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The impact of vegetarian diet in the prevention of type 2 diabetes mellitus

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Abstract

Review article aimed at investigating the possible mechanisms related to the vegetarian diet and type 2 diabetes mellitus. To do so, we conducted a comprehensive literature review from 2000 to 2012. Among the possible mechanisms linking the disease with vegetarian diet, we highlight how human genes interact with nutrients, mechanism explained by nutrigenetics science, which is able to prevent the rise of chronic diseases such as type 2 diabetes mellitus. Another related mechanism is the protection of antioxidants in oxidative metabolism, to prevent changes favorable to oxidative stress, an important trigger of chronic morbidities. This study helps provide an understanding of such mechanisms and shows a comparison between vegetarian and non-vegetarian (omnivorous) diets, and can be useful for nutrition professionals to understand how a vegetarian diet can help prevent type 2 diabetes mellitus.

Keywords: Diet. Vegetarian. Chronic Disease. Diabetes Mellitus Type 2. Antioxidants. Nutrigenomics.

Introduction

The incidence of noncommunicable chronic diseases (NCD) has increased alarmingly in developing countries in recent years. Such increase is due to poor dietary habits associated with sedentary behavior. Among such diseases is *diabetes mellitus* (DM), which is classified as type 1 (T1DM) and type 2 (T2DM).[1,2]

T1DM is characterized by the lack of insulin secretion and makes up 5.0% of all cases of diabetes in the USA, while T2DM accounts for 90.0% of the cases. In the latter, insulin secretion occurs normally or even in high levels, but the target cells of insulin are less sensitive than usual to this hormone.[2,3]

The disease can appear at any age: T1DM prevails in children, whereas T2DM arises more usually in adult life, and its incidence is associated with external factors, including lifestyle and endogenous factors such as genetic determination.[2]

Unlike T1DM, which depend permanently on insulin administration, T2DM can be controlled with weight loss and healthy diets, and a complete reversion of symptoms is possible. [2,3] Various studies have shown the importance of some nutrients and compounds present in foods in the prevention of NCDs, including DM. Among such studies, there are reports about the benefits of vegetarian diets, particularly among vegans, in reducing the occurrence of the disease.[2-6] The term "vegetarianism" refers to a wide range of dietary practices with numerous health implications.[3]

In a study of the Adventist Health Study series, vegetarians showed lower incidence of DM compared to non-vegetarians. It is possible that various factors found in vegetarianism protect against the disease, among them lower body weight, decreased cholesterol levels, low intake of simple carbohydrates, increased consumption of dietary fibers and complex carbohydrates, and non-intake of animal proteins and fats.[3]

Compared with vegetarian diet, it becomes clear the association of these studies, once the incidence of T2DM is closely related to environmental factors, among them high-fat, high-protein diets, sedentary habits and hyperphagia, which can solely or together favor the continuity of the disease.[3]

Historically, vegetarian diets were associated with some religious practices, but today health seems to the be main reason for the adherence to this diet in Eastern countries.[3] A great number of individuals around the world follow vegetarian diets, but in the majority of these countries vegetarians represent a small portion of the population, except in India, where about 35.0% of the people have followed a traditional vegetarian diet for many generations.[7]

Vegetarians are defined as people who do not consume animal foods and are divided into the following subgroups: ovo-lactovegetarians, lactovegetarians (these comprising the largest group), who exclude from the diet red meats, poultry, fish and seafood, but include dairy products and/or eggs. The strictest group is vegan, in which any animal-based product is excluded from consumption, including honey, and animal products such as wool and leather.[3,7]

Based on the results of the Adventist Health Study-2, it can be concluded that vegetarian diets have a high protective potential against T2DM, even after adjusting for age, gender, ethnicity, education, social status, lifestyle and body mass index (BMI), whereas pesco-vegetarian diets (which includes fish) and semi-vegetarian diets (which includes fish and small amounts of meat) provide intermediate protection. In vegans, researchers found a lower prevalence of T2DM, of 78.0%, which increases the possibilities of further studies to corroborate the relationship between vegetarianism and lower incidence of the disease.[8]

The present study aims to study the relationship of vegetarian diets with incidence of T2DM.

Methodology

An extensive literature survey was conducted, including articles available in electronic databases of scientific reliability, such as PubMed, Medline, Science Direct, Bireme, LILACS, as well as books and periodicals specialized on the subject. The searches were made in Portuguese, English and Spanish, using the following descriptors: vegetarianism and noncommunicable chronic diseases, oxidative stress and noncommunicable chronic diseases, vegetarianism and type 2 diabetes, vegetarianism and veganism, vegetarianism and chronic diseases, nutrigenomics and antioxidants. The period of the survey was from February to May 2013, considering articles published from 2000 on relating to the researched theme.

