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Regular paper

Plant-based diets contribute to lower circulating leptin in healthy subjects independently of BMI

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Much research has shown how important role leptin – a hormone secreted by adipose tissue – plays in the regulation of human body weight, mainly due to its appetite-decreasing effects. Under the conditions of energy balance, leptin is an indicator of the amount of triglycerides stored in adipose tissue. In contrast, in a state of hunger or overeating, it acts as an energy balance sensor, and when its level is too high, it fails to reduce food intake, disturbing maintenance of the proper body mass. Recent studies indicate that there is a relationship between a vegetarian diet and the decreased incidence of cardiovascular diseases, certain types of cancer and obesity. It has been noted that people on plant-based diets have lower body weight and percentage of body fat than omnivores. The aim of the study was to analyze the relationship between serum leptin concentrations and the type of diet. The 143 female volunteers on a vegetarian, vegan or omnivore diet were enrolled in the study. All participants had normal body weight (BMI≥18.5<24.9kg/m²). There were statistically significant differences in the serum leptin concentrations of the studied women. Both in the group of vegetarians and vegans circulating leptin was significantly lower (p<0.001) than in the group of omnivores, with the lack of differences in neither BMI nor in body fat content. This suggests that leptin levels are affected not only by the amount of stored fat, but also by the consumed food. This observation indicates the health-promoting properties of plant diets, by influencing circulating leptin.

Keywords: leptin, obesity, plant-based diets, vegan diet, vegetarian diet

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Abbreviations: BIA, bioelectrical impedance analysis; BMI, Body Mass Index; MUFA, monounsaturated fatty acids; PAL, Physical Activity Level; PCOS, polycystic ovary syndrome; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids; WHR, waist to hip ratio

INTRODUCTION

An appropriately planned vegetarian diet is considered nutritionally adequate (Melina *et al.*, 2016). Moreover, there are several papers documenting its positive role in the prevention and treatment of several diseases, including obesity (Oussalah *et al.*, 2020). Leptin, a hormone secreted from the adipose tissue cells, is deeply involved in appetite regulation and maintenance of energetic homeostasis. High levels of leptin (observed in obese subjects) result in leptin resistance, which is responsible for increased food consumption, disturbances in lipid and carbohydrate metabolism, and, consequently, further excessive fat accumulation (Park & Ahima, 2015). Thus, it is important to identify factors which may be helpful in lowering circulating leptin in order to keep sensitivity to this hormone. The essential factors affecting serum levels of this adipocytokine are the number and size of the adipocytes (Gogga *et al.*, 2011).

It is well-established that people following plant-based diets have lower BMI values, which contributes to lower levels of leptin in vegetarians (Dinu *et al.*, 2017; Kim & Bae, 2015). However, some findings suggest that diet composition may be relevant for leptin levels, even without reducing body mass (Ambroszkiewicz *et al.*, 2011; Kratz *et al.*, 2002; Winnicki *et al.*, 2002). The current study compared serum leptin concentrations between subjects on different diet types (omnivores, vegetarians, and vegans), with the same BMI (normal), in an attempt to investigate the impact plant-based diets may have on the circulating leptin.

Material and Methods

The study was approved by the local Independent Bioethics Commission for Scientific Research at the Medical University of Gdańsk (no: NKBBN/234/2016) and was part of the project: "The influence of meat-free diet on serum levels of leptin, obesity markers and gut microbiome in vegetarian and vegan subjects" (no: 01-0293/08/316).

Participants

A total of 143 female volunteers (47 vegans, 55 vegetarians and 41 omnivores) were recruited for the study. The group of vegetarians included lacto-, ovo- and lacto-ovo-vegetarians. Participants were classified as controls (meat-eaters) if they claimed to consume meat at least five times a week. Vegetarians and vegans consumed no meat or fish. The first group's diet included animal-derived products (dairy and/or eggs and/or honey), while the vegan group's diet comprised only plant products.

All women were apparently healthy and had a normal BMI (18.5–24.99). The basic characteristics of diet in studied groups are presented in Table 1.

Participants were recruited for the study via electronic media – information about the research, including its purpose, course and instructions on how to join,

Table 1. Comparison of basic characteristics in different diet groups. Me – median, QD – quartile deviation; WHR – waist to hip ratio.

Parameter	Diet type	Me	QD	N
Age [years]	vegan	25	4.5	47
	vegetarian	26	3.5	55
	omnivore	30	4.5	41
BMI [kg/m^2]	vegan	20.9	1.2	47
	vegetarian	21.3	1.4	55
	omnivore	21.3	1.2	41
Body fat [%]	vegan	24.4	3.1	47
	vegetarian	25.0	15.6	55
	omnivore	25.8	2.2	41
WHR	vegan	0.76	0.03	46
	vegetarian	0.75	0.04	55
	omnivore	0.78	3.03	41
Time on the diet [years]	vegan	2.3	1.1	47
	vegetarian	2.4	2.9	51

were issued on Facebook. The inclusion criteria for the study group were as follows: refraining from eating meat for at least three months continuously, absence of eating disorders, and not being pregnant. Subjects from the control group (omnivores) were supposed to consume meat regularly and meet the same additional criteria as the study group.

