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Rule Of Omega 3 On Liver

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Abstract:

Omega-3 (N-3) fatty acids are essential, polyunsaturated fatty acids (PUFAs), they cannot be synthesized in vivo. In diet, large quantities are found naturally in fish oil, flaxseed and some nuts. They derive from a-linolenic acid and mainly occur as eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA), which are both anti-inflammatory. These are then converted to active metabolites, in particular, molecules known as resolving and protecting. These recently discovered lipid products are yet to be fully omega-3 fatty acids play a vital role in supporting liver health by reducing inflammation, regulating lipid metabolism, improving insulin sensitivity, and providing antioxidant protection. Incorporating omega-3-rich foods such as fatty fish, flaxseeds, and walnuts into the diet, or considering omega-3 supplementation, can help to promote liver health and reduce the risk of liver diseases. However, it's essential to consult with a healthcare professional before making any significant changes to your diet or supplementation regimen, especially if you have existing liver conditions or are taking medications.

Keywords: Omega 3, Liver disease, NAFLD, EPA and DHA

1.Introduction

Nonalcoholic fatty liver disease (NAFLD) involves the excess accumulation of hepatic fat in the absence of alcohol consumption and is defined by the presence of steatosis (characterized by lipid droplets) in more than 5% of hepatocytes. The histological pattern of NAFLD can progress to nonalcoholic steatohepatitis (NASH). NAFLD is now one of the most common liver diseases worldwide. In Western countries and some regions of China, the prevalence of NASH and NAFLD is 1–5% and 15–39%, respectively. One-third of NASH patients have advanced fibrosis and 20% develop cirrhosis. The pathogenesis of NAFLD is multifactorial and includes excessive inappropriate dietary fat intake combined with peripheral insulin resistance, oxidative stress, and innate immunity. It is frequently associated with obesity, type 2 diabetes (T2DM), dyslipidemia, metabolic syndrome, and cardiovascular disease. Currently, several therapeutic approaches for NASH have been proposed. According to EASL-EASD-EASO guideline, patients without NASH or fibrosis should only receive counselling for healthy diet and physical activity and no pharmacotherapy for their liver condition and in overweight/obese NAFLD, a 7–10% weight loss is the target of most lifestyle interventions and results in improvement of liver enzymes and histology. No drug has currently been tested in phase III trials and is approved for NASH by regulatory agencies.(Lu et al., 2016) NAFLD is a worldwide health problem affecting one-third of the global population. The fate of patients with cirrhosis, we aim to describe the effects of omega-3 fatty acids on hepatic lipid metabolism and on inflammatory pathways affecting development of NAFLD. Furthermore, we discuss the role of omega-3 fatty acids as a potential treatment for NAFLD.(Scorletti & Byrne, 2013) The inflammatory process is the unifying principle that is pervasively involved in the pathophysiology of cholestasis and liver disease. Although the body of evidence is not yet sufficient to make concrete conclusions, there are suggestions that omega-3 fatty acid supplementation may be helpful in blunting this process.(Lee et al., 2007)The most striking evidence thus far supporting use of this treatment is the apparent dearth of side effects. acid supplementation is important in not only liver disease but whole-body health, with widespread literature suggesting beneficial effects in multiple disciplines, the potential applications are numerous. Omega-3 fatty acid supplementation offers an attractive alternative to other therapies, because it possesses both nutritional and therapeutic benefits. Future prospective studies using this promising potential therapy are necessary to confirm preliminary findings in animal studies and early clinical reports.(Lee et al., 2007)

2. Liver

The liver is the second-largest organ in the human body. Traditionally, the anatomy of the liver has been described on the basis of its external appearance/gross anatomy. However, with the increase in surgical procedures, for example resection and transplant, the need for a more functional description of the liver based on its vascular and biliary architecture evolved. Different models of functional anatomy of the liver have been described in the literature in the past, but Couinaud's model of functional anatomy of the liver is the most popular. The liver has dual vascular supply, with most of its supply coming from the portal vein and the remainder through the hepatic artery. In this article, we outline the functional anatomy of the liver along with its blood supply.

