CLINICAL NUTRITION

DOI: 10.12957/demetra.2020.43955

DEMETRA
Alimentação, Nutrição & Saúde

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This manuscript is part of an undergraduate thesis entitle "Hepatic Steatosis. Mechanisms of development of a reversible cell lesion from the nutritional aspect" written by Karina Amante Vieira, supervised by Felipe Perozzo Daltoé and co-supervised by Débora Kurrle Rieger, presented on December 2018 at the Federal University of Santa Catarina, SC, Brazil.

Nutritional treatment of non alcoholic fatty liver disease: relevant aspects of the macronutrient composition

Tratamento nutricional na doença hepática gordurosa não alcoólica: aspectos relevantes na composição de macronutrientes

Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a condition in which there is an excessive accumulation of fat into the liver tissue, non-related to abusive ethanol consumption. The etiology is multifactorial and mostly related to ether excessive lipid synthesis and/or reduced lipid excretion on genetically predisposed people. *Objective*: the aim of this manuscript is to describe the main mechanisms of NAFLD development, prevention and treatment with nutritional emphasis. *Methods:* review of literature. *Results:* although it is a condition related to fat liver accumulation, NAFLD seam not to be related only to the amount of dietary fat consumption but to sedentarism and positive caloric balance intake. *Conclusion:* the main treatment for NAFLD is weight loss aiming 10% of body weight, which often requires dietary changes and physical activities practices. Regarding to diet, there were compared studies with hypercaloric, normocaloric, hipocaloric, low carb/high fat, low fat/high carb and mediterranean diet for NAFLD control and patients quality of life improvement.

Keywords: Fatty Liver. Non-Alcoholic Fatty Liver Disease. Diet. Lipids. Carbohydrate.

Resumo

Introdução: A doença hepática gordurosa não alcoólica (DHGNA) é a condição na qual há acúmulo excessivo de gordura no tecido hepático, não causada pelo consumo excessivo de etanol. A etiologia desse acúmulo é multifatorial, mas parece ocorrer por mecanismos que envolvem a síntese excessiva de lipídios e/ou a redução da excreção dos mesmos em indivíduos geneticamente predispostos. *Objetivo:* este artigo tem como objetivo descrever os principais mecanismos de desenvolvimento da DHGNA, assim como sua prevenção e tratamento com foco nutricional. *Metodologia:* revisão de literatura. *Resultados:* de maneira geral, apesar de ser uma doença que envolve o acúmulo de gorduras no fígado, ela parece não estar relacionada ao consumo excessivo de gorduras em si, mas ao sobrepeso causado pelo sedentarismo e ao balanço calórico positivo. *Conclusão:* o principal tratamento da DHGNA envolve, portanto, perda de peso, objetivando redução lenta e gradual de cerca de 10% do peso corporal, a qual deve ser feita por readequação da dieta e prática de atividades físicas. Nesse sentido, também foram descritos e comparados estudos com dietas hipercalóricas, normocalóricas, hipocalóricas, *low carb/high fat*, *low fat/high carb*, dieta mediterrânea, entre outras, visando à melhor estratégia para a regressão da doença e melhora da qualidade de vida do paciente.

Palavras-chave: Esteatose hepática. Doença hepática gordurosa não alcoólica. Dieta. Lipídios. Carboidratos.

INTRODUCTION

The liver plays a fundamental role in the human body, performing >500 reactions to synthesis and degradation, among which are bile formation; glycogenesis; glycogenolysis; gluconeogenesis; urea synthesis; cholesterol metabolism; metabolism of steroids and thyroid hormones; iron storage; storage of vitamins A, D, E, K, and B12; synthesis of plasma proteins (albumin, globulin, transferrin, ceruloplasmin, coagulation factors, and lipoproteins); detoxification of various toxins; and biotransformation of xenobiotics. Therefore, any change in liver function has a great impact on the individual's health.[1]

Hepatic steatosis, also known as fatty liver degeneration, is a group of diseases characterized by accumulation of fat in the liver. At a cellular level, these diseases are characterized as reversible lesions of the hepatocytes that culminate in the accumulation of lipids into the cells. This accumulation may regress to the point of returning to normality if the etiological factors are removed or evolve into an irreversible cellular dysfunction that leads to necrosis in the functional tissue and development of more serious diseases such as hepatic cirrhosis and hepatocellular carcinoma.[2]

