Artículo de Revisión

Adipokines: The postprandial point of view

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SUMMARY

Adipokines comprise all the bioactive molecules produced by adipose tissue. The regulation of adipokines has been studied in recent years. However, as with other metabolism molecules, most of the studies has focused on fasting subjects, whereas relatively few papers have investigated postprandial regulation. The objective of this review is to describe our current knowledge regarding postprandial changes in the concentrations of the main adipokines and the possible variables that regulate the acute secretion of these molecules as well.

Keywords: Perceived social support, diabetes distress, depression.

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Fecha de Recepción: 4 de septiembre de 2023 Fecha de Aceptación: 17 de octubre de 2023

Introduction

Adipokines comprise all the bioactive molecules produced by adipose tissue which exert an endocrine or paracrine function in the body (1). It has been twenty years since the cloning of the leptin gene, the first adipokine characterized (2). At present, more than 600 of such molecules have been described and their numbers are on the increase (3). The description of adipokines set a milestone in the research of human physiology, since before its discovery the function of adipose tissue was believed to be mainly a storage for energy, thereby a little more than inert tissue. It is currently known that adipose tissue has an active participation in human beings' metabolism, as well as in other important related functions such as the regulation of appetite and satiety, endothelial function, the degree of inflammation and blood pressure, among others (4). In fact, adipose tissue is more than a monocelular adipocytes interwoven. Although they constitute the main cellular component, adipose tissue also includes macrophages and other immune system cells, fibroblasts, mesenquimal cells (preadipocytes) and cells of the vascular, neural and connective tissues (5). In fact, some adipokines, are not really or only secreted by adipocytes, but instead by the other kind of cells that inmerge in it (6).

Regulatory secretion and effects of adipokines have been extensively studied in recent years. However, as with other metabolism molecules, most of the studies have focused on fasting subjects, whereas relatively few papers have investigated these molecules' postprandial changes related to food quality and subjects inherent metabolism. Postprandial metabolism is a field of recent interest (7) because in modern life food patterns, human beings spend most of their day in postprandial period, while fasting is mostly limited to sleeping hours. However, most of the knowledge we have respect to adipokines and other molecules related to metabolism are on the fasted state, even though the

postprandial state seems to be an earlier predictor of metabolic and cardiovascular disease (8, 9). Although postprandial state seems to affect directly what happens on gastrointestinal tract and adipose tissue would only barely be affected late in the metabolism, it is important to remember that some of the adipokines are also expressed on gastrointestinal tract (10, 11) so changes in their concentration could be theoretically during both early and late postprandial metabolism. For these reasons we believe that studies carried out while fasting do not represent all aspects of the interaction between adipokines and individual metabolism as well as metabolic risk. The objective of this review is to describe current knowledge regarding postprandial changes in the concentrations of the main adipokines, as well as the possible variables that regulate the acute secretion of these molecules. We focus here on adipokines that have studies regarding postprandial concentration.

ASPECTS OF METABOLISM AFTER FOOD INGESTION

The definition of metabolism includes the physicochemical and molecular changes that take place in living beings which lead to the formation of sufficient energy to stay alive. The classification of metabolism between fasting and postprandial is more because of academic interest than a real physiologic difference, since the processes that take place are a continuum that even when occurred during the fasting period do not stop altogether after food ingestion; albeit, certainly the activity of many molecular processes may decrease or increase notably. Likewise, it is difficult to say at which moment the metabolic phenomena caused by the arrival of food cease, since it varies depending on sex, age, time of day when the food is eaten or even on the quantity or quality of the food (12). For example, while the absorption of 75 grams of carbohydrate occurs in its entirety within 3 hours after eating, an isocaloric fat load can travel up to 18 hours through the enterocyte (13).

In the same way, the extent at which different hormones intervene in postprandial metabolism differ depending on diet composition. Carbohydrates metabolism is directly influenced by insulin, which controls postprandial hyperglycemia and regulates other hormones that act as counter-regulators such as glucagon, epinephrine, growth hormone and cortisol. The glucose absorbed from food, in addition to serve as an energy source for the cells, is actively stored in the liver in the form of glycogen to be used later during the fasting period. Insulin plays a key role in this process, by suppressing hepatic glucose production and exercising thus a permissive action on glycogen storage (14).

Lipids, on the other hand, undergo a process of enzymatic absorption and digestion that requires the action of several lipases from the first contact of the food with the digestive tract up to its final absorption in the small intestine. Fatty acids in the form of free fatty acids, mono and diglycerides are absorbed either passively or by means of active transporters through the brush edge of the enterocyte, resynthesized to triglycerides and packed in chylomicrons containing apoB-48 before entering the circulation or being stored inside the enterocyte to be released in a subsequent meal (15). Interestingly, the chylomicrons that are released in the first hours after food ingestion are produced with lipids from previous meals, which has led to what is now called the cephalic phase of lipid mobilization, since it occurs by simply trying food that contains fat; e.g., pizza or cream cheese (16, 17). Once in circulation, the chylomicrons released by the intestine are catalyzed to release free fatty acids through the action of lipoprotein lipase, leaving remnants of chylomicrons poor in triglycerides that are easily cleared by the liver. The action of lipoprotein lipase is stimulated by insulin, so once again this hormone has an effect even on lipid metabolism. Upstream there are still other factors that interrelate the metabolism of nutrients, since the L cells of the intestine secrete a glucagon-like peptide type 1 (GLP-1) in response to exposure to carbohydrates or fats. This peptide, in addition to reduce the flow of postprandial

chylomicrons, stimulates the secretion of insulin so that the body can more effectively process the chylomicrons released earlier.

The nutrients that come from the diet will be used in the first place as energy; however, the body, anticipating a period of fasting, will reserve part of this energy as adipose tissue through a process called lipogenesis. This process includes the formation of triglycerides for storage in adipocytes, using fatty acids, as well as acetyl coenzyme A; this process is catalyzed by the lipoprotein lipase mentioned in the previous paragraph. The intake of nutrients thus influences the size and number of adipocytes, for they grow and differ as necessary to store more energy in the form of triglycerides. In turn, these adipocytes send signals to the body that influence numerous functions, through adipokines, which produce effects on pancreatic hormones that control much of the postprandial metabolism (18). In conclusion, food intake has a direct and early relationship with adipose tissue that seems to influence adipokine secretion.

