

Dietary intakes and leptin concentrations

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Review Article

Abstract

BACKGROUND: Leptin, a peptide contained 146 amino-acids, is mostly secreted from adipose tissue and it has a critical role on regulation of body weight, body fat mass, appetite, and food intakes. We tried to review the previous evidence regarding the effects of dietary intakes, including consumption of carbohydrates, fats and protein on concentrations of leptin concentration.

METHODS: We searched in PubMed search engine to January 2013 by using the following key words: dietary intake, diet, dietary fat, high-fat diet, dietary carbohydrate, high carbohydrate diet, dietary protein, high protein diet in combination with leptin, adipokine. Then, we recruited 35 articles to review in the present study.

RESULTS: It seems that beside the amount of fats, type of fatty acids have the key roles on circulating leptin concentration. Energy intake also significantly associated with the hormone. Studies regarding the association between carbohydrate intake and concentration of leptin have been reached to contradictory results. It seems that protein intake can increase the leptin activity.

CONCLUSION: Findings from several studies suggest that a diet display an important role on change the concentration of leptin.

Keywords: Diet, Carbohydrate, Protein, Fat, Leptin

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Introduction

Leptin, a 16 kDa protein, is a peptide contained 146 amino-acids that are discovered in 1994. Leptin is mostly secreted from adipose tissue, and it has a critical role on regulation of body weight and also body fat mass.¹⁻³ It markedly regulates energy expenditure, appetite, thermogenesis and food intakes. Leptin caused to increase fatty acids oxidation and decrease triglyceride synthesis and so that it attenuates lipogenic action of insulin and increases insulin sensitivity of muscle and liver. This hormone has the favorable effect on glucose homeostasis.⁴⁻⁷ Given the key role of leptin on regulation of body weight and prevention of obesity, it seemed that leptin levels were decreased during the elevation of body weight.⁸ But according to a large body of evidence, most obese humans have higher circulations of leptin.⁹ It has been indicated that obesity might induces state of leptin resistance.¹⁰

Inactivation of leptin receptors enhance leptin resistance and reduces satiety, and it enhances the risk of obesity.⁵ Therefore, treatment of obesity tends to increase leptin action in central nervous system

(CNS), which is able to decrease food intake and body fat through the reduction of energy intakes.^{1,5,8}

Expression and secretion of leptin is enhanced by estrogen, tumor necrosis factor- α , corticosteroids as well as glucose and insulin. In contrast, T₄, growth hormone, catecholamine, androgens and free fatty acids suppress the expression of this hormone.^{11,12} Among these parameters, diet-related factors display the important roles on augmentation and amelioration of this hormone.¹³⁻¹⁹

Among diet-related factors, dietary components including consumption of beverages, fatty acids, proteins and carbohydrates have been shown to have a significant association with concentrations of leptin.^{1,15,20-22} However, contradictory results are found in this regard. Based on several evidence diets rich in polyunsaturated fatty acids (PUFA) (ω_3 and ω_6) leads to increase circulating of leptin compared to diet rich in monounsaturated fatty acids (MUFA) and saturated fatty acids (SFA).²⁰ In contrast, according to some studies consumption of ω_3 fatty acids showed a reduction in leptin gene expression.^{23,24} High carbohydrate diet might

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increase leptin sensitivity in some studies.^{5,8} Beside percent consumption of carbohydrate, glycemic index and glycemic load of carbohydrate also have been indicated to have a critical role on concentrations of leptin.¹⁶

In this review article, we tried to review the previous evidence regarding the effects of dietary intakes, including consumption of carbohydrates, fats and protein on concentrations of leptin and also explain about potential underlying mechanism in this regard.

Materials and Methods

To investigate the relationship between dietary

intakes and concentrations of leptin, we searched in PubMed search engine from 2000 to January 2013 using the following key words to the topics: dietary intake, diet, dietary fat, high fat diet, dietary carbohydrate, high carbohydrate diet, dietary protein, high protein diet in combination with leptin, adipokine. All 265 articles with design of clinical trial, cohort and cross-sectional studies have been reviewed. 35 articles were recruited in this study, and others were excluded owing to lack of the direct relation with this issue, duplication and lack of full-text articles. Studies that investigated among association between dietary intakes and leptin concentrations are shown in table 1.

