Special Article

Effect of diet on adiponectin levels in blood

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Dietary management has been considered an alternative means of modulating adiponectin levels. The purpose of this review is to examine the scientific evidence regarding the effect of diet on adiponectin levels in blood. Clinical trials were selected from Medline until April 2010 using the following MeSH terms: adipokines OR adiponectin AND diet OR lifestyle. A total of 220 articles were identified in the initial search, and 52 studies utilizing three different methods of dietary management were included in the present review: low-calorie diets (n = 9 studies), modification of diet composition (n = 33), and diet plus exercise (n = 10). Daily intake of fish or omega-3 supplementation increased adiponectin levels by 14–60%. Weight loss achieved with a low-calorie diet plus exercise increased adiponectin levels in the range of 18–48%. A 60–115% increase in adiponectin levels was obtained with fiber supplementation. In conclusion, dietary management can be an effective therapeutic means of increasing adiponectin levels. Studies investigating different forms of adiponectin and changes in the types of adipose tissue are necessary in order to elucidate the mechanisms involved in the modulation of adiponectin levels.

INTRODUCTION

In recent years, understanding of the role played by adipose tissue has expanded. Currently, adipose tissue is considered an endocrine organ and not strictly a compartment for fat storage, because many hormones and proteins are produced by adipocytes. Adipokines, which are proteins secreted by adipose tissue, influence a variety of physiological processes, such as food intake control, energy homeostasis, insulin sensitivity, angiogenesis, blood pressure regulation, and blood coagulation.[1]

The expression of most adipokines increases with adipose tissue accumulation, and this increased expression is implicated in insulin resistance and atherosclerosis.[2] Visceral adipose tissue secretes the largest amounts of adipokines linked to inflammation, followed by subcutaneous fat tissue.[3] The type of adipose tissue seems to be more important than the quantity of adipose tissue, and visceral adiposity, rather than total adiposity, is more closely associated with comorbid conditions linked to overweight.[4] However, unlike the majority of proteins secreted by adipocytes, adiponectin is inversely correlated with excess body weight.[1,2]

Adiponectin is a 30-kDa protein produced exclusively by adipocytes of white adipose tissue and encoded by a gene located on chromosome 3q27. Circulating adiponectin is found in different isoforms, including those of low, medium, and high molecular weight. It has been suggested that high-molecular-weight adiponectin is the active biological form of the protein.[5] It is also suggested that the low-/high-molecular-weight adiponectin ratio is an important determinant of the physiological activity of adiponectin.[6]

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Adiponectin plays a significant role in the regulation of insulin sensitivity; in addition, it has anti-atherosclerotic and anti-inflammatory properties.[7,8] Low adiponectin levels have been associated with type 2 diabetes,[5,8] metabolic syndrome,[9,10] and cardiovascular disease.[11] The strong relationship between low adiponectin levels and diseases associated with obesity has prompted several studies on the potential of different therapeutic strategies to modulate blood levels of adiponectin,[12] with the aim of developing therapeutic approaches to minimize the presence and/or severity of these conditions.

Treatment with thiazolidinediones to improve insulin sensitivity appears to influence both the genetic expression and the blood levels of adiponectin, although the mechanism through which these effects occur has not yet been elucidated.[13] Weight loss induced by bariatric surgery also appears to increase adiponectin blood levels.[14,15] Moderate- to high-intensity exercise modifies blood levels of adiponectin, although it is not known whether the type of exercise influences these changes.[16]

Associations between certain dietary components or specific dietary patterns and adiponectin blood levels have been demonstrated in longitudinal studies.[17–19] The intake of fiber, whole grains, and foods with a low glycemic index was positively associated with adiponectin levels in a study conducted in men with type 2 diabetes.[17] Differences in the consumption of animal protein, omega-3 fatty acids, arachidonic acid, and cholesterol were also associated with adiponectin levels in a Japanese population.[18] Furthermore, a positive association between higher scores of Mediterranean diet adherence and higher adiponectin levels was observed in a study involving diabetic women.[19]

Thus, the aim of this study was to review the scientific evidence from clinical trials on diet (type of diet, food, or specific nutrient) alone or diet combined with exercise in the modulation of adiponectin blood levels.

LITERATURE SEARCH AND QUALITY OF STUDIES

Clinical trials were selected by a search of the Medline database (publications in English, Portuguese, and Spanish) using the Clinical Queries search engine; in addition, specific publications in the medical and nutrition fields were searched. Articles published until April 2010 were searched. The MeSH terms used were as follows: adipokines OR adiponectin AND diet OR lifestyle. The search was limited to studies conducted in humans. No limitations were set regarding follow-up or design of clinical trials. Studies on the effects of bariatric surgery, medications, or exercise only were excluded as well as studies conducted in children and adolescents.

A total of 220 potentially relevant articles were identified in the initial search. Following the evaluation of title and abstracts, 59 articles were selected for full-text reading. Seven articles were excluded on the basis of the exclusion criteria. In total, 52 studies[20–71] were eligible for inclusion in this review (Figure 1).

In 27 (51.9%) studies, evaluation of the intervention effect on adiponectin blood levels was the primary outcome, while in others, determination of adiponectin levels was a secondary outcome.[21–23,26–29,31,36,38–40,43,46,47,53–55,60,62,65,68,69,71] Most studies (90.4%) analyzed only the total adiponectin form, while the measurement of at least one of the adiponectin multimeric forms was performed in five studies.[26–28,42,71] More than half the studies (67.3%) described the method used for assessing compliance with the dietary intervention: records, recalls, and food diaries were the main strategies used.

Thirty-nine of the identified studies were randomized controlled trials,[25,27–29,31,33–40,42–61,63–65,68,69,71] while the others were single-arm intervention studies. Five (9.6%) studies described the method of randomization,[40,42,48,63,68] and just three studies reported the allocation concealment of participants.[40,48,63] Two studies did not report the inclusion criteria for participants.[20,60]
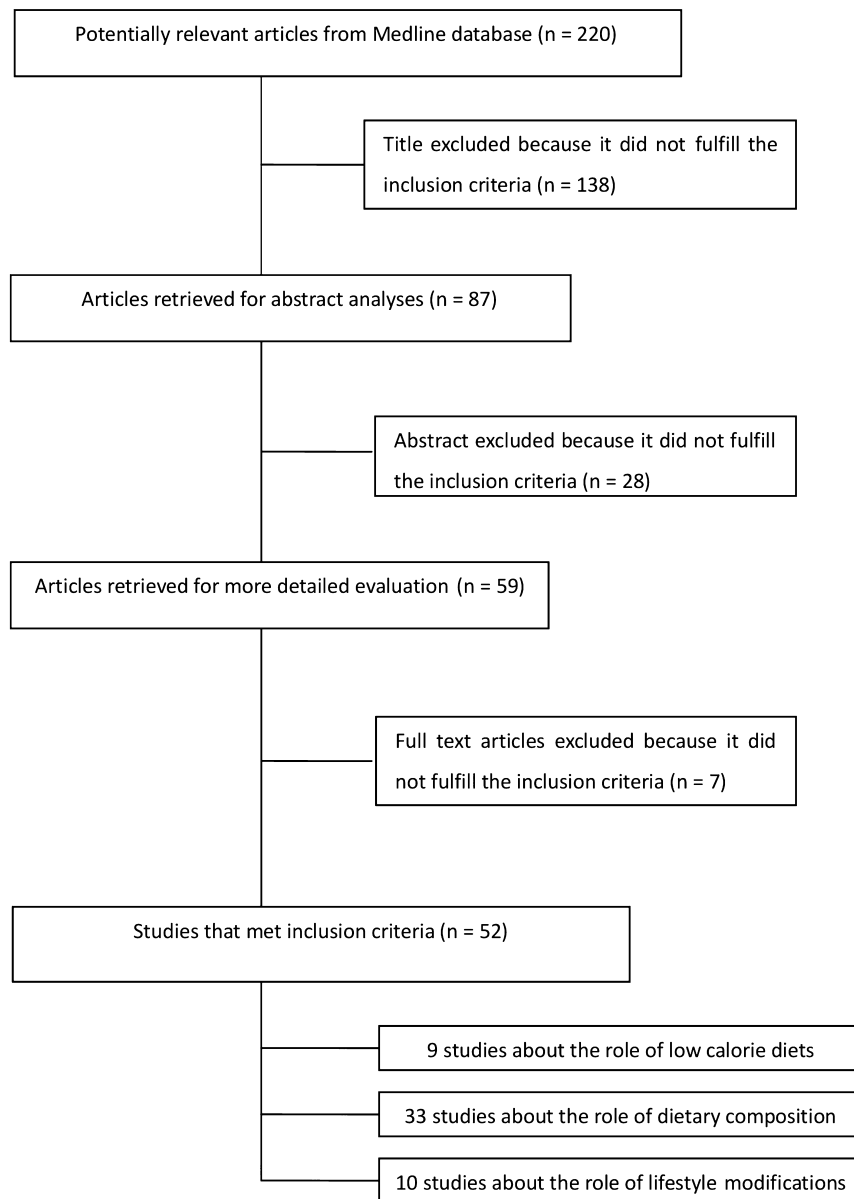
The number of participants ranged from 10[31] to 219.[70] Fifteen (28.8%) studies included only females,[20,23,24,26,29,31,32,45,49,51,55,63,65,66,70] and seven (13.5%) included only males.[22,28,39,40,53,54,69] Two studies did not report the gender of participants,[42,57] and other studies (n = 28) included both female and male participants. Most studies (76.9%) included only overweight participants.[20–24,26–38,43,45–48,50–52,55–59,62–71]