ADIPONECTIN

Adiponectin is the adipokine with the highest plasma concentration and its secretion is inversely proportional to the adiposity of an individual, so its plasma concentrations decrease in obese subjects (19) and increase when such patients lose weight (20). It is an acidic protein of 244 amino acids and weighing 30 kDa, whose primary structure includes a signal peptide, a variable region, a collagen-like domain and a globular domain (21). Although this protein is expressed mainly in adipose tissue, in completely differentiated adipocytes (22), there are data that suggest its production by cardiomyocytes and skeletal muscle (23). Adiponectin found in the circulation in the form of trimers (light molecular weight), hexamers (medium molecular weight) and a heavy molecular weight form that has from 12 to 18 parts (24). This hormone acts through three receptors: adipo R1, which shows ubiquitous expression, including skeletal muscle and liver; adipo R2, whose expression is restricted to the liver; and, T-cadherin, which shows abundant expression in endothelial cells, smooth and cardiac muscle cells (25). Through these receptors, it exercises the function of being an insulin sensitizer by performing several molecular actions in different tissues through the inhibition of the expression of phosphoenolpyruvate carboxykinase and glucose-6-phosphatase in the liver, thereby suppressing gluconeogenesis (26, 27). It also increases β-oxidation in skeletal muscle and suppresses the accumulation of lipids in the liver by stimulating the activity of the 5'AMP-activated protein kinase (AMPK) (26). On the other hand, it suppresses inflammatory responses and promotes macrophage polarization toward the anti-inflammatory M2 phenotype, in addition to exert anti-apoptotic effects on cardiac myocytes, pancreatic β cells and mitigating oxidative stress in endothelial cells and podocytes (28). These functions of adiponectin produce insulin sensitizing effects, therefore its high fasting concentration is considered a positive event from the metabolic point of view; conversely, lower concentrations are related to higher insulin resistance rates (29, 30).

Adiponectin exhibits a diurnal pattern of secretion with higher concentration during day and declining at the start of the late evening and reaching, this characteristic and its relative long half-life nadir early in the morning (31) (2.5 h) make difficult to translate its meal related concentration. The meal challenges and the characteristic of subjects studied, had produced different and sometimes contradictory results (Table 1).

Effect of metabolic status on postprandial adiponectin level

Adiponectin gene expression and secretion has been seen stimulated in vitro by insulin, insulin like growth factor 1 (IGF-1), growth hormone (GH) and leptin (32). Given that insulin is a hormone with notorious secretion changes after meals, it is logical to think that meals could affect adiponectin concentration in vivo as well. However, many of the studies that have assessed the postprandial concentration of adiponectin have failed to demonstrate a change in its secretion (Table 1) (33-37), although is not

Table 1.A. Continue in Table 1.B. Adiponectin postprandial research studies. Abbreviations: CHO (carbohydrates), SFA (saturated fatty acids), MUFA (monounsaturated fatty acids), PUFA (polyunsaturated fatty acids), UFA (unsaturated fatty acids), AUC (area under the curve), NASH (non-alcoholic steatohepatitis), M (men), W (women).

Author	Research subjects	Diet	Adiponectin response
Imbeault et al. (35)	15 healthy M	Standardized breakfast, 575 kcal (55% CHO, 30% fat, 15% protein)	No changes
Peake et al. (34)	29 W and 15 M with insulin resistance vs 24 controls and 20 family controls	Meal of 4250 Kj with 80 g of fat (40 g de saturated fat), 19 g of CHO and 47 g of protein	No changes
English et al. (38)	13 lean vs 11 obese subjects	M lunch of 714 Kcal and W of 551 Kcal (56.8% CHO, 31% fat, 12.2% protein)	↑ Concentration in obese subjects at 60’
Umeda et al. (41)	3 M and 7 W with DM2 who underwent bariatric surgery	Standardized liquid food of 353 Kcal (46.8% CHO, 12.5% lipids, 32.2% protein)	↑ Concentration 90 days after surgery at 60, 90 and 120’
Lozano et al. (44)	21 M between 18 and 30 y.o.a. with BMI <30 kg/m2	Fat load of 1 g/kg of weight with different composition of SFA, MUFA and PUFA	Larger AUC, with a peak value at 6 h with heavy load in PUFA
Kennedy et al. (46)	Normal-weight 17 M aged between 18 and 40 years	Cross-design with two diets: high fat (46 g of fat and 1210 Kcal) low fat (15 g of fat and 1214 Kcal)	↑ Concentration at 3 h
Lindegaard et al. (50)	13 obese with DM2 and 12 normoglycemic. All underwent gastric bypass.	Liquid food of 300 Kcal, 50% CHO, 35% fats and 15% protein)	No changes
Reddy et al. (55)	10 normoglycemic obese W	Food with 763 Kcal (50% CHO, 18% protein, 32% fats) in 10 or 40 minutes after intake	AUC was larger when the intake took 40 minutes
Phillips et al. (39)	10 thin, 10 obese and 10 obese with DM2	High-fat diet with 4,136 Kj (34% CHO, 51.5% fat and 14.5% protein)	No changes

always the case. Obesity has been constantly related to insulin resistance and hyperinsulinemia, so in order to explore phenotype as a modifier of postprandial adiponectin English and collaborators compared the adiponectin curve between lean and obese individuals, and found an elevation of up to 4 times in obese subjects with the peak value at 60 minutes, something that the authors attributed to a possible decrease in β–adrenergic stimulation of adipocytes and an increase in plasma insulin concentrations. (38). However, another two studies did not found a significant postprandial change after a high fat diet in overweight or obese subjects (39, 40). Another matter of importance is the postprandial changes in obese subjects after they lose weight that would be approached later.

Insulin resistance and subrogates have been extensively studied according to postprandial adiponectin changes. In that sense, postprandial adiponectin has been negatively correlated with changes in triglycerides (41-43) but, even when fasting and postprandial hypertriglyceridemia has been associated with insulin resistance, postprandial adiponectin has been inconstant in showing a relation with it. Whereas some studies have shown an inverse relationship between postprandial adiponectin and the Homeostatic Model Assesment of Insulin Resistance (HOMA-IR) value (40-42) or a direct relationship with the Matsuda index as a measure of insulin sensitivity

Table 1.B. Continue in Table 1.C. Adiponectin postprandial research studies. Abbreviations: CHO (carbohydrates), SFA (saturated fatty acids), MUFA (monunsaturated fatty acids), PUFA (polyunsaturated fatty acids), UFA (unsaturated fatty acids), AUC (área under the curve), NASH (non-alcoholic steatohepatitis), M (men), W (women).