Table 1. Studies regarding the association between dietary intakes and concentrations of leptin

Study	Type of study	Numbers/sex	Age (year)/BMI	Design and aim	Duration of study	Results
1	Parallel	55 obese men and women	Age: 25.7 ± 5.4 BMI: 23.0 ± 2.3	Effect of diets with 3 types of fat (olive, rapeseeds, sunflower oil)	2 weeks diet with SFA and 4 intervention diets	Serum levels of leptin effect on diet rich in α -linoleic acids
6	Parallel	18 women and men	Age: 45.3 ± 13.6 BMI: 27.1 ± 2.3	Effect of high carbohydrate low fat on serum level of leptin (35% fat, 45% CHO, 20% protein) compared to (15% fat, 65% CHO, 20% protein)	2 weeks weight maintenance, 2 weeks isocaloric and 12 weeks weight loss diet	No change was found in level of leptin and increase in leptin sensitivity
8	Cross sectional	31 (women and men) cirrhosis patients and 10 controls	Age: 54-57 BMI: 25.7-56.5	Assessing the association between energy intakes and leptin	-	No significant relationship was found
9	Parallel	19 lean and obese women	Age: 21.5 ± 1.9 BMI: 21.6 ± 1.8 Age: 34.6 ± 7.8 BMI: 49.8 ± 6.9	Isocaloric meals: 166 g CHO, 38 g protein and 70 g fat, 36 g protein	-	Significant lower levels of leptin after carbohydrate meals in obese women compared to lean women
16	Parallel	19 women and men	Age: 41 ± 11 BMI: 26.2 ± 2.1	Effect of high protein diet on leptin (50% CHO, 35% fat, 15% protein) compared to (50% CHO, 20% fat, 30% protein)	2 weeks normal diet with weight maintenance 2 weeks isocaloric high protein diet, 12 weeks high protein weight loss diet	Greater status of satiety with no change in plasma leptin after high protein diet
17	Cross sectional	165 healthy overweight and obese women in postmenopausal status	Age: 60.73 ± 6.7 BMI: 30.5 ± 3.9	Assessing the association between habitual dietary intakes and leptin	-	Inverse relationship between consumption of high carbohydrate and fat with hormone
18	Parallel	13 lean and overweight men	Age: 18-27 BMI: 20.8 ± 0.7 30.8 ± 1.7	High carbohydrate, low fat meals (80% CHO, 17% protein, 3% fat)	3 days	No significant difference was found
19	Parallel	200 women	Age: 100 women with ≤ 50 100 women: > 50 BMI: 25.7	Diet rich in fruits, vegetables and fiber with low amount of fat	12 months	Had no effect on leptin

Table 1. Studies regarding the association between dietary intakes and concentrations of leptin (Continue)

Study	Type of study	Numbers/sex	Age (year)/BMI	Design and aim	Duration of study	Results
20	Cross sectional	60 men and women with Type 1 diabetes	Age: 22.8 ± 6.8 BMI: 22.7 ± 2.3	Assessing the association between consumption of SFA and PUFA and leptin	-	Positive relationship with consumption of SFA and leptin in men/ positive and negative association between linolenic acid and arachidonic acids and leptin, respectively
25	Experimental	344 female rats	-	High fat diet in comparison with low fat with complex carbohydrate	20 months	Increase in plasma level of hormone by the high fat diet
26	Cross over	9 men and women	Age: 20-37 BMI: 18-26	High carbohydrate diet with different in glycemic index and fat in 4 groups	8 days	17% greater in diets with high glycemic index
27	Experimental	rats	-	Effect of type of fat in low calorie diet on leptin	10 weeks	60% increase in leptin concentration among fish oil and sunflower oil fed compared to beef tallow fed
28	Cross sectional	211 male and 205 female of Japanese-American in Hawaii and Japanese in Japan	Age: 40-59 BMI: < 25 and ≥ 25	Assessing the association between energy intake and serum leptin concentration	-	Inverse relationship between energy intake and serum level of leptin in obese persons
29	Parallel	44 healthy male	Age: 43 ± 5 BMI: 27.3 ± 3.2	Effect of low calorie diet on plasma leptin	4 days	39.4% decrease in leptin by the energy restricted diet

