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Diet and Exercise Treatment and Prevention for Non-alcoholic Fatty Liver Diseases Patients

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Abstract. Non-alcoholic fatty liver disease, a chronic metabolic disease, has been studied for decades. There is already well-recognized pathogenesis from pathology, epidemiology, physiology, gene expression, etc. While the understanding of the disease itself is increasing, therapies for this issue seem to have some obstacles: there has been no officially accepted direct pharmaceutical treatment(targeted drugs) until now. Nevertheless, lifestyle regulation has been investigated a lot to fill in this gap. Many researches have already given recommendations in fields of diets or physical activities. However, there is a lack of a comprehensive review to combine both perspectives and give an overview of the disease. This article will review the researches on the lifestyle recommendations for NAFLD patients from both diet and exercise aspects. All the references throughout this research, including journals and literature reviews, are conducted from online databases. The content will mainly discuss the effectiveness of different types of diet and how exercise taking place with respect to reducing the NAFLD risk factors. In brief, most current experimental/observational results suggest that a Mediterranean diet combining with moderate intense exercise could be remarkably beneficial in the management of NAFLD.

Keywords: NAFLD, diet, physical activities, Mediterranean diet, calories control

1. Introduction

NAFLD(non-alcoholic fatty liver disease) is a metabolic disease characterized by 5% excess hepatic fat tissue[1,2]. In recent decades, the risk factors, epidemiology, pathology, and certain therapies have been well studied. The Western lifestyle — commonly characterized by sedentary routines, high energy intake diets, and poor lifestyle — has been considered as the largest element that is responsible for NAFLD. However, genetics, environmental and other personal factors are considered to be essential factors of NAFLD as well. Because there are no officially accepted pharmaceutical or surgical treatments for NAFLD, most research has emphasized the importance of appropriate lifestyle, diet, and physical activities as prevention or treatment[1,2,3,4,5,6]. This article will review some commonly accepted dietary and sportive treatment in the field of nutrient science for NAFLD patients. Thus, the potential effectiveness of different dietary and physical activity plans will be discussed with respect of their interaction with the physiological system. Around 10 journals—which are published within 6 years—regarding the pathology, cause, co-morbidity and dietary recommendations are conducted through Google Scholar, PubMed, and other authorized journal publication channels, to form an overview of the topic. This review may provide a preliminary guideline to NAFLD patients and help with regulating their lifestyle, thereby trying to reduce the mortality or morbidity of NAFLD.

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However, the current knowledge of more specific dietary and sportive recommendations or plans for patients who already got co-morbidity from NAFLD(such as type 2 diabetes, cardiovascular diseases) has not been perfected yet. Plus, the complexity of epigenetics and genetic factors coping with NAFLD is still not clear, though they have been studied for many years. Both perspectives may worth larger effort to further study.

2. Methodology

This research was completely conducted through the Internet, specifically, several academic journal database such as PubMed, Google Scholar, or Science Direct. Throughout the whole research, certain queries were applied to filtrate valid sources: NAFLD, diet, nutrients, exercise, co-morbidity, treatment, and prevention. However, a few criteria were used to evaluate the validity of sources. Firstly, time manner was considered. The research will have to be published no longer than 10 years, and the ones published within the passed 5 years will be given higher precedence. The findings and discussion of sources would have to demonstrate some aspects of NAFLD, which could either be causes of it, its prevalence, dietary or exercise interaction,etc. Furthermore, any results/perspectives without experimental support or other forms of reference will not be taken in. Any journal with primary data will be considered first, and the ones with diagram/visual presentations will take higher priority as well. Plus, the critical thinking section, which would be an investigation on the limitation of dietary/sportive intervention toward NAFLD, will also be accepted as crucial information regarding the topic. Finally, ten academic journals in total were chosen and referred to.

This investigation will first conduct a biomedical definition of non-alcoholic fatty liver disease and briefly introduce its properties. After that, several pathology aspects will be introduced in a general scale, including the different stages of NAFLD pathological development, the simple pathogenesis, and relevant complications of NAFLD. Next, the dietary and other lifestyle-related resolution targets on NAFLD will be demonstrated from different points of view. The importance of appropriate lifestyle implements will be first stressed. Different macro and micro nutrients will then be related onto NAFLD pathogenesis and treatment to find out the biochemical interaction of nutrients and the NAFLD system. On a larger scale, the different types of diet composition and their effects on NAFLD patients will be evaluated, following their limitations and cautions. Meanwhile, the importance of physical activities and their functions in this system will be stressed and shown. Finally, the dietary plan and physical activities will be associated,thereby raising a practical lifestyle guideline.