2.1 Liver anatomy

the liver is divided into two lobes e the right and the left lobes of the liver e based on its external appearance. This division is based on the attachment of the falciform ligament anteriorly on the diaphragmatic surface and the fissure for the ligamentum teres and ligamentum venosum on the inferior surface of the liver. The quadrate and the caudate lobe of the liver belong to the right lobe of the liver. The liver, the largest organ in the body, weighs 1200–1500g and comprises one-fiftieth of the total adult body weight. It is relatively larger in infancy, comprising one-eighteenth of the birth weight. This is mainly due to a large left lobe. Sheltered by the ribs in the right upper quadrant, the upper border lies approximately at the level of the nipples. There are two anatomical lobes, the right being about six times the size of the left. Lesser segments of the right lobe are the caudate lobe on the posterior surface and the quadrate lobe on the inferior surface. The right and left lobes are separated anteriorly by a fold of peritoneum called the falciform ligament, posteriorly by the fissure for the ligamentum venosum, and inferiorly by the fissure for the ligamentum teres.(Jay H. Lefkowitch, n.d.) The liver has a double blood supply. The portal vein brings venous blood from the intestines and spleen and the hepatic artery, coming from the coeliac axis, supplies the liver with arterial blood. These vessels enter the liver through a fissure, the porta hepatis, which lies far back on the inferior surface of the right lobe. Inside the porta, the portal vein and hepatic artery divide into branches to the right and left lobes, and the right and left hepatic bile ducts join to form the common hepatic duct. The hepatic nerve plexus contains fibres from the sympathetic ganglia T7–T10, which synapse in the coeliac plexus, the right and left vagi and the right phrenic nerve. It accompanies the hepatic artery and bile ducts into their finest ramifications, even to the portal tracts and hepatic

parenchyma. The ligamentum venosum, a slender remnant of the ductus venosus of the fetus, arises from the left branch of the portal vein and fuses with the inferior vena cava at the entrance of the left hepatic vein.(Calder, 2010) The ligamentum teres, a remnant of the umbilical vein of the fetus, runs in the free edge of the falciform ligament from the umbilicus to the inferior border of the liver and joins the left branch of the portal vein. Small veins accompanying it connect the portal vein with veins around the umbilicus. Efferent vessels drain into glands around the coeliac axis. Some superficial hepatic lymphatics pass through the diaphragm in the falciform ligament and finally reach the mediastinal glands. Another group accompanies the inferior vena cava into the thorax and ends in a few small glands around the intrathoracic portion of the inferior vena cava.(Capanni et al., 2006) The inferior vena cava makes a deep groove to the right of the caudate lobe about 2cm from the midline. the bare area which lies to the right of the fossa for the inferior vena cava. The other areas without peritoneal covering are the fossae for the inferior vena cava and gallbladder. The liver is kept in position by peritoneal ligaments and by the intra-abdominal pressure transmitted by the tone of the muscles of the abdominal wall.(Jay H. Lefkowitch, n.d.)

2.2 Liver Functions

The liver is a vital organ in the human body with numerous essential functions. Here are the primary roles of the liver

2.2.1 Metabolism of Nutrients

Carbohydrate Metabolism: The liver helps maintain blood glucose levels by storing glucose as glycogen (glycogenesis) and releasing it when needed (glycogenolysis). It also synthesizes glucose from non-carbohydrate sources (gluconeogenesis). Lipid Metabolism The liver is involved in the synthesis, breakdown, and storage of fats. It produces bile, which helps in the digestion and absorption of dietary fats. The liver also synthesizes lipoproteins, cholesterol, and phospholipids. Protein Metabolism The liver synthesizes most blood plasma proteins, including albumin, clotting factors, and enzymes. It also converts excess amino acids into energy or stores them as fats and carbohydrates.(Ozougwu, 2017)

2.2.2 Detoxification

The liver detoxifies various metabolites, drugs, and toxins. It converts ammonia, a byproduct of protein metabolism, into urea, which is excreted in the urine. The liver also breaks down

alcohol and other toxic substances, making them less harmful and easier to excrete.(Ozougwu, 2017)

