

Systemic Review: Role of Lifestyle Interventions for The Treatment of Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Background: Non-alcoholic fatty liver sickness (NAFLD) is a variety of liver pathological conditions that intensely related to other chronic diseases including obesity and diabetes.

Objectives: Systematically evaluating the role of lifestyle interventions on reducing the activity of NAFLD.

Methods: Collecting all the studies regarding the effects of changing the diet, exercise or combination of both on the activity or markers of NAFLD during the period from 2006 to 2017.

Results: Database searches returned 122 citations with 92 included in more than one search then the final studied which include in this study was 19 articles. Five articles studied the effects of a combination of dietary and exercise interventions, four of these articles showed positive results regarding the Dietetic Association (ADA) Quality Criteria Checklist, while only one article showed a neutral results, i.e. 80.0% of the articles showed a positive effect of the combination of diet and exercise on the effect of NAFLD patients.

Conclusion: This review showed that the combination of healthy life interventions, including exercise and health diet, are effective in reducing the activity of NAFLD and could result in complete reversal of the condition. Thus NAFLD patients are advised to lose about 10% of their weight and engaging in regular exercises for 5 days per week.

Keywords: Systemic review, Lifestyle interventions, Management, Non-alcoholic fatty liver disease.

INTRODUCTION

Non-alcoholic fatty liver sickness (NAFLD) is a variety of liver pathological conditions that intensely related to other chronic diseases including obesity and diabetes. It is also defined as the hepatic factor for metabolic syndrome and the most long-established etiology for international chronic diseases of liver⁽¹⁾. The prevalence of NAFLD is as about 45% of the adult population around the world but also its incidence could differ depending the ethnicity and development of populations⁽²⁾. About 50% of NAFLD patients could develop complications as steatohepatitis, cirrhosis, fibrosis, liver failure and hepatocellular carcinoma^(3,4).

The NAFLD diagnosis can best be made in the absence of high ethanol intake and the exclusion of other comorbidities including hepatitis C, malnutrition and inflammatory bowel disease as well as excluding the other causes of steatosis^(4,5). Importantly, the disease can be delayed or even reversed during early stages using therapeutic agents and nutritional supplementation⁽⁶⁾. Although, there is no specific medication for NAFLD till now; changing the lifestyle and weight loss are still the best clinical management in all guidelines^(4,5).

Many studies showed that weight loss and increasing the physical activity pattern are related to

improvement in the metabolic syndrome thus reducing steatosis⁽⁶⁻⁹⁾.

The aim of this systemic review is to evaluate the interventions involving eating regimen, weight reduction and exercise which could decrease the activity and biomarkers of NAFLD in adults.

METHODS

Information sources and search strategy

Methods of the analysis and eligibility criteria were specified prior to the literature search with Prospero (CRD42016032764). The review was conducted by SK according to Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines at the 10 last years. The search terms were 'role of Lifestyle interventions for the treatment of non-alcoholic fatty liver disease.', 'NAFLD and weight loss' and 'NAFLD and diet/diet, reducing' for all available database. The searches were limited to clinical trials, human studies, English language and journal articles only.

RCTs in human adults of any gender/ethnicity with a diagnosis of NAFLD, non-alcoholic steatohepatitis (NASH), fibrosis or NAFLD-based cirrhosis made on validated biochemical, radiological or histological evidence were included;

other causes of fatty liver disease were excluded. Papers excluded from this review were: non-human studies, letters/case reports, studies relating to children, articles not reporting primary outcomes of interest or primary data reporting, and trials using non-invasive methods that have not been validated. Included trials had to have measured as primary outcomes either: changes in biochemical, radiological or histological markers of NAFLD in response to a diet, weight loss or exercise (or combination of these) intervention. The validity of eligible RCTs was assessed using the American Dietetic Association (ADA) quality assessment tool (10).

The study was done after approval of ethical board of King Khalid university Statistical analysis

Statistical analysis was performed using the Cochrane systematic reviews (Review Manager 5.3) (11).

RESULTS

Search Results

The identification and selection of eligible studies included in this review are illustrated in figure 1. Database searches returned 122 citations with 92 included in more than one search. Following removal of studies for the reason described in Fig. (1), the final studies which were included in this study were 19 articles. The different data of this study are shown in table 1.