Author	Research subjects	Diet	Adiponectin response
Katergari et al. (40)	28 overweight of obese M	High-fat diet with 140 g of nuts	No changes
Esposito et al. (43)	15 M and 15 W with DM2 and 15 controls by sex	Cross-design, 3 isoenergetic diets: high fat (60% fat), high in CHO low in fiber (4.5 g of fiber), high in CHO high in fiber (16.8 g of fiber).	↓ In patients with con DM2, with the high-fat diet and high in CHO low in fiber. ↓ in non-diabetics only with the high-fat diet
Shimabukuro et al. (36)	6 M and 6 W, normal weight, between 30 and 42 yoa	Cross-design, 3 diets: high in CHO (300 Kcal, 100% CHO), high in fat (342 Kcal, 30 g de fat per m2SC), standard (478 Kcal, 50.4% CHO, 32.7% fat, 16% protein)	No changes
Poppitt et al. (33)	18 M, normal weight, between 19 and 33 yoa	Two diets, a high ratio of SFA:UFA and another with low ratio of SFA:UFA	No changes
Derosa et al. (45)	141 M y 145 W, normal weight	Meal of 1,147 Kcal with 20% CHO, 68% fat and 12% protein	↓ concentration at 3, 6 and 9 h
Rubin et al. (42)	110 M between 45 and 65 years with and without metabolic syndrome	High-fat diet of 1,017 Kcal with 75 g CHO, 58 g fat, 30 g protein and 10 g of alcohol	↓ concentration at 5 and 6 h
Pietraszek et al. (37)	17 relative of patients with DM2 and 17 controls	Two diets of 847 Kcal, one high in MUFA (72% MUFA) and another high in SFA (79% SFA)	No changes
Dordevic et al. (49)	33 individuals, both genders	Three parallel groups with three beverages: placebo (water, aspartame/vanilla flavor), beverage high in CHO (1856 Kj) and beverage high in fat (1988 Kj)	↓ concentration at 2 h only in the placebo group

(40, 41); other studies have failed to demonstrate this relationship (38, 39, 44). In contrast, the postprandial adiponectin curve has been positively related to postprandial concentrations of High-density lipoprotein cholesterol (C-HDL) (40, 42).

Finally, the postprandial adiponectin curve has also been found in inverse relationship with inflammatory markers such as C-reactive protein, erythrocyte sedimentation rate, fibrinogens and uric acid, as well as with metalloproteinases 2 and 9 as markers of vascular remodeling (45), albeit the latter was not demonstrated in another study (46).

Effect of meals on adiponectin concentration

The kind of diet that the researchers use, is a possible variant that should be controlled. There are two types of diet that have been tried mainly: high-fat diets and high-carb diets. The former are interesting because the prolonged lipemia that they cause sharply decreases insulin sensitivity (47). However, the diets used in clinical studies vary in the percentage or amount of nutrients, also in the calories ingested. Hence, studies that have shown a decrease in postprandial adiponectin levels have been carried out using both high-fat diets (42, 45, 48) and high-carb diets (43, 49) and this has been demonstrated in individuals with metabolic syndrome, DM2 and

Table 1.C. Adiponectin postprandial research studies. Abbreviations: CHO (carbohydrates), SFA (saturated fatty acids), MUFA (monunsaturated fatty acids), PUFA (polyunsaturated fatty acids), UFA (unsaturated fatty acids), AUC (área under the curve), NASH (non-alcoholic steatohepatitis), M (men), W (women).

Author	Research subjects	Diet	Adiponectin response
Westerink et al. (53)	15 overwrite or obese and metabolic syndrome M	Two days of trial: 1) prolonged fast; 2) load of oral fat at 50 g of fat and 3.75 g of glucose by m^2SC	↑ Concentration at 2 h compared when they remained at fasting
Musso et al. (48)	32 patients with NASH diagnosed by biopsy and 32 healthy controls	Oral load of fat of 766 Kcal with 78.3 g of fat, 8.8 g of protein and 7 g of CHO.	↑ Concentration in the control patients at 6 and 8 h and ↓ in patients with NASH as of 2 hours up to the end of the study
Ciardi et al. (51)	12 M and 12 W, healthy	Crossed design: high-fat meal with 1080 Kcal (4.6% CHO, 91.2% fat, 4.2% protein) vs fasting	No changes
Stirban et al. (52)	34 patients with DM2	High-fat diet of 600 Kcal (41 g CHO, 40 g fat, 21 g protein)	No changes
Herpich et al. (57)	20 older and 22 younger women	Randomized. Dextrose or high fat dietery challenge	Remains stable after both test males
Bozzetto et al. (58)	37 M and 8 W with DM2	A CHO/Fibre diet or a MUFA diet for an 8-week period	Significantly increased after the CHO/fibre diet but not after the MUFA diet
Larsen et al. (59)	50 adults with obesity and 17 healthy normal weight	Oral glucose tolerance test	A slight initial peak, followed by a significant decrease at 8 h, in the NW. In the OB these changes were abolished
Adamska-Patruno et al. (60)	46 men, 21-58 years old, normal-weight and overweight/ obese	Crossover study. Every subject participated in two meal-challenge-tests with high-carbohydrate (HC), and normo-carbohydrate (NC) or high-fat (HF) meals	↑ at 60 min in normal-weight individuals after HC-meal.

also normal-weight subjects (42, 50) between 4 and 9 hours after food intake. In contrast, other studies found no changes in postprandial adiponectin despite using a high-fat diet (36, 37, 40, 51, 52), while others that used a mixed diet reported an increase in its concentration (48, 53). The reduction in adiponectin after a high-fat meal, instead of being due to a decrease in its secretion, has been attributed to an increase in liver clearance, though the factors controlling this clearance are not known (54). Other factors that have shown, in at least one study, an increase in the concentration of postprandial adiponectin are food intake over a prolonged period of time (40 vs. 10 minutes) (55) and food intake abundant in polyunsaturated fatty acids, enriched with nuts (44). Other studies have interesting reports with postprandial adiponectin after meals (Tabla 1) (56-59).

