

Specific dietary patterns and concentrations of adiponectin

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Background: One of the adipokines mostly secreted from adipose tissue is adiponectin. Adiponectin is well known as the anti-diabetic, anti-obesity and cardio-protective factor. Present study focused on the review the previous studies about relationship between adherence to healthy dietary pattern, independent of one or two special dietary components, and concentration of adiponectin. **Materials and Methods:** We searched in PubMed search engine from 2003 to July 2014 using the following key words: Healthy dietary pattern, mediterranean dietary pattern, dietary pattern, diet intervention and adiponectin and adipokines. Then, we recruited 10 articles to review in the present study. **Results:** Cohort studies that are examined this relationship among women showed the strong positive association in this regard. According to cross-sectional studies adherence to healthy dietary pattern like Mediterranean intervention with moderate weight loss had a positive association with concentration of adiponectin. **Conclusion:** It seems that adherents to the healthy dietary patterns have great levels of circulating adiponectin. However, it is not clear that whether the separate components of healthy dietary patterns like good sources of fats or protein or fibers mostly have important roles in these beneficial effects of such dietary patterns or not.

Key words: Adipokine, adiponectin, healthy eating pattern, mediterranean diet

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INTRODUCTION

One of the adipokines secreted from adipose tissue is adiponectin. Adiponectin is a peptide contains 244 amino acids^[1] and accounts for 0.01% of total plasma protein.^[2] Although this hormone is secreted from adipocytes, its concentration is negatively correlated with body fat mass.^[3] Plasma adiponectin concentration consists three types of complexes containing low molecular weight, medium molecular weight and high molecular weight (HMW) which HMW is the most abundant form as well as an active form of adiponectin.^[4,5] Two receptor isoforms are known for adiponectin (Adipo R₁ and Adipo R₂). Adipo R₁ and Adipo R₂ are predominantly expressed in the skeletal muscle and liver, respectively, and both of them also are expressed in the pancreatic β -cells.^[6] Adiponectin has the anti-obesity, anti-diabetic, anti-cancer, anti-inflammation properties as well as cardio protective effects that are supported by large body of evidence.^[7-10] Several studies indicated that adiponectin play the important roles on concentration of blood glucose and lipid profile.^[11-13] Life style related factors like physical activity and diet play the important roles on adiponectin.^[14-16] According to previous studies dietary patterns, which are rich in fiber, low fat dairy products, whole grain, and plant sources of protein

display the key role on protection against metabolic syndrome and cardiovascular diseases (CVDs).^[17-22]

Several investigations were conducted about the association between one of the special dietary components and concentration of adiponectin. Effects of fatty acids, dietary proteins, carbohydrate with low glycemic index and consumption of foods rich in fiber as well as high-fat diet on concentration of adiponectin are properly examined.^[2,3,5,11] It seems that weight loss diet can enhance the hormone. At least 10% weight loss may increase adiponectin concentration.^[23,24] Beside weight loss diets and dietary components such as omega 3 fatty acids or high protein foods intake, it seems that diverse dietary patterns play important roles on circulating of adiponectin.^[14-16] Therefore, diverse diets also can be a healthy pattern.

Healthy dietary pattern such as mediterranean dietary pattern have been shown to decrease risks for diabetes, cardiovascular disorders, and chronic diseases.^[1,12,25,26] The mechanisms underlying health effects of these dietary patterns are still uncertain. The beneficial roles of different healthy dietary pattern on prevention of chronic diseases may be mediated via the increase in adiponectin concentration. According to our knowledge,

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there is no review study to collect all these published papers on the association between healthy dietary patterns and the concentration of adiponectin. A review paper can more focus just on the link between dietary patterns and adiponectin levels. All foods and nutrients are usually eaten in the context of a dietary pattern, and none of us consume single nutrient or single food. Therefore, it is important to see the association between important biochemical indices like adiponectin that can have a role in health and disease with different dietary patterns. In the present study, because of the major role of the type of diet on concentration of adiponectin and also the role of adiponectin in the prevention of chronic diseases, we aimed to gather available data regarding the relationship between consumption of healthy eating pattern and circulation of adiponectin.

