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/m², 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 groups, 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...
to curb the concerning growth and the concomitant disease risk such as lipid profile disturbance and inflammatory disorders.\textsuperscript{[2,3]} Weight reduction is one of the most effective approaches to prevent and manage several associated-degenerative and metabolic disorders.\textsuperscript{[4]} Up to now, the proper macronutrients ratio of weight reducing diet remains uncertain\textsuperscript{[5]} in spite of the common recommendation of low-carbohydrate (CHO) diets, having insufficient evidence of the efficacy, and safety.\textsuperscript{[6]} Recently, there is increasing interests in low- or moderate- CHO/high-protein (HP) diet as a possible alternative solution.\textsuperscript{[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\textsuperscript{[9]} and decrease after weight loss.\textsuperscript{[10,11]} Furthermore, CRP is sensitive endothelial indicator dysfunctions (recently recognized as a causal factor in atherogenesis).\textsuperscript{[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.\textsuperscript{[12]} Decreases in body fat are associated with a reduction in the concentration of CRP\textsuperscript{[12]}

Farnsworth et al.\textsuperscript{[13]} and Skov et al.\textsuperscript{[14]} observed that a decrease occurs in TG with HP diets, whereas Parker et al.\textsuperscript{[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.\textsuperscript{[16]} The discussion goes on considering the most appropriate macronutrient composition of diets to obtain weight loss.\textsuperscript{[16]} In this research, we aimed to assess the result of different PRO and CHO ratio diets on lipid profiles and inflammation biomarkers.

\section*{METHODS}

\section*{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.\textsuperscript{[17]}

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

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

Females between 20 and 46 years and those who had body mass index (BMI) equal or more than 25 kg/m\textsuperscript{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.

\section*{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 50% 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.

\section*{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).

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 adhere 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 diet (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      | <0.001|
| P                        |               | 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±47.94      |       |
| 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-κB 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.[21] 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 (50% PRO, 40% CHO) and an HC-high fiber regime (50% CHO, >35 g total dietary fiber, and 20% PRO) were associated with reduction in HDL-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 TG and LDL-C, HDL-C in overweight and obese patients with heart failure.[33] Te Morenga et al.[27] observed that there was a minor, but insignificant decrease in TC and LDL-C reduced, significantly; in addition, it accompany with nonsignificant decrease in HDL-C levels. 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).

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.
attributed to greater reduction in adiposity and body weight [Table 2]. Due to the high-fat content of HP diets, these regimes can raise TG 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. Effects of HP diet on blood lipids are controversial. Farnsworth et al. and Skov et al. realized that HP diet decreased TG concentration and Parker et al. 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. In some studies it seems that replacing a portion of dietary CHO with PRO can show positive effects on TG/HDL-C ratio. 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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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Wilborn C, Beckham J, Campbell B, Harvey T, Galbreath M, La Bounty P, et al. Obesity: Prevalence, theories, medical consequences, management, and research directions. J Int Soc Sports Nutr 2005;2:4:31.
2. Clifton PM, Bastiaans K, Keogh JB. High protein diets decrease total and abdominal fat and improve CVD risk profile in overweight and obese men and women with elevated triacylglycerol. Nutr Metab Cardiovasc Dis 2009;19:548-54.
3. Kerk оказ C, Thomas A, Campbell B, Taylor L, Wilborn C, Marcello B, et al. Effects of a popular exercise and weight loss program on weight loss, body composition, energy expenditure and health in obese women. Nutr Metab (Lond) 2009;6:23.
4. Nakata Y, Okura T, Matsuo T, Tanaka K. Factors alleviating metabolic syndrome via diet-induced weight loss with or without exercise in overweight Japanese women. Prev Med 2009;48:351-6.
5. Klein S, Sheard NF, Pi-Sunyer X, Daly A, Wylie-Rosett J, Kulkarni K, et al. Weight management through lifestyle modification for the prevention and management of type 2 diabetes: Rationale and strategies: A statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. Diabetes Care 2004;27:2067-73.
6. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS Jr., Brehm BJ, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: A meta-analysis of randomized controlled trials. Arch Intern Med 2006;166:285-93.
7. Hession M, Rolland C, Kulkarni U, Wise A, Broom J. Systematic review of
randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. Obes Rev 2009;10:34-50.

8. Paddon-Jones D, Westman E, Mattes RD, Wolfe RR, Assrum A, Westerterp-Plantenga M. Protein, weight management, and satiety. Am J Clin Nutr 2008;87:1585S-61S.

9. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: Associations with obesity, insulin resistance, and endothelial dysfunction: A potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol 1999;19:972-8.

10. Esposito K, Ponzillo A, Di Palo C, Giugliano G, Masella M, Marfella R, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: A randomized trial. JAMA 2003;289:1799-804.

11. Kopp HP, Kopp CW, Festa A, Krzyzanowska K, Kriwanek S, Minar E, et al. Impact of weight loss on inflammatory proteins and their association with the insulin resistance syndrome in morbidly obese patients. Arterioscler Thromb Vasc Biol 2003;23:1042-7.

12. Selvin E, Paynter NP, Erler TP. The effect of weight loss on C-reactive protein: A systematic review. Arch Intern Med 2007;167:31-9.

13. Farnsworth E, Luscombe ND, Noakes M, Wittert G, Argyiou E, Clifton PM. Effect of a high-protein, energy-restricted diet on body composition, glycemic control, and lipid concentrations in overweight and obese hyperinsulinaemic men and women. Am J Clin Nutr 2003;78:31-9.