Duration of follow-up ranged from 3 days[30] to 3 years.[33] Only seven (13.5%) studies had a follow-up period equal to or greater than 1 year.[25,32,33,35,63,68,69] Dropouts were encountered in 21 (40.4%) studies,[25,32,33,35–37,44,45,49,51,53,56–58,60,62,63,65,68,69,71] and in nine of these,[25,33,35,37,56,57,62,68,71] the dropout rate exceeded 20%. Intention-to-treat analysis was performed in one study,[53] and five studies were unclear about whether there were losses to follow-up.[21,46–48,59]

The different dietary interventions among the studies included in this review were grouped into three categories: 1) Diets with caloric restriction (n = 9 studies, Table 1[20–28]); 2) Modification of diet composition (n = 33, Table 2[29–61]); and 3) Diet combined with exercise (n = 10, Table 3[62–71]). The influence of each type of dietary intervention on adiponectin levels is presented and discussed below.

EFFECT OF LOW-CALORIE DIETS ON ADIPONECTIN LEVELS

Nine (17.3%) studies analyzed the effect of calorie-restricted diets on adiponectin blood levels.[20–28] The details of these clinical trials are summarized in Table 1 in

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│  Potentially relevant articles from Medline database (n = 220)│
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│  Studies that met inclusion criteria (n = 52) │
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                          ├──────│ 33 studies about the role of dietary composition │
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                          └──────│ 10 studies about the role of lifestyle modifications │
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Figure 1 **Flow-chart of study selection.**

chronological order of publication. There was little consistency among the total numbers of calories of the diets included in the intervention arms of these studies (range 550–1,550 kcal/day).

Five studies[20–22,24,27] did not report changes in adiponectin blood levels with low-calorie diets, and in four of these,[20–22,24] the weight loss was less than 7%. Two trials[26,28] demonstrated significant increases in adiponectin values with a low-calorie diet (20% and 37%, respectively). A 17% increase in adiponectin was also reported in another study that adopted this intervention,[25] but this increase was without statistical significance. On the other hand, a reduction in adiponectin blood levels was observed in a short-term clinical trial that employed a calorie-restricted diet in normal-weight subjects.[23]

Among clinical trials that reported increases in adiponectin blood levels with a low-calorie diet, weight loss was equal to or greater than 7.4%, and the duration of follow-up ranged from 12 weeks to 12 months.[25,26,28] These data suggest that a low-calorie diet can increase adiponectin blood levels, especially when the intervention is administered over a longer period and a significant weight loss is induced.

A negative correlation between adiponectin levels and visceral adipose tissue storage and a positive correlation of this adipokine with subcutaneous adipose tissue

Table 1 **Effect of diets with calorie restriction on adiponectin blood levels and body weight in intervention studies.**

Reference	Study design, length of follow-up	Characteristics of patients	Interventions in study	Effects on adiponectin levels and body weight
Garaulet et al. (2004)[20]	Clinical trial, 4 weeks	33 females, 37 ± 6 years of age; BMI = 34.0 ± 4.0 kg/m²	Very-low-calorie liquid diet (~800 kcal/day) consumed in 4 portions per day, each containing 25% of the whole-day energy content.	Δ adiponectin: NS; Δ body weight: ↓ 7%
Xydakis et al. (2004)[21]	Clinical trial, 5 weeks	40 patients with MetS, 47.1 ± 0.9 years of age, 42.5% males; BMI = 38.3 ± 0.7 kg/m²	Very-low-calorie diet of 600–800 kcal/day consisting of meal replacement products (each serving contained 200 kcal) alone or in combination with lean beef, fish, or poultry.	Δ adiponectin: NS; Δ body weight: ↓ 7%
Imbeault et al. (2004)[22]	Clinical trial, 4 days	15 males, 24 ± 4 years of age; BMI = 28.4 ± 4.6 kg/m²	Diet with restriction of ~800 kcal/day.	Δ adiponectin: NS; Δ body weight: ↓ 1.12%
Wolfe et al. (2004)[23]	Clinical trial, 4 weeks	15 females, 22 ± 3 years of age; BMI = 23.3 ± 1.2 kg/m²	Diet with 1,000–1,200 kcal/day, with 31% of energy from protein, 25% of energy from lipids, and 44% of energy from carbohydrates.	Δ adiponectin: ↓ 16.2%; Δ body weight: ↓ 4.8% in BMI*
Anderlová et al. (2006)[24]	Clinical trial, 3 weeks	14 females, no description of patients' age; BMI = 48.0 ± 2.0 kg/m²	Diet with 550 kcal/day.	Δ adiponectin: NS; Δ body weight: ↓ 5% in BMI*
Weiss et al. (2006)[25]	Randomized clinical trial, 48 weeks	58 patients, 50–60 years of age, no description of patients' gender; BMI = 23.5–29.9 kg/m²; Follow-up losses = 15.6%	Hypocaloric diet: caloric intake reduced by 16% in 3 months and by 20% in 9 months. Exercise: increased energy expenditure through exercise by 16% in 3 months and by 20% in 9 months. Control: no change in dietary habits or lifestyle.	Δ adiponectin: NS in all groups; Δ body weight was different between groups: Diet: ↓ 8.6%; Exercise: ↓ 10.4%; Control: ↓ 1.5%
Polak J et al. (2007)[26]	Clinical trial, 12 weeks	20 females, 39.4 ± 9.5 years of age; BMI = 32.2 ± 6.4 kg/m²	Diet with restriction of 600 calories/day.	Δ adiponectin: ↑ 36%; Δ adiponectin forms: HMW: ↑ 5.5%; IMW: ↑ 8.5%; LMW: ↑ 18.1%; Δ body weight: ↓ 7.4%
O'Leary et al. (2007)[27]	Randomized clinical trial, 12 weeks	21 patients with impaired glucose tolerance, >60 years of age, 33.3% males; BMI = 30.0–40.0 kg/m²	Hypocaloric diet: 1,300 kcal/day. Control diet: 1,800 kcal/day. Both groups guided to practice 300 min/week of aerobic exercise.	Δ adiponectin NS in both groups; Δ body weight was different between groups: Hypocaloric diet: ↓ 8.1%; Control: ↓ 3.4%
Chan et al. (2008)[28]	Randomized clinical trial, 16 weeks	35 males with MetS, 46 ± 8 years of age; BMI = 34.0 ± 3.0 kg/m²	Hypocaloric diet: 1,500 kcal/day with 25% of energy from lipids, 55% of energy from carbohydrates, and 20% of energy from proteins. Control diet: 2,300 kcal/day, with 35% of energy from lipids, 40% of energy from carbohydrates, and 20% of energy from proteins.	Δ adiponectin: Hypocaloric diet: ↑ 20%; Control: NS; Δ body weight was different between groups: Hypocaloric diet: ↓ 12%; Control: NS

* Body weight data not reported.

Abbreviations: Δ, difference between final value and basal value; BMI, body mass index; HMW, high molecular weight; IMW, intermediate molecular weight; LMW, low molecular weight; MetS, metabolic syndrome; NS, nonsignificant ($P > 0.05$).