MATERIALS AND METHODS

For assessing the association between healthy dietary patterns and adiponectin level, we searched databases using two groups of key word including medical subject headings and other keywords from 2003 to July 2014: (1) "healthy dietary pattern," "mediterranean dietary pattern," "dietary pattern"; (2) "Adipokines," "adiponectin," "adipocytokines" and searched databases using keywords 1 in combination with 2.

Articles were screened by their title and then abstract were considered when needed. The significant change for each study was extracted as summary measures. Two reviewers independently checked the title, abstract and full-text article to find the related published articles. Studies, which had the inclusion criteria were chosen. Where a decision could not be made based on title/abstract for including the study, full-text was checked to determine articles for the final selection. Discrepancies between the two investigators were solved by discussion. Any clinical trial, cohort and cross-sectional studies that had the mentioned keywords in the title, abstract or keywords were included in the review. A total of 521 articles with several designs including clinical trial, cohort, and cross-sectional studies have been reviewed. We excluded studies owing to lack of the direct relation with this issue; for example the relationship between special dietary components such as omega 3 fatty acids or high fat, were excluded. Duplicated articles also were excluded and finally 10 articles were recruited in this study. We extracted data on publication (the first author's last name and year of publication), study design, gender, age, number of participants, mean \pm standard deviation (SD) of body mass index (BMI), mean \pm SD or odds ratio of dietary patens for adiponectin level, adjusted variables and results. Studies that investigated the association

between adherence to healthy dietary pattern and concentration of adiponectin are presented in Table 1.

Quality of each study was assessed, and a score from 0 to 27 according to Downs quality assessment scores was given. Downs's checklist is composed of 27 items that can assess risk of bias at the study and outcome level in individual studies. Some assessment questions were regarding the confounders and its adjustment, adverse events of the intervention, patient loss, blindness, interventions compliance and randomization. Higher scores reflected higher quality.

Healthy dietary patterns are defined as any dietary pattern that known as healthy diet in papers such as mediterranean diet, low glycemic index, Dietary Approaches to Stop Hyperte, high-vegetable diets and high fiber diet.

RESULTS

Cohort studies

Results from prospective studies indicate the strong effect of healthy dietary patterns on concentrations of adiponectin among women.^[12,26] One investigation was conducted among 987 females that were in the age range of 30-55 years. The results of the mentioned study revealed that adherence to the mediterranean dietary pattern are positively associated with plasma adiponectin status ($P < 0.01$). Plasma adiponectin level was 23% higher in women who followed this dietary pattern after adjustment for age and energy intake.^[12] Another cohort study conducted among 1922 women from Nurse's Health Study (NHS) study, aged 30-55 years, indicated the strong direct relationship between adherence to healthy eating pattern and adiponectin levels.^[26] Circulating total, and HMW of adiponectin, adiponectin were 24% and 32% greater in women who adhered the healthy eating pattern after adjustment for potential confounders.^[26]

These two prospective studies were conducted among females of NHS study. More prospective studies considering both sexes in different parts of the world are needed to clarify this association.

Case-control study

One study among 185 smoker/nonsmoker individuals indicated the direct relationship between following 5 years mediterranean diet and circulating adiponectin among nonsmoker people. In contrast, smoking status ameliorated the association between adherence to the diet and the hormone.^[25]

Cross-sectional studies

The cross-sectional studies that are examined the relationship between diverse healthy dietary patterns and adiponectin

Table 1: Studies regarding the association between healthy dietary pattern (including mediterranean diet) and concentrations of adiponectin

