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Non-alcoholic fatty liver golden standard therapy-exercise therapy

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ABSTRACT

Non-alcoholic fatty liver (NAFLD) is a serious chronic diseases, which harms to public health seriously. The article analyzes the risk factors for NAFLD. The evidences have shown that the drug treatment is unclear. Exercise therapy can Prevent NAFLD is accepted, which is the gold en standard for the treatment of NAFLD. Appropriate ways of exercise, intensity of exercise, time of exercise, frequency and duration of exercise, amount of exercise can ensure effectiveness of exercise therapy. Some basic scientific data is still lack of Evidence-based medicine on exercise therapy of NAFLD. We must further research on the clinical trials.

KEYWORDS

Non-alcoholic fatty liver; Exercise therapy.

INTRODUCTION

Fatty liver is an abnormal condition of the liver that is characterized by lipid accumulation in the hepatocytes to the extent that lipids account for more than five percent of liver weight and that is caused especially by injury, malnutrition, or hepatotoxins[1]. The clinical types are usually from course, etiology or pathology. The clinical types can be divided into acute or chronic in the course of the disease. The clinical types can be divided into non-alcohol, alcohol, drugs, genetic from the cause. The clinical types can be divided into simple fatty liver, fatty hepatitis and fatty liver cirrhosis from pathological types.

The most common type is non-alcoholic fatty liver disease (non-alcoholic fatty liver disease, NAFLD), NAFLD metabolism is more than one syndrome[2], such as dyslipidemia, hypertension, central obesity, diabetes or coronary heart disease. NAFLD can not only cause of acute hepatitis and chronic liver cirrhosis, may also lead to gene mutation which can bring about cancer.

THE EPIDEMIOLOGICAL DISTRIBUTION OF NAFLD

China is a high risk area in the pathogenesis of NAFLD. Fan JG[3] survey data show Chinese NAFLD after the incidence of viral hepatitis, is China's second largest liver disease. Shanghai city in 2008[4] random sampling 2226 cases, calculated the average incidence of the year in Shanghai City, NAFLD rate was 23.3%, that means the incidence of fatty liver in China already exceeds the rate of South Korea, Japan or other East Asian population[5,6]. Nowadays in china, NAFLD has become a major disease which seriously threatens people life safety. Unfortunately, there is no reliable way to prevent the rapid growth of the incidence of NAFLD.

RISK FACTORS OF NAFLD HAS THE DOUBLE CONTRADICTION

Many factors can induce the production of NAFLD, the research shows that risk factors for NAFLD than expected in the complex, such as obesity and weight loss, metabolic syndrome and deficiency of nutrition. The two seemingly opposite factors may induce the occurrence or deterioration of NAFLD.

TABLE 1 : Risk factors of NAFLD has the double contradiction

	Risk factors	result
Weigt	Obesity	The incidence of NAFLD in obesity is about 90%
	Rapid weight loss	Even nonalcoholic steatohepatitis (NASH)
Nutrition	Metabolic syndrome	Related to type 2 diabetes, obesity, hyperlipidemia and other metabolic syndrome
	Malnutrition	Leading to NAFLD with inflammation and fibrosis of liver cells.

Obesity or rapid weight loss may be the risk factors for NAFLD

Obesity is most important factor for NAFLD

Obesity is a risk factor in the pathogenesis of NAFLD. Fat accumulation in the liver weight is proportionate to body weight. So the BMI index and body fat is the most significant risk factors for fatty liver. Epidemiological investigation[7] shows, the incidence of western developed countries, ordinary people NAFLD rate is around 20-30%, however, the incidence of NAFLD in obesity is about 90%, the incidence of childhood obesity rate is 53%.

Rapid weight loss is also one of the risk factors of NAFLD.

A study of America[8] pointed out, weekly weight loss should not exceed 1.6kg. The study makes 41 pathological overweight lost an average of 34kg, resulting in 24% people appeared different degree of hepatitis and cirrhosis of the liver. Fasting, rapid weight loss, drugs and so on, can cause liver enzyme system is activated rapidly, and make liver malondialdehyde (MDA) and lipid peroxide rapid accumulation, and then induced NAFLD, even nonalcoholic steatohepatitis (NASH). On the other hand, rapid weight loss often means a quick rebound in weight, thereby increasing the burden on the liver. So the rapid weight loss is also important pathogenic factors of NAFLD.