The best known and most studied type of hepatic steatosis is alcoholic hepatic steatosis, caused by the excessive consumption of alcohol, with an estimated worldwide prevalence of 25%.[3] Non-alcoholic steatohepatitis (NASH), also known as non-alcoholic fatty liver disease (NAFLD), has a prevalence of 10% to 35% in the United States and it is been considered a major cause of liver disease.[4]

Among the major causes of NASH, nutritional factors stand out. The prognostic and therapeutic roles of nutritional issues in the management of patients with liver disease have long been known, and weight loss generally reduces the risk of hepatic steatosis.[5] In this sense, the literature presents diet as an important modulating factor of hepatic steatosis, although the evidence regarding the optimal dietary composition is still controversial, especially regarding macronutrients (carbohydrates, proteins, and lipids). Thus, this literature review was aimed at describing the main mechanisms of the development of NAFLD and suggesting the best nutritional approach options for the prevention and treatment of the disease.

Lipid metabolism

To understand the mechanism of the development of steatosis, which is a pathological accumulation of fat in the liver, first, how the lipid metabolism occurs under healthy conditions must be well understood.

Lipids are compounds ingested in the diet as triglycerides (three fatty acids esterified to glycerol) and must be digested to be absorbed as free fatty acids (FFAs). Digestion begins in the mouth, with small amounts of fat being hydrolyzed by the lingual lipase enzyme, and then in the stomach, with the onset of short- and medium-chain triglyceride (TG) hydrolysis through the action of gastric lipase. The remaining TG (approximately 70%) is hydrolyzed in the duodenum through bile salts and pancreatic lipase, thus forming the FFAs.[6,7]

In general, the final products of lipid digestion are FFAs, which are absorbed by diffusion in the proximal portion of the jejunum. Inside the epithelial cells of the intestine (the enterocytes), FFAs are re-esterified to glycerol and return to form TG. These, along with cholesterol, phospholipids, and liposoluble vitamins, join apoproteins to become soluble in aqueous solutions and are called chylomicrons. Only then do they proceed to the lymphatic and blood vessels.[6,7]

Inside the chylomicrons, TGs are again hydrolyzed to FFA and glycerol, this time by the lipoprotein lipase enzyme, and reach the cells through the capillary walls. This makes fatty acids available as an energy source in

various tissues of the body, including the liver. FFAs that are not used as energy can also be stored by cells. FFAs that have not been recruited by the body cells bind to albumin to be transported to the liver where they can still be used for the formation of very-low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) particles. The former is used to release fatty acids into the fatty and muscle tissues whenever needed. The latter act in the reverse path, removing free cholesterol from peripheral tissues and transporting it to the liver, where it will be eliminated in the form of AGL and bile salts. From the VLDL, low-density lipoprotein (LDL) can still be formed, which would still be the main cholesterol-carrying lipoprotein for the peripheral tissues.[6,7]

In short, liver cells control the serum levels and types of lipids circulating in the bloodstream, and either by an excessive intake of fatty acids into the liver or by some problem in their excretion by the organ, the lipids will accumulate in hepatocytes, causing hepatic steatosis.[5-7]

Hepatic steatosis

The increased amount of fatty acids inside hepatocytes causes mitochondrial dysfunction, increased oxidative stress, endoplasmic reticulum stress, production of reactive oxygen species, and an inflammatory condition known as steatohepatitis. Thus, cell respiration is affected, energy production is diminished, FFA oxidation is impaired, and FFA accumulation is potentiated, creating a vicious cycle.[7,8] The chronicity of this process causes cell death and the replacement of lost cells by repairing fibrous connective tissue, which results in cirrhosis. Loss of hepatocytes and their replacement by scar tissue cause gradual loss of organ function. Cirrhosis is the main cause of the need for liver transplantation.[9]

From among the main sources of FFA for hepatocytes, we highlight those deriving from i) the adipose tissue itself, ii) the biotransformation of carbohydrates into fats (known as *de novo* lipogenesis), and iii) the ingestion of fatty acids.[10]