Study	Type of study	Numbers/sex	BMI/age	Type of diet	Mean±SD or OR ^a	Adjusted variables	Results
Al-Attas <i>et al.</i> ^[25]	Case-control	185 smokers/nonsmokers	Age: 43±6.1-54.1±11.0 BMI: 23.2±2.5 ^b -27.2±3.6	Mediterranean diet for 5 years	13.2±1.8 ^c versus 11.2±1.6 ^d versus 7.6±1.2 ^e versus 10.2±1.5 ^f versus 8.3±1.2 ^g	-	Ameliorate the association between following the diet and adiponectin among smokers
Tsukinoki <i>et al.</i> ^[11]	Cross-sectional	202 Japanese male	Age: 41.7±11 BMI: 23.2±2.9	Effect of dietary factors, physical activity and lifestyle change	OR: 0.21 (0.06-0.74) ^h OR: 0.25 (0.07-0.91) ⁱ	Age, BMI, hypertension, lipids, glycemia, family members, platelet count	Positive association between adiponectin with physical activity, consumption of yellow vegetables and meal frequency
Nakamura <i>et al.</i> ^[16]	Cross-sectional	203 female/male Japanese in Hawaii and 249 male/female living in Japan	Age: 40-59 years BMI: 20-34	Diet rich in plant protein, carbohydrate and PUFA in comparison with western diet	Male in Japan: 10.5±5.5, in Hawaii: 6.7±3.2 Female, in Japan: 12.9±5.9, in Hawaii: 9.41±4.2	BMI for male and BMI and physical activity for female	Higher concentration of adiponectin in Japanese living in Japan than in Hawaii
Fragopoulou <i>et al.</i> ^[27]	Cross-sectional	532 male/female of ATTICA study		Mediterranean dietary pattern		Age sex and different biochemical factors	Higher level of adiponectin among individuals with adherent the dietary pattern
Cassidy <i>et al.</i> ^[30]	Cross-sectional	877 female twin pairs	Age: 47.8±12.3 BMI: 24.9±1.2	Fruit and vegetables pattern and traditional pattern	OR: 2.55 (-0.26-5.45) ^j	Age, lean mass, fat mass, energy intake, physical activity, smoking	A trend toward an association between fruits and vegetables intakes and adiponectin after adjustment for multivariable
Mantzoros <i>et al.</i> ^[11]	Cohort	987 female of NHS study	Age: 30-55 BMI: 23-38	Mediterranean diet	5.49±1.04 versus 6.91±1.06	Age and energy intake	23% higher of adiponectin in adherence of this diet
Fargnoli <i>et al.</i> ^[26]	Cohort	1922 women of NHS study	Age: 30-55 years BMI: 19-37	Healthy eating pattern	11.54±1.04 versus 12.88±1.04 ^k	Age, calorie, physical activity, BMI	24% and 32% greater of adiponectin and HMW in women who adhere the healthy dietary pattern after adjustment for age and energy intake
Rokling-Andersen <i>et al.</i> ^[14]	Clinical trial	188 male with diabetes and CVD risk factors	Age: 45±2.8 BMI: 28.5	Healthy diet with or without exercise	OR: 0.25 (0.08-0.43) in crude model and OR: 0.17 (-0.02-0.35) in adjusted model ^k	Percentage of body fat	Positive effect of 1-year diet intervention on adiponectin compared to control group

^aResults reported as the mean ± SD or OR; ^bP < 0.05; ^cLowest age (mean ± SD) is related to never smokers mediterranean diet adherents and highest age (mean ± SD) is related to ex-smokers mediterranean diet adherents; lowest mean ± SD for BMI is related to heavy smokers mediterranean diet adherents and highest mean ± SD for BMI is related to never smokers mediterranean diet adherents; ^dMean ± SD for never smokers mediterranean diet adherents; ^eMean ± SD for never smokers nonmediterranean diet adherents; ^fMean ± SD for heavy smokers mediterranean diet adherents; ^gMean ± SD for moderate smokers mediterranean diet adherents; ^hOR resulted from moderate physical activity (2 times/weeks); ⁱOR resulted from daily consumption of frequent meals with yellow deep vegetables; ^jLower mean ± SD for lowest quintiles of adherence and higher mean ± SD for highest quintiles of adherence; ^kP < 0.01 for crude model and P = 0.07 for adjusted model; ^lOR resulted from fruit and vegetable dietary pattern and P = 0.08. SD = Standard deviation; BMI = Body mass index; OR = Odds ratio; PUFA = Polyunsaturated fatty acid; CVD = Cardiovascular diseases; NHS = Nurse's Health Study; HMW = High molecular weight

have reached consistent results. Two observational studies investigated the presence of any link between adherence to mediterranean dietary pattern and concentration of adiponectin showed a positive correlation.^[25,27]