Data synthesis

Nothing will benefit human health and increase chances for survival of life on Earth as much as the evolution to a vegetarian diet.

Albert Einstein

Diabetes mellitus

DM is the most common of all endocrine disorders, comprising the most common NCDs today. Acute symptoms of the disease are attributable to an inadequate action of insulin, which is a hormone with the unique ability of reducing blood glucose levels. High blood sugar levels – hyperglycemia – is one of the most prominent characteristics of DM.[2]

Individuals with T2DM produce insulin but are resistant to the hormone. Among the factors that seem to be directly connected with the development of the disease, genetics and lifestyle are the most important, including obesity as frequent comorbidity, with 90.0% of type 2 diabetics being obese.[2]

The basic cause T2DM is still imprecise; there are several studies on the subject that point to various causes, among them obesity and insulin resistance. This theory holds that the adipose tissue produces a hormone called resistin, which causes insulin resistance, thus interfering with its action. In addition, the production of adiponectin hormone (which has the effect of increasing sensitivity to insulin) is decreased in obese individuals.[2]

Mahan et al.[9] describe as risk factors for the onset of T2DM genetic and environmental factors, added to family history of diabetes, and aging. The authors claim that adiposity and chronic obesity constitute sound risk factors for the development of the disease, even though small reductions of body weight may contribute significantly to the normalization of glycemia in pre-diabetic individuals.[9]

Insulin resistance is first observed in the target tissues, mainly in muscular, hepatic and adipose cells. In the early stages, hyperglycemia arises as an increase of postprandial or blood sugar levels caused by insulin resistance in the cell level, followed by a rise of fasting glucose concentrations. As insulin secretion diminishes, hepatic production of glucose increases, causing an increase of the preprandial or fasting blood glucose levels. Intensifying the problem is the deleterious effect of

hyperglycemia – the glucotoxicity that affects insulin secretion and sensitivity Such resistance in the adipocyte level triggers lipolysis, with an increase of circulating free fatty acids and contributing additionally to hyperglycemia.[9]

Diagnosis of type 2 *diabetes mellitus*

Classical DM symptoms include polydipsia, polyuria and sharp weight loss, associated with a high increase of blood sugar levels (≥ 200 mg/dl or 11.1 mmol/L).[3]

DM can be diagnosed by three ways, which are fasting plasma glycemia >126 mg/dl, random blood glycemia (> 200 mg/dl), in the presence of symptoms, and proof of tolerance to oral glucose. The most recent recommendation of the American Diabetes Association (ADA) is to maintain the levels of glycosylated hemoglobin (Hb A1c) < 7.0%.[10]

Metabolic factors and others affect most of DM complications, which include retinopathy, nephropathy and neuropathy. Atherosclerosis is the most common complication of the disease.[3]

Nutritional treatment for type 2 *diabetes mellitus*

Current recommendations for the diabetic population are not much different from those recommended for non-diabetics with respect to calorie and macronutrient intake. Recommended intake of protein from animal or plant source is of 15.0% to 20.0 of total caloric value (TCV), or more recently, 0.8g to 1kg of protein/kg of body weight. Regarding total fat, maximum recommended intake is 30.0% of TCV, limiting saturated fat to less than 7.0% of TCV; polyunsaturated fatty acids up to 10% of TCV, and monounsaturated fatty acids complementing in an individual basis; and cholesterol intake less than 200 mg/day. Carbohydrate intake is defined by the difference, after establishment of protein and lipid contents. Daily recommended consumption ranges from 45.0% to 60.0% of TCV, being sucrose up to 10.0%, fructose not added to foods and dietary fiber at least 20g/day or 14g/1000 kcal.[10,11]

Priority in nutritional treatment is to adopt interventions in lifestyle to improve possible alterations in glycemia, dyslipidemia and hypertension.[3]

Included in such lifestyle changes is adequate consumption of fruits and vegetables as sources of dietary fibers, vitamins and minerals. Among the minerals, zinc is crucial for diabetics. There are studies that associate zinc to the regulation of insulin production and the use of glucose by skeletal muscle and fat cells. Such role is associated to the fact that zinc is involved in the insulin synthesis, storage and release.[12-14]