3. Findings

NAFLD is a chronic acquired metabolic disease. The spectrum of NAFLD vary from individuals. But, pathologically speaking, it may generally be categorized into four stages. Firstly, the hepatic(liver) adipose tissue accumulated without much intervention from alcohol, causing a non-alcoholic fatty liver(NAFL). When NAFL further develop, the hepatic adipose tissue accumulated to approximately 7%-30%, the cell gains inflammation property thus the disease becoming non-alcoholic steatohepatisis(NASH). Long term inflammation then influence the basic composition of liver cell, thus turn the cells fibrous, and this is called liver fibrosis. Finally, when all the liver cells got fibrosis, the liver tissue gets totally dysfunction, causing cirrhosis[2]. There are many factors in charge of attaining NAFLD and its later progression. From perspective of nutrient science, the most common measures of NAFLD progression and treatment are: 1. Insulin resistance, insulin resistance may lead to insensitive reaction to insulin from hepatic tissue and other metabolic systems; in this case, the liver will continuing synthesized lipid with glucose; 2. Intrahepatic lipid content, measurement of lipid proportion in liver; 3. Body mass index(BMI) BMI is a proportion from body weight to height, a comprehensive measurement of body mass and composition[3,5,7,8,9,10]. Pointing on theses factors, many types of diets are proved to be effective, however, the major points in diet with respect to NAFLD are mostly emphasizing low carbohydrate, calories deficit and balancing[1,2,4,5,6]. Moreover, sedentary behaviour is another neglected but leading cause of NAFLD and other metabolic diseases. And sufficient physical activities may counter this effects[2,4].

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3.1. High protein diet

There are few primary resources that investigate how protein-rich diets are linked to NAFLD[4,5]. Nonetheless, some data suggests that a high protein diet can help with NAFLD management. A study investigated two types of high protein diets, which are composed of approximately 30% protein, 30% lipid, and 40% carbohydrate; as a result, this study concluded that high protein diets may reduce IHLC by 36%-48% in patients with T2DM[5]. Another Chinese study also investigated the normal protein level diet, and the result turned out positively as well. However, with the same research group, they then researched on low protein and high carbohydrate diets acting upon NAFLD; in the end, the diet did not improve any indexes despite slight weight loss, but the differences in carbohydrates should be taken into consideration[5]. High quality protein may provide a better substrate for lipoprotein synthesis, lower carbohydrate consumption increases the likelihood of consuming fat as an energy source, and amino acid hydrolysis requires more energy[1]. On the other hand, there is a contradiction regarding these subjects. Some research shows that some protein-enriched diets may even provide negative assistance to NAFLD, and this situation varies from animal protein to plant protein[1,2,3,5]. In a closer view, animal protein is usually consumed through red or processed meats. Red meats may introduce high saturated fatty acids and a high level of iron, two factors that show a positive correlation with IHLC and the risk of NAFLD[1,5].

3.2. Intermittent calories restriction/intermittent fasting

Intermittent calories restrictions(ICR) is a diet plan that emphasizes on the rhythm and frequency of intake rather than the composition of diets. Much research has shown that consuming energy at night or prolonging the normal prandial period can disrupt the normal metabolism rate, putting additional strain on the liver and other metabolic systems[4]. ICR is characterized by a period of very low or no calorie intake plus a fasting period of taking in high energy foods[5]. In most cases, people will fast(or eat very few calories) for one or two days and then eat normally for the rest of the week. In a random control trial(RCT), participants took an average of 9 days of a very low calorie diet. The results turned out to be that half of the participants had reduced pathological fatty liver indexes[4]. Moreover, a conclusion has been drawn that factors like intensity of ICR, WL, and BMI reduction have a linear correlation with reductions in NAFLD risks[3,4]. Moreover, this study combined ICR with moderate physical exercise such as paved walks; the elements may contribute to metabolism and lowering BMI. For the other half of the participants, there are many factors that may drive the result away from expectations, including the potential high fat diet in the normal intake period[4]. In general, a number of studies have shown that ICR has beneficial effects in its early stages, such as increasing insulin sensitivity, decreasing adipose mass, and improving cardiovascular metabolism[4].

3.3. Mediterranean diet

The Mediterranean Diet(MED Diet) is the most investigated and proved to be potentially the most effective dietary lifestyle in terms of chronic disease management[1,2,4,5,6,7,8]. The MED Diet originated in the Mediterranean region, characterized by relatively higher fat intake but mostly monounsaturated fatty acids (MUFA) or polyunsaturated fatty acids(PUFA)[6]. In the MED Diet, olive oil and nuts are major sources of oil. As a result, the MED dietary oil is high in Omega-3 PUFA, fatty acids that may aid in the normal synthesis of adipose tissues and lipoprotein[5,6]. Moreover, the MED diet emphasizes rich fruits and vegetables, plus whole grains and legumes. This meal composition provides sufficient dietary fiber and vitamins[4,5]. The main protein recourse from the MED diet is from fish or seafood rather than red meat and dairy products, another difference compared to other diets(especially the Western ones). In general, approximately 35%-45% of lipids, 35%-45% of carbohydrates, and 15%-25% of protein exist in the MED diet[6]. Figure 1 demonstrates the very general composition of the MED Diet.