14. Skov AR, Toubro S, Bulow J, Krabbe K, Parving HH, Astrup A. Changes in renal function during weight loss induced by high vs low protein diets in overweight subjects. Int J Obes (Lond) 1999;23:1170-7.

15. Parker B, Noakes M, Luscombe N, Clifton P. Effect of a high-protein, high-monounsaturated fat weight loss diet on glycemic control and lipid levels in type 2 diabetes. Diabetes Care 2002;25:425-30.

16. Nield L, Summerbell CD, Hooper L, Whitaker V, Moore H. Dietary advice for the prevention of type 2 diabetes mellitus in adults. Cochrane Database Syst Rev 2008. DOI: 10.1002/14651858.CD005102.pub2.

17. Noakes M, Keogh JB, Foster PR, Clifton PM. Effect of an energy-restricted, high-protein, low-fat diet relative to a conventional high-carbohydrate, low-fat diet for weight loss in overweight and obese hyperinsulinaemic men and women. Am J Clin Nutr 2003;78:60S-7.

18. Santos MG, Pegoraro M, Sandrini F, Macuco EC. Risk factors for the development of atherosclerosis in childhood and adolescence. Arq Bras Cardiol 2008;90:276-83.

19. Heilbronn LK, Noakes M, Clifton PM. Energy restriction and weight loss on very-low-fat diets reduce C-reactive protein concentrations in obese, healthy women. Arterioscler Thromb Vasc Biol 2001;21:968-70.

20. Azadbakht L, Izadi V, Surkan PJ, Esmaillzadeh A. Effect of a high protein weight loss diet on weight, high-sensitivity C-reactive protein, and cardiovascular risk among overweight and obese women: A parallel clinical trial. Int J Endocrinol 2013;2013:971724.

21. Azadbakht L, Atabak S, Esmaillzadeh A. Soy protein intake, cardiorenal indices, and C-reactive protein in type 2 diabetes with nephropathy: A longitudinal randomized clinical trial. Diabetes Care 2008;31:648-54.

22. Jovinge S, Hamsten A, Tornvall P, Prouder A, Bävenholm P, Ericsson CG, et al. Evidence for a role of tumor necrosis factor alpha in disturbances of triglyceride and glucose metabolism predisposing to coronary heart disease. Metabolism 1998;47:113-8.

23. Niklas B, You T, Pahor M. Behavioural treatments for chronic systemic inflammation: Effects of dietary weight loss and exercise training. CMAJ 2005;172:1199-209.

24. Sharman MJ, Volek JS. Weight loss leads to reductions in inflammatory biomarkers after a very-low-carbohydrate diet and a low-fat diet in overweight men. Clin Sci (Lond) 2004;107:365-9.

25. Ratiliff JC, Mutungi G, Puglisi MJ, Volek JS, Fernandez ML. Eggs modulate the inflammatory response to carbohydrate restricted diets in overweight men. Nutr Metab (Lond) 2008;5:6.

26. Seshadri P, Iqbal N, Stern L, Williams M, Chicoano KL, Daily DA, et al. A randomized study comparing the effects of a low-carbohydrate diet and a conventional diet on lipoprotein subfractions and C-reactive protein levels in patients with severe obesity. Am J Med 2004;117:398-405.

27. Te Morenga LA, Levers MT, Williams SM, Brown RC, Mann J. Comparison of high protein and high fiber weight-loss diets in women with risk factors for the metabolic syndrome: A randomized trial. Nutr J 2011;10:40.

28. Krebs NF, Gao D, Gralla J, Collins JS, Johnson SL. Efficacy and safety of a high protein, low-carbohydrate diet for weight loss in severely obese adolescents. J Pediatr 2010;157:252-8.

29. Foster GD, Wyatt HR, Hill JO, McGuickin BG, Brill C, Mohammed BS, et al. A randomized trial of a low-carbohydrate diet for obesity. N Engl J Med 2003;348:2082-90.

30. Brinkworth GD, Noakes M, Parker B, Foster P, Clifton PM. Long-term effects of advice to consume a high-protein, low-fat diet, rather than a conventional weight-loss diet, in obese adults with type 2 diabetes: One-year follow-up of a randomised trial. Diabetologia 2004;47:1677-86.

31. Brehm BJ, Seeley RJ, Daniels SR, D’Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab 2008;93:1617-23.

32. Rolland C, Hessien M, Murray S, Wise A, Broom I. Randomized clinical trial of standard dietary treatment versus a low-carbohydrate/high-protein diet or the LighterLife Programme in the management of obesity. J Diabetes Sci Technol 2009;3:207-17.

33. Volek JS, Feinman RD. Carbohydrate restriction improves the features of metabolic syndrome. Metabolic syndrome may be defined by the response to carbohydrate restriction. Nutr Metab (Lond) 2005;2:31.

34. Wood RJ, Volek JS, Liu Y, Shachter NS, Contois JH, Fernandez ML. Carbohydrate restriction alters lipoprotein metabolism by modifying VLDL, LDL, and HDL subfraction distribution and size in overweight men. J Nutr 2005;136:384-9.

35. Evangelista LS, Heber D, Li Z, Bowerman S, Hamilton MA, Fonarow GC. Reduced body weight and adiposity with a high-protein diet for weight loss in severely obese adolescents. Am J Clin Nutr 2005;81:1298-306.

36. Schoeller DA, Buchholz AC. Energetics of obesity and weight control: Does diet composition matter? J Am Diet Assoc 2005;105 5 Suppl 1:S24-8.

37. National Cholesterol Education Program Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) NIH Publication No. 01-3670, Washington, DC; 2001.