Effects of bariatric surgery on adiponectin postprandial concentration.

Umeda and collaborators measured the postprandial adiponectin curve in 10 subjects with type 2 diabetes mellitus (DM2) who underwent bariatric surgery before such procedure, and at 7 and at 90 days after. They found a significant increase in the postprandial measurement when they have already lose significant weight at 90 days but not before (41). Conversely, Lindegaard and collaborators did the same on both subjects with DM2 and normoglycemic obese, with measurements before surgery, at one week, at 3 months and a year, and despite that after a year AUC was higher than in the other measurements,

postprandial values in that curve were not different from the fasting value (50).

In conclusion, despite these contradictory results, adiponectin could have no change or decrease with a high-fat diet and can also have no change or increase with a balanced diet. Most of these changes occur late in the postprandial period, usually after 4 hours of food intake. An aspect that has been scarcely explored in these studies is the molecules responsible for transporting the signal from the digestive tract to the adipose tissue in order to modify the concentration of adiponectin.

LEPTIN

Leptin is a 167 amino acid peptide belonging to the cytosine family of interleukin 6 (60). It was the first adipokine to be cloned (2) and is mainly secreted in subcutaneous adipose tissue, but it also expresses in placenta, mammary and gastric epithelium, skeletal muscle and brain (10). Leptin is an anorexigenic hormone that acts in the hypothalamus, through the ObR receptor, which has six isoforms, named from A to F, and since it is a receptor in the cytosine family, it acts through the system of the Janus 2 kinase (JAK2) and its STAT3 effectors. In order to act, it requires crossing the blood-brain barrier, which it does through a saturable transporter. The functions of leptin are widely varied and will not be described in detail in this paper, as there are excellent recent reviews regarding this issue (61). However, it is important to notice that almost all of them are permissive functions that involve the processes of satiety, reproductive function, secretion of hypothalamic hormones, immune function and metabolic actions, the latter largely insulinomimetic.

Leptin secretion is proportional to the amount of adipose tissue, even though there is a circadian rhythm with larger secretion at night and at early nadir in the morning, such rhythm is influenced and can be modified by diet (62). In women, an ultraradian rhythm with greater secretion in the luteal phase has also been described, and they secrete more leptin than men, however this difference is not as marked as in the case of adiponectin and there are factors known to reduce its secretion such as exposure to cold conditions, adrenergic stimulation, smoking, thiazolidinediones and hormones such as GH, thyroid hormones and melatonin (63).

Effect of metabolic status on postprandial leptin concentration

Gender is a factor that influences leptin secretion and with respect to postprandial responses, Carroll and collaborators found a greater suppression of postprandial leptin in men on a high carbohydrate diet, compared to women (64), in accordance with other studies that have found higher concentration of postprandial leptin in women in an hourly leptin measurements base over 12 – 24 hours, (65-66). In none of the studies above, the body mass index or adiposity measured by bioimpedance were related to a different response from leptin to the food stimulus (64-65).

On the other hand, even though it has been mentioned that an important regulator of the postprandial response of leptin is insulin, the studies that have assessed this relationship have yielded conflicting results. Some of them have reported that at a higher concentration of insulin, there is either a greater secretion of leptin or a lower decrease in its secretion (49, 67-68), while others show a greater short-term reduction in the secretion of leptin in the presence of high-carbohydrate foods with an increase in insulin secretion (69-71); and, even there are studies which fail to demonstrate any possible relationship between insulin secretion and leptin secretion (65,72-73), or they do not find a postprandial change in leptin before the stimulus granted by the authors (74-76). Therefore, it can be said that it is not clear if insulin regulates or how it regulates leptin secretion at least during the postprandial period.

Effect of meals on postprandial leptin concentration

Leptin secretion has also been evaluated in response to a high-fat diet. In healthy patients, a greater decrease in leptin was found after high-fat food (77), even more than in comparison with high-carbohydrate food (49). The same has been observed in first-degree relatives of patients with type 2 diabetes mellitus, or with prediabetes (37) or even with a diagnosis of type 2 diabetes

mellitus (78). On the other hand, other authors ascertained that high-fat food does not produce a difference in the behavior of leptin compared with that of subjects subjected to prolonged fasting, both in patients with normal weight and in patients with overweight or mild obesity and metabolic syndrome (51, 53, 79). Moreover, the direct infusion of fat or protein into the digestive tract has failed to produce a change in the postprandial concentration of leptin (80), neither does the presence of fat in the food appear to be a factor that uniformly causes changes in postprandial leptin secretion.

On the other hand, Stirban et al. found in a group of diabetic patients that the administration of foods with a high degree of cooking caused a greater reduction of leptin at 2 and 4 hours after ingestion compared to food with a low degree of cooking, isocaloric and balanced, which the authors attributed to a greater amount of advanced glycosylation end products in these foods (81).

Effects of bariatric surgery on postprandial leptin concentration.

Bariatric surgery is the most effective method for long-term weight loss. This decrease in adipose tissue produces a decrease in fasting leptin concentration. In the same way, both Roux Y gastric bypass and sleeve gastrectomy cause a decrease in postprandial leptin levels, as well as in the area under the postprandial leptin curve, these lower levels are not different from fasting leptin levels nevertheless (82-85).

RESISTIN

It is a protein of 108 amino acids with a structure similar to adiponectin. Although this protein is secreted by adipocytes, the site of the greatest secretion in humans is mainly M2 monocytes and macrophages, so the stimuli that trigger its secretion are inflammation, lipopolysaccharides and interleukin 6. Resistin has been related above all to insulin resistance in liver in mice (11).

Effect of meals on postprandial resistin concentration

With regard to the postprandial secretion of this adipokine, it has been studied in healthy subjects for which there are again discordant results, as Yamauchi and collaborators found a reduction 4 hours after the intake of a balanced mixed diet and 3 and 4 hours after a load with 75 g of glucose (86); Gruendel and collaborators determined that the intake of a mixed balanced meal causes a lower decrease in the secretion of resistin from 50 to 350 minutes after the intake of a mixed and balanced liquid food compared with subjects who remained fasting during such period of time (87)---83); while in a study by Westerink and collaborators, in which they used a high-fat diet with overweight men and metabolic syndrome, the decrease in postprandial resistin was not statistically different from that presented by the same patients when they were left on a prolonged fast (53). On the contrary, in another study in which patients with non-alcoholic steatohepatitis (NASH) were evaluated versus controls, also subject to a high-fat diet, patients with NASH, who had lower rates of insulin sensitivity, had a higher elevation in postprandial resistin levels after 4 hours after food intake (48).

