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Review Article

The Consumption of Omega-3 as Part of the Treatment and Prevention of Non-Alcoholic Fatty Liver Disease (NAFLD)

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Abstract

It is common to hear about the liver, and how this organ can easily get sick or damaged by excessive alcohol consumption. However, there is a condition that is not necessarily related to alcohol intake, this is non-alcoholic fatty liver disease (NAFLD), and it can be prevented or modified in its early stages of evolution [1].

Keywords: Non-Alcoholic Fatty Liver Disease (NAFLD); Metabolic Syndrome; Hepatocyte; Omega-3:

But why does this condition occur?

NAFLD is a not well-known condition, it can be caused by some modifiable risk factors that play an important role in the development of the disease. A sedentary life, for example, performing less than 30 minutes of physical activity per week, a poor-quality diet, abundant in energy (Kcal/day), high intakes of saturated fats, fructose and simple sugars, are essential factors for developing called metabolic syndrome (characterized by central obesity, hypertriglyceridemia, diabetes mellitus, high blood pressure, hyperglycemia, insulin resistance, among others) and NAFLD is part of it [2,3].

NAFLD is worrisome since it occurs in at least one third of the adult population and is considered one of the most frequent causes of chronic liver disease in children [1], so great care must be taken considering that in Mexico at least 7 of every 10 adults and 1 of every 3 children is overweight and obese [4].

NAFLD is an excessive accumulation of fat in the liver in the form of triglycerides, which presents various clinical forms, from the initial phase of the disease with the accumulation of fat in the liver tissue (composed of functional liver cells called hepatocytes) known as simple steatosis, to an inflammation and damage to the liver tissue that is non-alcoholic steatohepatitis. The latter carries an increased risk of cirrhosis and liver cancer (Figure 1) [5]. The disorders that occur in the metabolic syndrome are the result of the abnormal production of cytokines, which regulate the inflammatory response (secreted in adipose tissue), there is a greater increase in proinflammatory substances in relation to anti-inflammatory substances. Overfeeding leads directly to obesity and NAFLD, a situation that leads to inflammation of the hepatocyte, due to an increase in the appetite-regulating hormone, leptin. There is insulin resistance, which increases the production of free fatty acids, hepatic cholesterol and therefore NAFLD. Also, there is an increase in oxidative stress at the level of the endoplasmic reticulum within

the hepatocyte, activating the hormone hepcidin (produced in the liver) that increases hepatic iron uptake, increasing liver cholesterol, contributing to the development of NAFLD [6].

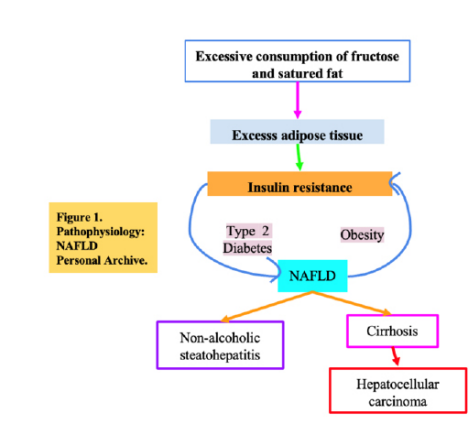

Figure 1: The whole potato plant.

How do I know if I have NAFLD?

To establish the diagnosis of NAFLD clinical tests are required, one of the methods is biopsy, which is the gold standard to determine the presence of the pathology. However, there are other more accessible and less invasive methods such as ultrasound, computerized axial technology and magnetic resonance imaging [5]. It is very important to perform any of these medical tests if the risk factors mentioned above are present.

And what is the relationship of NAFLD with Omega-3?