Metabolic syndrome or malnutrition can cause NAFLD

Metabolic syndrome is a risk factor for NAFLD

Historic evaluation[9] demonstrated that a series of metabolism in type 2 diabetes as the representative of the syndrome is associated with NAFLD. Some scholars[10] think that NAFLD is a component of the metabolic syndrome. However, the latest research results that NAFLD does not belong to the metabolic syndrome, the mechanism behind many worthy of in-depth study of the problem.

USA government[11] in 2013 February to historical data were comprehensive evaluation, summarize 3846 cases of excess nutritional status in patients with metabolic syndrome, 30.2% patients have fatty liver, and then analysis to obtain the conclusion: according to the severity of NAFLD is closely associated with the metabolic syndrome, but there is no evidence

that NAFLD is a component of metabolic syndrome, also cannot prove that NAFLD is the characterization of metabolic syndrome.

A number of studies[12] have demonstrated that, NAFLD is highly related to type 2 diabetes, obesity, hyperlipidemia and other metabolic syndrome. Previous studies showed that NAFLD and metabolic syndrome contact may be insulin resistance (IR), IR directly affects the synthesis and decomposition of TC and TG, lead to the peroxide accumulation. TNF-α, IL-1 β, IL-6, NF-kB, natural killer cells, osteopontin, leptin, adiponectin, angiotensinogen, norepinephrine, osteopontin, endoplasmic reticulum stress hormones in the IR process plays a transmission function, any one disorder may lead to the occurrence of NAFLD. Gene, racial, Hedgehog (HH) pathway and so on, further analysis shows that NAFLD is a complex disease. The matrix and logic behind all kinds of appearance, it is still not clear.

Malnutrition which is an important factor in NAFLD

Malnutrition also induces fatty liver. Malnutrition[13] means that deficiency of high density lipoprotein, resulting in fat metabolism disorder and the incidence of NAFLD is rising sharply. Lack of vitamin D, osteopontin, osteocalcin, and osteoprotegerin, fetuin-A not only can lead to osteoporosis, but can lead to NAFLD. Imbalance of intestinal flora[14] leads to choline too little, so as to made metabolism disorder, then leading to NAFLD. The lack of vitamin E, vitamin C, magnesium, alpha lipoic acid, potassium, can lead to NAFLD with inflammation and fibrosis of liver cells.

DIAGNOSIS AND TREATMENT OF NAFLD

NAFLD diagnosis standard appeared significant differences between China and USA.

NAFLD diagnosis standard is the different between China and USA. Chinese standard about fatty tissue is greater than 33%, American definition that there are more than 5% fatty can be diagnosed as NAFLD, in which no inflammation and no liver cell damage that is called NAFL. In accordance with the American diagnostic standard, the early prevention and treatment of NAFLD may be more effective.

The cognition of NAFLD is opposite. The review of the American government in 2013[11] thinks that NAFLD is not part of the metabolic syndrome, and China standard thinks that NAFLD is a component part of the metabolic syndrome. Chinese guide[15] states "metabolic syndrome with unexplained serum alanine aminotransferase (ALT) and (or) aspartate aminotransferase (AST), glutamine transferase (GGT) increased continuously for more than half a year to consider NAFLD", and America guide does not have any recommendation.

The treatment for NAFLD concept also has some obvious differences. If the improper use of drugs in the treatment of metabolic syndrome, is likely to aggravate the burden of the liver. So NAFLD syndrome drug metabolism in patients with limited American standards than China standards more stringent. USA Medical institutions[12] does not recommend normolipidemic subjects using the Omega-3 fatty acids and statin lipid-lowering drugs, not recommended for normal glucose patients using metformin and rosiglitazone-hypoglycemic drugs, is prohibited due to the existence of adverse cardiovascular effects, pioglitazone may also exist for a long time the safety problem, does not allow use vitamin E for diabetics, the experimental results also show that ursodeoxycholic acid is possible without any clinical curative effect.

Exercise therapy is the gold standard for the treatment of NAFLD.

There are many methods to treat NAFLD. Weight loss drugs (orlistat etc.), hypoglycemic agents (metformin, troglitazone, pioglitazone and rosiglitazone etc.), lipid-lowering drugs (clofibrate, bezafibrate, atorvastatin or other statins etc.), antioxidants (vitamin C, vitamin E, glutathione), cell protective agent (such as taurine, ursodeoxycholic acid etc.), Chinese medicine (Chinese herbal medicine, massage, acupuncture, bloodletting etc.), and multiple therapy is often used. Diversity has also led to that not enough samples passed Randomized controlled trials. Emmanuel[16] think, from the evidence based medicine, there is no evidence to show that a treatment of NAFLD have conclusive value.

