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RESEARCH ARTICLE

NON-ALCOHOLIC STEATOHEPATITIS: NON-PHARMACOLOGICAL TREATMENT STRATEGIES: A MINI REVIEW

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ABSTRACT

Among them, non-alcoholic steatohepatitis (NASH), consists of a stage of greater severity and is characterized by the presence of hepatic steatosis, hepatocellular ballooning, micro and macro vesicular steatosis, with inflammatory response, and hepatic fibrosis, has emerged as a cause of chronic liver disease that may lead to severe clinical conditions, which include cirrhosis and hepatocellular carcinoma (HCC).Still in the present moment there is no pharmacological treatment for NAFLD and NASH. However, changes related to the lifestyle of these patients appear as an alternative to generate health benefits of these patients, the RPE and diet modification, as the only way to set this disease. Recents studies have demonstrated that the regular practice of physical exercise associated with a macronutrient intake management causes benefits related to weight loss, body mass index, improve of lipogenic imbalance, inflammatory response, and histological profile in patients. However it is not known fully what the role of RPE and diet modification remaining unclear. The objective of this review is to investigate the role non-pharmacological treatment strategiesin path physiological process in NASH.

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INTRODUCTION

Non-Alcoholic Steatohepatitis (NASH) to one of the leading causes of liver disease leading to severe clinical conditions, including cirrhosis and hepatocellular carcinoma (HCC), (Jarvisen, 2015). NAFLD characterizes a wide spectrum of factors, among them Non-Alcoholic Steatohepatitis (NASH), which is characterized by the hepatic steatosis, hepatocyte ballooning, micro and macro vesicular steatosis, with inflammatory response, and hepatic fibrosis (Pellicoro, 2014; Bataller, 2015). There is still no pharmacological treatment for NASH, which leverages the performance of tools such as RPE and dietary modifications in the intake of macronutrients, which generate, among other benefits such as significant weight loss, body mass index, modifications in body composition and mitochondrial activity, improve of lipogenic imbalance, inflammatory response, and decrease of fibrosis profile in patients (Oliveira et al., 2016; Kistler et al., 2011).

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However it is not known fully what the role of RPE and diet modification remaining unclear. The objective of this review is to investigate the role of non-pharmacological treatment strategiesin NASH.

DEVELOPMENT: For the following review we selected some relevant topics found in the literature to structure comments related to the performance of regular physical exercise in patients with non-alcoholic fatty liver disease and NASH; with emphasis on the regular practice of physical exercise and dietary interventions in these patients with NAFLD / NASH

INSTALLATION OF NAFLD

The NAFLD development process is multifactorial, involving genetic, immunologic, metabolic, and connected to the individual's lifestyle, and these have important associations that lead to a decrease in the health condition of the patient (Fearly, 2012). Among the major mediators this insulin resistance, it indicates an inhibition of transporters GLUT-2 e GLUT-4 (glucose transporter 2 and 4) and insulin receptor

substrate 1 and 2 (IRS-1 e IRS-2). The metabolic deregulation lipogenic causes excessive production by addition to an imbalance in the rate of storage and lipid oxidation with intrahepatic triglyceride installation (Neuschwander, 2013).This metabolic dysregulation causes excessive lipogenic production, through this, to a decompensation in the storage rate and oxidation of lipid, with installation of intrahepatic triglycerides. This accumulation is accompanied by an oxidative energy deficit, gradually cause the NAFLD. (Rinella, 2016; Mehal *et al*., 2011) With this way of lipogenic signaling free to transcribe and express their factors, there is an immediate immune response through a macrophage signaling pathway and subsequent expression of inflammatory pro cytokines such as interleukin 6, 2 (IL-6 and IL-2) and tumor necrosis factor alfa (TNF-a). This inflammatory process tends to activate major signaling pathways in the production of oxidative stress with ROS production (Fallowfield, 2007).In addition, this process immunomodulatory causes activation of signaling cascades fibrogenesis via deposition of collagen in the extracellular matrix (Sechang, 2014; Gonçalves, 2013).Such elements directly impact the health of patients with NAFLD, leading to more chronic disease conditions, directly impact the health of the patient with NAFLD, causing more chronic conditions of this disease. In addition, lifestyle variables with levels of physical activity and di*et al*so contribute to such phenomena. Physical inactivity causes an increased inflammatory state, and reduces the oxidative capacity of acids free fatty (FFA) and when it is associated with high intake of simple carbohydrates (CHO), high dietary levels of saturated fats and decrease the consumption of acids mono unsaturated fatty and polyunsaturated fats, which contribute to systemic deregulation and installation of pathogenic process of NAFLD (Oliveira *et al.,* 2016).