VISFATIN

Visfatin is another protein abundantly produced by adipocytes; it has metabolic and immune-system related activities. From the metabolic point of view, it has insulin-like mimetic effects in cultured adipocytes and lowers plasma glucose in mice. It also induces leukocyte activation and stimulates the production of TNF-alpha and interleukin 6. There are few postprandial studies on this adipokine; however, its secretion could be increased mainly by postprandial hyperglycemia as suggested by a study with hyperglycemic clamp (88). The high-fat diet has failed to demonstrate postprandial changes in visfatin secretion (51).

VASPIN

Vaspin is a protein that keeps structural homology with the serine protease inhibitor family without having such a function. It is an adipokine of secretion mainly of visceral fat and that correlates positively with age and body mass index. Also its secretion is increased by doing exercise. The postprandial secretion of vaspin

has been evaluated together with the exploration of the circadian secretion of this adipokine in healthy men aged between 18 and 30 years; in this population vaspin showed an increase with respect to the fasting average and in the times before food and a decrease in its concentration after the ingestion of a balanced and isocaloric meal (89). This behavior is the opposite of insulin secretion and allows theorizing about a link between the action or secretion of both hormones.

Conclusion

The different variables inherent to the possible diversity in the diet of human beings make it difficult to predict the behavior of the various metabolites, including adipokines in the postprandial stage. However, current studies suggest that nutrients are only modifiers of the secretion of adipokines, without having a clearly established direct relationship. The various forms of food that humans try across the globe and their lives must be incentives to study these metabolites as regards the regional modifications caused by diet.

References

1. Blüher, M. Adipokines-removing road blocks to obesity and diabetes therapy. Mol Metab. 2014 Jan;3(3):234-40
2. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. Nature. 1994;372:425-32.
3. Blüher, M. Adipose tissue dysfunction in obesity. Exp Clin Endocrinol Diabetes. 2009 Jun;117(6):241-50.
4. Freitas-Lima LC, Andrade-Braga V, Franca-Silva MS, Campos-Cruz J, Sousa-Santos SH, Oliveira-Monteiro MM, Moura-Balarini C. Adipokines, diabetes and atherosclerosis: an inflammatory association. Front Physiol. 2015;6:304. Doi:10.3389/fphys.2015.00304
5. Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. Obesity Reviews. 2010;11(1):11-18. Doi:10.1111/j.1467-789X.2009.00623.x
6. Fasshauer M, Blüher M. Adipokines in health and disease. Trends Pharmacol Sci. 2015 Jul;36(7):461-70. doi: 10.1016/j.tips.2015.04.014
7. Rodríguez-Ayala E, Gallegos-Cabrales EC, González-López L, Laviada-Molina HA, Salinas-Osornio RA, Nava-González EJ, et al. Towards precisión medicine: defining and characterizing adipose tissue dysfunction to identify early immunometabolic risk in symptom-free adults from the GEMM family study. Adipocyte.2020;9(1):153-69.
8. Cavalot F, Petrelli A, Traversa M, Bonomo K, Fiora E, Conti M, et al. Postprandial blood glucose is a stronger predictor of cardiovascular events than fasting blood glucose in type 2 diabetes mellitus, particularly in women: lessons from the San Luigi Gonzaga Diabetes Study. J Clin Endocrinol. Metab. 2006;91(3):813-9.
9. Anderson RA, Evans ML, Ellis FR, Graham J, Morris K, Jackson SK, et al. The relatonship between post-prandial lipaemia, endotelial function and oxidative stress in healthy indivduals and patients with type 2 diabetes. Atherosclerosis. 2001; 154(2);475-83.
10. Margetic S, Gazzola C, Pegg GG, Hill RA. Leptin: a review of its peripheral actions adn interactions. Int J Obes Relat Metab Disord. 2002;26:1407-33.
11. Acquarone E, Monacelli F, Borghi R, Nencioni A, Odetti P. Resistin: a reappraisal. Mech Ageing Dev. 2019;178:46-63. doi: 10.1016/j.mad.2019.01.004
12. Milan AM, Cameron-Smith D. Digestion and postprandial metabolism in the elderly. Advances in food and nutrition research. 2015;76:79-124.
13. Meyer C, Dostou JM, Welle SL, Gerich JE. Role of human liver, kidney and skeletal muscle in postprandial glucose