The scientific and reasonable exercise therapy[8] was recommended as the highest level of A, not only can correct the NAFLD lipid metabolism disorder, also can reduce the risk of NASH and liver fibrosis, more effective control of NAFLD associated with metabolic syndrome.

Compared with drug therapy, reasonable exercise therapy has not to worry about the side effects of drugs and other iatrogenic risk, is more suitable for large sample randomized control study. In recent years, USA[11], Japan[17], South Korea[18] and other developed countries research institutions are working on NAFLD historic evaluation, national census nature of the screening, large sample randomized controlled study, associated with other major diseases on several aspects, exercise therapy effects and so on.

EXERCISE THERAPY OF NAFLD

Exercise therapy has a wide applicable people, lower cost, but still has some risk. We must research ways of exercise, intensity of exercise, time of exercise, frequency or cycle of exercise. If lost weight too fast, malnutrition or other metabolic abnormalities, The incidence of NAFLD disease will increase.

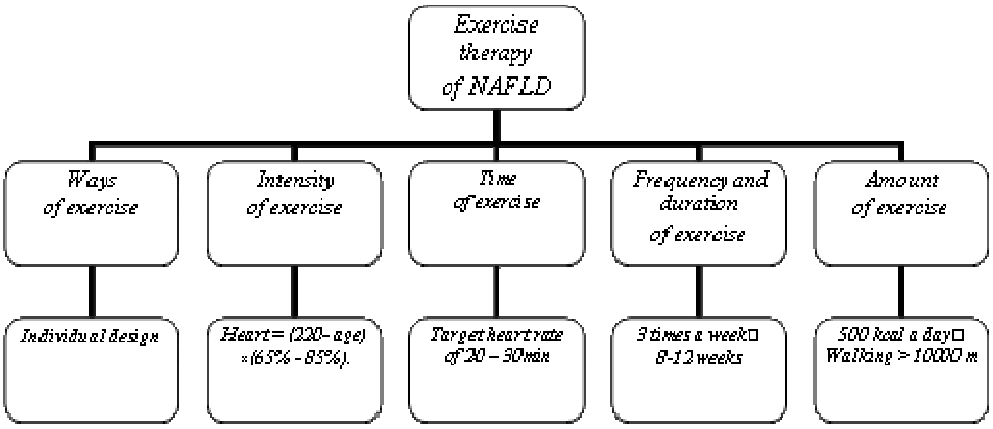

Figure 1 : Exercise therapy of NAFLD

Ways of exercise

Exercise therapy of fatty liver needs to control weight, on the other hand, can not lose weight too fast. Ways of exercise must be easy to insist for a long time. The body often gets exercise and do not feel fatigue.

Exercise should focus on their own interests and personal habits, it is for long-term exercise to achieve clinical efficacy. Because of individual differences, such as environment, lifestyle, sports, and different fatty liver severity, must exercise program by individual design.

Intensity of exercise

Exercise intensity evaluation mainly from the maximal oxygen uptake (VO2max) is difficult to measure. There is a formula between exercise intensity and oxygen consumption. Heart rate can be used to control of aerobic exercise intensity.

Moving target heart rate is too low, no consumption of fat tissue. Moving target heart rate is too high, while improving the glucose uptake, without increasing the consumption of adipose tissue; only the target heart rate maintained at a reasonable level, can effective consumption of fatty tissue. The ideal state of aerobic exercise is the maximum heart rate of 65% ~ 85% as the target heart rate. Formula is Target Heart Rate = (220- age) ×(65% - 85%).

Considering that NAFLD should not too fast, choose 65%-75% heart rate as the basis for the exercise intensity. The NAFLD prevalence about 50 years of age, the heart rate is about 110-128 times in 1 min. The intensity of exercise is acceptable for most of the people.

Time of exercise

Time of exercise has three modes: unit of exercise time, period of exercise, right exercise time.

Unit of time, most of scholars think that the aerobic exercise to reach the appropriate target heart rate of 20 ~ 30min can effectively fat consumption. Keep in the medium intensity exercise (such as 65%VO2max), fatty acid consumption rate varies with the time of steady growth, the coupling mechanism of the exercise intensity and time, may be one of the key physical therapy to prevent NAFLD.