Prior to the onset of the study, all included women provided informed consent – their participation in the project was fully voluntary. They underwent two consultations with a dietitian. During the first consultation, they provided detailed information about the specificity and longevity of their diet and health status.

Anthropometric measurements

The following anthropometric parameters were measured in all participants:

- body mass (Jawon Medical X-contact 350) and height (stadiometer Physical activity, medium CA 213, Germany), for calculating body mass index (BMI) value
- circumference of waist and hip (tape measure Seca 201), essential for calculating waist-to-hip ratio (WHR)
- body composition (the content of body fat) was estimated with the bioelectrical impedance analysis (BIA) method (Jawon Medical X-contact 350).

Peripheral venous blood was obtained from subjects after an overnight fast. Immediately after collection, the blood was centrifugated to obtain serum. Collected samples were stored at –32°C before analysis. An immunoenzymatic test (ELISA) was used (Demeditec Diagnostics GmbH, Germany) to determine serum leptin levels, and a microplate reader was used (Biorad, USA) for visualization. The standard curve was calculated using GraphPad Prism 4.0 (GraphPad, San Diego, CA, USA). The range of values of standard samples provided by the manufacturer was 1–100 ng/ml. Samples of known values were used in further analyses as additional controls.

Physical activity

Physical activity assessment was based on PAL (Physical Activity Level) values, which were attributed according to the information provided by all women during an interview with a dietitian. All participants were assigned to one of three categories – low physical activity (PAL≤1.69), medium physical activity (PAL 1.7–1.99) or high physical activity (PAL≥2.0) (FAO/WHO/UNU 2004).

Statistical Analysis

All calculations were made using Statistica 12 (Statsoft). Serum leptin concentrations, BMI, and body fat were compared using the Kruskal-Wallis test, with Dunn's test applied post-hoc. The same tests were used for comparisons of age and WHR between analysed groups. Time on diet was compared between two plant-based diet groups with Mann-Whitney test. Pearson's chi-squared test was applied to check if the level of physical activity is the same in each group. For Spearman's rank correlation coefficient was used to identify correlations between leptin levels and age and time on the diet (for plant-based diets). A multivariable regression model was used to determine the contribution of different factors affecting serum leptin levels. $p<0.05$ was considered statistically significant.

RESULTS

Statistically significant differences were observed in serum leptin levels between both plant-diet groups

Table 2. Serum levels of leptin in different diet groups [ng/ml]. Me – median, QD – quartile deviation, Min – minimum value, Max – maximum value.

Diet type	Me	QD	Min	Max	N
vegan	6.1	3.1	1.0	18.3	47
vegetarian	6.9	4.6	1.1	20.8	55
omnivore	8.8	5.3	3.0	29.2	41

Table 3. Analysis of correlation between leptin levels, age and plant-based diet duration. RS – Spearman's rank correlation coefficient.

Diet type	Parameter	R_S	*p* value	N
BMI [kg/m²]	vegan	0.42	0.003	47
	vegetarian	0.18	0.19	55
	omnivore	0.43	0.005	41
Body fat [%]	vegan	0.39	0.006	47
	vegetarian	0.34	0.01	55
	omnivore	0.52	<0.001	41
Age [years]	vegan	–0.05	0.74	47
	vegetarian	–0.22	0.11	55
	omnivore	0.02	0.88	41
Time on the diet [years]	vegan	–0.08	0.60	47
	vegetarian	0.003	0.98	51

and omnivores ($H_{2,143}$=14.72, p<0.001) (Table 2). Medians were lower in vegans (p=0.001) and vegetarians (p=0.004) than in meat-consumers.

There were no differences in BMI values ($H_{2,143}$=1.77, p=0.41) and the percentage of body fat content ($H_{2,143}$=2.57, p=0.28) between all groups. Although body fat tended to be higher in omnivores than in vegans and vegetarians, the differences in this parameter did not reach statistical significance.

Low PA was detected in 48.7% of omnivorous, 58% of vegetarians and 40.4% of vegans, high PA level was presented in only 3 subjects (2 omnivorous and 1 vegetarian). No differences were observed in physical activity level between groups (χ^2=6.26, p=0.18). A positive statistically significant relationship was found for circulating leptin and body fat content in all groups, but there were no correlations between leptin levels and age or plant diet duration (Table 3).

The multivariable regression model showed that factors influencing the level of leptin in the examined women were type of diet (p<0.001) and body fat percentage (p<0.001), while age, BMI, time on the diet and physical activity had no impact on this parameter (Table 4).