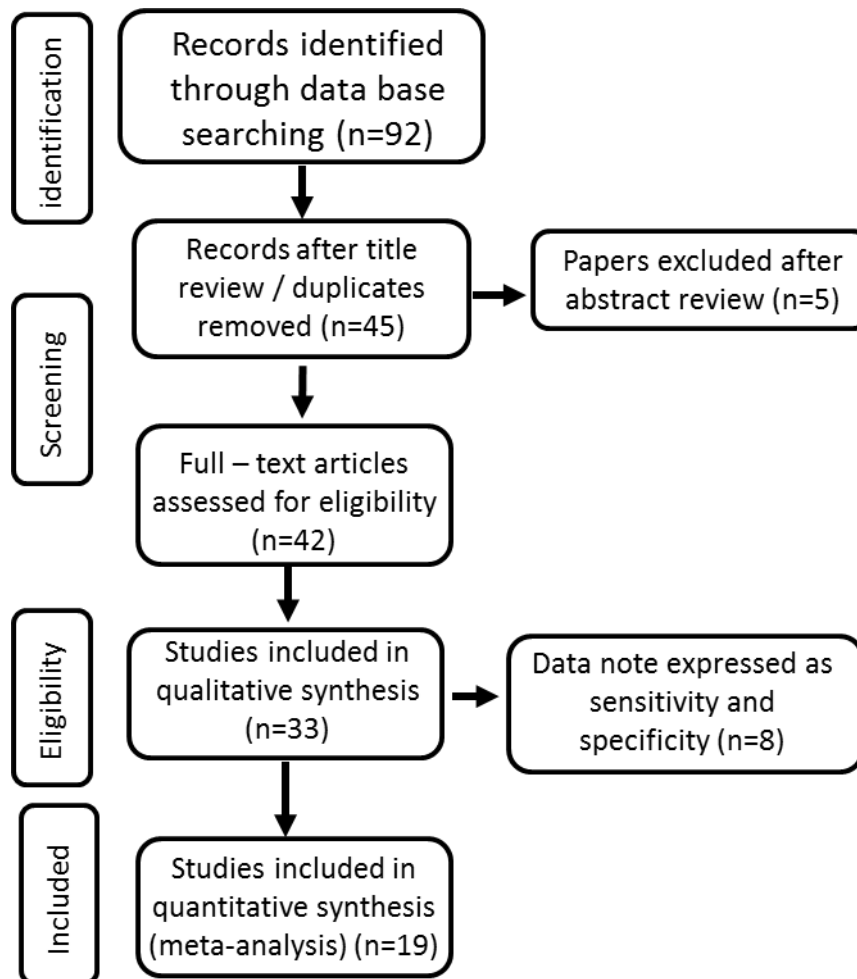


Fig. (1): Flow chart for identification and selection of studies in the systematic review

The articles in this study were divided into three classes of intervention and information was recorded from each included trial, as shown in table (1):

1. Dietary interventions
2. Exercise interventions
3. Dietary and exercise intervention.

Table 1 Main characteristics of studies included in the systemic review.

Ref. No.	Author (year)	Title	Age Range	No. of cases	Outcome measures	Conclusion
(12)	<i>Tock , 2006</i>	Nonalcoholic fatty liver disease decrease in obese adolescents after multidisciplinary therapy	15–19	73	significant reduction in visceral adiposity and nonalcoholic fatty liver disease prevalence	The short-term treatment suggests a profound impact on the control of obesity-related comorbidities in young people
(13)	<i>de Piano , 2012</i>	Long-term effects of aerobic plus resistance training on the adipokines and neuropeptides in nonalcoholic fatty liver disease obese adolescents	15–19	58	higher magnitude of change in the subcutaneous fat, glycemia, total cholesterol (TC), low-density lipoprotein-cholesterol, ALT, and adiponectin in response to AT+ RT than in the control group (AT). All patients who underwent the AT+ RT	The long-term interdisciplinary therapy with AT+ RT protocol was more effective in significantly improving noninvasive biomarkers of NAFLD
(14)	<i>George , 2009</i>	Effect of a lifestyle intervention in patients with abnormal liver enzymes and metabolic risk factors	40-64	152	Reduction in liver enzymes was greatest in the moderate-intensity intervention group and least in the control group	Moderate and even low-intensity lifestyle counselling interventions targeting improvement in physical activity and nutritional behaviors and modest weight loss are a practical and effective method for improving the health