Vegetarianism: origin and guidelines

Vegetarianism appeared about five million years ago, a time when diets consisted of fruits and vegetables. In the Paleolithic Age, the most recent ancestral, *Homo neanderthalensis,* introduced hunting and the consumption of meat. Afterwards, human populations became sedentary and included animal meats to their diets. Around 3200 B.C, religious groups, who believed that abstinence from meat created a karmic power that facilitated reincarnation, adopted vegetarianism in Egypt. Later on, around 155 to 255 A.C, vegetarianism was practiced as a form of purification of the soul in Christian religions.[15] In 1847, the first vegetarian association was created in England, followed by the foundation of the first German vegetarian society and the creation of the American Vegetarian Society in New York, 1850.[16] Sylvester Graham fostered vegetarianism in the USA and became known for his struggle for using "Graham" whole grain in the making of bread. [17]

The adequacy of a diet containing little or no meat was assessed during the World Wars, in Denmark (World War I) and Norway (1940 to 1945). The favorable effect of such dietary restriction was evidenced by the decreased mortality rate from cardiovascular diseases. This period is referred to as the golden age of vegetarianism. During this time, vegetarianism has lost much of its stigma of "occultism" and advanced in a more scientific basis.[16] Since the 1980s, people have been more concerned with healthier lifestyle, along with nonviolence conscientiousness and respect for animals. Ever since, animal rights organizations and the promotion of vegetarianism or veganism have gained strength and developed worldwide actions.[15]

In Nutrition, professionals in this area no longer see vegetarians as "potentially malnourished", and, in addition, vegetarian diets have been used successfully in clinical practice for treatment of NCDs.[14]

The American Dietetic Association defines vegetarianism as a practice that consists of partial or total exclusion of animal products from the diet, being this a dietary practice of vegetarians, corresponding to individuals who include totally or especially vegetable foods in their diets and in principle exclude any form of animal food.[18]

Messina et al.[19] and Sabaté[20] claim that there are many reasons why people decide to follow a vegetarian diet, among them ethical, environmental, religious aspects, and especially health concern.

The ethical reason is based on environmental destruction, once the livestock industry causes serious environmental impacts and the risk of hunger. It has been reported that for each kilo of meat produced five kilos of grains are required.[19,20] Other factor is religious, which is based on the belief that killing is strictly wrong. Regarding the health factor are dietary habits associated with practices of healthier lifestyle.[19,20]

Vegetarian dietary intake and its benefits and risks

Leitzmann[21] says that the vegan diet based solely on vegetables has advantages and disadvantages compared to the omnivorous diet. When comparing the vegetarians with non-vegetarians, or omnivores, the first is considered healthier. This is explained by the fact that this group tends to consume less total fats, saturated fats and cholesterol, and a larger amount of dietary fibers. Vegetarians usually consume more grains, vegetables, legumes, fruits, and a greater amount of soybean, nutrients such as vitamins C, E, folic acid and magnesium. But some authors question the small intake of other vitamins and minerals, such as zinc, vitamin B_{12}, vitamin A, vitamin D, and calcium.[3]

The beneficial effect of the vegetarian diet on NCDs may be due to the presence of antioxidant vitamins such as vitamin E, vitamin C, β-carotene and flavonoid, as well as folic acid, linoleic acid and dietary fibers present in fruits and vegetables. As LDL cholesterol oxidation is a key step in the pathogenesis of atherosclerosis, vitamin E, β-carotene and flavonoids prevent such oxidation.[14]

Rauma & Mykkänen[22] showed that vegetarians have higher levels of tissue antioxidants when compared to omnivores, which was assessed by the level of antioxidant vitamins in the plasma or serum (vitamin C, vitamin E, β-carotene). According to these authors, good antioxidant vitamins status is explained by high consumption of fruits, vegetables and nuts. It is possible that the beneficial effects of fruits and vegetables on health are mediated by many dietary components and several protecting mechanisms, including the antioxidant defense.

Added to eating habits, other factors relating to lifestyle, such as physical activity, abstinence from alcohol and tobacco, have effects on the antioxidant status. According to Rauma & Mykkänen,[22] to determine the antioxidant potential of a vegetarian diet *versus* an omnivorous diet, more studies are needed to evaluate the total antioxidant capacity, not only determining the isolated status of a single antioxidant.

According to Key et al.,[23] typical vegetarian diets, especially vegan diets, are related to lower risk of occurrence of diseases such as T2DM, obesity, cancer and cardiovascular diseases, which have showed a considerable increase among non-vegetarians, possibly due to the consumption of meats, with increased levels of saturated fats and cholesterol. The authors however remind that due to the exclusion of some nutrients in the vegans' dietary patterns, a satisfactory diet planning in terms of their nutritional needs is necessary.

