipid profiles and hs-CRP levels within the groups, but there were no significant differences between groups.

Keywords: C-reactive protein, diet, inflammation, lipid profile

INTRODUCTION

The rate of overweight and obesity is increasing over the world.[1] A large number of researches are attempting

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to curb the concerning growth and the concomitant disease risk such as lipid profile disturbance and inflammatory disorders.[2,3] Weight reduction is one of the most effective approaches to prevent and manage several associated-degenerative and metabolic disorders.[4] Up to now, the proper macronutrients ratio of weight reducing diet remains uncertain[5] in spite of the common recommendation of low-carbohydrate (CHO) diets, having insufficient evidence of the efficacy, and safety.[6] Recently, there is increasing interests in low- or moderate- CHO/high-protein (HP) diet as a possible alternative solution.[7,8]

The mechanisms underlying increased concentrations of inflammatory factors and their variation because of weight reduction are not yet completely understood. Insulin resistance, obesity Elevate C-reactive protein (CRP) levels[9] and decrease after weight loss.[10,11] Furthermore, CRP is sensitive endothelial indicator dysfunctions (recently recognized as a causal factor in atherogenesis).[12] Diet and physical activity-induced weight reduction are related to improve components of the metabolic syndrome (high-density lipoprotein cholesterol [HDL-C], triglycerides [TG], waist circumference, fasting glucose, and the blood pressure) and CRP concentrations.[12] Decreases in body fat are associated with a reduction in the concentration of CRP.[12]

Farnsworth *et al.*[13] and Skov *et al.*[14] observed that a decrease occurs in TG with HP diets, whereas Parker *et al.*[15] found a reduction of low-density lipoprotein cholesterol (LDL-C) level with an HP diet. However, more research is needed if form either protein (PRO) or CHO HP diets on blood lipids.[16] The discussion goes on considering the most appropriate macronutrient composition of diets to obtain weight loss.[16] In this research, we aimed to assess the result of different PRO and CHO ratio diets on lipid profiles and inflammation biomarkers.

METHODS

Characteristics and participants

In our parallel designed randomized controlled clinical trial, sixty female were athletes who attended in aerobic gyms in Isfahan city from that 56 individuals completed this trial. The number samples were calculated by following formula and the primary information from the study by Noakes *et al.*[17]

$$N = \left(\frac{1+\varphi}{4}\right)\left(\frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2}{\Delta^2}\right) + \frac{Z^2_{1-\alpha/2}}{2(1+\varphi)} \approx 25$$

$$\varphi = 1, \alpha = 5\%, Z_{1-\alpha/2} = 1.96, Z_{1-\beta} = 1.28, \Delta = 1$$

Females between 20 and 46 years and those who had body mass index (BMI) equal or more than 25 kg/m^2 enrolled in the project. Women should be physical active three times per week, with for the duration of 60 min per training session. Our exclusion criteria including being pregnant, lactating, with a history of renal disorders, Type 1 or 2 diabetes, elevated blood pressure, or cardiovascular diseases. All participants who were suitable for this study signed informed consent. Three-day food records (including 1 weekend day and 2 nonconsecutive weekdays) were completed at the beginning and at the end of the 8-week period. This trial is registered with randomized controlled trial IRCT201402245062N7.

Study procedures and variable assessment

Subjects were divided equally into two groups using permuted block randomization method; HP diet (45% of energy from CHO, 25% from PRO, and 30% fat) and balanced diet (BD) (CHO 55%, PRO 15%, and fat 30%).

All subjects had a 500 kcal reduction of total energy (TE) diet, which were calculated by Harris–Benedict formula (655.1 + [9.56 × weight (kg)] + [1.85 × height (cm)] − [4.68 × age (year)]) for 8 weeks. Dietary intake was determined by a 3-day food record at baseline and every 2 weeks. Food intakes were recorded at three different weekdays (the 1st day of the week, the middle of the week, and on the weekend).

Subjects were weighed at baseline and at the end of the study while they had light clothing and no shoes with an accuracy of 0.1 kg (Seca, Model 770, Hamburg, Germany). Height was measured without shoes using unstretchable meter with an accuracy of 0.5 cm in standing position. BMI was calculated by weight in kg/height by meter square. Fasting blood samples were obtained at baseline and after the 8th week following the intervention.

High-sensitive CRP (hs-CRP) was measured by latex-ALTA kit (Biosystem, Tehran, Iran). TG and cholesterol were assessed by glycerol phosphate oxidase/peroxidase method. HDL-C was measured by phosphotungstate/Mg-cholesterol oxidase/peroxidase.