Another study conducted among a sample of Japanese in Japan and Japanese emigrants living in Hawaii indicated higher serum adiponectin concentration in Japan than in Hawaii. Japanese people consumed diet rich in plant sources of protein, more polyunsaturated fatty acid and carbohydrate in comparison with population in Hawaii, which adhered to the western-style dietary pattern.^[16] Author stated that the difference in concentration of adiponectin between two groups was related to BMI among men and mostly attributed to difference in BMI and physical activity among women.^[16] Lifestyle with moderate physical activity and consumption of the high amount of yellow deep vegetables substantially reduced risk of hypoadiponectinemia among Japanese male.^[1]

In another study, high consumption of low-fat dairy products, whole grain cereals as well as low consumption of refined grains positively enhanced plasma adiponectin level in 220 healthy women.^[28] In a study conducted among 780 type 2 diabetic men from the Health Professional's Follow-up Study, adherence to a low glycemic index diet with high amount of fiber could substantially increase plasma adiponectin level after adjustment for potential confounders.^[29] One study conducted among 877 female twin pairs in the aged of 47.8 ± 12.3 years, indicated a trend toward the relationship between adiponectin and fruit and vegetables intake after adjustment for several potential variables.^[30]

Clinical trial studies

Results from a clinical trial suggested that adherence to diet similar to healthy dietary pattern positively increase the concentration of adiponectin.^[14,31-33]

One investigation conducted among 188 male with several risk factors of diabetes and CVDs, indicated that some interventions including advice to reduce energy intake from fat and saturated fatty acids, consumption of fish and fish products, as well as consumption of fiber rich foods had beneficial effects on plasma adiponectin concentration compared to control group. This favorable impact was predominantly explained by decrease in fat mass.^[14] Consumption of diet rich in complex carbohydrate and fiber for 6 weeks substantially enhanced level of adiponectin in overweight and obese subjects.^[31] One clinical trial performed among patients with type 2 diabetes, and healthy individuals suggested that high-fat diet with low fiber intake induced the reduction of adiponectin.^[33]

DISCUSSION

The evidence from cohort, cross-sectional and clinical trial studies suggests a significant positive relationship between healthy dietary pattern such as mediterranean diet, low glycemic index and high fiber diet and concentration of adiponectin.

Although, there several original papers in this regard, we need to have a review to be more focused on these results. Considering dietary pattern instead of a single food or nutrient can be a more concise way to judge about the link between diet and diseases. Therefore, it is important to see the association between important biochemical indices like adiponectin that can have a role in health and disease with different dietary patterns. This is the first review in this regard.

Mediterranean diet is characterized by consumption of high amount of whole grains, olive oil (which is rich in monounsaturated fatty acids), vegetables and fruits, as well as moderate intake of fish and dairy products and lower consumption of red meat, sweets and saturated fatty acids and maybe these components play the important role on changes the circulation of adiponectin. However, the mechanism underlying this relationship and also which of the components exactly have the beneficial role on this effect are still unknown.^[12] So, low-calorie diet with high amount of fibers and unsaturated fats as well as consumption of carbohydrate with low glycemic load of mediterranean diet have beneficial effects on circulating of adiponectin. Some studies mentioned the important role of secondary outcomes of healthy dietary pattern like weight loss on augmentation of adiponectin levels, but it is still under debate.^[34-37] However, body weight and body fat can have a role in the association between different dietary patterns and serum adiponectin levels. In some cases, after adjusting for the weight and BMI, the association between dietary patterns and adiponectin was attenuated. This result showed that this association is modified by the weight or BMI to some extent.