Vegetarians' intake of vitamins and minerals, particularly vegans, in general is a controversial issue. When assessing zinc intake, Yen et al.[24] and Li[25] claim that there seems to be no difference in consumption between omnivores and vegetarians, but the bioavailability of this mineral in vegetarian diets is lower, due to the higher content of phytic acid which acts as a chelating agent. Key et al.[7] report that in general severe dependence of zinc is not observed in Western vegetarian diets, once whole grains, wheat germen, nuts, cereals, vegetables and tubers are important sources of the mineral. It however warns that consumption may be at or below the recommended levels, which are 11 mg/day for men aged 19 to 70 years or over and 8 mg/day for women aged 19 to 70 years or over.[14]

Regarding calcium, according to data of the American Dietetic Association (ADA) published in 2003, some authors claim that vegetarian diets have low contents of this mineral, below the recommended levels, and that, in addition, there are anti-nutritional factors, such as oxalates, that hinder its absorption. But ADA reminds that there are diverse plant-based sources of calcium and that dark-green leafy vegetables such as broccoli, kale, watercress, among others, have low contents of oxalate and can provide high bioavailability of calcium (around 49.0% to 61.0%) when compared to tofu, fortified juices and cow's milk (which has an approximate bioavailability of 32.0%). This meets the daily needs for this mineral, because according to determination of the Institute of Medicine (IOM), the recommended daily intake is of 1000 mg/day for men and women aged 19 to 50 years, 1200 mg/day for women aged 50 years and 1200 mg/day for men over 70 years of age. [18,26]

Regarding selenium, vegetarians have a similar profile to non-vegetarians. The sources of this mineral are grains, legumes and vegetables, and Brazil nut (or Pará nut) is the main source. Other sources of this mineral are oysters, crustaceous, swine and bovine meats and poultry. Studies indicate that there are risks to the nutritional status of vegetarians regarding selenium, due to the highly varied and inconsistent intake of this mineral, especially by women, whose intake is insufficient. However, such deficiency is not very common, once IOM recommendation is that people from 14 years, of both sexes, should consume 55 μg/day.[14,26]

As for the intake of vitamins B_{12} and D, studies indicated that there is deficiency of B_{12} mainly in vegans, but ovo-lactovegetarians can obtain this vitamin by consuming eggs and dairy products.[14] Some authors say that there is no guarantee of vitamin B_{12} intake by vegans, and supplementation, specialized formulations or fortified foods are necessary.[14,27] Other authors report that with respect to the consumption of omega 3 and omega 6, vegetarian diets often present adequate amounts of omega 6 and low intake of omega 3. Exception is when there is adequate consumption of fish, eggs or a great amount of algae.[28]

Alternatives to increase the low supply of omega 3 include the use of other food sources of this nutrient, such as eggs from chicken fed omega 3 (EPA and DHA), some microalgae (sources of DHA) and sources of ALA, the precursor for EPA and DHA, such as flax seeds, walnuts, canola oil, and soybean.[29,30]

Table 1, at the end of this paper, presents a summary of the articles used in the discussion of the mechanisms that relate T2DM with vegetarian diet.

Table 1. Summary of the literature review about the relationship of vegetarian diet with type 2 diabetes mellitus. 2013.

Authors	Title	Year	Objective	**Results**
MARQUES, Inês Margarida	**Zinc, chrome and diabetes mellitus**	2000	Review of the relationship of T2DM with zinc and chrome intake and evaluation of the benefits of supplementation in diabetics.	Zinc reduces hyperglycemia by increasing insulin activity. Vegetarian diets may have a chelating agent of this mineral due to the presence of anti-nutritional factors.

Authors	Title	Year	Objective	**Results**
VEIGA, Meirelles C.M	**Vegetarian diets: Characterization, nutritional implications, and controversies**	2001	Review of the advances of knowledge on the theme and discussion of the implications of the vegetarians' dietary pattern and their nutritional status.	Benefit of the vegetarian diet in reducing the prevalence of T2DM and risk of micronutrients deficiency.
JENKINS, DJ; et al.	**Type 2 diabetes and vegetarian diet**	2003	To analyze the studies on the incidence of DM and the practice of vegetarianism.	Vegetarian diet has a portfolio of natural products that can reduce glycemia and improve the lipid profile. Anticipation of what this kind of diet will produce.
FROST, G	**Veganism and its relationship with insulin resistance and intramyocellular lipid**	2004	To test hypotheses of dietary factors of the vegan diet on improved insulin sensitivity and improved lipid profile.	Vegans present better biochemical profile and cardioprotective effects, such as protection of β-pancreatic cells.