Since NAFLD is becoming more common and is linked to some diseases with a great impact on health, such as diabetes and obesity, new nutritional agents have been sought to prevent and treat this disease, making it a priority in public health. Therefore, omega-3 long-chain polyunsaturated fatty acids (in this article they are referred to as Omega-3) turn out to be a focus of interest in NAFLD due to their role in its prevention and treatment [6]. Omega-3 are long-chain fatty polyunsaturated fatty acids found in food in three main forms: eicosapentaenoic acid (20:5, EPA), docosahexaenoic acid (22:6 DHA), and alpha-linolenic acid (18:3, to wing). EPA, DHA and ALA are considered essential fatty acids, which means that they must be ingested through the diet, since the body cannot synthesize them on its own. Since they are found in different foods (algae, fish such as salmon, sardines, tuna, and vegetable fats such as chia seeds, walnuts, almonds, flaxseed, among others), their consumption is related to some benefits for human health. For example, omega-3 prevent layers of cholesterol from sticking to the arteries (atherotic plaques), contributing to the reduction of total cholesterol, triglycerides and very low-density cholesterol (VLDL) levels in the blood, providing protection to the hepatocyte (hepatoprotective activity) and the cardiovascular system [3,6].

Treatment

Traditionally, treatment focuses on nutritional intervention, with a specialized diet for the person, that is, individualized and with approaches ranging from weight reduction, modifying some elements of the diet or supplementation of antioxidants and vitamin E [7]. However, a study carried out over 12 months in a sample of 108 people with NAFLD and obesity compared treatment in two groups: one with omega-3 supplementation (1 dose per day of 1g) against the use of a placebo (sunflower oil) in conjunction with an individualized eating plan, both groups had a healthy lifestyle intervention. At the end of the study, it was observed that the prevalence of NAFLD was lower in the group that consumed omega-3, in addition to a greater decrease in BMI, lower fasting insulin levels and liver function tests (significant decrease in alanine aminotransferase ALT and aspartate aminotransferase AST). Although both groups had a decrease in these values, the intervention with omega-3 supplementation had a positive effect on the reduction of NAFLD and is considered a viable strategy for its treatment [8].

Mechanisms by which omega-3 help improve NAFLD

It is known that the EPA and DHA fatty acid molecules are ligands of some receptors that are involved in various pathways, and for an organism, a metabolic pathway or the functioning of a cell to be regulated, part of its control is regulated by genes, and these are regulated by other factors through the "nuclear receptors", the omegas-3 are a type of factor that act as a ligand for nuclear receptors (Figure 2).

There are two types of receptors which they are related to omega-3 (Figure 3). The SREBP-1c receptor (controls cholesterol metabolism and other glycolytic pathways) that is reduced in the presence of omega-3 by proteolysis via proteasomal catabolism, causing a decrease in lipogenesis and glycogenesis. Overexpression of this receptor induces NAFLD, as a consequence of excessive con-

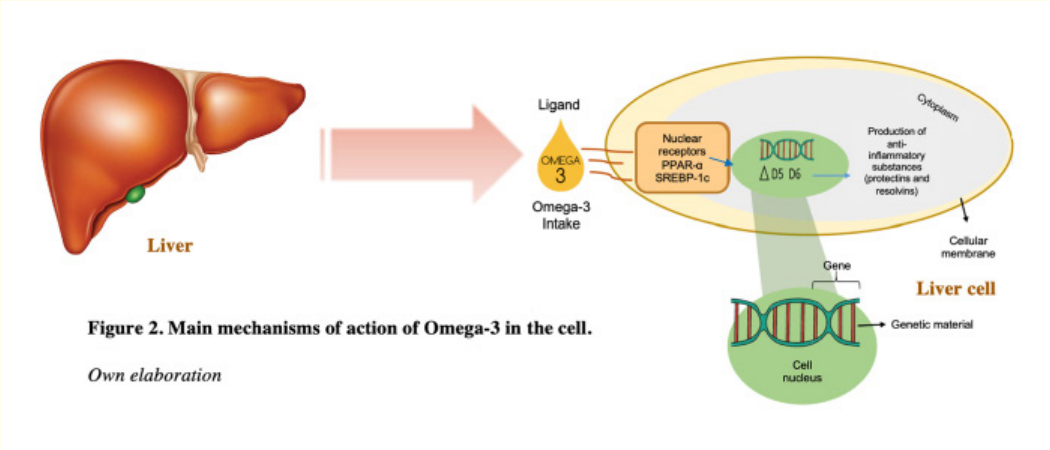

Figure 2: Main mechanisms of action of Omega-3 in the cell.