2.2.3 Bile Production

The liver produces bile, a yellow-green fluid essential for digestion. Bile contains bile salts, which emulsify fats in the small intestine, facilitating their digestion and absorption. Bile is stored in the gallbladder and released into the small intestine as needed.(Ozougwu, 2017)

2.2.4 Storage of Vitamins and Minerals

The liver stores various vitamins and minerals, including vitamins A, D, E, K, and B12, as well as iron and copper. These stores are released into the bloodstream as needed to maintain adequate levels and support various bodily functions.(Ozougwu, 2017)

2.2.5 Synthesis of Blood Proteins

The liver synthesizes most of the proteins found in blood plasma, including albumin, which helps maintain the osmotic pressure of blood, and clotting factors, which are crucial for blood coagulation.(Ozougwu, 2017)

2.2.6 Regulation of Blood Clotting

The liver produces clotting factors necessary for blood coagulation. It also synthesizes anticoagulant proteins that prevent excessive clotting, thus maintaining a balance in the coagulation system.(Ozougwu, 2017)

2.2.7 Immune Function

The liver contains immune cells called Kupffer cells, which are macrophages that capture and digest bacteria, worn-out cells, and other debris from the blood. This helps in protecting the body from infections(Ozougwu, 2017).

2.2.8 Excretion of Bilirubin

Bilirubin, a byproduct of the breakdown of red blood cells, is processed by the liver. The liver converts bilirubin into a form that can be excreted in bile and urine. This process prevents the buildup of bilirubin in the blood, which can cause jaundice.(Ozougwu, 2017)

2.2.9 Hormone Metabolism

The liver plays a role in the metabolism of hormones, including the inactivation and excretion of hormones such as insulin, estrogen, and cortisol.(Ozougwu, 2017)

2.2.10 Synthesis of Biochemicals Necessary for Digestion

The liver synthesizes various biochemicals necessary for digestion, including bile acids and cholesterol, which are crucial for the digestion and absorption of fats.(Ozougwu, 2017)

2.3 Liver Disease

Liver diseases encompass a wide range of conditions that affect the liver's ability to function properly.(Tajir & Shimizu, 2013) Here are some of the most common liver diseases:

2.3.1 Hepatitis

Hepatitis refers to inflammation of the liver and can be caused by viruses, alcohol, drugs, or autoimmune diseases. The most common types are viral hepatitis:

- **Hepatitis A:** Transmitted through contaminated food or water, usually acute and self-limiting.
- **Hepatitis B:** Spread through contact with infectious body fluids, can be acute or chronic.
- **Hepatitis C:** Primarily spread through blood-to-blood contact, often becomes chronic.
- **Hepatitis D:** Occurs only in conjunction with hepatitis B.
- **Hepatitis E:** Typically transmitted through contaminated water, usually acute.

2.3.2 Non-Alcoholic Fatty Liver Disease (NAFLD)

NAFLD is characterized by the accumulation of fat in the liver in people who drink little or no alcohol. It ranges from simple fatty liver (steatosis) to non-alcoholic steatohepatitis (NASH), which includes liver inflammation and damage.

2.3.3 Alcoholic Liver Disease

This disease results from excessive alcohol consumption, leading to fatty liver, alcoholic hepatitis, and cirrhosis. Chronic alcohol abuse causes inflammation, liver cell damage, and scarring.

2.3.4 Cirrhosis

Cirrhosis is the late stage of scarring (fibrosis) of the liver caused by many forms of liver diseases and conditions, such as hepatitis and chronic alcoholism. It can lead to liver failure, where the liver no longer functions properly.

2.3.5 Liver Cancer

The most common type of primary liver cancer is hepatocellular carcinoma (HCC). It often occurs in people with chronic liver diseases, such as hepatitis B or C or cirrhosis. Secondary liver cancer, or metastatic liver cancer, occurs when cancer from another part of the body spreads to the liver.

2.3.6 Hemochromatosis

Hemochromatosis is a genetic disorder that causes the body to absorb too much iron from food, leading to iron overload. The excess iron is stored in various organs, including the liver, leading to damage.