(15)	Hallsworth , 2011	Resistance exercise reduces liver fat and its mediators in non-alcoholic fatty liver disease independent of weight loss	33-72	38	relative reduction in liver lipid, Lipid oxidation	This is the first study to demonstrate that resistance exercise specifically improves NAFLD independent of any change in body weight.
(16)	Eckard , 2013	Prospective histopathologic evaluation of lifestyle modification in nonalcoholic fatty liver disease: a randomized trial	18-70	56	significant change was found in pre- to post-NAFLD activity score	Lifestyle modification improved liver histology, as verified by repeat biopsy, after a 6-month intervention
(17)	Angulo, 2007	Obesity and Nonalcoholic Fatty Liver Disease		129	The impact of NAFLD on health-related quality of life is currently being evaluated. Several studies have found a significant detrimental impact due to several comorbidities that are associated with the metabolic syndrome	Further studies are necessary to determine the impact of NAFLD on health-related quality of life, as well as the extent to which preventing the development of the metabolic syndrome will prevent NAFLD
(18)	Bacchi , 2013	Both Resistance Training and Aerobic Training Reduce Hepatic Fat Content in Type 2 Diabetic Subjects With Nonalcoholic Fatty Liver Disease (the RAED2 Randomized Trial)	40-70	31	hepatic fat content was markedly reduced	Resistance training and aerobic training are equally effective in reducing hepatic fat content among type 2 diabetic patients with NAFLD

(19)	Balducci , 2015	Volume-dependent effect of supervised exercise training on fatty liver and visceral adiposity index in subjects with type 2 diabetes The Italian Diabetes Exercise Study (IDES)	40-60	606	AST, ALT, FLI and VAI decreased significantly	Fatty liver index (FLI) and visceral adiposity index (VAI) decrease with supervised training in a volume-dependent manner
(20)	Cuthbertson , 2016	Dissociation between exercise-induced reduction in liver fat and changes in hepatic and peripheral glucose homoeostasis in obese patients with non-alcoholic fatty liver disease	50-52	50	quantify changes in hepatic and peripheral insulin sensitivity, a pre-determined	Patients with NAFLD exercise-induced reduction in liver fat is related to the improvement in cardiorespiratory fitness and accompanied by an improvement of peripheral (muscle and adipose) but not hepatic IR.
(21)	George AS, 2009	Effects of Physical Activity in Patients with Nonalcoholic Fatty Liver Disease	35-55	141	Lipid profile and liver enzymes decreased	Lifestyle counseling interventions are effective in improving physical activity behavior. Maintaining or increasing physical activity provides health benefits for patients with fatty liver
(22)	Johnson , 2009	Exercise Training Reduces Hepatic and Visceral Lipids in Obese Individuals Without Weight Loss	30-52	23	Significantly reduced visceral adipose tissue volume. reduction in plasma free fatty acids	Regular aerobic exercise reduces hepatic lipids in obesity even in the absence of body weight reduction

(23)	Kantartzis , 2009	High cardiorespiratory fitness is an independent predictor of the reduction in liver fat during a lifestyle intervention in non-alcoholic fatty liver disease	35-56	170	The most pronounced changes were found for liver fat (231%, p <0.0001). resolution of NAFLD	Cardiorespiratory fitness, independently of total adiposity, body fat distribution and exercise intensity, determines liver fat content in humans, suggesting that fitness and liver fat are causally related to each other
(24)	Keating , 2015	Effect of aerobic exercise training dose on liver fat and visceral adiposity	40.0-49.0	48	There was a significant change in group time interaction in liver fat, which reduced in HI:LO , LO:HI and LO:LO but not in PLA. Significant reduction in VAT	All of the aerobic exercise regimens employed reduced liver fat and VAT by a small amount without clinically significant weight loss.
(25)	McCarthy , 2012	The Role of Diet and Nutrient Composition in Nonalcoholic Fatty Liver Disease	Adult	125	Improving insulin sensitivity. Here we review the literature and discuss the role of diet and nutrient composition in the management of NAFLD	The role of weight loss in the treatment of fatty liver is well established. Based on data from cardiovascular or diabetes trials and limited studies in patients with NAFLD
(26)	Chen , 2008	Effects of Therapeutic Lifestyle Program on Ultrasound-diagnosed Nonalcoholic Fatty Liver Disease	28-45	54	Significant improvements in anthropometric indices, total cholesterol, insulin sensitivity, liver biochemistry,	Diet plus exercise is more efficacious than exercise alone in the lifestyle modification treatment of NAFLD