Statistical analysis

We used SPSS (version 18; SPSS Inc., Chicago, IL, USA) for data analysis. One-way multivariate analysis of covariance was used when necessary. $P < 0.05$ was defined as being significant. Quantitative data were shown as mean ± standard deviation, and qualitative data were appeared in frequency (percentage). Normality of studied variables was assessed by the Kolmogorov–Smirnov test. Positive skewed data were subjected to logarithmic transformation. Within group, analysis was performed using paired samples *t*-test, and between groups analysis were conducted using independent samples *t*-test, and Chi-square test was utilized to compare qualitative variables.

RESULTS

Fifty-six individuals were registered in the study; however, the trial was completed only by fifty participants. In this study, six individuals were excluded from the trial: One subject was not interested in completing the rest of the study, two subjects had surgery and diseases, and three subjects did not show up for the final measurement for private reasons. The data for the fifty subjects who completed the trial were entered for analysis. The flow diagram of the study is shown in Figure 1.

Energy, percentage of CHO, fat, and PRO in both groups were significantly different (at the baseline and at the end of the intervention). Respectively, *P* value for energy <0.01 in BD diet and 0.002 in HP diet, *P* value for percentage of CHO 0.006 in BD and 0.025 in HP diets, *P* value for percent of fat 0.02 in BD and 0.022 in HP diets, and *P* value for percent of PRO 0.028 in BD and 0.017 in HP diets. However, a difference of cholesterol, saturated fatty acid, monounsaturated fatty acid, and polyunsaturated fatty acid were not significant (at the baseline and at the end of the intervention). Respectively, *P* value for cholesterol 0.91 in BD and 0.89 in HP diets, *P* value for saturated fatty acid 0.45 in BD and 0.79 in HP diets, *P* value for monounsaturated fatty acid 0.11 in BD and 0.36 in HP diets, and *P* value for polyunsaturated fatty acid 0.47 in BD and 0.88 in HP diets.

At baseline, average of circulating levels of LDL-C in subjects on HP diet was more than standard PRO group (but mean difference LDL-C at baseline and after 8 weeks in HP diet was 9.84 and BD diet 1.15), and these values increased, significantly after intervention, but this increase was greater in BD diet than the other diet. ($P = 0.023$ vs. $P < 0.01$, respectively HP, BD diet).

Mean plasma levels of HDL in BD group were more than in HP group. After intervention, HDL concentrations in both groups increased. This difference was significant and mean of increasing in BD diet was more than in HP diet (4.1 vs. 5.1 mg/dl).

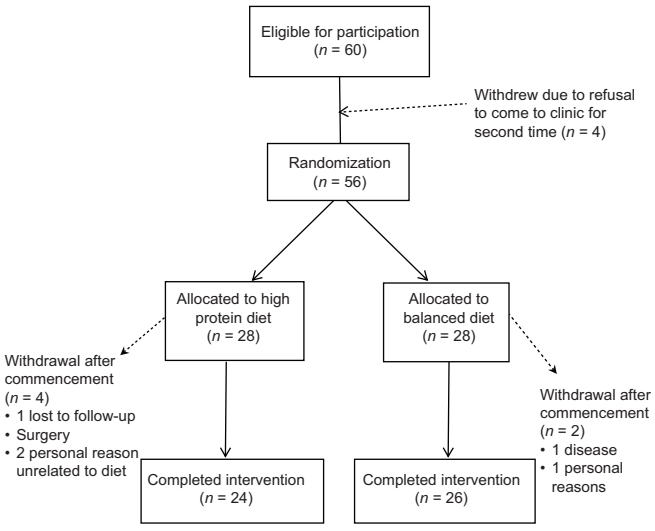

Figure 1: Schematic representation of randomization

Results show that TG levels increased in both interventions. We observed that after TG levels increased in both diets intervention; however, this increase was not statistically significant in HP diet (TG change as 16# ±47 vs. 17# ±30.9 mg/dl for HP in comparison with BD diet) ($P < 0.05$).

Mean plasma levels of total cholesterol (TC) in HP diet was less than in BD diet. After the intervention, levels of TC decreased, but it was not significant, and this reduction in HP group was more than BD group (−2.03 in HP diet and −5.39 in BD diet).

There were marginally significant decreases in hs-CRP level, after intervention in HP and BD diets. A 0.55 reduction in hs-CRP levels in HP group ($P = 0.086$) and 0.74 decline in second group was observed ($P = 0.057$). There was no difference between diets for these variables [Table 1].

DISCUSSION

We assessed the effects of HP and BD on hs-CRP and lipid profiles (LDL-C, HDL-C, TG, and TC) among overweight and obese women who did aerobic exercise three times per week with duration of 60 min per training session. Our findings demonstrated that hs-CRP concentrations decreased significantly.