2.3.7 Wilson's Disease

Wilson's disease is a genetic disorder in which excess copper builds up in the body, particularly in the liver and brain. It can cause liver disease, neurological symptoms, and psychiatric problems.(Tajir & Shimizu, 2013)

2.3.8 Primary Biliary Cholangitis (PBC)

PBC is a chronic autoimmune disease that slowly destroys the bile ducts in the liver. Bile builds up and damages the liver tissue, leading to cirrhosis.

2.3.9 Primary Sclerosing Cholangitis (PSC)

PSC is a disease of the bile ducts that causes inflammation and scarring, leading to blockages and liver damage. It is often associated with inflammatory bowel disease.

2.3.10 Acute Liver Failure

Acute liver failure is a rapid loss of liver function, typically in individuals without pre-existing liver disease. It can be caused by drug toxicity (such as acetaminophen overdose), viral hepatitis, and other factors.

2.3.11 Autoimmune Hepatitis

Autoimmune hepatitis is a chronic condition where the immune system attacks liver cells, causing inflammation and liver damage. It can lead to cirrhosis and liver failure if untreated.

2.3.12 Liver Abscess

A liver abscess is a pus-filled mass inside the liver caused by infection, such as bacterial or amoebic infection. It requires prompt medical treatment.

3.Omga3. unsaturated fatty acid

Omega-3 fatty acids (w-3 FAs) are essential fatty acids with diverse biological effects in human health and disease. Reduced cardiovascular morbidity and mortality is a well-established benefit of their intake. Dietary supplementation may also benefit patients with dyslipidaemia, atherosclerosis, hypertension, diabetes mellitus, metabolic syndrome, obesity, inflammatory diseases, neurological/ neuropsychiatric disorders and eye diseases. Consumption of v-3 FAs during pregnancy reduces the risk of premature birth and improves intellectual development of the fetus. Fish, fish oils and some vegetable oils are rich sources of v-3 FAs. According to the UK Scientific Advisory Committee on Nutrition guidelines (2004), a healthy adult should consume a minimum of two portions of fish a week to obtain the health benefit. This review outlines the health implications, dietary sources, deficiency states and recommended allowances of v-3 FAs in relation to human nutrition.(Yashodhara et al., 2009)

3.1 Omega-3 and HEALTH

omega-3 FAS IN HEALTH Studies of Paleolithic nutrition and that of the hunter–gatherers have shown that the ancient populations consumed much less saturated fat, roughly equal amounts of v-6 and v-3 FAs (ratio of 1–2:1) and much lower amounts of trans-fatty acids than the present-day Western populations.43 44 The current Western diet is very high in v-6 FAs (the ratio of v-6 FA to v-3 FA is 20–30:1) because of decreased fish consumption and increased consumption of food items rich in v-6 FAs.44 Consumption of higher amounts of v-6 FAs

increases the plasma concentrations of eicosanoid metabolic products from arachidonic acid, specifically prostaglandins, thromboxanes, leukotrienes, hydroxy fatty acids and lipoxins. These bioactive products contribute to the formation of thrombi and atheromas in blood vessels, development of allergic and inflammatory disorders, and excessive cell proliferation.44 v-3 FAs on the other hand counteract these deleterious effects of v-6 FAs by decreasing the production of thromboxane A2 (a potent vasoconstrictor and platelet aggregator), prostaglandin E2 metabolites and leukotriene B4 (inducer of inflammation and leucocyte chemotaxis and adherence), and increasing concentrations of vasodilatory prostacyclins such as prostaglandin(Yashodhara et al., 2009)