homeostasis. Am J Physiol Endocrinol Metab. 2002;282:E419-27.
14. Reza-Albarrán AA. Capítulo 4. Secreción y acciones fisiológicas de la insulina. En Tratamiento del paciente diabético con insulina. 1ª edición. Editorial Corporativo Intermédica S.A. de C.V. 2008. Pp 59-76.
15. Mjos OD, Faergeman O, Hamilton RL, Havel RJ. Characterization of remnants produced during the metabolism of triglyceride-rich lipoproteins of blood plasma and intestinal lymph in the rat. J Clin Invest. 1975;56:603-15.
16. Chavez-Jauregui RN, Mattes RD, Parks EJ. Dynamics of fat absorption and effect of sham feeding on postprandial lipemia. Gastroenterology. 2010;139:1538-48.
17. Heath RB, Jones R, Frayn KN, Robertson MD. Vagal stiumlation exagerates the inhibitory ghrelin response to oral fat in humans. J Endocrinol. 2004;180:273-81.
18. Marroqui L, Gonzalez A, Ñeco P, Caballero-Garrido E, Vieira E, Ripoll C, Nadal A, Queasada I. Role of leptin in the pancreatic B-cell: effects and signaling pathways. J Mol Endocrinol. 2012;49:R9-R17.
19. Hu E, Liang P, Spiegelman BM. AdipoQ is a novel adipose-specific gene dysregulated in obesity. J Bio Chem. 1996 May;271(18):10697-703.
20. Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsuzawa Y, Chao CL, et al. Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein adiponectin. J Clin Endocrinol Metab. 2001 Aug;86(8):3815-9.
21. Swarbrick MM, Havel PJ. Physiological, pharmacological, and nutritional regulation of circulating adiponectin concentrations in humans. Metab Syndr Relat Disord. 2008 Jun;6(2):87-102
22. Scherer PE, Williams S, Fogliano M, Baldini G, Lodish HF. A novel serum protein similar to C1q, produced exclusively in adipocytes. J Biol Chem. 1995 Nov;270(45):26746-9
23. Liu Y, Chewchuk S, Lavigne C, Brulé S, Pilon G, Houde V, et al. Functional significance of skeletal muscle adiponectin production, changes in animal models of obesity and diabetes, and regulation by rosiglitazone treatment. Am J Physiol Endocrinol Metab. 2009 Sep;E297(3):657-64.
24. Pajvani UB, Hawkins M, Combs TP, Rajala MW, Doebber T, Berger JP, et al. Complex distribution, not absolute amount of adiponectin, correlates with thiazolidinedione-mediated improvement in insulin sensitivity. J Biol Chem. 2004 Mar;279(13):12153-62.
25. Wang ZV, Scherer PE. Adiponectin, the past two decades. J Mol Cell Biol. 2016 Febr;8(2):93-100.
26. Yamauchi T, Kamon J, Minokoshi Y, Ito Y, Waki H, Uchida S, et al. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. Nat Med. 2002 Nov;8(11):1288-95.
27. Combs TP, Berg AH, Obici S, Scherer PE, Rossetti L. Endogenous glucose production is inhibited by the adipose-derived protein Acrp30. J Clin Invest. 2001 Dec;108(12):1875-81.
28. Ruan H, Dong LQ. Adiponectin signaling and function in insulin target tissues. J Mol Cell Biol. 2016 Febr;8(2):101-109.
29. Coker RH, Williams RH, Yeo SE, Kortebein PM, Bodenner DL, Kern PA, et al. Visceral fat and adiponectin: associations with insulin resistance are tissue-specific in women. Metab Syndr Relat Disord. 2009 Feb;7(1):61-7.
30. Ryan AS, Berman DM, Nicklas BJ, Sinha M, Gingerich RL, Meneilly GS, et al. Plasma adiponectin and leptin levels, body composition, and glucose utilization in adult women with wide ranges of age and obesity. Diabetes Care. 2003 Aug;26(8):2383-8.
31. Gavrila A, Peng CK, Chan JL, Mietus JE, Goldberger AL, Mantzoros CS. Diurnal and ultradian dynammics of serum

adiponectin in healthy men: comparisn with leptin, circulating soluble leptin receptor, and cortisol patterns. J Clin Endocrinol Metab. 2003;88(6):2838-2843.
32. Fang H, Judd RL. Adiponectin regulation and function. Compr Physiol. 2018;8:1031-63.
33. Poppitt SD, Keogh GF, Lithander FE, Wang Y, Mulvey TB, Chan YK, et al. Postprandial response of adiponectin, interleukin-6, tumor necrosis factor-alpha, and C-reactive protein to a high-fat dietary load. Nutrition. 2008 Apr;24(4):322-9.
34. Peake PW, Kriketos AD, Denyer GS, Campbell LV, Charlesworth JA. The postprandial response of adiponectin to a high-fat meal in normal and insulin-resistant subjets. Int J Obes Relat Metab Disord. 2003 Jun;27(6):657-62.
35. Imbeault P, Pomerleau M, Harper ME, Doucet E. Unchanged fasting and postprandial adiponectin levels following a 4-day caloric restriction in Young healthy men. Clin Endocrinol. 2004;60:429-433.
36. Shimabukuro M, Chinen I, Higa N, Takasu N, Yamakawa K. Ueda S. Effects of dietary composition on postprandial endotelial function and adiponectin concentrations in healthy humans: A crossover controlled study. Am J Clin Nutr. 2007 Oct;86(4):923-8.
37. Pietraszek A, Gregersen S, Hermansen K. Acute effects of dietary fat on inflammatory markers and gene expression in first-degree relatives of type 2 diabetes patients. Rev Diabet Stud. 2011;8:477-89.
38. English PJ, Coughlin SR, Hayden K, Malik IA, Wilding JP. Plasma adiponectin increases postprandially in obese , but not in lean subjects. Obes Res. 2003 Jul;11(7):839-44.
39. Phillips LK, Peake JM, Zhang X, Hickman IJ, Briskey DR, Huang BE, et al. Postprandial total and HMW adiponectin following a high-fat meal in lean, obese and diabetic men. Eur J Clin Nutr. 2013 Mar;67(3):377-84.
40. Katergari SA, Passadakis P, Milousis A, Passadaki T, Asimakopoulos B,Mantatzis M, et al. Subcutaneous and total fat at L4-L5 and subcutaneous, visceral and total fat at L3-L4 are important contributors of fasting and postprandial adiponectin level. Endocr Res. 2015 Mar;40(3):127-32.
41. Umeda LM, Pereira AZ, Carneiro G, Arasaki CH, Zanella MT. Postprandial adiponectin levels are associated with imporvements in postprandial trigycerides after Roux-en-Y gastric bypass in type 2 diabetic patients. Metab Syndr Relat Disord. 2013 May;11(5):343-8.
42. Rubin D, Helwig U, Nothnagel M, Lemke N, Schreiber S, Folsch UR, et al. Postprandial plasma adiponectin decreases after glucose and high fat meal and is independently associated with postprandial triacylgycerols but not with -11388 promoter polymorphism. Br J Nutr. 2008 Jan;99(1):76-82.
43. Esposito K, Nappo F, Giuliano F, Di PC, Ciotola M, Barbieri M, et al. Meal modulation of circulating interleukin 18 and adiponectin concentrations in healthy subjects and in patients with type 2 diabetes mellitus. Am J Clin Nutr. 2003 Aug;78(8):1135-40.
44. Lozano A, Perez-Martinez P, Marin C, Tinahones FJ, Gado-Lisa J, Cruz-Teno C, et al. An acute intake of a walnut-enriched meal improves postprandial adiponectin response in healthy youn adults. Nutr Res. 2013 Dec;33(12):1012-8.
45. Derosa G, Ferrari I, D'Angelo A, Salvadeo SA, Fogari E, Gravina A, et al. Effects of a standardized oral fat load on vascular remodelling markers in healthy subjects. Microvasc Res. 2010 Jul;80(1):110-5.
46. Kennedy A, Spiers JP, Crowley V, Williams E, Lithander FE. Postprandial