CRP is produced by the liver. Increasing of CRP levels has been correlated with cardiovascular disease, obesity, diabetes, smoking, and sedentary lifestyle.[18] These findings are consistent with Heilbronn *et al.*[19] that stated that CRP level is decreased following of weight reduction while its decrease had not been affected by dietary compositions, even though they suggested that HP diet can be effective in decreasing CRP concentrations more effective in women with hypertriglyceridemia. Azadbakht *et al.*[20] stated that CRP levels improved marginally among overweight and obese women who adherence HP diet compared to high-carbohydrate (HC) diet (PRO, CHO, and fat: 25%, 45%, and 30% vs. 15%, 55%, and 30%, respectively). Noakes *et al.*[17] observed that CRP concentrations decreased with weight loss in a group HP group (34% PRO, 20% fat, and 46% CHO) and a HC (17% PRO, 20% fat, and 34%) diets, with no significant effect of diet ($P = 0.447$) (time was more important than diet). A longitudinal randomized, parallel trial assessed the effect of soy PRO on CRP concentrations among patients with Type 2 diabetes. Soy PRO group (a diet including 0.8 g PRO/kg body weight (35% animal PROs, 35% textured soy PRO, and 30% vegetable PROs) had a significant reduction in CRP levels compared to placebo group (a similar diet containing 70% animal PROs and 30% vegetable PROs).[21]

Table 1: Comparisons mean±standard deviation lipid profiles and high-sensitive C-reactive protein in both of groups before and after intervention and between groups

	Balanced diet	High-protein diet	*P*
LDL-C* (mg/dl)			
Before intervention	97.18±25.24	109.09±29.5	0.784
After intervention	108.75±25.69	118.93±21.74	
P	<0.001	0.023	
HDL-C† (mg/dl)			
Before intervention	50.26±10.76	49.40±10.73	0.529
After intervention	55.45±10.03	53.59±10.92	
P	<3.59±	0.002	
TG‡ (mg/dl)			
Before intervention	93±51.62	121.86±59.01	0.663
After intervention	110±66.97	137.92±71.79	
P	0.007	0.099	
TC§ (mg/dl)			
Before intervention	190.42±40.01	210.57±46.47	0.75
After intervention	185.03±46.67	208.53±37.94	
P	0.53	0.73	
LDL/HDL			
Before intervention	1.99±0.52	2.28±0.5	0.895
After intervention	1.97±0.48	2.25±0.55	
P	0.642	0.695	
TG/HDL			
Before intervention	2.07±1.33	2.67±1.42	0.753
After intervention	1.97±1.23	2.60±1.39	
P	0.382	0.633	
Hs-CRP‖ (mg/dl)			
Before intervention	2.1±1.8	2.34±2.71	0.358
After intervention	1.35±1.39	1.78±2.19	
P	0.057	0.086	

P<0.05 was considered statistically significant. *LDL-C=Low-density lipoprotein cholesterol, †HDL-C=High-density lipoprotein cholesterol, ‡TG=Triglyceride, §TC=Total cholesterol, ‖Hs-CRP=High-sensitive C-reactive protein

Nuclear factor-κβ modulates expression of inflammatory cytokines, including tumor necrosis factor alpha (TNF-α). Circulating levels of TNF-α have been positively associated with elevated TG and heart failure.[22] CRP has been demonstrated that predict cardiovascular diseases more than other cytokines.[23] Sharman and Volek[24] reported that CRP and TNF-α reduced significantly after weight loss with very low-CHO (PRO, fat, and CHO as percentage of TE were 20%, 25%, and 55%) and low-fat diet (30%, 60%, and <10%, respectively PRO, fat, and CHO) in overweight men. In a study, Ratliff *et al.*[25] demonstrated that carbohydrate-restricted diet (CRD) (% energy from CHO: Fat: PRO = 17:57:26). Seshadri *et al.*[26] found that decrease in CRP concentration after dietary intervention was modestly decreased in both diet groups (low-CHO diet [reduce CHO intake to ≤30 g/day], conventional diet [≤30% of these calories from fat]). However, the response of CRP to diet differed depending on whether baseline level was in a high-risk (>3 mg/dl) or low- to intermediate-risk (≤3 mg/dl) range ($P = 0.04$).

Our findings indicated that there was a minor, but insignificant decrease in TC by following the diet for 8 weeks. Circulating TG was not significant increased; however, there was a significant increase in HDL-C and LDL-C levels in both diets, but increasing in LDL-C in BD was greater than HP diet. Te Morenga *et al.*[27] demonstrated that both an HP diet (30% PRO, 40% CHO) and an HC-high fiber regime (50% CHO, >35 g total dietary fiber, and 20% PRO) were associated with reduction in LDL-C and TG levels. HP low-carbohydrate diet leads to a significant reduction in TG and LDL-C concentrations while it is accompanied with nonsignificant decrease in HDL-C levels.[28] Foster *et al.*[29] and Brinkworth *et al.*[30] found that low carbohydrate and HP (LCHP) diets (40%, 30%, and 30%, respectively CHO, PRO, and fat) can have favorable effects on serum HDL-C.