3.2 Structure, Naming, and Metabolic Relationships of Omega-3 Fatty Acids

Fatty acids are hydrocarbon chains with a carboxyl group at one end and a methyl group at the other. The carboxyl group is reactive and readily forms ester links with alcohol groups, for example those on glycerol or cholesterol, in turn forming acylglycerols (eg, triacylglycerols, phospholipids) and cholesteryl esters. Fatty acids containing double bonds in the hydrocarbon chain are referred to as unsaturated fatty acids; a fatty acid containing 2 double bonds is called a polyunsaturated fatty acid (PUFA). Fatty acids have common names and systematic names. They are also referred to by a shorthand nomenclature that denotes the number of carbon atoms in the chain, the number of double bonds, and the position of the fi rst double bond relative to the methyl (ω; sometimes called n) carbon. Omega-3 fatty acids are so called because the fi rst double bond is on carbon number 3, counting the methyl carbon as carbon number The simplest omega-3 fatty acid is alpha-linolenic acid (ALA) (18:3ω-3). Alpha-linolenic acid is synthesized from linoleic acid (18:2ω-6) by desaturation,(Clària et al., 2011) catalyzed by delta-15 desaturase (confusingly, the desaturase enzymes are named according the fi rst carbon carrying the newly inserted double bond, counting the carboxyl carbon as carbon number 1). Animals, including humans, do not possess the delta-15 desaturase enzyme and thus cannot synthesize ALA. Plants possess delta-15 desaturase and so are able to synthesize ALA. Although animals cannot synthesize ALA, they can metabolize it by further desaturation and elongation; desaturation occurs at carbon atoms below carbon number 9 (counting from the carboxyl carbon) and mainly occurs in the liver. Alpha-linolenic acid can be converted to stearidonic acid (18:4ω-3) by delta-6 desaturase and then stearidonic acid can be elongated to 20:4ω-3 (Figure 1). This fatty acid can be further desaturated by delta-5 desaturase to yield eicosapentaenoic acid (EPA) (20:5ω-3) (Figure 1). A pathway for further conversion of EPA to docosahexaenoic acid (DHA) (22:6ω-3) exists; this pathway involves addition of 2 carbons to

form docosapentaenoic acid (DPA) (22:5ω-3), addition of 2 further carbons to produce 24:5ω-3(Philip C. Calder, n.d.)

3.3 Types of Omega-3

EPA and DHA: Eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA) come mainly from cold-water fish, so they are sometimes called marine omega-3s. Salmon, mackerel, tuna, herring, and sardines contain high amounts of EPA/DHA. EPA and DHA can be made from another omega-3 fat called alpha-linoleic acid (ALA), so they are more accurately termed "conditionally essential" fats. But because the conversion from ALA to EPA/DHA may not be sufficiently efficient, EPA/DHA are best obtained directly from food sources. ALA: Alpha-linolenic acid (ALA), the most common omega-3 fatty acid in most Western diets, is found in plant oils (especially canola, soybean, flax), nuts (especially walnuts), chia and flax seeds, leafy vegetables, and some animal fats, especially from grass-fed animals. It can be converted into EPA and DHA, but the conversion rate is limited so we are still uncertain whether ALA alone can provide optimal intakes of omega-3 fatty acids. (Swanson et al., 2012) The simplest omega-3 fatty acid is alpha-linolenic acid (ALA) (18:3 ω-3). Alpha-linolenic acid is synthesized from linoleic acid (18:2 ω-6) by desaturation, catalyzed by delta-15 desaturase (confusingly,). Animals, including humans, do not possess the delta-15 desaturase enzyme and thus cannot synthesize ALA. Plants possess delta-15 desaturase and so are able to synthesize ALA. Alpha-linolenic acid can be converted to sardonic acid (18:4 ω-3) by delta-6 desaturase and then sardonic acid can be elongated to 20:4ω-3 This fatty acid can be further desaturated by delta-5 desaturase to yield eicosatetraenoic acid (EPA) (20:5 ω-3) (Figure 1)., counting the carboxyl carbon as carbon number 1 path- way for further conversion of EPA to docosahexaenoic acid (DHA) (22: 6ω-3) exists; this pathway involves addition of 2 carbons to form docosapentaenoic acid (DPA) (22:5 ω-3), addition of 2 further carbons to produce 24:5 ω-3 desaturation to form 24:6ω(Philip C. Calder, n.d.)

here are three main types of omega-3 fatty acids:

- EPA (eicosatetraenoic acid). EPA is a "marine omega-3" because it's found in fish.
- DHA (docosahexaenoic acid). DHA is also a marine omega-3 found in fish.
- ALA (alpha-linolenic acid). ALA is the form of omega-3 found in plants.