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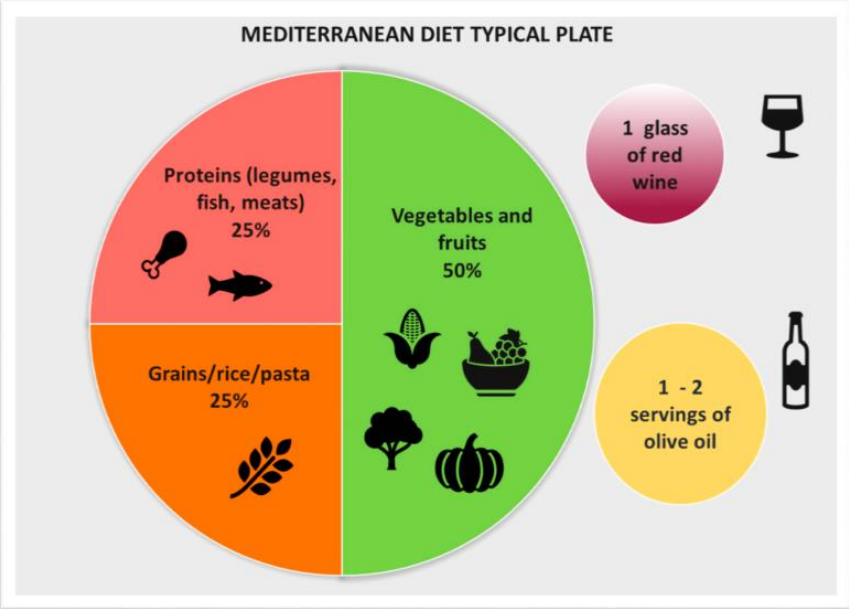

Figure 1. Typical composition of meditarrean diet [6].

MED Diet has the advantages on rich MUFA, PUFA, dietary fibers, and less added sugar, fructose [4,5,6]. Currently, the macro-nutrients in MED Diet show beneficial influences on adipose and glucidic metabolism, thus also beneficial to non-alcoholic fatty liver diseases. MUFA can induce the MetS-related risks such as lowering triglycerides level in bloods, cholesterol in high density lipoprotein, glycemic level as well as general body fats [6]. A study of providing NAFLD patients with MUFA enriched diets, and the results turned out with positive effects. In that study, the researcher found MUFA in MED Diet and mostly came from olive oil, which may improve the steatosis condition, though the body weight did not lose much [6]. When it comes to PUFA, it may drag down the pressure of the cardiovascular system by decreasing insulin resistance, raising the anti-inflammation ability, reducing hepatic adipose accumulation and slowing steatosis. These benefits are clearly expressed through omega-3 fatty acids [2,5,6]. Notably, some research states that to receive most benefits from omega-3 fatty acids, there should be relatively lower omega-6 fatty acids intake. The best status is to have a low ratio of omega-6 to omega-3[6]. However, there is a lack of evidence to describe the function of omega-3 fatty acids in fibrosis management. Dietary fibers, another emphasis in MED Diet, may moderately adjust gut microbiota, making them regulate NAFLD risk factors 2,4]. MED Diet is enriched in whole grain and vegetables. This brings the consumer a large amount of dietary fibers. Compared to other processed/refined carbohydrates, fibers has a lower calorie s density, which provides higher satiety. There are many studies already proved that dietary fibers may regulate the bacteria biome in intestines to produce larger amount of short-chain fatty acids, which has anti-inflammation functions, and accelerate fatty acids metabolism, thus causing a decline in hepatic triglyceride level and blood cholesterol level [6]. Low added sugar is also present in the MED Diet, which is another factor that benefits NAFLD and other MetS [1,6,7,8]. It is reported that there is a linear relationship between artificial refined sugar, high-fructose additives, high carbohydrate mass products and NAFLD development [1,6]. In Western Diet, fructose and corn syrup (dense in fructose and sucrose-fructose plus glucose) beverages is a heavy burden for NAFLD patients. There are already massive researches summarized that overdosed fructose are account for high IHLC and de-novo lipogenesis (DNL, new born liver adipose) [1,5,6]. Fructose is one of the most effective substrate for synthesizing lipid tissues, and fructose may alter the glycolysis expression into DNL expression in hepatic cells, which is the mechanism that further boosting IHLC growth [2]. Lastly, low consuming in red meats yields low intake of saturated fatty acids and cholesterol. Besides that, many

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processed/red meats might contain high iron elements, which is another abnormal index found in most NAFLD and other MetS patients [1,2,5,8].