Several studies have reported an improvement in TG levels with low-CHO diet (approximately 40% CHO, 30% fat, and 30% PRO)[29,31] and while Rolland *et al.*[32] did not observe the same results. Rolland *et al.* observed that there were significant decrease in TC, TG, LDL-C, HDL-C in LighterLife program (36% CHO, 36% PRO, and 28% fat) compared with measurement at baseline, but in LCHP group (20% CHO,40% PRO, and 40% fat) there was a significant improvement in LDL-C, with no significant changes in TC, HDL-C, and TG. Volek and Feinman[33] reported that serum TC and LDL-C reduced, significantly with replacing dietary CHO content with PRO. The study on 29 men participated in 12-week trial demonstrated that CRD (10% CHO, 65% fat, and 25% PRO) lead to weight loss and it can decrease TG and Apo lipoprotein C-I, Apo C-III, Apo E, involved in TG metabolism, significantly; in addition, it accompany with lower levels of atherogenic particles such as small and very small LDL, and increasing HDL particle size. Furthermore, there are significant relations between reduction in abdominal fat mass and improving lipoprotein size.[34] Thus, CRD can improve lipoprotein profiles (HDL-C, TG, and LDL-C levels) in overweight men. Evangelista *et al.*[35] showed that in overweight and obese patients with heart failure who adherence a HP diet (40% CHO, 30% PRO, and 30% fat) experienced greater reduction in TC, TG, and LDL-C levels and more increase in HDL-C concentration compared to BD diet (55% CHO, 15% PRO, and 30% fat). More improvements in lipid profiles were observed in patients following HP diet compared to BD diet are

Table 2: Age, weight, and body mass index at baseline and after intervention between two groups

Variable	BD diet†	HP diet†	*P*‡
Weight (kg)			
Before intervention	73.17±7.92	77.48±11.14	
After intervention	70.82±8.16	74.8±11.51	0.691
P	<0.001	<0.001	
BMI* (kg/m^2)			
Before intervention	28.87±2.9	30.59±4.52	0.837
After intervention	27.84±3.01	29.48±4.68	
P	<0.001	<0.001	
Age (year)	38.62±6.24	37.07±8.81	0.46

*BMI=Body mass index, †BD=Balanced diet, HP=High-protein diet, ‡*P*<0.05 was considered statistically significant

attributed to greater reduction in adiposity and body weight [Table 2]. Due to the high-fat content of HP diets, these regimes can raise TC and LDL-C levels, so patients should consume more plant sources than animal sources of PRO, which minimizes this potential risk. Nonetheless, long-term variations of HP diet on lipid profiles warrant further investigation. The mechanism that more weight reductions correlated with higher PRO diet are still unknown, but it speculates that more weight reductions may be related to more energy expenditure in patients who consume higher PRO in diets. Weight loss improved cardiovascular disease markers in the following of HP and HC diets; TG levels diminished with HP diets more than HC diets in women with elevated TG levels. This finding confirms that lower CHO content in HP diet causes very low-density lipoprotein and TG production reduction.[36] Effects of HP diet on blood lipids are controversial. Farnsworth *et al.*[13] and Skov *et al.*[14] realized that HP diet decreased TG concentration and Parker *et al.*[15] observed a significant decrease in LDL-C of individuals with this regime. An important concern about consuming HP diets, especially those rich in animal PRO sources, is its direct correlation with higher cholesterol and saturated fatty acids intake and higher cardiovascular diseases risk. However, roles of CHO and PRO contents of diet have gotten less attention. It is accepted that animal PROs showed atherogenic effects and that diets with high complex CHOs content can decrease heart disease risk. It seemed that effects of HP and HC diet can be confounded by other dietary components including dietary fiber, total fat, and TE intake. In some studies seem that replacing a portion of dietary CHO with PRO can show positive effects on TG/HDL-C ratio.[37] Several limitations of this study require consideration. First, we studied our trial on overweight and obese women, and therefore, we cannot generalize our findings to the general population. Second, measurement error and bias of food record could have impacted on our observed relationship. Third, the short period of the trial can affect on the observed relationship.

CONCLUSIONS

In this trial, we observed that both diets had positive effects on CRP, and HDL. LDL increased significantly in both groups following the different diet with a greater increase in those following the BD. We were unable to achieve significant increasing in TG among overweight and obese women in this study. Further investigations need to confirm these findings and due to the controversial fact of similar trials findings, it seems that more research is necessary to elucidate the potential mechanisms that may explain the changes in anthropometric measurements following an HP diet.

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This study extracted from MSc dissertation, approved by Ethical Committee of Isfahan University of Medical Sciences (code 292047).

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Conflicts of interest

There are no conflicts of interest.

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