In a healthy state, fat tissue provides approximately 75% of FFA to the liver tissue. Lipids derived from diet also have the liver as their main destination, but the amount of fat stored in the liver is up to four times greater than that provided by diet. *De novo* lipogenesis, in turn, would be responsible for only 5% to 10% of the supply of circulating FFA. In patients with hepatic steatosis, the contribution of fat tissue decreases to 60%, even though it has the highest percentage, while that of dietary fat, especially saturated and trans fatty acids, increases to 15%, and the *de novo* lipogenesis pathway becomes unregulated, increasing to approximately 25%.[10]

Non-alcoholic fatty liver disease

NAFLD is characterized by excessive accumulation of fat in liver tissue due to some interference in the fatty acid metabolism by hepatocytes that is unrelated to excessive alcohol intake. According to the consensus of the Brazilian Society of Hepatology, excessive alcohol consumption is considered to be >140 g/ethanol/week for men (±21 doses) and 70 g/ethanol/week for women (±14 doses). The liver is considered to be steatotic when the accumulation of hepatic fat is ≥5%.[11]

NAFLD is the leading cause of chronic liver disease and is predicted to become the leading cause of liver transplantation by 2030.[9] The prevalence of NAFLD in eutrophic individuals without known risk factors is approximately 16%.[6] As age increases, so does the prevalence of NAFLD. As the years progress, the prevalence rates of other metabolic complications that potentiate NAFLD also increase.[12]

The pathophysiology of NAFLD is quite complex. Currently, NAFLD is assumed to develop as a result of multiple factors acting on genetically predisposed patients.[7]

In the genetic field, studies have linked single-nucleotide phospholipase 3 (PNPLA3), variant rs738409, polymorphism to the development and progression of NAFLD. The protein that encodes the PNPLA3 gene is expressed mainly in hepatocyte cell membranes and closely related to fat accumulation in these cells. It is activated after feeding and in cases of insulin resistance.[7,13]

Apparently, a strong relationship exists between insulin resistance and the development of NAFLD, but whether insulin resistance leads to hepatic steatosis or whether hepatic steatosis leads to insulin resistance is unclear, as patients with insulin resistance cannot absorb circulating glucose. As a reflection of high serum glucose levels, increased insulin production occurs in the pancreas, which causes increased serum levels of VLDL, which possesses most circulating TGs.[14] In addition, hyperinsulinemia stimulates *de novo* lipogenesis, which in turn potentiates the accumulation of fatty acids in liver cells.[15]

For these reasons, patients with diabetes mellitus 2 (DM2) are also more prone to develop NAFLD, which can worsen DM2. Obese patients with DM2 have, on average, an accumulation of intrahepatic lipids of up to 80% greater than that of non-diabetic obese patients.[15]

One of the most important factors in the etiopathogenesis of NAFLD seems to be obesity. However, the type of fat and its body distribution seem to be more important than the amount of fat itself. People with higher visceral fat accumulation have a higher risk of developing NAFLD than people with subcutaneous fat accumulation, regardless of their body mass indexes (BMIs).[16] This is because visceral fat tissue is an endocrine organ that, when hypertrophied, tends to produce more proinflammatory than anti-inflammatory cytokines. These inflammatory molecules ultimately have the ability to enhance peripheral insulin resistance.[6] The liver itself, when with fat accumulation in its cells, begins to secrete proinflammatory molecules (IL-6 and TNF-a, PCR), which potentiates the condition and predisposes the patient to other diseases such as atherosclerosis and myocardial infarction.[13]

Finally, besides the main comorbidities that are risk factors for the development of NAFLD (obesity, overweight, DM, dyslipidemias, and cardiovascular diseases),[13] NAFLD can arise as a consequence of surgeries (ileojejunal bypass and biliodigestive derivations), use of anabolic steroids and other drugs, medicines (amiodarone, corticosteroids, estrogens, and tamoxifen), environmental toxins or chemical products, and prolonged parenteral nutrition, or by association with diseases such as hepatitis C, polycystic ovarian syndrome, hypothyroidism, sleep apnea syndrome, hypogonadism, lipodystrophy, abetalipoproteinemia, and acid lipase deficiency.[1,6,8]

