Effect of lifestyle change on the management of metabolic syndrome and nonalcoholic fatty liver in adolescents: a systematic review

Efeito da mudança no estilo de vida no tratamento da síndrome metabólica e do fígado gorduroso não alcoólico em adolescentes: uma revisão sistemática

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ABSTRACT

Objective: To evaluate the impact of interventions related to lifestyle change in the management of metabolic syndrome and nonalcoholic fatty liver disease in adolescents. Methods: Systematic review covering randomized clinical trials in adolescents aged 12 to 18 years with a diagnosis of metabolic syndrome and/or nonalcoholic fatty liver disease, with a minimum intervention period of three months. We included the Pubmed, Embase, and Cochrane databases. We included studies published in English, Spanish, Portuguese, Italian, French, German, and

Swedish. Results and conclusion: A total of 1.676 articles were found and, after adequate evaluation, five articles considered relevant to the objective of this systematic review. Dietary interventions have been shown to be effective in weight reduction, BMI, lipid profile, and intrahepatic fat. In the form of aerobic training associated with resistance training, interventions in physical activity were effective in reducing the prevalence of nonalcoholic fatty liver disease. The high and low-intensity training resulted in the improvement of biomarkers related to the disease. In patients with risk factors for metabolic syndrome, dietary, psychological, and physical activity intervention reduced fat mass, lipid profile, and C-reactive protein. It is important to highlight the multidisciplinary role of interventions, demonstrating the importance of integrated care to adolescent health.

Keywords: adolescent, fatty liver, metabolic syndrome, obesity.

RESUMO
Objetivo: Avaliar o impacto das intervenções relacionadas à mudança de estilo de vida no manejo da síndrome metabólica e da doença não alcoólica do fígado gorduroso em adolescentes. Métodos: Revisão sistemática cobrindo ensaios clínicos aleatórios em adolescentes de 12 a 18 anos com diagnóstico de síndrome metabólica e/ou doença hepática gordurosa não alcoólica, com um período mínimo de intervenção de três meses. Incluímos as bases de dados Pubmed, Embase, e Cochrane. Incluímos estudos publicados em inglês, espanhol, português, italiano, francês, alemão e sueco. Resultados e conclusão: Foi encontrado um total de 1.676 artigos e, após avaliação adequada, cinco artigos considerados relevantes para o objetivo desta revisão sistemática. As intervenções dietéticas demonstraram ser eficazes na redução de peso, IMC, perfil lipídico e gordura intra-hepática. Na forma de treinamento aeróbico associado ao treinamento de resistência, as intervenções na atividade física foram eficazes na redução da prevalência da doença hepática gordurosa não alcoólica. O treinamento de alta e baixa intensidade resultou na melhoria dos biomarcadores relacionados com a doença. Em pacientes com fatores de risco para síndrome metabólica, a intervenção na dieta, psicológica e na atividade física reduziu a massa gorda, o perfil lipídico e a proteína C reativa. É importante destacar o papel multidisciplinar das intervenções, demonstrando a importância do cuidado integrado à saúde do adolescente.

Palavras chave: adolescente, fígado adiposo, síndrome metabólica, obesidade.

1 INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is a comprehensive term. It refers to a spectrum of diseases, ranging from steatosis without inflammation or necrosis to hepatocyte injury and cell death, called nonalcoholic hepatic steatosis.[1] Studies suggest that the prevalence of NAFLD associated with overweight may be up to 70%, compared to 7% in those with a healthy weight.[2,3] Therefore, other factors influence risk, such as preferential fat deposition in visceral tissue.[4-7] NAFLD is often associated with central obesity, insulin resistance, and dyslipidemia, characteristics of metabolic syndrome (MS).[8]

All guidelines for the management of NAFLD converge on the importance of lifestyle changes, characterized by a nutritional program appropriate to age and regular physical

activity.[9] Some studies reported that, even in the absence of weight loss, lifestyle interventions could positively affect the components of MS.[10-12] There is no specific dietary recommendation for the treatment of NAFLD. A balanced and hypocaloric diet, accompanied by moderate physical activity, is recommended for weight reduction to occur healthily.[13] Marchesini et al.,[14] observed that a 7% to 10% reduction in body weight seems sufficient to improve hepatic steatosis.

Faced with these issues, the modification of lifestyle focused on nutrition, exercise, and behavioral changes is fundamental to the management of NAFLD and MS in adolescents and highly desirable, considering the severe effects of these diseases. This systematic review aims evaluate the impact of interventions related to lifestyle change in the management of metabolic syndrome and nonalcoholic fatty liver disease in adolescents.