Table 2 **Effect of diet composition on adiponectin blood levels and body weight in intervention studies.**

Reference	Study design, length of follow-up	Characteristics of patients	Interventions in study	Effects on adiponectin levels and body weight
Different proportions of dietary macronutrients				
Arvidsson et al. (2004)[29]	Randomized clinical trial, 10 weeks	40 females, 21–49 years of age; BMI = 30.9–47.7 kg/m²	Diet rich in lipids: 40–45% of energy from lipids, 15–20% of energy from proteins, and 40–45% of energy from carbohydrates. Control diet: 20–25% of energy from lipids, 15–20% of energy from proteins, and 60–65% of energy from carbohydrates.	Δ adiponectin: NS in both groups; Δ body weight: NS in both groups
Mostad et al. (2004)[30]	Clinical trial, 3 days	19 patients with type 2 diabetes, 62.0 ± 17.0 years of age, 52.6% males; BMI = 30.1 ± 6.5 kg/m²	Diet with lipid restriction (24% of energy from lipids), 50% of energy from carbohydrates, and 22% of energy from proteins.	Δ adiponectin: ↑ 12%; Δ body weight: NS
Berk et al. (2005)[31]	Randomized clinical trial crossover, 6 days	11 females, 22–44 years of age; BMI > 28 kg/m²	Diet rich in lipids: 50% of energy from lipids and 35% of energy from carbohydrates. Control diet: 30% of energy from lipids and 55% of energy from carbohydrates.	Δ adiponectin: NS in both groups; Body weight data not reported
Kasim-Karakas et al. (2006)[32]	Clinical trial, 32 weeks	22 females, 61 ± 11 years of age; BMI = 29.1 ± 1.4 kg/m²; Follow-up losses = 9.1%	Diet with 15% of energy from lipids.	Δ adiponectin: ↑ 12.9%; Δ body weight: ↓ 6.3%
Cardillo et al. (2006)[33]	Randomized clinical trial, 144 weeks	132 patients, 55 ± 10 years of age, 83% males; BMI > 35 kg/m²; Follow-up losses = 59.8%	Hypocaloric diet with lipid restriction: diet with 500-calorie restriction and <30% of energy from lipids. Diet with carbohydrate restriction: normocaloric diet with <30 g/day of carbohydrates.	Δ adiponectin: NS in both groups; Δ body weight: NS in both groups
de Luis et al. (2007)[34]	Randomized clinical trial, 12 weeks	90 patients, 42.9 ± 15.8 years of age, 30% males; BMI = 35.8 ± 5.9 kg/m²	Diet with lipid restriction: 27% of energy from lipids, 52% of energy from carbohydrates, and 20% of energy from proteins. Diet with carbohydrate restriction: 38% of energy from carbohydrates, 26% of energy from proteins, and 36% of energy from lipids.	
Keogh et al. (2008)[36]	Randomized clinical trial, 8 weeks	117 patients, 50.0 ± 8.3 years of age, no description of patient's gender; BMI = 33.7 ± 4.1 kg/m²; Follow-up losses = 29.1%	Diet with carbohydrate restriction and rich in saturated fatty acids: calorie restriction of 30%; 35% of energy from proteins, 61% of energy from lipids (20% from saturated fatty acids), and 4% of energy from carbohydrates. Diet rich in carbohydrates and with saturated fatty acid restriction: calorie restriction of 30%; 21% of energy from proteins, 30% of energy from lipids (<8% from saturated fatty acids), and 46% of energy from carbohydrates.	Δ adiponectin: NS in both groups; Δ body weight: NS in both groups
Keogh et al. (2007)[35]	Randomized clinical trial, 52 weeks	36 patients, 48.7 ± 1.5 years of age, 32% males; BMI = 33.0 ± 4.0 kg/m²; Follow-up losses = 22.2%	Hypocaloric diet with carbohydrate restriction: calorie restriction of 30%; 33% of energy from carbohydrates, 27.5% of energy from lipids, and 40% of energy from proteins. Hypocaloric diet rich in carbohydrates: calorie restriction of 30%; 60% of energy from carbohydrates, 20% of energy from lipids, and 20% of energy from proteins.	Δ adiponectin: NS in both groups; Δ body weight: NS in both groups
Al-Sarraj et al. (2009)[37]	Randomized clinical trial, 12 weeks	39 patients, 18–50 years of age, 35.9% males; BMI > 25 kg/m²; Follow-up losses = 30.4%	Diet with carbohydrate restriction: 20–25% of energy from carbohydrates, 50–55% of energy from lipids, and 25–30% of energy from proteins. American Heart Association diet: 55% of energy from carbohydrates, 25–30% of energy from lipids, and 15–20% of energy from proteins.	Δ adiponectin was different between groups: Diet with carbohydrate restriction: ↑ 7.8%; American Heart Association diet: ↑ 16.4%. Δ body weight was different between groups: Diet with carbohydrate restriction: ↓ 8.4%; American Heart Association diet: ↓ 5.9%

Table 2 **Continued**

Reference	Study design, length of follow-up	Characteristics of patients	Interventions in study	Effects on adiponectin levels and body weight
Quality of dietary lipids				
Paniagua et al. (2007)[38]	Randomized clinical trial crossover, 4 weeks	11 patients, 62.0 ± 9.4 years of age, 36.4 % males; BMI = 32.6 ± 7.8 kg/m²	Diet rich in saturated fatty acids: 47% of energy from carbohydrates and 38% of energy from lipids (23% from saturated fatty acids, 9% from monounsaturated fatty acids, and 6% from polyunsaturated fatty acids). Diet rich in monounsaturated fatty acids: 47% of energy from carbohydrates and 38% of energy from lipids (9% from saturated fatty acids, 23% from monounsaturated fatty acids, and 6% from polyunsaturated fatty acids). Diet rich in carbohydrates: 65% of energy from carbohydrates and 20% of energy from lipids (6% from saturated fatty acids, 8% from monounsaturated fatty acids, and 6% from polyunsaturated fatty acids).	Δ adiponectin: NS in all groups Body weight data not reported
Lithander et al. (2008)[39]	Randomized clinical trial crossover, 3 weeks	18 males with dyslipidemia, 39.7 ± 13.9 years of age; BMI = 25.9 ± 4.2 kg/m²	Diet with high ratio of saturated/unsaturated fatty acids: 18% of energy from saturated fatty acids, 10% from monounsaturated fatty acids, and 7% from polyunsaturated fatty acids. Diet with low ratio of saturated/unsaturated fatty acids: 13% of energy from saturated fatty acids, 12% from monounsaturated fatty acids, and 8% from polyunsaturated fatty acids	Δ adiponectin: NS in both groups Δ body weight: NS in both groups
Damsgaard et al. (2008)[40]	Randomized clinical trial, 8 weeks	66 males, 19–40 years of age; BMI = 22.8 ± 1.8 kg/m²	Intervention diet: supplementation with fish oil (5 mL/day). Control diet: supplementation with olive oil (5 mL/day).	Δ adiponectin: NS in both groups Body weight data not reported
Guebre-Egziabher et al. (2008)[41]	Clinical trial, 10 weeks	17 patients, 27.1 ± 1.9 years of age, 58.8% males; BMI = 22.4 ± 0.4 kg/m²	Diet with intake of fish (100-g portion, 3 times/week) plus 20 mL/day of vegetable oil.	Δ adiponectin: ↑ 17% Δ body weight: NS
Tsitouras et al. (2008)[42]	Randomized clinical trial crossover, 6 weeks for control diet and 8 weeks for intervention diet	12 patients, >60 years of age, 50% males; BMI = 22–30 kg/m²	Intervention diet: 4 portions of fat fish/week plus 1 tablespoon of fish oil/day. Control diet: 4 portions of lean fish/week.	Δ adiponectin: NS in both groups Δ body weight: NS in both groups
Kratz et al. (2008)[43]	Randomized clinical trial, 12 weeks	33 patients, 37.6 ± 13.8 years of age, 38.5% males; BMI = 28–33 kg/m², Follow-up losses = 24.2%	Diet rich in omega-3 fatty acids: 49.8% of energy from carbohydrates, 15.9% from proteins, and 34% from lipids, of which 3.5% are omega-3 fatty acids. Control diet: 49.8% of energy from carbohydrates, 15.9% from proteins, and 34% from lipids, of which 0.5% are omega-3 fatty acids.	Δ adiponectin: NS in both groups Δ body weight: NS in both groups
Lara et al. (2007)[44]	Randomized clinical trial crossover, 4 weeks	48 patients, 20–55 years of age, 33.3% males; BMI = 18.5–29.9 kg/m², Follow-up losses = 14.6%	Diet with fish: 50% of energy from carbohydrates, 15% from proteins, and 35% from lipids, including 125 g/day of salmon. Diet without fish: 50% of energy from carbohydrates, 15% from proteins, and 35% from lipids, not including fish intake.	Δ adiponectin: NS in both groups Body weight data not reported
Krebs et al. (2006)[45]	Randomized clinical trial, 24 weeks	116 females, 44.7 ± 13.2 years of age; BMI = 35.0 ± 5.5 kg/m²; Follow-up losses = 19.8%	Intervention diet (omega-3 supplementation): weight-loss program plus supplementation of 5 oil capsules/day, including 1.3 g of eicosapentaenoic fatty acids and 2.9 g of docosahexaenoic fatty acid per capsule. Placebo diet: weight-loss program plus supplementation with 5 oil capsules/day, including 2.8 g of linoleic fatty acid and 1.4 g of oleic fatty acid per capsule. Control diet: supplementation with 5 oil capsules/day, including 2.8 g of linoleic fatty acids and 1.4 g of oleic fatty acid per capsule, without weight-loss program. Weight-loss program = hypocaloric diet plus exercise.	Δ adiponectin was different between groups: Intervention diet (omega-3 supplementation): ↑ 22.1% Placebo diet: ↓ 1.9% Control diet: ↑ 5.8% Δ body weight was different between groups: Intervention diet (omega-3 supplementation): ↓ 11% Placebo diet: ↓ 12.4% Control diet: NS