Authors	Title	Year	Objective	Results
DE BIASE, Simone Grigoletto et al	**Vegetarian diet and cholesterol and triglycerides levels**	2005	To determine values of triglycerides and total cholesterol, LDL and HDL in vegetarians and non-vegetarians.	Significant reduction of the lipid profile in vegetarians. Risks associated with veganism such as anemia and congenital hypothyroidism in babies breastfed by vegan mothers.
CAMPBELL, T.Collin	**The China Study**	2006	To evaluate the effect of reduced intake of proteins from animal source.	Exclusion of endogenous insulin administration in the assessed group and reduction of 30.0% of cholesterol serum levels.
BARNARD, Neal D.; COHEN, Joshua	**A low-fat vegan improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes**	2006	To investigate the effect of low-fat intake on improved glycemic control and cardiovascular risk factors in T2DM.	Reduction of 43.0% of use of medications by vegans; reduction of HbA1c (glycated hemoglobin); reduction of body weight and LDL. Significant improvement of glycemic control and lipid profile of individuals with T2DM.
MOLINA, Teixeira	**Nutritional status and lifestyle in vegetarians and omnivores**	2006	Assessment and description of the nutritional status and aspects of lifestyle in vegetarians and non-vegetarians.	Unfavorable lipid profile; higher BMI and waist-hip ratio in omnivores. Increased risk of developing NCDs by excessive intake of proteins and fats.

Authors	Title	Year	Objective	Results
BARNARD, Neal	**El impacto de una dieta vegana em las personas con diabetes tipo 2**	2007	To compare the effects of vegan diet with ADA recommendations.	Reduced levels of LDL in vegans (21.0%) and in ADA recommendations (9%). Reduced weight in vegans (5.8kg) and ADA recommendations (4.3kg). Greater indices reduction compared to those observed in patients using medications.
SABRY,M.O.D. ;SÁ,M.L.B.;SA MPAIO,H.A.C	**The Paleolithic diet in the prevention of chronic diseases**	2007	Comparison of the effect of Paleolithic diet with Mediterranean diet in diabetics.	Allusion to the reduction of NCDs with Paleolithic diet.
TEIXEIRA, Rita de Cássia et al	**Cardiovascular risks in vegetarians and omnivores: a comparative study**	2007	To describe and assess cardiovascular risk in vegetarians and omnivores aged 35 to 64 years residing in Grande Vitória-ES.	Imbalanced omnivorous diets with excessive intake of animal proteins and fats may trigger NCDs. Evidenced benefits of the vegetarian diet in diminishing such risks.
SIMÕES, Shirley Kelly dos Santos; CAMPOS, Florisbela A.C. Siqueira	**Nutritional status of vegetarian individuals**	2008	To assess the relationship between high-lipid diets with the lipid profile of vegetarians.	Vegetarian diet, like other diets, has positive and negative aspects. Support that healthy dietary habits and lifestyle influence health directly.

Authors	Title	Year	Objective	Results
TONSTAD, Serena; BUTLER, Terry; YAN, Ru; FRASER, Gary E	**Type of vegetarian diet, body weight, and prevalence of type 2 diabetes**	2009	To assess the incidence of T2DM in vegetarians and non-vegetarians.	Reduction of half of the risks of T2DM in vegans and ovo-lactovegetarians.
BARNARD ND; et al	**A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial**	2009	To compare the effects of a low-fat vegan diet with the conventional diets recommended to diabetics.	Reduced body weight and improved lipid profile in both diets. Regarding reduction of use of specific medication, the vegan diet had better results.
PARENTE, Rita	**Vegetarian diet: key nutrients intake during the lifecycle and in athletes and prevention of DC**	2010	Analysis of vegetarians' dietary pattern and the influence of this diet on NCDs.	High potential of vegetarian diets in the control of T2DM with 78% lower prevalence in vegans.
PEDRO, Nelson	**Vegetarian diet: facts and contradictions**	2010	To analyze the characteristics of vegetarian diet and its nutritional deficiencies.	Vegetarian diet is beneficial to the control of diseases such as high blood pressure, hypercholesterolemia, T2DM and obesity.
MARTINS, Márcia Cristina Teixeira	**Vegetarian nutrition: advances and perspectives**	2011	Editorial	Benefits of vegetable and oleaginous foods intake and increased risk of NCSs with red meats consumption.