Nutritional approach in the prevention and treatment of NAFLD

The approach to preventing and treating NAFLD should include strict control of the metabolic risk factors often associated with the disease.[13,17,18] Among these, slow and progressive weight loss is widely recommended, aiming for long-term adherence.[5,11,17]

In this sense, the recommended weight loss is between 7% and 10%. Strategic diets that generate a caloric deficit of 500 to 1,000 kcal/day and lead to a weight loss of 0.5 to 1 kg/week, which are considered the most appropriate and safe method, may be used.[19] If the weight loss is too fast, it causes various side effects such as increased inflammation and hepatic fibrosis.[20,21]

The most important factor in reducing the percentage of hepatic fat seems in fact to be the control of energy intake. Hypercaloric diets, regardless of their composition, cause an increase in the percentage of hepatic fat. In the normocaloric models, the percentage of liver fat is increased in high-fat/low-carbohydrate diets and decreased in low-

fat/high-carbohydrate diets. Finally, in hypocaloric models, liver fat is significantly reduced, regardless of the type of macronutrient distribution and diet models.[22]

The consensus of the Brazilian Society of Hepatology states that the diet of patients with NAFLD should be low in carbohydrates and fructose (primarily from industrialized products) but not too restricted to the point of, for example, achieving ketosis.[11] In contrast, according to the clinical guidelines of the European Association for the Study of the Liver, European Association for the Study of Diabetes, and European Association for the Study of Obesity, in addition to energy restriction and the reduction in the consumption of processed, fructose-rich foods and beverages, the macronutrient composition should follow the Mediterranean diet.[17] This is characterized by reduced intake of refined grains and sugars and increased intake of monounsaturated and omega-3 fatty acids.[23]

High consumptions of refined and industrialized grains and especially fructose-rich foods are strongly correlated with NAFLD. Sugars such as fructose and glucose are metabolized in the liver, and their excess consumption contributes to increase in the levels of triglycerides and hepatic lipogenesis. In addition, they contribute to the exacerbation of *de novo* lipogenesis, increased levels of triglycerides in circulation, and decreased insulin sensitivity.[24,25]

Fructose is a simple sugar present in fruits and honey and is an important component of two sweeteners, sucrose (table sugar, fructose disaccharide, and glucose) and high-fructose corn syrup (a mixture of fructose and glucose monosaccharides) used in the food industry as a sugar substitute.[24,25]

Some studies have shown that fructose is different from glucose with respect to its potential to increase plasma triglyceride levels and hepatic fat accumulation. The fact that the total amount of fructose converted into triglycerides is relatively small (1%–3% of fructose) has led some scientists to contest the importance of fructose in stimulating liver lipid synthesis and accumulation.[26,27] In spite of this, most studies still reported that high fructose intake is related to the increased propensity to develop hepatic steatosis and cirrhosis.[28,29]

Studies that compared individuals with cirrhosis-free NAFLD with controls matched for age, sex, and BMI found that individuals with NAFLD consumed two to three times as much fructose from sugary beverages as the controls.[29] Other studies also suggested that consumption of fructose (especially from soft drinks) is related to the severity of hepatic fibrosis in a dose-dependent manner.[30,31] Finally, although fruits also contain fructose, the literature makes it clear that they are less likely to induce metabolic problems of this order because of the lower fructose content per fruit (compared with soft drinks) and because of their flavonoid, epicatechin, ascorbate, and other antioxidant components, which can combat the effects of fructose.[32-34]

The lipid composition of diets can also influence the accumulation of intrahepatic lipids. However, the amount of lipid consumed is as important as the type of lipid ingested, as different types of fatty acid generate different metabolic responses and levels of oxidative stress.[35] NAFLD would be related to high consumption of trans and saturated fatty acids and lower amounts of polyunsaturated fatty acids.[21] In general, diets with reduced compositions of trans and saturated fats and appropriate amounts of polyunsaturated and monounsaturated lipids have a protective effect against NAFLD.[23,36-38] The fat intake in the Mediterranean diet is approximately 30–40% of the total energy value, and the proportion of monounsaturated fatty acids is twice that of saturated ones.[39]

RESULTS

The most relevant scientific studies in the nutritional approach for patients with NAFLD are presented in chart 1, where the main results of the respective studies can also be found, such as changes in weight, percentage of liver fat, histological evaluation, liver enzyme levels, and insulin resistance.