Itoh et al. (2007)[46]	Randomized clinical trial, 12 weeks	52 patients with MetS, 52.2 ± 2.8 years of age, 40.4% males; BMI = 30.1 ± 0.9 kg/m²	Intervention diet (omega-3 supplementation): 25 calories/kg/day and supplementation with 1.8 g/day of eicosapentaenoic fatty acid. Control diet: 25 calories/kg/day and supplementation with 1.8 g/day of palmitic fatty acid.	Δ adiponectin was different between groups: Intervention diet (omega-3 supplementation): ↑ 59.6% Control diet: ↑ 6.4 % Δ body weight: NS in both groups
Nelson et al. (2007)[47]	Randomized clinical trial, 8 weeks	57 patients, 38.5 ± 11.4 years of age, 19% males; BMI = 30.3 ± 5.0 kg/m²	Intervention diet (omega-3 supplementation): usual diet plus supplementation with omega-3 (5% of total energy). Control diet: usual diet.	Δ adiponectin was different between groups: Intervention diet (omega-3 supplementation): ↓ 8.8% Control diet: ↑ 2.1% Δ body weight: NS in both groups
Micallef & Garg (2009)[48]	Randomized clinical trial, 3 weeks	60 patients with dyslipidemia, 55.4 ± 1.0 years of age, 45% males; BMI = 26.9 ± 0.5 kg/m²	Placebo: sunflower oil. Placebo with plant sterols: sunflower oil with 2 g/day of plant sterols. Fish oil: 1.4 g/day of omega-3 capsules. Fish oil plus plant sterols: 1.4 g/day of omega-3 capsules with 2 g/day of plant sterols.	Δ adiponectin was different between groups: Placebo: ↓ 1% Placebo with plant sterols: ↑ 10% Fish oil: ↑ 20% Fish oil plus plant sterols: ↑ 30% Body weight data not reported
Vega-Lopez et al. (2009)[49]	Randomized clinical trial cross-over, 5 weeks	37 females with LDL cholesterol > 120 mg/dL, 64.2 ± 7.5 years of age; BMI = 5.6 ± 3.6 kg/m²; Follow-up losses = 18.9%	Diet enriched with corn oil: 12.1% of energy from polyunsaturated fatty acids. Diet enriched with partially hydrogenated soybean oil: 5.9% of energy from polyunsaturated fatty acids.	Δ adiponectin: NS in both groups Δ body weight: NS in both groups

Different source of dietary carbohydrates and proteins by foods or supplements

Ludvik et al. (2008)[57]	Randomized clinical trial, 20 weeks	88 patients with type 2 diabetes, 59.2 ± 1.7 years of age, 52.2% males; BMI = 30.5 ± 0.7 kg/m²; Follow-up losses = 30.1%	Intervention diet: supplementation with 4 g of Caiapo potato extract daily. Control diet: supplementation with 4 g of placebo daily.	Δ adiponectin was different between groups: Intervention diet: ↑ 11% Control diet: ↑ 3% Δ body weight: NS in both groups
Lucotti et al. (2006)[50]	Randomized clinical trial, 3 weeks	33 patients with type 2 diabetes and MetS, 56.4 ± 1.4 years of age, 24.2% males; BMI = 39.1 ± 0.5 kg/m²	Intervention diet (L-arginine supplementation): supplementation with 8.3 g/day of L-arginine. Control diet: supplementation with placebo. Both diets with 1,000 calories/day plus 450 min/week of aerobic exercise.	Δ adiponectin was different between groups: Intervention diet: ↑ 40% Control diet: NS Δ body weight: NS in both groups
Mahon et al. (2007)[51]	Randomized clinical trial, 11 weeks	61 females, 58 ± 2 years of age; BMI = 29.6 ± 0.8 kg/m²; Follow-up losses = 11.5%	Lacto-ovo vegetarian diet plus beef: 250 kcal/day of beef. Lacto-ovo vegetarian diet plus chicken: 250 kcal/day of chicken. Lacto-ovo vegetarian diet: 250 kcal/day of carbohydrate/fat foods. Control diet: usual diet.	Δ adiponectin: NS in all groups Δ body weight was different between groups: Lacto-ovo vegetarian diet plus beef: ↓ 8.1% Lacto-ovo vegetarian diet plus chicken: ↓10.4% Lacto-ovo vegetarian diet: ↓ 7.4% Control diet: ↓ 1.5%
Ouellet et al. (2008)[52]	Randomized clinical trial crossover, 4 weeks	19 patients, 40–65 years of age. 52.6% males; BMI > 25 kg/m²	Intervention diet (dietary cod protein): diet with 58–68% of energy from proteins, cod fillet being the main protein source. Control diet: diet with 58–68% of energy from proteins, with lean dairy products, beef, and pork being the main protein sources.	Δ adiponectin: NS in both groups Δ body weight: NS in both groups
Wennersberg et al. (2009)[58]	Randomized clinical trial, 24 weeks	121 patients with MetS, 30–65 years of age, 34% males; BMI > 25 kg/m²; Follow-up losses = 6.6%	Intervention diet: diet with 3–5 portions of dairy products per day. Control diet: usual diet, without modification of dairy products intake.	Δ adiponectin: NS in both groups Δ body weight: NS in both groups