3.4 Dietary Sources and Typical Intakes of Omega-3 Fatty Acids

Green leaves contain a signifi can't proportion (typically 50%) of their fatty acids as ALA, however green leaves are not rich sources of fat. Several seeds and seed oils and some nuts contain signifi cant amounts of ALA. Linseeds (fl axseeds) and their oil typically contain 45% to 55% of fatty acids as ALA,(Clària et al., 2011) while soybean oil typically contains 5% to 10% of fatty acids as ALA. Rapeseed oil and walnuts also contain ALA. Corn oil, sunfl ower oil, and saffl ower oil are rich in linoleic acid but contain very little ALA. Typical intakes of ALA among Western adults are 0.5 to 2 g/d.2,3 The main PUFA in most Western diets is the omega-6 fatty acid LA (18:2ω-6), which is typically consumed in 5- to 20-fold greater amounts than ALA.2,3 Seafood is a source of the longer chain, more unsaturated omega-3 PUFAs. Fish can be classifi ed into lean fi sh that store lipid in the liver (eg, cod) or "fatty" ("oily") fi sh that store lipid in the fl esh (eg, mackerel, herring, salmon, tuna, and sardines). Compared with other foodstuffs, fi sh and other seafood are good sources of the very long-chain omega-3 fatty acids EPA, DPA, and DHA. However, different types of fi sh contain different amounts of these fatty acids and different ratios of EPA to DHA. This is partly dependent upon the metabolic characteristics of the fi sh and also upon their diet, water temperature, season, and other variables. Nevertheless, it is clear that a single lean fi sh meal (eg, one serving of cod) could provide about 0.2 to 0.3 g of very long-chain omega-3 fatty acids, while a single oily fi sh meal (eg, one serving of salmon or mackerel) could provide 1.5 to 3 g of these fatty acids.(Philip C. Calder, n.d.)

4.Rule of Omega-3 and Liver

Fish oil has become the hot topic in nutrition and health care in general over the past few years. With any therapy that receives inordinate attention from the lay press, though, scientists and health care providers must approach this issue with a healthy dose of professional skepticism. However, contrary to previous "fads", the benefits of fish oil have a strong foundation in physiological theory and peer-reviewed scientific and clinical studies, with the most notable being efficacy in certain aspects of treating heart disease.Fish oil is primarily composed of omega-3 fatty acids, which, along with omega-6 fatty acids, make up the essential fatty acids. These cannot be synthesized by the human body and thus must be derived from exogenous sources. Fish, marine animals, and nuts are particularly rich in omega-3 fatty acids whereas omega-6 fatty acids are concentrated in animal products, vegetable oils, and trans-fatty acids that typify the modern Western diet. Research relevant to liver disease has recently been gaining

momentum with very encouraging preliminary studies which are establishing benchmarks in the field. Long-chain omega-3 fatty acids belong to a family of polyunsaturated fatty acids that are known to have important beneficial effects on metabolism and inflammation. Such effects may confer a benefit in specific chronic noncommunicable diseases that are becoming very prevalent in Westernized societies [e.g., nonalcoholic fatty liver disease (NAFLD)]. Typically, with a Westernized diet, long-chain omega-6 fatty acid consumption is markedly greater than omega-3 fatty acid consumption. (Madonna et al., 2011)The potential consequences of an alteration in the ratio of omega-6 to omega-3 fatty acid consumption are increased production of proinflammatory arachidonic acid–derived eicosanoids and impaired regulation of hepatic and adipose function, predisposing to NAFLD. NAFLD represents a spectrum of liver fat–related conditions that originates with ectopic fat accumulation in liver (hepatic steatosis) and progresses, with the development of hepatic inflammation and fibrosis, to nonalcoholic steatohepatitis (NASH). (Masterton et al., 2010)If the adipose tissue is inflamed with widespread macrophage infiltration, the production of adipokines may act to exacerbate liver inflammation and NASH. Omega-3 fatty acid treatment may have beneficial effects in regulating hepatic lipid metabolism, adipose tissue function, and inflammation(Scorletti & Byrne, 2013)