Chart 1. Comparison between the types of nutritional intervention performed and the results achieved

Author,year	Type of study	Population	Intervention	Duration	Results				
					Weight	Liver fat	Histology	Enzymes	IR*
Kirk et al., 2009[41]	Experimental randomized, controlled	22 obese adults	1000 kcal/day + HCD deficit (65% CHO or >180 g/day, 20% LIP, and 15% PTN) or 1000 kcal/day + LCD deficit (10% CHO or <50 g/day, 75% LIP, and 15% PTN)	48 hours	Similar reduction in both groups: 2.0% ± 0.2%	Reduction of approximately 10% with HCD and approximately 30% with LCD		No significant changes	23.8 ± 5.9 reduction with HCD and 40.3 ± 6.1 reduction with LCD
				11 weeks or 7% weight loss	Similar reduction in both groups: 7.5% ± 0.4%.	Reduction of approximately 42% with HCD and approximately 38% with LCD		No significant changes	27.1 ± 5.1 reduction with HCD and 44.0 ± 4.7 reduction with LCD
Elias et al., 2010[48]	Uncontrolled experimental	31 obese patients with NASH	Deficit of 500–1000 kcal/day (15% PTN, 55% CHO, and 30% LIP)	6 months	Reduction ≥5%	Reduction		Significant improvement of GGT and ALT levels	Reduction from 4.2 ± 2.9 to 2.4 ± 1.5
de Luis et al., 2008[52]	Uncontrolled experimental	142 non-diabetic obese patients	Hypocaloric (1520 kcal/day) with 52% CHO, 25% LIP, and 23% PTN	3 months	≥5%			Significant reduction in GGT, ALT, and AST levels	Reduction from 3.1 ± 1.6 to 1.9 ± 1.7

Chart 1. Comparison between the types of nutritional intervention performed and the results achieved. (Continues.)

Author,year	Type of study	Population	Intervention	Duration	Results				
					Weight	Liver fat	Histology	Enzymes	IR*
Okita et al., 2001[53]	Uncontrolled experimental	14 obese patients with NASH	Hypocaloric (25 kcal/kg) with 20.8% PTN, 25% LIP, and 54.2% CHO	6 months	Reduction of 2.4 ± 0.9 kg	Reduction		Significant reduction in ALT and AST levels	
Thomas et al., 2006[49]	Uncontrolled experimental	10 patients with NASHGD	500 kcal/day reduction (46% CHO, 35% LIP, and 18% PTN)	6 months	4% reduction (3.4 kg)	No significant changes		No significant changes	No significant changes
de Luis et al., 2010[55]	Randomized experiment	162 obese patients	Hypocaloric (1500 kcal/day) with LFD (53% CHO, 20% PTN, and 27% LIP) or LCD (38% CHO, 26% PTN, and 36% LIP)	3 months	Approximately 4 kg regardless of diet type			LFD reduced ALT, AST, and GGT levels, while LCD reduced ALT and GGT levels	From 12.1 ± 4.6 to 3.1 ± 1.8 reduction with LFD and from 8.1 ± 9.1 to 4.2 ± 2.4 reduction with LCD

Chart 1. Comparison between the types of nutritional intervention performed and the results achieved. (Continues.)