Table 2 **Continued**

Reference	Study design, length of follow-up	Characteristics of patients	Interventions in study	Effects on adiponectin levels and body weight
Zemel et al. (2010)[59]	Randomized clinical trial crossover, 4 weeks	20 patients, 31 ± 10.3 years of age, 70% males; BMI > 25 kg/m²	Intervention diet: diet with 3 portions of dairy products/day, 7 providing 1,200–1,400 mg of calcium/day. Control diet: diet with 3 portions of soybean extract/day, providing 500–600 mg of calcium/day.	Δ adiponectin was different between groups: Intervention diet: ↑ 151% Control diet: ↓ 63% Body weight data not reported
Moderate alcohol consumption				
Sierksma et al. (2004)[53]	Randomized clinical trial crossover, 17 days	24 males, 45–65 years of age; BMI = 26.7 ± 3.0 kg/m²; Follow-up losses = 4.2%	Intervention diet: 125 mL of whisky/day (40 g of alcohol). Control diet: 125 mL of water/day.	Δ adiponectin was different between groups: Intervention diet: ↑ 11% Control diet: NS Body weight data not reported
Beulens et al. (2007)[54]	Randomized clinical trial crossover, 3 weeks	20 males, 18–25 years of age; BMI = 20.1 ± 1.0 kg/m² (n = 11) and 31.3 ± 3.9 kg/m² (n = 9)	Intervention diet: 5% of energy from beer (990 mL/day, providing 40 g of alcohol/day). Control diet: 990 mL/day of nonalcoholic beer.	Δ adiponectin was different between groups: Intervention diet: ↑ 11% Control diet: NS Δ body weight was different between groups: Intervention diet: ↓ 0.6 ± 0.2 kg Control diet: ↓ 1.3 ± 0.2 kg (Basal and final values of body weight not reported, just the difference)
Dietary fiber supplementation				
Grunberger et al. (2007)[56]	Randomized clinical trial, 12 weeks	66 patients with type 2 diabetes, 57.5 ± 9.2 years of age, 46.8% males; BMI > 30 kg/m²; Follow-up losses = 30.3%	Intervention diet: supplementation with 1 g FBCx® per meal (6 times/day of a soluble dietary fiber derived from corn). Control diet: supplementation with 1 g placebo per meal (6 times/day).	Δ adiponectin was different between groups: Intervention diet: ↑ 60% Control diet: NS Δ body weight NS in both groups
Fragala et al. (2009)[55]	Randomized clinical trial, 8 weeks	22 females, 38.3 ± 6.8 years of age; BMI > 25 kg/m²	Intervention diet: supplementation with modified cellulose and acetylated fatty acids (400 mg/day). Control diet: supplementation with placebo.	Δ adiponectin was different between groups: Intervention diet: ↑ 115.6% Control diet: ↑ 73% Δ body weight was different between groups: Intervention diet: ↓ 10.6% Control diet: ↓ 4.8%
Other dietary interventions				
Sano et al. (2007)[60]	Randomized clinical trial, 12 weeks	61 patients with dyslipidemia, 30–70 years of age, 47.5% males; BMI = 24.2 ± 0.6 kg/m²; Follow-up losses = 16.4%	Diet with grape seed extract supplement providing different amounts of proanthocyanidin: Group 1: 0 mg of proanthocyanidin. Group 2: 200 mg of proanthocyanidin. Group 3: 400 mg of proanthocyanidin.	Δ adiponectin: NS in all groups Δ body weight: NS in all groups
Kajiyama et al. (2008)[61]	Randomized clinical trial crossover, 8 weeks	30 patients with type 2 diabetes and 6 patients with impaired glucose tolerance, 58.6 ± 4.7 years of age, 50% males; BMI = 23.4 ± 3.5 kg/m²	Intervention diet: diet with 900 mL of hydrogen-enriched water daily. Control diet: diet with 900 mL of pure water daily.	Δ adiponectin: NS in both groups Δ body weight: NS in both groups

Abbreviations: Δ, difference between final value and basal value; BMI, body mass index; LDL, low-density lipoprotein; MetS, metabolic syndrome; NS, nonsignificant (P > 0.05).

Table 3 **Effect of diet plus exercise on adiponectin blood levels and body weight in intervention studies.**

Reference	Study design, length of follow-up	Characteristics of patients	Interventions in study	Effects on adiponectin levels and body weight
Monzillo et al. (2003)[62]	Clinical trial, 24 weeks	35 patients with normal glucose tolerance or impaired glucose tolerance or type 2 diabetes, 49.3 ± 1.9 years of age, patients'gender not described; BMI = 36.7 ± 0.9 kg/m², Follow-up losses = 31.4%	Lifestyle modification program, including low-calorie diet (restriction of 500 kcal/day) plus at least 150 min/week of moderate-to-intense exercise.	Δ adiponectin: NS in all groups, but ↑ 29.5% in patients with type 2 diabetes (*P* = 0.01) Δ body weight: ↓ 7%
Esposito et al. (2003)[63]	Randomized clinical trial, 96 weeks	120 females, 34.6 ± 5.0 years of age; BMI = 34.9 ± 2.4 kg/m²; Follow-up losses = 6.7%	Intervention group: low-calorie Mediterranean-style diet (1,400 kcal/day) and increased physical activity (individual counseling) to achieve a weight reduction of 10%. Control group: general information provided about healthy food choices and exercise.	Δ adiponectin was different between groups: Intervention group: ↑ 48.2% Control diet: ↑ 8.5% Δ body weight was different between groups: Intervention diet: ↓ 14.7% Control diet: ↓ 3.2%
Brekke et al. (2004)[64]	Randomized clinical trial, 16 weeks	77 parents of patients with type 2 diabetes, 25–55 years of age, 63.6% males; BMI = 25.8 ± 3.2 kg/m²	Diet group: less than 30% of energy from lipids, less than 10% of energy from saturated fatty acids, and more than 12 g of fiber/1,000 kcal. The intake of fish and low-glycemic-index foods was prescribed. Diet plus exercise group: diet similar to diet group, plus 120 –150 min/week of walking. Control group: no change in lifestyle was encouraged.	Δ adiponectin was different between groups: Diet group: ↓ 5.4% Diet plus exercise group: ↑ 11.1% Control group: ↓ 0.95% Δ body weight was different between groups: Diet group: ↓ 1% Diet plus exercise group: ↓ 2.1% Control group: ↓ 0.6%
Giannopoulou et al. (2005)[65]	Randomized clinical trial, 14 weeks	40 females with type 2 diabetes, 50–70 years of age; BMI = 34.6 ± 1.1 kg/m²; Follow-up losses = 17.5%	Diet group: low-calorie diet (restriction of 600 kcal/day), with 40% of energy from lipids, especially monounsaturated fatty acids, 40% of energy from carbohydrates, and 20% of energy form proteins. Exercise group: supervised walking program of 180–240 min/week. Diet plus exercise group: both interventions combined.	Δ adiponectin: NS in all groups Δ body weight was different between groups; Diet group: ↓ 5.8% Exercise group: ↓ 6% Diet plus exercise group ↓ 1.8%
Manigrasso et al. (2005)[66]	Clinical trial, 12 weeks	15 females, 47.2 ± 6.7 years of age; BMI = 39.0 ± 7.3 kg/m²	Low-calorie diet with 1,200 kcal/day and increased physical activity.	Δ adiponectin: NS in all groups Δ body weight: ↓ 7.4%
Barbato et al. (2006)[67]	Clinical trial, 16 weeks	53 patients, 32.5 ± 6.5 years of age, 25.5% males; BMI = 32.8 ± 1.6 kg/m²	Low-calorie diet (restriction of 500–1,000 kcal/day) and increased moderate aerobic activity (at least 30 min/day).	Δ adiponectin: NS Patients grouped according to weight loss: Group A: ↓ 7.8% Group B: ↓ 0.3%

Table 3 Continued

Reference	Study design, length of follow-up	Characteristics of patients	Interventions in study	Effects on adiponectin levels and body weight
Corpeleijn et al. (2007)[68]	Randomized clinical trial, 48 weeks	147 patients with impaired glucose tolerance, >40 years of age, patients' gender not described; BMI > 25 kg/m²; Follow-up losses = 29.9%	Intervention group: diet with 55% of energy from carbohydrates, 30 –35% from lipids, and 10–15% from proteins, plus moderate physical activity. Control group: general guidance about healthy food choices and exercise.	Δ adiponectin: NS in both groups Δ body weight was different between groups: Intervention group: ↓ 3% Control group: body weight data not reported
Rokling-Andersen et al. (2007)[69]	Randomized clinical trial, 48 weeks	219 males, 45.1 ± 2.5 years of age; BMI = 28.6 ± 3.4 kg/m²; Follow-up losses = 14.2%	Diet group: increased consumption of fish, vegetables, and fiber-rich foods, and reduced consumption of sources of saturated fatty acids and cholesterol. Exercise group: 180 min/week of exercise. Diet plus exercise group: both interventions combined. Control group: no intervention.	Δ adiponectin between groups: Diet group: NS Exercise group: NS Diet plus exercise group: NS Control group: ↓ 28.5% Δ body weight between groups: Diet group: ↓ 4.4% Exercise group: ↓ 1% Diet plus exercise group: ↓ 6.3% Control group: ↑ 1.1%
Hainer et al. (2008)[70]	Clinical trial, 3 weeks	67 females, 48.7 ± 12.2 years of age; BMI = 32.4 ± 4.4 kg/m²	Diet with 1,100 kcal/day plus daily physical activity supervised by a personal trainer, plus counseling to encourage behavioral changes.	Δ adiponectin: NS Δ body weight: ↓ 4.5%
Christiansen et al. (2010)[71]	Randomized clinical trial, 12 weeks	79 patients, 18–45 years of age, 50.8% males; BMI = 30–40 kg/m²; Follow-up losses = 25.3%	Diet group: 8 weeks of very-low-energy diet (600 kcal/ day) followed by 4 weeks with a weight-maintenance diet. Exercise group: exercise without diet restriction. Diet plus exercise group: 8 weeks of very-low-energy diet (800 kcal/day) followed by 4 weeks of weight-maintenance diet combined with exercise throughout the 12 weeks.	Δ adiponectin was different between groups: Diet group: ↑ 18.6% Exercise group: ↓ 5.7% Diet plus exercise group: ↑ 19.7% No difference was observed between groups regarding adiponectin forms (HMW, IMW, and LMW) Δ body weight was different between groups: Diet group: ↓ 3.5% Exercise group: ↓ 11.4% Diet plus exercise group: ↓ 11.6%

Abbreviations: Δ, difference between final value and basal value; BMI, body mass index; HMW, high molecular weight; IMW, intermediate molecular weight; LMW, low molecular weight; MetS, metabolic syndrome; NS, nonsignificant ($P > 0.05$).

storage are described in the literature. In this sense, it is possible that visceral fat loss can increase adiponectin levels in overweight subjects, while subcutaneous fat loss can result in a reduction in adiponectin levels in normal-weight subjects.[23]

It is also remarkable that 44.4% of nine manuscripts[20,21,23,24] did not state whether compliance with the intervention (hypocaloric diet) was evaluated, which could be an important determinant of the outcome, since it is directly associated with the weight loss induced by a hypocaloric diet.