3.4. Other diet composition

3.4.1. Alcohol. Alcohol intake is quite a contradictory factor with respect to NAFLD and other MetS. Several researches found that a moderate drinking lifestyle-lower than 20mg alcohol/day (less than two glasses of wine) and drinking everyday-demonstrated healthy effect on NAFLD issues [6]. In this case, some doctors recommend an appropriate daily intake of alcohol. On the other hand, more recent studies gave results that moderate alcoholism shows a lower proportion with treated NAFLD compare to those complete abstainers. Furthermore, moderate drinkers sometimes demonstrates higher possibility of further development in NAFLD, from NAFLD to NASH or liver fibrosis [5]. In short, the exact effects of alcohol on NAFLD patients need to be researched more to find out the implicit interacted factors.

3.4.2. Coffee. Though there are many unclear factors in coffee, in terms of its effects on NAFLD, most existing studies agree that coffee can positively affect overall metabolic and certain organ's health [1,2,4,5,8]. Some researches present data that: "Any coffee consumption was associated with 29% lower risk of NAFLD, a 30%-39% lower risk of fiber fibrosis, and a 39% lower risk of liver cirrhosis" [5]. For other liver diseases, there are evidences demonstrated a inversely proportional relationship between dose of coffee to liver-related deaths and liver fibrosis (within a recommended dose) [5]. A study found a significant difference in coffee consumption between the NASH/Liver fibrosis patients and well controlled NAFLD ones [6]. Under such circumstances, there are recommendations of drinking less than 3 cups of coffee per day [5]. The beneficial effect brought by coffee could be explained by an assistance in Beta-oxidation of hepatic tissues, and certain phenolic substances may help with metabolic issues.

3.5. Physical activities and exercises

Sedentary behaviour has clearly been proved to be associated with more than 30 types of chronic/metabolic diseases disregarding their diet composition and other lifestyles [4,5]. An epidemiological study presents a significant difference in changes of getting HCC between people who regularly exercise and those do not [5]. Physical activity is critical in metabolism regulation and body weight control, especially in terms of insulin and lipoprotein [4,5]. Regular exercise may help to improve appetite-control, raise insulin sensitivity and metabolize low density lipoprotein, thus liver may export more triglycerides [5]. In certain analysis, athletes with excellent cardiovascular function and physical exercise capacity usually demonstrate a higher variety of micro biome [5]. However, there is no clear recommendations for types of exercise to manage MetS and NAFLD. Some evidences suggest aerobic exercise due to the higher energy consumption and more training on cardiovascular functions, but there seems to be no obvious differences between medium intentisy aerobics and high intensity aerobics toward NAFLD/WL issues [5]. On the other hand, resistance training (mostly anaerobic exercises) shows a higher capacity in patients who are poor in cardiorespiratory conditions [5]. In the end, most analysis reaches consensus on a significant benefit from dietary therapy coping with physical activities with respect to most MetS and NAFLD patients [1,2,3,5,7,8,10]. Exercise corporate with diet control usually shows a large improvement in IR, WL, and IHLC [4,5,6]. MED Diet with physical activities yields a really positive measurement in hepatic steatosis of NAFLD patients [5].

4. Discussion

Though the prevalence of NAFLD is not in a serious scale, the treatment or prevention regarding the issue can be basic and straightforward. In current stage of researches, the most essential risk factors for NAFLD are weight, IHLC, IR, and gut bacteria biome. Directly pointing on these factors, physical

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activities/exercises should be consistently implemented, with combinations toward several dietary controls. Amount on, NAFLD patients should mainly focus on carbohydrate and fat control(their weight in total intake), total calories intake and macro-nutrient composition in meals. Since most types of dietary plan may contribute to regulating NAFLD, patients should carefully design their diet depending on personalized health condition. Plus, without considering the main diet source, coffee can be an additional save material to assist in this progression. Beside the primary composition of management plan, consistency should be take in considered to ensure a long-term liver health security as well as the whole metabolic system. Lastly, since physical activities, diet, and coffee may influence people's circadian rhythm and both physical/emotional status, patients should take their social activities into consideration and balance them.

5. Conclusion

To summarize, calories-controlled Mediterranean diet combining appropriate type/intensity of physical activities and assisted with coffee seems to be the most effective lifestyle modification for NAFLD and the patients. Of course, if patients have got co-morbidity already, they should take the mixed interactions into account. This article concluded some of the most well-accepted NAFLD strategies. However, it is a bit weak on more evidence to discuss micro-nutrients and potential genetic factors in the whole picture. In the end, for the whole field of NAFLD research, the complex genetic, nutrition, pathology, and co-morbidity may all be further studied, in an attempt to build a more smooth and comprehensive recommendation.

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