Authors	Title	Year	Objective	Results
TURNER-MCGRIEVY; et al	**Decreases in dietary glycemic index are related to weight loss among individuals following therapeutic diets for type 2 diabetes**	2011	To assess the effect of alterations in the glycemic index (GI) and glycemic load (GL), weight loss and changes in HbA1c in ADA's conventional diet in the control of T2DM.	Low-GI foods can be a determinant factor of the success of ADA's diet and vegan diet in the prevention and treatment of T2DM.
KAHLEOVA H. et al.	**Vegetarian diet improves insulin resistance and oxidative stress markers more than conventional diet in subject with type 2 diabetes**	2011	Comparison of the benefits of conventional diets in diabetics and vegetarian diets combined or not with exercises.	Vegetarian diet improves insulin resistance compared to conventional diet for diabetics; increased improvement with addition of physical activity.
PEREIRA, Josecleide Calixto	**Vegetarianism and obesity under the genetics perspective: a literature review on obesity and vegetarianism**	2012	Literature review to describe the relationship of obesity with consumption of animal protein	Vegetarianism as an effective strategy to reduce prevalence of obesity and NCDs such as T2DM.

Authors	Title	Year	Objective	Results
TRAPP, Caroline; LEVIN, Susan	**Preparing to prescribe plant-based diets for diabetes prevention and treatment**	2012	To discuss the researches conducted on the practice of vegetarianism, with its benefits and risks.	Vegetarianism favors decreased risks in developing T2DM and in the control of the disease by reducing fats intake and improving metabolic control.
THOMS, Tricha	**Improvement in management of type 2 diabetes with a plant-based diet compared to a conventional diabetes diet**	2012	To assess studies on vegetarian diet associated with the prevention of T2DM and reduced use of medications by this group.	Significant reduction of the use of hypoglycemiants in the group of vegetarians and greater body loss among vegetarians, improved glycemic index.

Discussion

Among the various mechanisms that are related to NCD pathogenesis are changes in the oxidative metabolism, which seem to be associated with the breakdown of the homeostasis of the oxidative metabolism and increased risk of such diseases.[31]

Studies by Sabry, Sá & Sampaio[32] say that diets like the Paleolithic diet (based on the consumption of lean meats, fish, shellfish, fruits, vegetable roots, eggs, nuts and abstention from grains and cereals) are effective in diminishing NCDs. According to Gottlieb, Morassutti & Cruz,[31] the Paleolithic pattern of diseases consisted primarily of parasitic diseases. In this period, physical activity was intense, and this and other factors probably led to the selection of genes involved in the regulation of the oxidative metabolism, being the human genome selected to live in an environment with oscillations between energy storage and intense energy expenditure.

Sabry, Sá & Sampaio[32] argue that animal-based protein intake has shown a better relationship with reduced risks of NCDs than diets based on vegetables and whole grains, such as the Mediterranean and vegetarian diets. These arguments support the idea that the Paleolithic diet would contribute to a reduced incidence of T2DM and NCDs, and that the vegetarian diet would not contribute to reduce the risks of these diseases.

Simões et al.[33] agree with such statements and are less prone to the vegetarian diet, arguing that not specifically this kind of diet has benefits against NCDs, but rather the fact that healthy eating habits and lifestyle have direct influence on health, not only the exclusion of animal foods from the diet.

Authors such as Marques[10] state that vegetarian diets may be disadvantageous due to micro-mineral and vitamin deficiencies, with emphasis on zinc as a key factor. According to the author, this mineral has a hypoglycemic feature because it enhances insulin activity. Corroborating such theory, Solomons[34] reported that extrinsic factors reduce zinc bioavailability, such as nonheme iron found in eggs and vegetables, ethylenediaminetetraacetic acid (EDTA), dietary fiber, calcium, copper and specific foods such as cow's milk, cheese, coffee, lemon and celery, besides phytic acid, present in numerous foods included in the vegetarian diet. All these factors, according to the author, contribute to low bioavailability of zinc because they act as chelating agents of this mineral.

Still on the subject, De Biase et al.[35] suggested that the benefits of vegetarian diet are of effective importance, such as the significant reduction of the lipid profile among their followers,

but argue that this group has prominent risk of developing anemia. They also point to the high risk that babies breastfed by vegan mothers have in showing congenital hypothyroidism, but did not clearly explain the mechanism.

Contrary to the theories that do not consider the vegetarian diet beneficial in the prevention of NCDs, Tonstad et al.[36] and Parente[37] claim that the reduction of risk of T2DM in vegetarians is higher than in omnivores, indicating that there was a reduction of half of the risks of the disease, especially among vegans and ovo-lactovegetarians, besides the high potential that the vegetarian diet has in controlling T2DM, with prevalence 78.0% lower among vegans. Pedro[38] was also favorable to this premise, based on the fact that his studies demonstrated that there was a better control of diseases such as high blood pressure, hypercholesterolemia, T2DM and obesity in vegetarians. This idea was also supported by Martins,[39] who reported the benefits of diets based on vegetable and oleaginous foods, pointing out to the increased risk of NCDs among omnivores.