EFFECT OF DIET COMPOSITION ON ADIPONECTIN LEVELS

Thirty-three (63.5%) studies analyzed the role of diet composition in the modulation of adiponectin levels.[29–61] The details of these clinical trials are summarized in Table 2, grouped according to the type of dietary intervention.

The dietary interventions that induced a significant increase in adiponectin blood levels are described as follows. 1) Low-fat diets: Diets providing 15%[30] and 24%[32] of energy from fat. 2) Carbohydrate restriction: Diet providing 20–25% of energy from carbohydrate.[37] 3) Fish intake: Consumption of fish (300 g/week) plus vegetable oil (20 mL/day)[41] or fish oil supplementation (4 g/day) in combination with plant sterols (2 g/day).[48] 4) Dietary fiber supplementation: Intake of two 1 g tablets of FBCx® (a soluble dietary fiber derived from corn) per fat-containing meal (at least 20 g of fat)[56] or supplementation with modified cellulose (1,200 mg/day) in combination with a weight-loss program.[55] 5) Supplementation with extract of *Ipomoea batatas* (Caiapo): 4 g/day of white-skinned sweet potato *Ipomoea batatas* (Caiapo) extract.[57] 6) L-arginine supplementation: L-arginine (8.3 g/day) included in a hypocaloric regimen and exercise training program.[50] 7) Increased consumption of dairy products: Increased intake of dairy products (3–5 portions/day).[59] 8) Alcohol consumption: Intake of four glasses of whisky[53] or three cans of beer[54] daily (40 g ethanol).

The mechanism through which these dietary interventions result in increased adiponectin levels is unclear. Of the dietary fatty acids, omega-3 polyunsaturated fatty acids (eicosapentaenoic and docosahexaenoic acid) have received a great deal of attention as prophylactic agents against cardiovascular disease and insulin resistance. Improvement in insulin sensitivity resulting from omega-3 intake is strongly related to the increase in adiponectin levels and is observed later than that resulting from Caiapo intake, dietary fiber supplementation, and moderate alcohol consumption. The increase in adiponectin levels promoted by these interventions appears to mediate the improvement in insulin sensitivity.[53,54,56,57]

In nine studies,[29–37] the intervention consisted of diets with different proportions of macronutrients, but in most of these studies (70%), this approach did not result in a change in adiponectin levels. These findings suggest that the proportion of dietary macronutrients does not influence the secretion of adiponectin by adipocytes. Furthermore, the content of saturated and monounsaturated fatty acids likewise failed to influence adiponectin levels,[38,39] as opposed to omega-3 supplementation, which was effective in increasing adiponectin levels in most of the studies reviewed.[41–44,46–48]

Dietary components with antioxidant potential did not increase adiponectin levels in two randomized clinical trials that determined the effects of hydrogen-enriched water[61] and grape seed extract supplementation.[60] A moderately increased intake of dairy products beneficially affected adiponectin in a short-term study,[60] although this benefit was not previously observed in a study with a 6-month follow-up period.[58]

EFFECT OF DIET PLUS EXERCISE ON ADIPONECTIN LEVELS

In 10 (19.2%) studies, the aim was to evaluate the role of diet combined with exercise in adiponectin modulation.[62–71] The details of these clinical trials are summarized in Table 3 in chronological order of publication.

Low-calorie diets (diets with 1,100–1,300 kcal/day or diets with a restriction of 500–1,000 kcal/day) were part of the intervention in seven studies.[62,63,65–67,70,71] In one of these studies, the Mediterranean diet was used,[63] while in another, a carbohydrate-restricted diet that was high in monounsaturated fatty acids was prescribed,[66] and in yet another, a diet with prudent macronutrient distribution (55% of calories from carbohydrates, 15% from proteins, and 30% from lipids) was adopted.[71] The composition of the low-calorie diet was not described in four studies.[62,66,67,70] Three randomized clinical trials included a diet without caloric restriction as part of the intervention.[64,68,69] Fish consumption as well as the intake of foods rich in fiber was investigated in two studies.[64,69] Consumption of foods with a low glycemic index[64] and a lower intake of saturated fatty acids and cholesterol[69] was also examined.

In all 10 studies that investigated the effect of diet plus exercise on adiponectin levels, the lifestyle modification program focused on regular practice of aerobic exercise, with variations in duration (120–240 min/week) and intensity of exercise (moderate to severe). One study report did not describe the physical activity program prescribed.[66] In four studies, exercise was supervised.[65,68,70,71]

Four studies demonstrated a significant increase in adiponectin levels when diet was combined with exercise.[62–64,71] A Mediterranean diet with caloric restriction combined with personalized counseling for aerobic exercise promoted a 15% weight loss and increased adiponectin values by 48%.[63] These data support the hypothesis that greater weight loss (at least 7%) is needed to increase adiponectin levels with hypocaloric diets.

Current evidence indicates a possible synergistic effect of physical activity and a calorie-restricted diet on adiponectin modulation.[64,69,71] This could be due to the positive effect of both interventions on insulin sensitivity. However, weight loss is crucial, because exercise without significant weight loss does not appear to improve adiponectin levels.[16,69]

CONCLUSION

The present review compiles scientific evidence regarding the effect of dietary management on adiponectin levels. Daily intake of fish or omega-3 supplements was effective in increasing adiponectin levels by about 14–60%, with consistent results among the studies. Another successful way to increase adiponectin levels was weight loss achieved with a low-calorie diet plus exercise: the increase in adiponectin levels with this type of intervention ranged from 18% to 48%. Other therapeutic possibilities still in the early stages of investigation (only two studies) include dietary fiber supplementation (resulting in a 60–115% increase in adiponectin levels). It is unclear in the literature if the magnitude of effect of these dietary interventions has clinical relevance. Although low adiponectin levels are associated with several cardiovascular risk factors, such as diabetes, overweight, and metabolic syndrome,[8,10–12] the amount of adiponectin increase required to protect against these disorders has not been established.

Significant weight loss (greater than 7%) has been repeatedly shown to increase adiponectin levels.[72] Weight changes of this magnitude can be obtained with a hypocaloric diet alone or combined with exercise, and the increase in adiponectin appears to be related more to the amount of weight lost than to the method used. Small changes in body weight may not accurately represent body fat reduction, especially the visceral fat mass and the size of adipocytes, which are probably the most important determinants of the synthesis and secretion of adiponectin.[43]

Multiple studies have shown a correlation between adiponectin levels and insulin sensitivity, which remains even after adjustment for adiposity.[73,74] In this context, it is possible that the increase in adiponectin levels achieved with dietary interventions could be greater in subjects with higher insulin resistance.

The lack of consistent evidence indicating that adiponectin levels are regulated by specific dietary interventions could be explained by the evaluation of only total adiponectin in the majority of studies. The high-molecular-weight form of adiponectin and the low-/high-molecular weight adiponectin ratio could be a better determinant of adiponectin physiological activity than the plasma concentrations of each isolated form or total adiponectin.[6]

In view of the strong relationship between low adiponectin levels and overweight, diabetes, dyslipidemia, metabolic syndrome, and cardiovascular disease, the identification of strategies to modulate adiponectin levels may help decrease the presence or severity of these disorders. Further studies, which include an evaluation of changes in body composition (type of adipose tissue) and an investigation of the effects of dietary intervention on all forms of adiponectin, especially the high-molecular-weight form, may help elucidate the mechanisms involved in the modulation of this adipokine.