Favorable influences of healthy dietary pattern were appeared because of its components.^[26] However, one clinical trial and one cross-sectional studies suggested that increase in concentration of adiponectin was occurred due to changes in BMI and body fat mass.^[14,16] Adherence to healthy dietary pattern tends to have a lower risk of several chronic diseases including diabetes, metabolic syndrome, atherosclerosis, and CVD. The mechanisms underlying these favorable effects of healthy dietary pattern are still under debate. It is possible that these dietary pattern decrease risk for chronic diseases through the elevation of adiponectin.^[14,16,25,26]

Unsaturated fats are one of the important components of healthy dietary pattern. These fatty acids are ligands of peroxisome proliferation activated receptor γ (PPAR γ) which stimulate the secretion and expression of adiponectin. Adiponectin is involved in fatty acids oxidation, reduce triglyceride storage in skeletal muscle, increase high-density lipoprotein via the activated of PPAR α and catabolism of apo AI^[38-41] and so play the important roles on protection against dislipidemia and cardiovascular disorders. ω_3 levels of serum phospholipids were substantially greater among individuals with a higher concentration of the hormone after adjustment for age, BMI and other fatty acids.^[42] In one investigation in Japan, adherents to healthy dietary patterns had higher levels of fish intake (best source of ω_3 fatty acids).^[16] ω_3 fatty acids like docosahexaenoic acids and eicosapentanoic acid caused to increase concentration of adiponectin mediated by activated the PPAR γ receptors and enhancement in liver AMP kinase.^[43-45] Based on results from one review article, daily consumption of fish and other sources of ω_3 fatty acids were able to elevate the hormone up to 60%.^[46]

Adherence to diet rich in fiber and complexes carbohydrate leads to improve concentration of adiponectin. According to the studies, diets rich in high amount of fiber increase the adiponectin level.^[31] It is suggested that supplementation of the diet with fiber enhance concentration of adiponectin up to 115%.^[46] Adiponectin is inversely correlated with insulin resistance, obesity and also it stimulates insulin sensitivity and metabolism of glucose.^[47] Consumption of foods with low glycemic index such as fruits and vegetables as well as legumes play a key role in protection against inflammation, metabolic syndrome and CVD^[17,20,21] and these beneficial effects may be occurred through the elevation of adiponectin. However, in one study effects of mediterranean diet on augmentation of the hormone remained either after adjustment for fiber intake.^[11] In addition, daily consumption of yellow deep vegetables significantly enhances the hormone among healthy Japanese men.^[1] So increase in adiponectin leads to stimulate glucose utilization and oxidation of fatty acids by activating of AMP kinase in skeletal muscle and elevate insulin sensitivity.^[10]

It seems that adherence to healthy dietary pattern with moderate weight loss tends to provide the higher levels of adiponectin especially among overweight and obese subjects.^[14] Increase in hormone was observed by the $\geq 10\%$ weight loss.^[36] Obesity leads to augmentation of inflammatory markers including tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) which decrease expression of adiponectin.^[48]

Healthy dietary patterns have usually healthy components like legumes, soy, whole grain, fruit, vegetables, good kinds

of fats and usually do not have high amounts of unhealthy items which can have a role in the link between these kinds of pattern and diseases.

There are some limitations in this review. Analyses of prospective studies were conducted with large samples of women. However, to the best of our knowledge, no prospective study has assessed this association among both sexes in patients with chronic diseases. Fewer clinical trials are available in this regard, and most of them were conducted among small samples of people. In addition, no clear report in the review of articles has explained the mechanisms underlying this association.

CONCLUSION

Results from a large body of evidence suggested that healthy dietary pattern such as mediterranean diet plays an important role on serum adiponectin level. More studies should be conducted to determine whether any of beneficial components of healthy dietary patterns has most positive effects on adiponectin.

AUTHOR'S CONTRIBUTION

VI Searched the related papers, read the papers, and drafted the paper. LA approval of the final version of the manuscript, revising the draft, and agreed for all aspects of the work.

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