Some studies express favorable opinions with respect to the benefits of vegetarian diet when related to T2DM, among which the study by Meirelles,[40] who observed in his study a reduced prevalence of this type of DM among vegetarians, but stressed the risks of micronutrients deficiency. Jenkins et al.[6] noted that the vegetarian diet has a portfolio of natural products that might contribute to the reduction of glycemia and improve the lipid profile of the followers of this diet.

There were also studies that reported the exclusion of hypoglycemic medications in patients. Campbell[41] observed the exclusion of exogenous administration of insulin in a group of vegetarians, who showed a reduction of 30.0% in serum cholesterol levels. Following the same rationale, Barnard et al.[8,42] and Thoms[4] observed a reduction of the use of medication among vegetarians, loss of body mass (BMI reduction), and a significant improvement of the glycemic index, once again showing an improved lipid profile in individuals with T2DM.

The vegetarian diet is referred to as a promising alternative to improve the quality of life. Pereira[43] underlined that vegetarianism may be an effective strategy to reduce the prevalence of diseases such as T2DM and obesity, a benefit that can be explained by the theory described in the study by Trapp,[44] who supports that vegetarian diets reduce the risk of developing T2DM and help in the control of the disease because of reduced intake of fats and effective metabolic control.

The study conducted by Teixeira et al.[45] agrees with the one by Trapp,[44] and when they compared vegetarian diets with omnivorous diets, they found that the latter were characterized by an imbalance of nutrients associated with excessive intake of protein and animal fat, which can trigger NCDs.

Comparisons between vegetarian diets with conventional diets for diabetics, as indicated by ADA, were also found in the reviewed studies. Turner et al.[46] found that both the vegetarian diet and the one recommended by ADA had satisfactory results in the prevention and treatment of T2DM, having as determinant factor the consumption of foods with low glycemic content. Kahleova et al.[47] observed, in such comparison, that vegetarian diets have better response to differentiated insulin compared to conventional diets, and such response is maximized when it includes physical activities.

By analyzing the studies, it was possible to find two approaches that can be deemed as a form to explain the relationship of vegetarian diet with the incidence of T2DM. The first is the *nutrigenetics* theory, and the second the *antioxidant* theory.

Based on the nutrigenetics principle, the studies conducted by Kuh et al.[48] and Martin and Oshima[49] showed that NCDs share various modifiable risk factors relating to their etiology, such as physical inactivity, inadequate diet, smoking, obesity and dyslipidemia, as well as genetic origin (mutations and genetic polymorphisms), which may cause increased susceptibility to this kind of diseases.

Nutrigenetics deals with the effects of genetic variation in diet-disease interaction, which includes the identification and characterization of the gene related to or even responsible for the diverse responses to nutrients. The purpose of this science is to develop a recommendation that can show to each individual the risks and benefits of consuming specific diets or dietary components.[50] In addition, nutrigenetics also studies the influence of several nutrients on the gene expression – this scientific approach may potentially help the prevention of NCDs.[51]

The effect of a food component on a certain phenotype can vary due to genetic polymorphisms. In simplest form, it is a genetic variation that makes that nutrients and other food compounds have a distinct interaction and therefore produce a different phenotype.[50]

It is important to consider that the natural genes dynamics and nutrients interaction may occur during long periods and that interactions from long exposure to the same diet with multifactorial diseases may also occur.[51] However, the same authors mention that diet components may have a modulating effect on the phenotypes dependent on genetic variation, and key associations of polymorphisms with nutrients may occur.

Steemburgo, Azevedo & Martínez[51] predict a significant increase of T2DM until 2030, as well as of obesity, factors that require changes in lifestyle, characterized by high calorie intake and physical inactivity. These factors, associated with a strong genetic component, have a key role in the T2DM pathogenesis.

Mori et al.[52] reported that the most frequent polymorphism described for DM was the gene *PPAR*-γ*2*. This is one of the isoforms of *PPAR*-γ, the gene responsible for the activation of receptors that regulate several genes involved in the metabolism of lipids and glucose.