BMI: Body mass index; PUFA: Polyunsaturated fatty acid; SFA: Saturated fatty acid; CHO: Carbohydrate

Results

Carbohydrate intake and concentrations of leptin: results from studies evaluated the association between adherence to high carbohydrate diet and leptin concentration have been shown to reach contradictory results.^{5,6,16,17,30}

Consumption of carbohydrate with high glycemic load may leads to leptin resistance.^{6,17} However, consumption of the high amount of fiber and high carbohydrate diet were found to have a decreased concentration of leptin and increase in insulin sensitivity, respectively.^{5,8,16} One crossover clinical trial study conducted among 9 healthy individuals indicated that high glycemic index carbohydrate diet increased diurnal rhythm of leptin.⁷ Consumption of 80% carbohydrate in 13 lean and overweight men had not shown a significant difference in concentration of leptin. However, oxidation of carbohydrate was substantially lower in obese subjects that may be due to leptin resistance in obese individuals.¹⁷

One parallel intervention study conducted among 18 men and women individuals suggested that adherence to high carbohydrate diet [65% carbohydrate (CHO), 15% fat, 20% protein] had not

significant effect on concentration of leptin in comparison with subjects consumed control diet (45% CHO, 30% fat, 20% protein). This diet enhanced leptin sensitivity.⁵ It seems that leptin response implicate after consumption of carbohydrate meals among obese subjects,^{8,17} one cross-sectional study conducted among 165 overweight and obese women, in the age range of 50-75 years, showed that significant inverse association between consumption of habitual high carbohydrate and fat intakes and leptin concentration after adjustment for potential confounders ($\beta = -0.11$, $P = 0.04$).¹⁶ Adherence to diet rich in fruits, vegetables and fiber with lower amounts of fat during 12 months had not showed the substantial effect on leptin level in healthy women.¹⁸

Fats intake and leptin levels: most studies regarding the relationship between high-fat diet and concentration of leptin were found that there is a positive association between intake of higher fats and leptin level.^{8,31} Furthermore, type of fats including SFA, MUFA and PUFA play the key roles on augmentation or reduction of circulating leptin concentration.^{1,19,21,25} However, contradictory results were observed in this regard.^{14,26}

One cross-sectional study conducted among

individuals with type 1 diabetes had shown that men consumed more SFA had more concentration of leptin.¹⁹ Consumption of linoleic acid and arachidonic acids among women had a positive and negative correlation with serum levels of leptin, respectively.¹⁹ In one parallel clinical trial conducted among 55 obese subjects, adherence to diet rich in α -linolenic acid source (rapeseed oil) in 4 weeks led to increase in serum level of leptin compared with individuals who followed the diet rich in MUFA and ω_6 sources (olive oil and sunflower oil, respectively).¹

High-fat diet substantially enhanced plasma level of leptin in rats.³¹ In one parallel intervention study, consumption of the meal with 70 g fat and 36 g protein showed no significant change in postprandial leptin among 19 lean and obese women compared to high carbohydrate diet.⁸ In one experimental study rats, fed fish oil and safflower oil energy restricted diet had 62% reduction in leptin levels compared to beef tallow fed.²¹ In contrast, energy-restricted diet independent of the type of fats could increase leptin production in rats.¹⁴

Protein intake and leptin levels: fewer studies examining the effect of high protein diet on leptin concentration.^{13,15} It seems that high protein low-calorie diet tend to increase in leptin activity.¹⁵

Results from one parallel clinical trial conducted among 19 participants (men and women) indicated that adherence to high protein diet (30% protein) in 2 weeks of iso-calorie diet did not enhance the area under curve (AUC) of leptin compared to control diet (15% protein). Furthermore, leptin AUC markedly decreased during 12 weeks energy restricted high protein diet.¹⁵ It seems that higher protein intake could increase leptin sensitivity despite any increase in the hormone concentration.¹⁵ Augmentation of high dietary protein during second trimester of gestation led to significantly increase plasma level of leptin in one experimental study.¹³ Results from other experimental investigation found no substantial effect of high protein diet on serum level of leptin.²⁷