NASH: NUTRITIONAL INTERVENTION: Dietary intervention appears to be of paramount importance for the prevention, treatment and rehabilitation of NASH patients. Since the onset of this pathology is dependent on an exaggerated carbohydrate intake (CHO),(Oliveira *et al.,* 2016) which provides sensitivity and resistance to insulin, through Inhibition of their receptors (IRS). This process produces an excessive mobilization of free fatty acids that convert into intrahepatic triglycerides, which in turn provoke an inflammatory response, a decrease in the FFA oxidation rate and the production of reactive oxygen species (ROS). There is a need to maintain a balanced diet, respecting the proportions of macronutrients in NASH patients, since they must decrease the level of lipid storage and increase their capacity to oxidize them, generating a better quality in their clinical condition (Neuschwander, 2013). It should increase the intake of mono and polyunsaturated fatty acids, since they participate in important lipogenic modulations in hepatic metabolism; furthermore the decrease of a high calorie diet is indicated for maintaining equilibrium in FFA synthesis. In addition, the need to be metabolically active through the practice of regular physical exercise, since physical inactivity reduces the oxidative rate and increase in path physiological processes such as inflammatory response, ROS production and liver fibro genesis which will be discussed later in this review

NASH: REGULAR EXERCISE IN CONTAINING THE FIBROGENIC ADVANCE: Among the conditions found in the path physiology of NASH is liver fibrosis in a chronic consisting immunogenetic process, which occurs through the NASH by sequential aggressions in the parenchymal hepatocytes caused by the fat deposition and inflammation. This active inflammation via macrophage (M1), generating an activation dormant hepatic stellate cells, which in turn transdifferentiation into myofibroblasts express genes such as Transforming growth factor beta (TGF-β), decorin (DCN), elastin (ELN) and collagen (COL), giving the liver tissue a hardened fibrous appearance (Mehal *et al*., 2011). Liver fibrosis is associated with major changes in both the quantity and composition of the extracellular matrix (ECM). In advanced stages of the liver contains about six times more than the normal ECM, including collagens (I, III and IV), fibronectin, laminin, hyaluronic and proteoglycans. The ECM accumulation results from an imbalance between the increased synthesis of inhibitors of metalloproteinases (TIMP) and decreased degradation of fibrotic mesh by matrix metalloproteinases(MMPs) (Fallowfield, 2007).

About this perspective a study conducted in by Oh *et al*. 2014 demonstrated in patients with nonalcoholic fatty liver disease that PA in the form of walk with a quantity of 240 minutes per week decreased liver stiffness which demonstrates that this element is applied properly and supervised manner can modulate the fibrogenic profile of these patients.Such benefits generated by the regular practice of physical exercise, are structured in metabolic increases, resulting in increased oxidative rate of free fatty acids (FFA), directly contributing to improve the liver metabolic phenotype in NASH. Exercise training in appropriate intensity preserves the extracellular matrix events linked to oxidative stress which results in an excessive release of ROS which can clutter cell functionality thus cannot control the deposition of essential membrane proteins cell as keratin, collagen, elastin, and others. (Gonçalves et al., 2013)

Conclusion

Regular PE practice associated with diet modifications appears as a fundamental non pharmacological tool in the clinical management of patients with NASH in need of an effective treatment, as it still does not have in the drug market a medication that is used to contain the path physiological processes.

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