adiponectin and gelatinase response to a high-fat versus an isoenergetic low-fat meal in lean, healthy men. Nutrition. 2015 Jun;31(6):863-70.
47. Pedrini MT, Niederwanger A, Kranebitter M, Tautermann C, Ciardi C, Tatarczyk T, et al. Postprandial lipaemia induces an acute decrease of insulin sensitivity in healthy men independently of plasma NEFA levels. Diabetologia. 2006;49(7):1612-8.
48. Musso G, Gambino R, Pacini G, De Michieli F, Cassader M. Prolonged saturated fat-induced, glucose-dependent insulinotropic polypeptide elevation is associated with adipokine imabalance and liver injury in nonalcoholic steatohepatitis: dysregulated enteroadipocyte axis as a novel feature of fatty liver. Am J Clin Nutr. 2009;89:558-67.
49. Dordevic AL, Pendergast FJ, Morgan H, Villas-Boas S, Caldow MK, Larsen AE, Sinclair AJ, Cameron-Smith D. Postprandial responses to lipid and carbohydrate ingestión in repeated subcutaneous adipose tissue biopsies in healthy adults. Nutrients. 2015;7:5347-61.
50. Lindegaard KK, Jorgensen NB, Just R, Heegaard PMH, Madsbad S. Effects of Roux-en-Y gastric bypass on fasting and postprandial inflammation-related parameters in obese subjects with normal glucose tolerance and in obese subjects with type 2 diabetes. Diabet Metab Syndr. 2015;7:12.
51. Ciardi C, Tatarczyk T, Tschoner A, Kranebitter A, Niederwanger A, Ebenbichler CF, Patsch JR, Pedrini MT. Effect of postprandial lipemia on plasma concentrations of A-FABP, RBP-4 and visfatin. Nutr Metab Cardiovasc Dis. 2010;20:662-8.
52. Stirban A, Nandrean S, Götting C, Stratmann B, Tschoepe D. Effects of n-3 polyunsaturated fatty acids (PUFAs) on circulating adiponectin and leptin in subjects with type 2 diabetes mellitus. Horm Metab Res. 2014;46:490-2.
53. Westerink J, Hajer GR, Kranendonk EG, Schipper HS, Monajemi H, Kalkhoven E, Visseren FLJ. An oral mixed fat load is followed by a modest anti-inflamatory adipocytokine response in overweight patients with metabolic syndrome. Lipids. 2014;49:247-254.
54. Wiest R, Moleda L, Farkas S, Scherer M, Kopp A, Wönckhaus U, Büchler C, et al. Splachnic concentrations and postprandial release of visceral adipokines. Metabolism Clinical Experimental. 2010;59:664-70.
55. Reddy NL, Peng C, Carreira MC, Halder L, Hattersley J, Piya MK, et al. Enhanced thermic effect of food, postprandial NEFA suppression and raised adiponectin in obese women who eat slowly. Clin Endocrinol (Oxford). 2015 Jun;82(6):831-7.
56. Herpich C, Kochlik B, Haß U, Weber D, Grune T, Norman K. Altered Adiponectin response in older women following dextrose and high-fat dietary Challenges. Mol Nutr Food Res. 2021 Sep;65(17):e2100487. doi: 10.1002/mnfr.202100487. Epub 2021 Aug 4.
57. Bozzetto L, Polito R, Nigro E, Prinster A, Della Pepa G, Costabile G, Vetrani C, Vitale M, Daniele A, Rivellese AA, Annuzzi G. Dietary influence on adiponectin in patients with type 2 diabetes. Eur J Clin Invest. 2021 Aug;51(8):e13548. doi: 10.1111/eci.13548. Epub 2021 Apr 2.
58. Larsen MA, Isaksen VT, Paulssen EJ, Goll R, Florholmen JR. Postprandial leptin and adiponectin in response to sugar and fat in obese and normal weight individuals. Endocrine. 2019 Dec;66(3):517-525. doi: 10.1007/s12020-019-02102-9. Epub 2019 Oct 11.
59. Adamska-Patruno E, Ostrowska L, Goscik J, Fiedorczuk J, Moroz M, Kretowski A, Gorska M. The differences in

postprandial serum concentrations of peptides that regulate satiety/hunger and metabolism after various meal intake in men with normal vs. excessive BMI. Nutrients. 2019 Feb 26;11(3):493. doi: 10.3390/nu11030493.