4.1 Hepatic and Adipose Tissue Function, Inflammation, and Nonalcoholic Fatty Liver Disease

The liver has a central anatomic location in the gastrointestinal tract and is the major metabolic organ for anabolic and catabolic processes. The liver is linked to the intestine (a) through a unique vasculature that converges in the portal vein and (b) through the enterohepatic biliary circulation. The liver has a wide range of functions, inter alia detoxification, hormone production, and plasma protein synthesis. A major function of the liver is to affect lipid metabolism (e.g., cholesterol synthesis, de novo lipogenesis, and synthesis of apolipoprotein B100). Among these other functions, the liver stores glycogen, lipid soluble vitamins, iron, and copper. The liver is not designed to store lipid, and lipid ac cumulation in hepatocytes is toxic. The quantity and the composition of food are relevant factors with regard to fat accumulation in the hepatocytes. Over the past three decades, the food habits of the general population have been changing toward a diet characterized by an increased consumption of fat and carbohydrate(X. Pan & Hussain, 2012). NAFLD is a spectrum of fat-related liver conditions, and hepatic lipid accumulation plays a pivotal role in the pathogenesis and progression of NAFLD. In the jejunum, dietary TGs are hydrolyzed by pancreatic lipase, resulting in the release of fatty

acids and monoacylglycerol that in turn are absorbed in the small intestine and utilized to synthesize TG. Subsequently, TG can be synthesized and stored in adipose tissue or metabolized in the liver (X. Pan & Hussain, 2012). Dietary TG is packaged into chylomicrons, and hepatic TG is packaged into very-low-density lipoproteins (VLDLs) in order to transport TG to peripheral tissues. Chylomicrons are assembled in the enterocytes during the absorpti The effect of omega-3 fatty acids on TGs primarily involves the suppression of hepatic VLDL apoB production and apoB pool size. Several tracer studies have demonstrated the effects of omega-3 fatty acids on VLDL metabolism. Chan et al. showed a reduction of TG plasma concentration in obese people after six weeks of treatment with high doses (4 g) of fish oil capsules comprising 45% EPA and 39% DHA. This reduction was mainly due to the effects of omega-3 fatty acids on VLDL apoB pool size; the effect of omega-3 fatty acids on VLDL particles was to favor the conversion of VLDL to LDL(Chan et al., 2003).This effect involves a decrease in triacylglycerol synthesis by 35% and an increase in fatty acid mitochondrial oxidation. In particular, omega-3 fatty acids induce the aggregation of apoB after its secretion from the endoplasmic reticulum (ER). In the Golgi, this aggregate material is oxidized and remains in the cell, where it is susceptible to the autophagic process(M. Pan et al., 2008)

4.2 Enterohepatic Circulation and Nonalcoholic Fatty Liver Disease

Imbalances in gut microbiota can increase fat absorption and energy harvest, causing liver fat accumulation, and in addition to the mechanisms discussed above, recent studies have shown the potential role of the gut microbiota in the pathogenesis and progression of NAFLD. The liver, biliary tract, intestine, portal venous circulation, colon, systemic circulation, and kidney are all involved in the enterohepatic circulation of bile acids.(Hegde et al., n.d.) Bile acid, water, electrolytes, phosphatidylcholine, cholesterol, and bilirubin are all components of bile, an iso-osmotic micellar solution produced by the liver. Bile acid synthesis is important for lipid digestion and absorption, cholesterol catabolism, fat-soluble vitamin absorption, and glucose and energy homeostasis. Bile acids are produced by cholesterol in two pathways: (a) a “classic” or natural pathway in which cholesterol is converted to 7-α hydroxycholesterol by a rate-limiting enzyme, cholesterol 7α-hydroxylase (CYP7A1); and (b) an “alternate” acidic pathway, in which cholesterol is converted to 27-hydroxy-cholesterol with 27-hydroxylase. These two pathways form the primary bile acids, i.e., chenodeoxycholic acid and cholic acid. In the intestine, gut microbiota deconjugate and dehydroxylate primary bile acids to form secondary bile acids, i.e., urodeoxycholic acids, deoxycholic acid, and lithocholic acid. Bile acids are natural ligands for farnesoid X receptor (FXR), a nuclear receptor expressed in the liver,

intestine, kidney, and adipose tissue. Chenodeoxycholic acid is the most effective endogenous ligand for FXR CYP7A1 is a rate-limiting enzyme that has a pivotal role in the regulation of bile acid synthesis. CYP7A1 transcription is inhibited by bile acids, steroid hormones, inflammatory cytokines, insulin, and growth factors(Spadaro et al., 2008).