Author,year	Type of study	Population	Intervention	Duration	Results				
					Weight	Liver fat	Histology	Enzymes	IR*
Viljanen et al., 2009[42]	Uncontrolled experimental	34 obese patients	Hypocaloric (50% CHO, 7% LIP, and 43% PTN)	6 weeks	Reduction of 11.2 ± 2.9 kg	60% reduction			40% reduction
Jang et al., 2018[55]	Randomized experiment	106 patients with NASHGD	LCD educational intervention or LFD educational intervention	8 weeks	Reduction of ~2.9kg with LCD and reduction of ~1.1kg with LFD	Larger reduction with LCD		Further reduction of ALT and AST levels with LCD	
Haufe et al., 2011[40]	Randomized and controlled experiment	170 patients with obesity or overweight	Deficit of 30% of the calories normally consumed with LCD (<90g CHO, 0.8g PTN/kg and ≥30% LIP) or LFD (20% LIP, 0.8g PTN/kg and the rest of CHO)	6 months	Reduction between 6 and 8kg regardless of diet type	47% reduction with LCD and 42% reduction with LFD		Similar reduction in ALT and AST levels in groups	Non significant changes
Browning et al., 2011[56]	Randomized and controlled experiment	18 patients with NASHGD	Hypocaloric 1200kcal/day for women and 1500kcalday for men (16% PTN, 34% LIP and 50% CHO) or LCV <20g/day (33% PTN, 59% LIP and 8% CHO)	2 weeks	Similar reduction in both groups ~4.3 ± 1.5 kg	55 ± 14% reduction with LCD and 28 ± 23% reduction with hypocaloric		No significant changes	

Chart 1. Comparison between the types of nutritional intervention performed and the results achieved. (Continues.)

Author,year	Type of study	Population	Intervention	Duration	Results				
					Weight	Liver fat	Histology	Enzymes	IR*
Benjaminov et al., 2007[57]	Pilot	14 candidates for bariatric surgery	CDV (<30g CHO/day)	4 weeks	14% reduction	Reduction	Improvement in steatosis, necrosis, inflammation and fibrosis	No significant changes	
Tendler et al., 2007[50]	Uncontrolled Experimental / Pilot	5 obese patients with NASH	LCKD (<20g CHO/day)	6 months	~12.8kg	Reduction	Improvement in steatosis, the degree of inflammation and fibrosis	No significant changes	Reduction of ~28.44
Ryan et al., 2013[58]	Experimental randomized *cross over*	20 patients with non-diabetic NAFLD	Mediterranean diet (rich in MUFA and PUFA with ~40% LIP, 40% CHO and 20% PTN) or LFD (30% LIP, 50% CHO and 20% PTN)	6 weeks	Reduction of 1.0 ± 0.5kg in the Mediterranean diet and 2.4 ± 0.6kg in LFD	39 ± 4% reduction in Mediterranean diet and 7 ± 3% reduction in LFD		No significant changes	Improved only with the Mediterranean diet, from 4.7 ± 1.6 to 3.0 ± 1.4

NAFLD = non-alcoholic fatty liver disease; IR = insulin resistance; CHO = carbohydrate; LIP = lipids; PTN = protein; LCD = low-CHO diet; VLCD = very-low-CHO diet; LCKD = low-CHO diet at ketogenic levels; HCD = high-CHO diet; LFD = low-fat diet; HFD = high-fat diet; MUFA = monounsaturated fatty acid; PUFA = polyunsaturated fatty acid.* A resistência à insulina foi avaliada através do HOMA-IR.
* Insulin resistance was evaluated using homeostasis model assessment-insulin resistance index.

DISCUSSION

NAFLD is the accumulation of fat in the liver, which leads to significant cellular dysfunction and it can result in chronic inflammatory conditions that lead to loss of organ function.[2] Most patients and even many health-care professionals think that a solution to the condition of excess fat accumulation in the liver would be simply the reduction of dietary fat intake *per se*. However, as discussed throughout this work, we observed that the development of NAFLD is complex and multifactorial and includes genetic predisposition and the presence or absence of comorbidities and associated diseases.[13,16]

The primary approaches to the treatment and prevention of NAFLD should therefore prioritize weight loss to improve the condition. This should be done in a balanced manner, with the objective of reducing approximately 10% of the initial weight through adequate diet and exercise (at least 150 minutes per week).[10,11,17]

Although the distributions of macronutrients and the constant villainization of fats and carbohydrates remain debatable, the use of low-calorie diets has reached a consensus. With this approach, studies have shown a consistent reduction in liver fat levels.[36,40-43]

Some authors argue that low-carbohydrate diets are more effective in treating NAFLD than low-fat diets.[40] The main theory behind this argument is that in individuals with NAFLD, *de novo* lipogenesis via metabolic pathways that convert excess carbohydrates to FFA in the liver is more active than in healthy individuals.[44] Thus, excess carbohydrates in the diet can be potentially more harmful than excess fat.