(27)	Promrat , 2010	Randomized Controlled Trial Testing the Effects of Weight Loss on Nonalcoholic Steatohepatitis	35-55	65	Reduction of NAS of at least 3 points	Weight reduction achieved through lifestyle intervention leads to improvements in liver histology in NASH
(28)	Sullivan , 2012	Trial of Exercise Effect on Intrahepatic Triglyceride Content and Lipid Kinetics in Nonalcoholic Fatty Liver Disease		18	Decreased in lipid profile	Physical activity guidelines has small but beneficial effects on IHTG content, but does not improve hepatic lipoprotein kinetics in obese persons with NAFLD
(29)	Takahashi , 2015	Simple Resistance Exercise helps Patients with Nonalcoholic Fatty Liver Disease	42-58	53	Hepatic steatosis grade, mean insulin and ferritin levels, and the homeostasis model assessment- estimated insulin resistance index were significantly decreased	Exercise comprising squats and push- ups helps to improve the characteristics of metabolic syndrome in patients with non-alcoholic fatty liver disease
(30)	Zelber-Sagi , 2014	Effect of resistance training on non- alcoholic fatty- liver disease a randomized- clinical trial	20-65	128	HRI score was reduced significantly	RT improves hepatic fat content accompanied by favorable changes in body composition and ferritin. RT may serve as a complement to treatment of NAFLD.

1. Dietary interventions

Six articles studied the effects of dietary intervention on NAFLD, four of these studies gave positive results, only 2 articles had a neutral results regarding the Dietetic Association (ADA) Quality Criteria Checklist , i.e. the dietary intervention showed a positive results in about 66.7% of the articles used.

Five articles studied the effects of a combination of dietary and exercise interventions, four of these articles showed positive results regarding the Dietetic Association (ADA) Quality Criteria Checklist, while only one article showed a neutral results, i.e. 80.0% of the articles showed a positive effect of the combination of diet and exercise on the effect of NAFLD patients.

2. Exercise interventions

Eight articles studied the effects of exercise on NAFLD, five of the articles gave a final conclusion that the exercise has positive effect on the fatty liver regarding the Dietetic Association (ADA) Quality Criteria Checklist, while 3 article showed a neutral effect, i.e. 62.5% of the article had positive results of exercise

Quality assessment

Using the ADA quality assessment criteria (Figure. 2), out of 19 studies, 13 studies that were presented in Figure. 2 showed that they were rated as positive, high-quality trials. Seven of the 13 trials, insufficient information was provided to make an informed decision regarding the adequacy of randomized trials.

3. Combination interventions

Item	Paper No.	Author	Validity Questions										Overall Quality rating		
			1	2	3	4	5	6	7	8	9	10			
Diet	(12)	Tock													Neutral
	(17)	Angulo													Neutral
	(22)	Johnson													Positive
	(25)	McCarthy													Positive
	(27)	Promrat													Positive
	(29)	Takahashi													Positive
Exercise	(13)	de Piano													Neutral
	(18)	Bacchi													Positive
	(16)	Hallsworth													Neutral
	(19)	Balducci													Positive
	(21)	George													Neutral
	(24)	Keating													Positive
	(28)	Sullivan													Positive
	(30)	Zelber-Sagi													Positive
Combined	(14)	George													Positive
	(16)	Eckard													Positive
	(20)	Cuthbertson													Positive
	(23)	Kantartzis													Positive
	(26)	Chen													Neutral

Figure 2: American Dietetic Association (ADA) Quality Criteria Checklist carried out on the 24 eligible trials.

(1) Clear Research Question; (2) Unbiased Selection of Participants; (3) Randomization/Group Comparability; (4) Description of Withdrawals; (5) Blinding; (6) Study Procedures Described; (7) Clearly Defined Outcomes; (8) Appropriate Statistical Analysis;(9) Results Support Conclusion; (10) Funding or Sponsorship Bias Unlikely.

DISCUSSION

This review suggested that the lifestyle changes could contribute to lowering the activity of the disease (NAFLD). Also, weight loss for up to 10% of the weight among NASH patients by dietary restrictions with combination of half to an hour practice could restrict the activity of the diseases. In addition, the current guidelines reflected that diet and exercise are the corner stones for increasing the favorable outcomes and improving the NAFLD activity markers⁽⁵⁾.

Many studies showed that dietary restrictions and exercise could result in improving the insulin for metabolic syndrome, thus decreasing the activity of the diseases^(10,17-18,23,26,30).

Also, the exercise showed a significant association with improvement of the disease activity among many subjects^(21-22,24,28-30).

On the other hand, most of the subjects in the studies using combination of both dietary restrictions and exercise would significantly decrease the levels of the disease and its markers and could result in complete elimination of the disease^(14,16,18-20,22-25,27-30).

CONCLUSION

This review showed that the combination of healthy life interventions including exercise and health diet are effective in reducing the activity of NAFLD and could result in complete reversal of the condition. Thus NAFLD patients are advised to lose about 10% of their weight and engaging in regular exercises for 5 days per week.

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