REFERENCES

1. Ahima RS. Metabolic actions of adipocyte hormones: focus on adiponectin. Obesity (Silver Spring). 2006;14(Suppl 1):9S–15S.
2. Matsuzawa Y. Adiponectin: identification, physiology and clinical relevance in metabolic and vascular disease. Atheroscler Suppl. 2005;6:7–14.
3. Hermsdorff HH, Monteiro JB. Visceral, subcutaneous or intramuscular fat: where is the problem? Arq Bras Endocrinol Metabol. 2004;48:803–811.
4. Hajer GR, van Haeften TW, Visseren FL. Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. Eur Heart J. 2008;29:2959–2971.
5. Silha JV, Krsek M, Skrha JV, Sucharda P, Nyomba BLG, Murphy LJ. Plasma resistin, adiponectin and leptin levels in lean and obese subjects: correlations with insulin resistance. Eur J Endocrinol. 2003;149:331–335.
6. Dridi S, Taouis M. Adiponectin and energy homeostasis: consensus and controversy. J Nutr Biochem. 2009;20:831–839.
7. Lihn AS, Pedersen SB, Richelsen B. Adiponectin: action, regulation and association to insulin sensitivity. Obes Rev. 2008;6:13–21.
8. Sheng T, Yang K. Adiponectin and its association with insulin resistance and type 2 diabetes. J Genet Genomics. 2008;35:321–326.
9. Okamoto Y, Kihara S, Funahashi T, Matsuzawa Y, Libby P. Adiponectin: a key adipocytokine in metabolic syndrome. Clin Sci (Lond). 2006;110:267–278.
10. Ryo M, Nakamura T, Kihara S, et al. Adiponectin as a biomarker of the metabolic syndrome. Circ J. 2004;68:975–981.
11. Swarbrick MM, Havel PJ. Physiological, pharmacological and nutritional regulation of circulating adiponectin

concentrations in humans. Metab Syndr Relat Disord. 2008;6:87–102.

12. Pischon T, Girman CJ, Hotamisligil GS, Rifai N, Hu FB, Rimm EB. Plasma adiponectin levels and risk of myocardial infarction in men. JAMA. 2004;291:1730–1737.

13. Patel SR, Mailloux LM, Coppola JT, Mindrescu C, Staniloae CS. Pioglitazone increases adiponectin levels in nondiabetic patients with coronary artery disease. Coron Artery Dis. 2008;19:349–353.

14. Yang WS, Lee WJ, Funahashi T, et al. Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. J Clin Endocrinol Metab. 2001;86:3815–3819.

15. Trakhtenbroit MA, Leichman JG, Algahim MF, et al. Body weight, insulin resistance, and serum adipokine levels 2 years after 2 types of bariatric surgery. Am J Med. 2009;122:435–442.

16. Simpson KA, Singh MA. Effects of exercise on adiponectin: a systematic review. Obesity (Silver Spring). 2008;16:241–256.

17. Qi L, Rimm E, Liu S, Rifai N, Hu FB. Dietary glycemic index, glycemic load, cereal fiber, and plasma adiponectin concentration in diabetic men. Diabetes Care. 2005;28:1022–1028.

18. Nakamura Y, Ueshima H, Okuda N, et al. Relation of dietary and other lifestyle traits to difference in serum adiponectin concentration of Japanese in Japan and Hawaii: the INTER-LIPID Study. Am J Clin Nutr. 2008;88:424–430.

19. Mantzoros CS, Williams CJ, Manson JE, Meigs JB, Hu FB. Adherence to the Mediterranean dietary pattern is positively associated with plasma adiponectin concentrations in diabetic women. Am J Clin Nutr. 2006;84:328–335.

20. Garaulet M, Viguerie N, Porubsky S, et al. Adiponectin gene expression and plasma values in obese women during very-low-calorie diet. Relationship with cardiovascular risk factors and insulin resistance. J Clin Endocrinol Metab. 2004;89:756–760.

21. Xydakis AM, Case CC, Jones PH, et al. Adiponectin, inflammation, and the expression of the metabolic syndrome in obese individuals: the impact of rapid weight loss through caloric restriction. J Clin Endocrinol Metab. 2004;89:2697–2703.

22. 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 (Oxf). 2004;60:429–433.

23. Wolfe BE, Jimerson DC, Orlova C, Mantzoros CS. Effect of dieting on plasma leptin, soluble leptin receptor, adiponectin and resistin levels in healthy volunteers. Clin Endocrinol (Oxf). 2004;61:332–338.

24. Anderlová K, Kremen J, Dolezalová R, et al. The influence of very-low-calorie-diet on serum leptin, soluble leptin receptor, adiponectin and resistin levels in obese women. Physiol Res. 2006;55:277–283.

25. Weiss EP, Racette SB, Villareal DT, et al. Improvements in glucose tolerance and insulin action induced by increasing energy expenditure or decreasing energy intake: a randomized controlled trial. Am J Clin Nutr. 2006;84:1033–1042.

26. Polak J, Kovacova Z, Jacek M, et al. An increase in plasma adiponectin multimeric complexes follows hypocaloric diet-induced weight loss in obese and overweight premenopausal women. Clin Sci. 2007;112:557–565.

27. O'Leary VB, Jorett AE, Marchetti CM, et al. Enhanced adiponectin multimer ratio and skeletal muscle adiponectin receptor expression following exercise training and diet in older insulin-resistant adults. Am J Physiol Endocrinol Metab. 2007;293:421–427.

28. Chan DC, Watts GF, Ng TW, Yamashita S, Barrett PH. Effect of weight loss on markers of triglyceride-rich lipoprotein metabolism in the metabolic syndrome. Eur J Clin Invest. 2008;38:743–751.

29. Arvidsson E, Viguerie N, Andersson I, Verdich C, Langin D, Arner P. Effects of different hypocaloric diets on protein secretion from adipose tissue of obese women. Diabetes. 2004;53:1966–1971.

30. Mostad IL, Qvigstad E, Bjerve KS, Grill VE. Effects of a 3-day low-fat diet on metabolic control, insulin sensitivity, lipids and adipocyte hormones in Norwegian subjects with hyper-triacylglycerolaemia and type 2 diabetes. Scand J Clin Lab Invest. 2004;64:565–574.

31. Berk ES, Kovera AJ, Boozer CN, Pi-Sunyer FX, Johnson JA, Albu JB. Adiponectin levels during low- and high-fat eucaloric diets in lean and obese women. Obes Res. 2005;13:1566–1571.

32. Kasim-Karakas SE, Tsodikov A, Singh U, Jialal I. Responses of inflammatory markers to a low-fat, high-carbohydrate diet: effects of energy intake. Am J Clin Nutr. 2006;83:774–779.

33. Cardillo S, Seshadri P, Iqbal N. The effects of a low-carbohydrate versus low-fat diet on adipocytokines in severely obese adults: three-year follow-up of a randomized trial. Eur Rev Med Pharmacol Sci. 2006;10:99–106.

34. de Luis DA, Aller R, Izaola O, Gonzalez Sagrado M, Bellioo D, Conde R. Effects of a low-fat versus a low-carbohydrate diet on adipocytokines in obese adults. Horm Res. 2007;67:296–300.

35. Keogh JB, Brinkworth GD, Clifton PM. Effects of weight loss on a low-carbohydrate diet on flow-mediated dilatation, adhesion molecules and adiponectin. Br J Nutr. 2007;98:852–859.

36. Keogh JB, Brinkworth GD, Noakes M, Belobrajdic DP, Buckley JD, Clifton PM. Effects of weight loss from a very-low-carbohydrate diet on endothelial function and markers of cardiovascular disease risk in subjects with abdominal obesity. Am J Clin Nutr. 2008;87:567–576.

37. Al-Sarraj T, Saadi H, Calle MC, Volek JS, Fernandez ML. Carbohydrate restriction, as a first-line dietary intervention, effectively reduces biomarkers of metabolic syndrome in Emirati adults. J Nutr. 2009;139:1667–1676.

38. Paniagua JA, Gallego de la Sacristana A, Romero I, et al. Monounsaturated fat-rich diet prevents central body fat distribution and decreases postprandial adiponectin expression induced by a carbohydrate-rich diet in insulin-resistant subjects. Diabetes Care. 2007;30:1717–1723.