DISCUSSION

It is known that leptin is deeply involved in the regulation of lipid and carbohydrate metabolism and, as such, it controls adiposity and body mass (Gogga *et al.*, 2011). Moreover, since increased levels of this adipokine (characteristic of obesity) are an important risk factor for the development of metabolic syndrome (with additional comorbidities such as diabetes mellitus type 2 and cardiovascular diseases; Ghadge & Khaire, 2019), it is of great importance to identify factors that may influence leptin expression and secretion. Generally, leptin concentrations are proportional to the amount of stored lipids, i.e. number and size of the adipose tissue cells (Gogga *et al.*, 2011). People on plant-based diets usually have lower BMI than those on meat-containing diets (Turner-McGrievy *et al.*, 2017), what may entail higher leptin concentrations. In a small preliminary study, we have shown that people on different types of vegetarian diet had lower circulating leptin than omnivores, and this observation correlated with lower body fat content (Gogga *et al.*, 2019). However, the aim of the following study was the comparison of serum leptin between subjects on different diet types (omnivores, vegetarians and vegans), with statistically the same fat content and BMI. Results of multiple regression analysis indicated that type of diet used, and the body fat percentage are independent predictors of leptin levels.

Similar results have been previously described involving differences in leptin concentrations in subjects with statistically the same BMI and usual diet. As an example, in a cross-sectional study, circulating leptin was measured in 831 healthy women. The so-called 'healthy plant-based diet index' (which included whole grains, fruits, vegetables, nuts, legumes, oils, tea/coffee) was associated with lower plasma leptin (Baden *et al.*, 2019).

Based on both animal experiments and human trials, it appears that the crucial dietary factor influencing circulating leptin is fatty acid composition. In rats, a high-fructose and coconut oil diet elevated serum leptin levels compared with a high-fructose and soybean oil diet and control groups (Lin *et al.*, 2017). In a study encompassing women with polycystic ovary syndrome (PCOS), authors observed a positive correlation between circulating leptin and the intake of total fat and particular lipid fractions, namely MUFA and PUFA, and total cholesterol

Table 4. Multivariate regression model predicting serum levels of leptin (the adjusted R2 of the model was 0.23). Physical activity was assessed as low, medium or high based on the PAL ratio values. N – 142. SE – standard error.

Regression model	B	SE	Beta	p value
Constant	–118.7	58.6		<0.05
Type of diet	0.761	0.22	0.26	<0.001
Age [years]	–0,084	0.05	–0.12	0.12
Body fat [%]	0.749	0.21	0.47	<0.001
BMI [kg/m²]	–0.258	0.44	–0.07	0.56
Physical activity	0.354	0.56	0.07	0.53

(Polak *et al.*, 2020). Saturated fatty acids also had an impact on circulating leptin also in pregnant women, whose total serum SFA levels were positively correlated with concentrations of this hormone (Lepsch *et al.*, 2016). Moreover, a similar result was also observed in healthy non-obese women after implementing a high-fat diet based on rapeseed oil (rich in MUFA and ALA) for four weeks. This diet slightly increased leptin levels in men and significantly increased these levels in women (Kratz *et al.*, 2002). It is known that fatty acid composition differs when comparing vegetarians – especially vegans – with omnivores, as they consume more PUFA and significantly less SFA (Clarys *et al.*, 2014), which, to some extent, may be responsible for the observed results.

Some authors have suggested that dietary fibre may have an impact on leptin levels. In a study of young, healthy women from Japan, high fibre intake was associated with lower leptin concentrations, and this was independent of BMI (Murakami *et al.*, 2007). As for food groups, intake of vegetables and pulses was also negatively correlated with circulating leptin (Murakami *et al.*, 2007), and these products are consumed by people on plant-based diets in considerable amounts, higher than in the general population (Clarys *et al.*, 2014). The influence of fibre intake on circulating leptin was also examined in an interventional trial. In a randomized, controlled, double-blind study, healthy adults were given muffins either enriched with resistant starch or the same muffins without additional fibre. After a 6-week study of the group consuming enriched muffins, lower serum leptin concentrations were observed, without changes in total calorie intake or in body composition (Maziarz *et al.*, 2017).

The above findings correspond with results obtained by Rostami and others (Rostami *et al.*, 2017), who showed that diet composition affects leptin gene expression in adipocytes (both in visceral and subcutaneous fat depots). They found that in adults, the expression of the leptin encoding gene was positively related to the amount of consumed SFA, while a higher intake of MUFA and PUFA decreased gene expression of this adipokine, which was observed as lower mRNA levels in adipose tissue cells. These findings suggest the role of a habitual diet, especially the fatty acid composition, in determining blood leptin concentrations through epigenetic factors.

The main limitations of our study are relatively small study groups, as well as the lack of a very detailed analysis of the diet. However, although the following study was a cross-sectional one, we demonstrated an association between leptin and diet type in very homogeneous groups, considering sex and age, and anthropometric features – especially BMI and body fat content.

CONCLUSIONS

Our results show that plant-based diets may be associated with lower circulating leptin levels in healthy subjects, thus it seems reasonable to suggest that properly planned vegetarian diets may possibly provide protection against obesity and related negative health outcomes in a safe and cost-effective manner. However, these findings need confirmation in thorough clinical studies.

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