When comparing low- and very-low-carbohydrate diets with a low-fat diet, we found that the former provides greater weight loss in the short term, decreased insulin resistance, reduced abdominal and subcutaneous fats, and improved lipid profiles and insulin sensitivity. However, in general, both presented positive short-term effects, thereby contributing to an improvement in the prognosis of NAFLD.[45,46] Moreover, the low-fat diet took longer to demonstrate its beneficial effects.[41]

The mechanism responsible for the early beneficial effects of low-carbohydrate diets on liver metabolism is unknown, but it is speculated to be related to the greater decrease in plasma insulin concentrations in individuals receiving this diet.[41]

Although low-carbohydrate diets lead to a greater change in liver fat content and metabolic function than low-fat diets in the initial period, both models showed a decrease in liver fat content over time.[41]

Regarding the composition of fats in the diet, the type of lipid seems to elicit the biggest difference. Studies showed that diets rich in polyunsaturated fatty acids, especially omega 3, and monounsaturated fatty acids have beneficial and protective effects in relation to NAFLD. By contrast, a diet rich in saturated fatty acids contributes to the evolution of NAFLD by worsening insulin resistance and lipid profiles, and increasing liver fat.[18,23,38] Despite this, excess fat, without excess calorie, is an unlikely predisposing factor for the development of NAFLD.[38]

As for the ingestion of proteins in the context of NAFLD, only few studies suggested benefits. Nevertheless, protein intake can reduce the adverse effects of high-fat diets and thereby induce satiety, increase lean mass, increase basal metabolic rate, and increase insulin sensitivity.[21,47] Even so, the effect of different protein types on NAFLD and the amount needed for macronutrient distribution are unclear.

Another important factor in the treatment of NAFLD but that is often overlooked in the literature is diet duration. In general, studies with restrictive diets are short term. The longest period found in the evaluated studies was 6 months. Most studies used a hypocaloric protocol with moderate calorie reduction of 500 to

1000 kcal/day.[41,48,49] One study used a ketogenic protocol,[50] and only one compared low-carbohydrate and low-lipid protocols.[43] Both decreased body weight, total body fat, visceral fat, and intrahepatic lipid content. However, none of the studies evaluated their subjects after the protocol was finalized to verify if the effects persisted.

Regardless of the type of diet used, the focus is that the regression of NAFLD should be initiated by weight loss. Awareness of restrictive diets whose effects are studied only in the short term is necessary. Rapid weight loss, despite reducing liver fat, worsens inflammation and fibrosis of the liver, improving one aspect of the disease and damaging the other.[43] In addition, diets that are difficult to adhere to usually lead to food compensation and overfeeding, which culminate in the recovery of the previous weight or even an overall increase, often leading to worsening of the condition as compared with the state before the start of the diet.[50] In individuals with NAFLD, a modest weight gain of 3 to 5 kg already leads to an increase in hepatic fat,[51] and attention must be paid to each individual and to the use the most appropriate diet therapy.

CONCLUSION

NAFLD has complex, multifactorial development mechanisms and is often associated with obesity. As treatment measures, reduction of the initial weight by approximately 10% through adequate diet and exercise (at least 150 minutes per week) are recommended.

With regard to the adequacy of the diet, the aim should be at the global control of energy consumption. Hypercaloric diets, regardless of their composition, cause an increase in liver fat percentage. In normocaloric diets, the percentage of liver fat increases in high-fat/low-carbohydrate diets and decreases in low-fat/high-carbohydrate diets. In hypocaloric diets, liver fat is significantly reduced regardless of the type of macronutrient distribution and dietary models. The Mediterranean diet has been described as a good therapeutic option, as it includes reduced carbohydrate intake and increased monounsaturated fatty acid and omega 3 intakes.

Weight loss should be slow and gradual, as abrupt loss can generate important side effects such as subsequent overeating

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Contributors

Vieira KA participated in the compilation of the data and writing of the manuscript; Rieger DK participated in the analysis and interpretation of the data, and writing and revision of the manuscript; Daltoé FP participated in the conception and design of the study and reviewed the written manuscript.

Conflict of Interest: The authors declare that they have no conflict of interest

Received: July 12, 2019
Accepted: May 01, 2017