60. Brennan AM, Mantzoros CS. Drug insight: the role of leptin in human physiology and pathophysiology-emerging clinical applications. Nat Clin Pract Endocrinol Metab. 2006;2:318-27.
61. Mantzoros CS, Magkos F, Brinkoetter M, Sienkiewicz E, Dardeno TA, Kim SY, Hamnvik OPR, Koniaris A. Leptin in human physiology and pathophysiology. Am J Physiol Endocrinol Metab. 2011;301:E567-84.
62. Fogteloo AJ, Pijl H, Roelfsema F, Frölich M, Meinders AE. Impact of meal timing and frequency on the twenty-four-hour leptin rhythm. Horm Res. 2004;62:71-8.
63. Mantzoros CS, Magkos F, Brinkoetter M, Sienkiwicz E, Dardeno TA, Kim SY, Hamnvik OP, Koniaris A. Leptin in human physiology and pathophysiology. Am J Physiol Endocrinol Metab. 2011;301:E567-E584
64. Carroll JF, Kaiser KA, Franks SF, Deere C, Caffrey JL. Influence of BMI and gender on postprandial hormone response. Obesity. 2007;15 (10):2974-83.
65. Stanhope KL, Griffen SC, Bair BR, Swarbrick MM, Keim NL, Havel PJ. Twenty-four hour endocrine and metabolic profiles following consumption of high-fructose corn syrup, sucrose, fructose and glucose sweetened beverages with meals. Am J Clin Nutr. 2008;87:1194-203
66. Lu G, Thomas-Geevarghese A, Anuurad E, Raghavan S, Minolfo R, Ormsby B, et al. Relationship of postprandial nonesterified fatty acids adipokines, and insulin across gender in human immunodeficiency virus-positive patients undergoing highly active antiretroviral therapy. Metab Syndr Relat Disord. 2009;7(3):199-204.
67. Chearskul S, Yothathai T, Sriussadaporn S. Postprandial leptin response to thai meals with different macronutrient mixtures. Southeast Asian J Trop Med Public Health. 2006;37:778-83.
68. Romon M, Lebel P, Velley C, Marecaux N, Fruchart JC, Dallongeville J. Leptin response to carbohydrate or fat meal and association with subsequent satiety and energy intake. Am J Physiol 1999;277:E866-61.
69. Koutsari C, Karpe F, Humphreys SM, Frayn KN, Hardman AE. Plasma leptin is influenced by diet composition and exercise. Int J Obes. 2003;27:901-6.
70. Barkoukis H, Marchetti CM, Nolan B, Sistrun SN, Krishnan RK, Kirwan JP. A high glycemic meal suppresses the postprandial leptin response in normal healthy adults. Ann Nutr Metab. 2007;51:512-18.
71. Masuo K, Katsuya T, Ogihara T, Tuck ML. Acute hyperinsulinemia reduces plasma leptin levels in insulin-sensitive Japanese men. AJH. 2005;18:235-243.
72. Erdmann J, Lippl F, Wagenpfeil S, Schusdziarra V. Differential Association of basal and postprandial plasma ghrelin with leptin, insulin, and type 2 diabetes. Diabetes. 2005;54:1371-8.
73. Krog-Mikkelsen I, Sloth B, Dimitrov D, Tetens I, Björck I, Flint A, et al. A low glycemic index diet does not affect postprandial energy metabolism but decreases postprandial insulinemia and increases fullness ratings in healthy women. J Nutr 2011;141:1679-84.
74. Di Francesco V, Zamboni M, Zoico E, Mazzali G, Dioli A, Omizzolo F, et al. Unbalanced serum leptin and ghrelin dynamics prolong postprandial satiety and inhibit hunger in healthy elderly: another reason for the “anorexia of aging”. Am J Clin Nutr. 2006;83:1149-52.
75. Smeraglio AC, Kennedy EK, Horgan A, Purnell JQ, Gillingham MB. Change in postprandial substrate oxidation after a high fructose meal is related to body

mass index (BMI) in healthy men. Nutr Res. 2013;33(6):435-41.
76. Guerci B, Hadjadj S, Quilliot D, Ziegler O, Drouin P. No acute response of leptin to an oral fat load in obese patients and during circadian rhythm in healthy controls. Eur J Endocrinol. 2000;143:649-55.
77. Poppitt SD, Leahy FE, Keogh GF, Wang Y, Mulvey TB, Stojkovic M, Chan YK, et al. Effect of high-fat meals and fatty acid saturation on postprandial levels of the hormones ghrelin and leptin in healthy men. Eur J Clin Nutr. 2006;60:77-84.
78. Iraklianu S, Melidonis A, Tournis S, Konstandelou E, Tsatsoulis A, Elissaf M, Sideris D. Postprandial leptin responses after an oral fat tolerance test. Diabetes care. 2001;24(7):1299-1300.
79. Fernández-García JC, Murri M, Coin-Aragaüez L, Alcaide J, El Bekay R, Tinahones FJ. GLP-1 and Peptide YY secretory response after fat load is impaired by insulin resistance, impaired fasting glucose and type 2 diabetes in morbidly obese subjects. Clin Endocrinol (Oxf). 2014;80(5):671-6.
80. Ullrich S, Otto B, Hutchison AT, Luscombe-Marsh N, Horowitz M, Feinle-Bisset C. Comparative effects of intraduodenal protein and lipid on ghrelin, peptide YY, and leptin reléase in healthy men. Am J Physiol Regul Integr Comp Physiol. 2015;308:R300-4.
81. Stirban A, Negrean M, Götting C, Stratmann B, Gawlowski T, Mueller-Roesel M, Kleesiek K, et al. Leptin decreases posprandially in people with type 2 diabetes, an effect reduced by the cooking method. Horm Metab Res. 2008;40:896-900.
82. Dimitriadis , Daskalakis M, Kampa M, Peppe A, Papadakis JA, Melissas J. Alterations in gut hormones after laparoscopic sleeve gastrectomy. A prospective clinical and laboratory investigational study. Ann Surg. 2013;257:647-54.
83. Jacobsen SH, Olesen SC, Dirksen C, Jorgensen NB, Bojsen-Moller KN, Kielgast U, et al. Changes in gastrointestinal hormone responses, insulin sensitivity, and beta-cell function within 2 weeks after gastric bypass in non-diabetic subjects. Obes Surg. 2012;22:1084-96.
84. Lee WJ, Chen CY, Chong K, Lee YC, Chen SC, Lee SD. Changes in postprandial gut hormones after metabolic surgery: a comparison of gastric bypass and sleeve gastrectomy. Surg Obes Relat Dis. 2011;7:683-90.
85. Ramón JM, Salvans S, Crous X, Puig S, Goday A, Benaiges D, Trillo L, Pera M, Grande L. Effect of Roux-en-Y gastric bypass vs sleeve gastrectomy on glucoes and gut hormones: a prospective randomised trial. J Gastrointest Surg. 2012;16:1116-22.
86. Yamauchi J, Osawa H, Takasuka T, Ochi M, Murakami A, Nishida W, et al. Serum resistin is reduced by glucose and meal loading in healthy human subjects. Metabolism Clinical Experimental. 2008;57:149-56.
87. Gruendel S, Weickert MO, Garcia AL, Wagner K, Pfeiffer AFH, Harsch, Koebnick C. Serum resistin increases in a postprandial state during liquid meal challenge test in healthy human subjects. J Endocrinol Invest. 2006;29:RC27-RC30.
88. Haider DG, Schaller G, Kapiotis S, Maier C, Luger A, Wolzt M. The reléase of the adipocytokine visfatin is regulated by glucose and insulin. Diabetologia. 2006;49:1909-1914.
89. Jeong E, Youn BS, Kim DW, Kim EH, Park JW, Namkoong C, et al. Circadian rhythm of serum vaspin in healthy male volunteers: relations to meals. J Clin Endocrinol Metab. 2010;95(4):1869-75.
90.