Period of exercise time of NAFLD patients can be divided into three steps: one is the warm-up phase, about 5 to 10 minutes, to ensure the full range of stretching limbs joints. The second exercise step, about 20 to 30 minutes, the motion target heart rate control in 65%-75%VO2max to achieve the purpose of slight depletion in adipose tissue. The third step, about 5 to 10 minutes, recover the muscle to relax state.

Right time is very important. Previous studies showed that, the afternoon or evening is more suitable for exercise. The best time is 30-60 minutes walk after dinner, is the largest energy consumption time of a day. Shanghai area in China[19] medical diagnosis of new onset patients with fatty liver in 182 cases, were randomly divided into intervention group and control group, results showed: the intervention group taking a walk after supper is better by ultrasonic examination.

Frequency and duration of exercise

Frequency of Exercise refers to the interval of the movement. Recovery of muscle glycogen is about 24-48 hours after exercise. So the intermittent training helps to relieve muscle fatigue, while avoiding excessive weight loss. An American study[20] showed NAFLD needs 150min exercise weekly, can produce weight loss. In other words, the weekly exercise frequency is 3 times can achieve the purpose of exercise.

Duration of exercise is the 8-12 weeks of exercise, can show the clinical effect. Submaximal exercise therapy (50%VO2max)[21] after 8 weeks of treatment seems to improve mild fatty liver (aged 55 ± 12, BMI 33 ± 5 kg/m2, 17 ± 9% fatty liver degeneration), plant nerve disorder, regulation of hemodynamics. South Korea[18] screening of 72359 without diabetic adults, part of the crowd after 3 months of regular exercise, results show the incidence of NAFLD decreased.

Amount of exercise

Amount of exercise refers to the sum of energy consumed by the body in different sports. It means the intensity of

exercise times the time of exercise, can show a movement of the total energy consumption, can also show a period of energy consumption, so many research often to use kcal, which is the key point evaluation.

Research[8] in the United States believe that NAFLD patients on an average day 500 kcal, weekly 0.45 kg weight loss is the ideal state, could help control weight and does not cause significant side effects, thus effective control of nonalcoholic fatty liver disease. Another randomized controlled[18], according to the results of after 48 weeks people lose weight by an average of 7% in sports training, ALT average also dropped significantly.

Some scholars[22] set the number of daily walk to represent amount of exercise, think less than 5000 steps a day is a sedentary lifestyle. NAFLD patients after 3-14 days great amount exercise (> 10000 m) on foot, compared with small amount of exercise (walking < 5000 m), change immediately, the former improvement in insulin sensitivity, blood glucose, while the latter does not have any change. The experiment indicates a small amount of exercise (walking < 5000 m) can not alleviate the negative factors of NAFLD.

EXERCISE THERAPY REMAINS CONTROVERSIAL

Lifestyle changes are the first line therapy in American NAFLD treatment program. Moderate energy intake, balanced nutrition diet, reasonable exercise, became the golden therapy in USA. Exercise therapy is the most effective to prevention or treatment of NAFLD, has received worldwide recognition. USA guide has been on BMI quantification, weight drop in at least 3% ~ 5% can alleviate fatty liver, more than 10% weight loss can alleviate the inflammation and necrosis of liver.

Many scholars have put forward different views, a series of retrospectively reviewes explains the improper weight loss is one of the main reason of NAFLD. Scientists[8] have suggested, that the "second hit" during the development of NAFLD, oxidative stress and lipid peroxidation may be the key to liver damage. The author thinks, operation, fast fat loss, weight loss drugs, high intensity exercise, or etc can increase the liver the "second hit", which can produce peroxide accumulation resulting in lipid metabolic disorder. That is why the rapid weight loss may lead to the deterioration of NAFLD.

CHINA MUST MAKE THE CLINICAL GUIDE ON NAFLD EXERCISE THERAPY

After the historic evaluation and survey of nonalcoholic fatty liver disease, NAFLD exercise therapy need to be further explored in China. Many researchers provides basic data on exercise prescription for NAFLD, such as ways of exercise, intensity of exercise, time of exercise, frequency and duration of exercise, amount of exercise etc. but exercise prescription has not yet reached the clinical standard. A treatment for the gold standard must be clear to all kinds of parameters and its reliability and validity.

China should build up a medical standard for NAFLD exercise therapy, design a scientific and reasonable exercise prescription, clinical test carry out in accordance with the principles of RCT. After the medical standard is established, china may decrease significantly the incidence of NAFLD.

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