sumption of energy (calories) from fat or carbohydrates, and with the administration of omega-3, the infiltration of fat in the liver is significantly reduced [3,6].

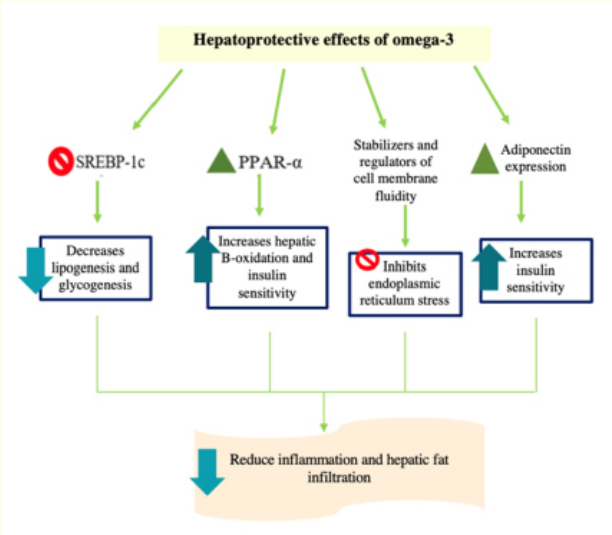

Figure 3: Protective effects of Omega-3 in the liver, mainly EPA and DHA.

Omega-3 will cause the PPAR-α receptor (peroxisomal proliferator-activated receptor - alpha), to activate, increasing hepatic β-oxidation, lipid catabolism and insulin sensitivity. Likewise, it should be noted that SREBP-1c is regulated by PPAR-α, so if it is increased, therefore SREBP-1c will be decreased, thus favoring the oxidation of fatty acids in the liver and the reduction of plasma lipids [3,6]. Has been shown that omega-3 administration, insulin sensitivity increase in liver, as well as skeletal muscle and adipose tissue. Adiponectin is a hormone that is produced in adipose tissue, participates in the metabolism of glucose and fatty acids, is related to metabolic syndrome and its low concentrations are associated with insulin resistance and therefore with NAFLD. Therefore, omega-3 administration activates adiponectin expression, thus increasing insulin sensitivity, which also activates PPAR-α (Figure 3) [6].

Omega-3 carry out their anti-inflammatory effect from the production of substances (protectins and resolvins). The synthesis of these begins with a series of elongation and desaturation reactions by two very important enzymes: D6 desaturase and D5 desaturase. Its production causes several beneficial modifications in the inflammation process, such as a reduction in the number of neutrophils and proinflammatory cytokines (Figure 2). An inflammatory state is a defense mechanism of the organism due to environmental stimuli. The inflammatory response involves the interaction of various cell types, as well as the production of lipid derivatives such as prostaglandins, leukotrienes, and proinflammatory cytokines, among others. Some diseases have inflammation as their main con-

dition and therefore a high concentration of these pro-inflammatory substances [3].

Conclusion

Thanks to the different mechanisms by which omega-3 can positively modify the state of NAFLD, they are considered a very effective treatment for this condition. However, they can also be used as a preventive method to reduce the risk of suffering from NAFLD, since being essential fatty acids, one of their greatest advantages is that they can be obtained from food, which is why the recommendation would be to include them in the diet routinely, that is to say that people consume foods rich in omegas-3 such as those mentioned above in this article without having to have any supplementation, to obtain this great benefit.

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