39. Lithander FE, Keogh GF, Wang Y, et al. No evidence of an effect of alterations in dietary fatty acids on fasting adiponectin over 3 weeks. Obesity (Silver Spring). 2008;16:592–599.

40. Damsgaard CT, Frøkiaer H, Andersen AD, Lauritzen L. Fish oil in combination with high or low intakes of linoleic acid lowers plasma triacylglycerols but does not affect other cardiovascular risk markers in healthy men. J Nutr. 2008;138:1061–1066.

41. Guebre-Egziabher F, Rabasa-Lhoret R, Bonnet F, et al. Nutritional intervention to reduce the n-6/n-3 fatty acid ratio increases adiponectin concentration and fatty acid oxidation in healthy subjects. Eur J Clin Nutr. 2008;62:1287–1293.

42. Tsitouras PD, Gucciardo F, Salbe AD, Heward C, Harman SM. High omega-3 fat intake improves insulin sensitivity and reduces CRP and IL6, but does not affect other endocrine axes in healthy older adults. Horm Metab Res. 2008;40:199–205.

43. Kratz M, Swarbrick MM, Callahan HS, Matthys CC, Havel PJ, Weigle DS. Effect of dietary n-3 polyunsaturated fatty acids on plasma total and high-molecular-weight adiponectin concentrations in overweight to moderately obese men and women. Am J Clin Nutr. 2008;87:347–353.

44. Lara JJ, Economou M, Wallace AM, et al. Benefits of salmon eating on traditional and novel vascular risk factors in young, non-obese healthy subjects. Atherosclerosis. 2007;193:213–221.

45. Krebs JD, Browning LM, McLean NK, et al. Additive benefits of long-chain n-3 polyunsaturated fatty acids and weight-loss in the management of cardiovascular disease risk in overweight hyperinsulinaemic women. Int J Obes (Lond). 2006; 30:1535–1544.

46. Itoh M, Suganami T, Satoh N, et al. Increased adiponectin secretion by highly purified eicosapentaenoic acid in rodent models of obesity and human obese subjects. Arterioscler Thromb Vasc Biol. 2007;27:1918–1925.

47. Nelson TL, Stevens JR, Hickey MS. Adiponectin levels are reduced, independent of polymorphisms in the adiponectin gene, after supplementation with alpha-linolenic acid among healthy adults. Metabolism. 2007;56:1209–1215.

48. Micallef MA, Garg ML. Anti-inflammatory and cardioprotective effects of n-3 polyunsaturated fatty acids and plant sterols in hyperlipidemic individuals. Atherosclerosis. 2009;204:476–482.

49. Vega-López S, Matthan NR, Ausman LM, et al. Substitution of vegetable oil for a partially-hydrogenated fat favorably alters cardiovascular disease risk factors in moderately hypercholesterolemic postmenopausal women. Atherosclerosis. 2009;207:208–212.

50. Lucotti P, Setola E, Monti LD, et al. Beneficial effects of a long-term oral L-arginine treatment added to a hypocaloric diet and exercise training program in obese, insulin-resistant type 2 diabetic patients. Am J Physiol Endocrinol Metab. 2006;291:906–912.

51. Mahon AK, Flynn MG, Stewart LK, et al. Protein intake during energy restriction: effects on body composition and markers of metabolic and cardiovascular health in postmenopausal women. J Am Coll Nutr. 2007;26:182–189.

52. Ouellet V, Weisnagel SJ, Marois J, et al. Dietary cod protein reduces plasma C-reactive protein in insulin-resistant men and women. J Nutr. 2008;138:2386–2391.

53. Sierksma A, Patel H, Ouchi N, et al. Effect of moderate alcohol consumption on adiponectin, tumor necrosis factor-alpha, and insulin sensitivity. Diabetes Care. 2004;27:184–189.

54. Beulens JW, de Zoete EC, Kok FJ, Schaafsma G, Hendriks HF. Effect of moderate alcohol consumption on adipokines and insulin sensitivity in lean and overweight men: a diet intervention study. Eur J Clin Nutr. 2008;62:1098–1105.

55. Fragala MS, Kraemer WJ, Volek JS, et al. Influences of a dietary supplement in combination with an exercise and diet regimen on adipocytokines and adiposity in women who are overweight. Eur J Appl Physiol. 2009;105:665–672.

56. Grunberger G, Jen KL, Artiss JD. The benefits of early intervention in obese diabetic patients with FBCx: a new dietary fibre. Diabetes Metab Res Rev. 2007;23:56–62.

57. Ludvik B, Hanefeld M, Pacini G. Improved metabolic control by Ipomoea batatas (Caiapo) is associated with increased adiponectin and decreased fibrinogen levels in type 2 diabetic subjects. Diabetes Obes Metab. 2008;10:586–592.

58. Wennersberg MH, Smedman A, Turpeinen AM, et al. Dairy products and metabolic effects in overweight men and women: results from a 6-mo intervention study. Am J Clin Nutr. 2009;90:960–968.

59. Zemel MB, Sun X, Sobhani T, Wilson B. Effects of dairy compared with soy on oxidative and inflammatory stress in overweight and obese subjects. Am J Clin Nutr. 2010;91:16–22.

60. Sano A, Uchida R, Saito M, et al. Beneficial effects of grape seed extract on malondialdehyde-modified LDL. J Nutr Sci Vitaminol (Tokyo). 2007;53:174–182.

61. Kajiyama S, Hasegawa G, Asano M, et al. Supplementation of hydrogen-rich water improves lipid and glucose metabolism in patients with type 2 diabetes or impaired glucose tolerance. Nutr Res. 2008;28:137–143.

62. Monzillo LU, Hamdy O, Horton ES, et al. Effect of lifestyle modification on adipokine levels in obese subjects with insulin resistance. Obes Res. 2003;11:1048–1054.

63. Esposito K, Pontillo A, Di Palo C, et al. Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial. JAMA. 2003;289:1799–1804.

64. Brekke HK, Lenner RA, Taskinen MR, et al. Lifestyle modification improves risk factors in type 2 diabetes relatives. Diabetes Res Clin Pract. 2005;68:18–28.

65. Giannopoulou I, Fernhall B, Carhart R, et al. Effects of diet and/or exercise on the adipocytokine and inflammatory cytokine levels of postmenopausal women with type 2 diabetes. Metabolism. 2005;54:866–875.

66. Manigrasso MR, Ferroni P, Santilli F, et al. Association between circulating adiponectin and interleukin-10 levels in android obesity: effects of weight loss. J Clin Endocrinol Metab. 2005;90:5876–5879.

67. Barbato KB, Martins Rde C, Rodrigues Mde L, Braga JU, Francischetti EA, Genelhu V. Effects of greater-than-5% weight reduction on hemodynamic, metabolic and neuroendocrine profiles of grade I obese subjects. Arq Bras Cardiol. 2006;87:12–21.

68. Corpeleijn E, Feskens EJ, Jansen EH, Mensink M, Saris WH, Blaak EE. Lifestyle intervention and adipokine levels in subjects at high risk for type 2 diabetes: the Study on Lifestyle Intervention and Impaired Glucose Tolerance Maastricht (SLIM). Diabetes Care. 2007;30:3125–3127.

69. Rokling-Andersen MH, Reseland JE, Veierød MB, et al. Effects of long-term exercise and diet intervention on plasma adipokine concentrations. Am J Clin Nutr. 2007;86:1293–1301.

70. Hainer V, Hlavatá K, Gojová M, et al. Hormonal and psychobehavioral predictors of weight loss in response to a short-term weight reduction program in obese women. Physiol Res. 2008;57(Suppl 1):S17–S27.

71. Christiansen T, Paulsen SK, Bruun JM, Ploug T, Pedersen SB, Richelsen B. Diet-induced weight loss and exercise alone and in combination enhance the expression of adiponectin receptors in adipose tissue and skeletal muscle, but only diet-induced weight loss enhanced circulating adiponectin. J Clin Endocrinol Metab. 2010;95:911–919.

72. Franz MJ, Van Wormer JJ, Crain AL, et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. J Am Diet Assoc. 2007;107:1755–1767.

73. Steffes MW, Gross MD, Schreiner PJ, et al. Serum adiponectin in young adults – interactions with central adiposity, circulating levels of glucose, and insulin resistance: the CARDIA study. Ann Epidemiol. 2004;14:492–498.

74. Weyer C, Funahashi T, Tanaka S, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. J Clin Endocrinol Metab. 2001;86:1930–1935.