One intervention study conducted among 17 non-diabetic male suggested that low protein diet (0.6 g/kg) decrease plasma level of leptin that not to be mediated through insulin-related mechanism.³² In contrast, serum leptin concentration was markedly greater in rats with low protein diet, and food intake enhanced due to augmentation of leptin in one experimental study.³³ Increase of leptin concentration suggested that low protein diet might lead to the state of leptin resistance.³³

Energy intake and concentration of leptin: it seems that energy restriction reduces concentration of leptin and high energy intake induces state of leptin resistance.^{7,34,35} A cross-sectional study conducted among a sample of patients with liver cirrhosis showed that there is an inverse relationship between fasting leptin and resting energy expenditure. Energy intake was found to have no substantial correlation with fasting concentration of leptin.⁷ Serum level of leptin was substantially negatively correlated with dietary energy intake in obese individuals in one cross-sectional study among a sample of Japanese-American in Hawaii and Japanese in Japan.³⁴ One intervention study conducted among 44 healthy men suggested that energy restricted diet decreased 39.4% fasting leptin concentration.³⁵

Discussion

Findings from several studies suggest that a diet display an important role on change the concentration of leptin.^{5,8,15} It seems that beside the amount of fats, type of fatty acids have the key roles on circulating leptin concentration.^{1,2} Energy intake also significantly associated with the hormone.^{34,35}

Carbohydrate intake has an important role on regulation of leptin level that may be due to change in insulin secretion.⁸ It is supported by evidence that carbohydrate meal induces greater postprandial leptin concentrations than fat meal.²⁸ According to evidence leptin deficiency leads to state of obesity, as well as insulin resistance and glucose tolerance impairment.²⁹ In the other hand, obese subjects have more concentration of leptin that tends to be the state of leptin resistance.³⁶ In addition, concentration of leptin implicates in subjects with Types 1 and 2 diabetes.^{37,38}

Obesity is one of the important factors in the etiology of metabolic syndrome, diabetes and cardiovascular diseases³⁹⁻⁴¹ and dietary intakes have the important role on controlling the obesity and chronic diseases.³¹ Consumption of high glycemic load of carbohydrates enhance concentration of the hormone.⁶ In addition, intake of the high amount of fiber causes to increase the leptin sensitivity and controls the secretion of leptin.⁴² It is possible that the leptin response is different in diverse types of carbohydrates. Also, the effect of high carbohydrate intake on leptin concentration may implicate in obese subjects.⁸

Sex and body fat are two most important factors in concentration of leptin that are supported by evidence.⁴³ Weight loss and starvation also can

decrease circulating of leptin.⁴⁴ According to evidence, SFA enhance the risk of obesity that may be mediated through a change in concentration of the hormone. Experimental studies showed that high-fat diets may elevate the leptin concentration.^{44,45}

It seems that a diet rich in MUFA and PUFA decrease the concentration of the hormone especially in women compared to SFA.¹ Dietary patterns rich in MUFA and PUFA usually characterized by high amount of fiber sources as well as low glycemic index of carbohydrate that lead to the lower concentration of leptin.⁴⁶ Given the important role of estrogen on expression of leptin, it is possible that the type of fatty acids has more effects on women than men.¹

To the best of our knowledge, fewer evidence is available regarding the impact of high protein diet on leptin concentration. It seems that higher protein intake increases satiety and enhances the leptin concentrations in CNS as well as elevates leptin sensitivity which tends to be weight maintenance.¹⁵ However, different protein sources were found to have diverse effects on health status.^{47,48}

Based on studies, individuals who consumed more energy from protein were found to have greater satiety. Increase in dietary protein intakes promotes an inverse energy balance and body fat loss. On the other hand, protein intake tends to increase energy expenditure that may be related to leptin action.¹

Conclusion

Findings from several studies suggest that a diet display an important role on change the concentration of leptin.

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Conflict of Interests

Authors have no conflict of interests.

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