5.Literature Review

E. Scorletti1 and C.D. Byrne in 11/12/16 they did a Review about Omega-3 Fatty Acids, Hepatic Lipid Metabolism, and Nonalcoholic Fatty Liver Disease in which they said otential beneficial effects of omega-3 fatty acids in liver and adipose tissue to ameliorate nonalcoholic fatty liver disease. In liver, long-chain omega-3 fatty acids regulate hepatic lipid metabolism by increasing hepatic fatty acid oxidation and inhibition of SREBP-1c and ChREBP activity (nuclear transcription factors that stimulate hepatic de novo lipogenesis). In adipose tissue, omega-3 fatty acids have a potential antiinflammatory effect by inhibiting macrophage recruitment and activation; decreasing fatty acid release; decreasing adipokine and cytokine secretion, and favorably affecting the enterohepatic circulation. Furthermore, omega-3 fatty acids upregulate CYP7A1 expression, increasing bile acid synthesis and excretion. The potential beneficial consequence of these effects is to ameliorate NAFLD. Abbreviations: ChREBP, carbohydrate regulatory element–binding protein; CYP7A1, cholesterol 7α-hydroxylase; NAFLD, nonalcoholic fatty liver disease; SREBP, sterol regulatory element–binding protein; TG, triglyceride.

G. S. MASTERTON*, J. N. PLEVRIS & P. C. HAYES in 8 December 2009 did a Review article about omega-3 fatty acids – a promising novel therapy for non-alcoholic fatty liver disease in which they said Non-alcoholic fatty liver disease is a common and growing problem worldwide.1, 99–100 Although frequently asymptomatic and relatively benign, NAFLD has the potential to progress to cirrhosis. Cirrhosis, when decompensated, has a poor prognosis.101 Currently, the mainstays of treatment are dietary advice, help and encouragement to lose weight, and exercise, and energetic treatment of co-existing disorders, especially, Type 2 diabetes and hypertension. Treatment strategies to date may be grouped into those that address weight loss, improve insulin sensitivity, are antioxidant, anti-TNF or have other mechanisms of action, but none has become an established intervention. Omega-3 fatty acids have been suggested as a treatment for NAFLD.20 They have several potential mechanisms of action, the most important being to alter hepatic gene expression, thereby switching intracellular metabolism from lipogenesis and storage to fatty acid oxidation and catabolism. There is also evidence that they improve insulin

sensitivity, are anti-inflammatory and reduce TNF levels thus offering several potential therapeutic mechanisms.

6. CONCLUSIONS

Complex mechanisms operate to regulate hepatic lipid homeostasis in normal physiology, and it is plausible that some or all of these mechanisms are perturbed at least in part in NAFLD. The accumulation of liver lipid occurs as a result of disturbances in several metabolic and inflammatory pathways that are affected by (a) diet, (b) regulation of de novo lipogenesis, (c) adipose tissue function, (d) regulation of bile synthesis and excretion, and (e) regulation of the enterohepatic circulation. Currently, only weight loss and increases in physical activity (where appropriate) decrease hepatic fat, and to date no therapy is licensed for NAFLD. hypertriglyceridemia (e.g., omega-3 fatty acids) may contribute to decreased fatty liver deposition and liver inflammation. Omega-3 fatty acids regulate hepatic lipid metabolism through several discrete mechanisms that may be beneficial in NAFLD: 1. activation of PPARs, which in turn increases hepatic fatty acid β-oxidation, apoB100 secretion, and autophagic degradation, causing a reduction in VLDL synthesis; 2. inhibition of SREBP-1c and ChREBP acivity, reducing hepatic de novo lipogenesis; and 3. reduction of inflammation by inhibiting NF-κB, inhibition of production of inflammatory cytokines including TNF-α and IL-1β receptors, and reduction of arachidonic acid–derived eicosanoids. Furthermore, omega-3 fatty acids may have beneficial effects (a) on lipid storage by regulating intra-adipocyte lipolysis, (b) by downreguating the production of proinflammatory cytokine, and (c) by upregula

7.References

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