Frederikson et al.[53] and Mori et al.[52] reported that polymorphism associated with improved sensitivity to the action of insulin and protection against the development of T2DM is the replacement of an alanine with proline in position 12 (Pro12Ala). The authors observed that individuals with polymorphism in gene *PPAR*-γ*2* (Pro12Ala) had a higher susceptibility to develop T2DM with increased consumption of saturated and trans fat, whereas other group with the same polymorphism was less likely to develop T2DM, with improved insulin sensitivity, after making changes in the diet by reducing saturated fat, increasing intake of total dietary fibers and physical activity. Another polymorphism associated with DM is *ApoE* (-219G→T), which was examined by Laakso et al.[54] regarding its insulin sensitivity.

Apo are families of polypeptides that determine the metabolic destination of lipids in plasma and their uptake by tissues, and their primary function is to activate and inhibit the enzymes involved in the metabolism of lipoproteins.[51] *ApoE* is a protein present in HDL cholesterol, in very low-density lipoprotein (VLDL) and chylomicrons; it also part of chylomicrons remnants and intermediate-density lipoprotein (IDL).[51]

Laakso et al.[54] reported that there are evidences that *ApoE* changes the effect of insulin and that the polymorphism of the *ApoE* gene alters proteins structure and function. According to the authors, the most described polymorphism is -219G→T, which seems to have an important relation with insulin resistance.

Moreno et al.[55] carried out a clinical trial and found that all individuals with polymorphism had a lower insulin sensitivity, regardless of the diet consumed but those who have the gene G of this same polymorphism had improved insulin sensitivity by consuming a diet rich in monounsaturated fat and carbohydrates.

Another approach that would explain the influence of the vegetarian diet in the prevention or incidence of T2DM is that the oxidative stress in diabetic patients is increased because of hyperglycemia. Regarding the development of metabolic syndrome, numerous studies report that in these individuals there are decreased levels of vitamin E, retinol, vitamin C and carotenoids, which are substances with antioxidant properties. [31]

This theory is based on the role of dietary antioxidants and free radical production by endogenous and exogenous sources.[31] Antioxidants are substances that delay or prevent oxidative

stress. Non-enzymatic or exogenous antioxidants are basically found in vegetables and have a complementary role in preventing the harmful effects of free radicals on the body, minimizing their effects.[31]

With the epidemiologic transition since the Paleolithic Age, foods with higher contents of dietary fibers, vitamins and bioactive compounds with antioxidant potential have been replaced by foods rich in simple carbohydrates, of easy absorption, saturated fats, salt and potassium. The oversupply of unhealthy foods associated with sedentary lifestyle cause the cells to function in a feedback cycle, as in T2DM.[31]

According to Gottlieb, Morassutti & Cruz,[31] during human evolution there was a form of adaptation of energy storage to maintain homeostasis during times of scarcity and climate changes. With such genetic adaptation since the Neolithic period, an imbalance between excessive foods intake and less calorie expenditure began. As a consequence of the increased stores of glucose, lipids and proteins available for the citric acid cycle, promotion of more H^+ donors was formed, increasing the proton gradient and production of reactive species of O_2 (free radical), which cause damages to the cell macromolecules.

Oliveira et al.,[56] Meyer et al.[57] and Urakawa et al.[58] showed that excess glucose in the bloodstream slows down cellular respiration, with no consumption of glucose yet, thus reproducing the symptoms of T2DM.

There are studies, such as the one conducted by Leonard & Robertson,[59] who conclude that sedentary lifestyle, associated with a hypercaloric diet, are factors that contribute to the imbalance of the cellular energy metabolism. This study suggests that oxidative stress can be a primary event and the trigger of diseases such as T2DM.

Chalabi et al.,[60] in a review study on nutrigenetics and antioxidants, mentioned that free radicals are involved in oxidative cell damages and that the body can benefit from diets that have as complementary source mineral cofactors and exogenous antioxidants provided by the intake of fruits and vegetables. Among the most well-known, the authors cite β-carotene, ascorbic acid (vitamin C), and phenolic compounds. The authors also mention that most of the NCDs, such as DM and cardiovascular diseases, involves complex interactions between the diet and several genes.

Both nutrients and other food compounds, diets and lifestyle, are factors that can alter gene expression, resulting in alterations of metabolic functions.[61]

Final considerations

In this study, it could be seen that there is strong evidence that the adoption of a vegetarian diet is associated with a better control of T2DM. Such association may have a direct connection with the gene-nutrient interaction studied by nutrigenetics and the protection of exogenous antioxidants.

Further studies are needed for a better understanding of the mechanisms of the vegetarian diet. It is crucial that the professionals of nutrition understand the basic principles of nutrigenetics, once it has the potential to clarify several mechanisms so far poorly understood, and thus promoting a considerable improvement of the professional's dietotherapeutic conduct.

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