2 METHODS

We conducted a systematic review, including studies published until November 2017, in the following electronic databases: MEDLINE (accessed through Pubmed), EMBASE, and Cochrane Central Register of Controlled Trials. Subsequently, the search was updated until September 2018.

2.1 SEARCH STRATEGY

The following terms and their variations were used as a search strategy for Pubmed:

#1 ((Adolescents [MeSH Terms]) OR (Adolescence[tiab]) OR (Teen[tiab]) OR (Teenagers[tiab]) OR (Youth[tiab]) OR Child OR Children OR Childhood OR (Pediatrics [MeSH Terms])) AND

#2 (Fatty Liver [MeSH Terms]) OR (Nonalcoholic Fatty Liver Disease[tiab] OR (Non-alcoholic Fatty Liver Disease [tiab]) OR (Fatty Liver Disease [tiab]) OR (Hepatic Steatosis[tiab]) OR (fatty liver, nonalcoholic[tiab]) AND

#3 (Metabolic Syndrome X [MeSH Terms]) OR (Dysmetabolic Syndrome X[tiab]) OR (Metabolic Cardiovascular Syndrome[tiab]) OR (Metabolic X Syndrome[tiab]) OR (Syndrome X, Insulin Resistance[tiab]) OR (Syndrome X, Dysmetabolic[tiab]) AND

#4 ((Diet[MeSH Terms]) OR (Diet Therapy[tiab]) OR (Diet Modification[tiab]) OR (Dietary Modifications[tiab]) OR (Healthy Diet[tiab]) OR (Healthy Eating[tiab]) OR (Healthy Diets[tiab]) OR (Healthy Eating Indices[tiab]) OR (Healthy Eating Habits[tiab]) OR (Healthy Food Habits[tiab]) OR (Good Food Habits[tiab]) OR (Nutritional Support[tiab]) OR (Healthy Nutrition[tiab])) OR

#5 ((Exercise[MeSH Terms]) OR (Acute Exercise[tiab]) OR (Exercise Training[tiab]) OR (Aerobic Exercises[tiab]) OR (Exercise, Acute[tiab]) OR (Exercises, Aerobic[tiab]) OR (Physical Activities[tiab]) OR (Physical Exercise[tiab]) OR (Training, Exercise[tiab]) OR (Aerobic Exercise[tiab]) OR (Exercise, Isometric[tiab]) OR (Exercise, Physical[tiab]) OR (Isometric Exercise[tiab]) OR (Physical Activity[tiab])) OR (Physical Education and Training[tiab]))OR

#6 ((Healthy Lifestyle[MeSH Terms]) OR (Life Style[tiab]) OR (Lifestyle[tiab]) OR (Life Styles[tiab]) OR (Lifestyles[tiab]) OR (Health Behavior[tiab]) OR (Behavior Therapy[tiab]) OR (Behavior Control[tiab]) OR (Counseling[tiab]) OR (Family Therapy[tiab]) OR (Health Promotion[tiab]) OR (Behavior Modification[tiab]) OR (life style change[tiab]) OR (life style changes[tiab]) OR (life style modification[tiab]) OR (lifestyle change[tiab]) OR (lifestyle modification[tiab])) AND

#7 ((clinical [Title/Abstract] AND trial [Title/Abstract]) OR clinical trials as topic [MeSH Terms] OR clinical trial [Publication Type] OR random[Title/Abstract] OR random allocation [MeSH Terms])

2.2 INCLUSION AND EXCLUSION CRITERIA

The studies were selected based on the following criteria: a) mean age of the participants between 12 years and 18 years; b) with diagnostic criteria for MS and or NAFLD; c) randomized clinical trials; d) minimum period of three months of intervention; e) published in English, Spanish, Portuguese, Italian, French, German, or Swedish.

Studies with the following characteristics were excluded: a) severe diseases; b) pregnant women; c) use of enteral nutrition or parenteral nutrition; d) use of medicines; e) use of food supplements; e f) studies published only in abstract form.

2.3 STUDY SELECTION

Two reviewers independently evaluated the titles and abstracts of the studies identified in the electronic search according to the previously established eligibility criteria. In the absence of adequate information in the abstract, the studies were evaluated by reading the full text. The evaluation by the reviewers was not masked as to the authors and the results of the studies. The third reviewer researcher was not activated, as there were no significant differences between the first two reviewers.

2.4 EVALUATION OF THE QUALITY OF STUDIES

The internal quality of the studies was verified through the Cochrane risk of bias and Jadad scale.[15,16] The following domains were evaluated: random sequence generation, allocation concealment, blinding of participants and professionals, blinding of evaluators and outcome, incomplete outcomes, reporting of selective outcomes, and other sources of bias. Each domain was classified as low risk of bias, uncertain risk of bias, or high risk of bias.

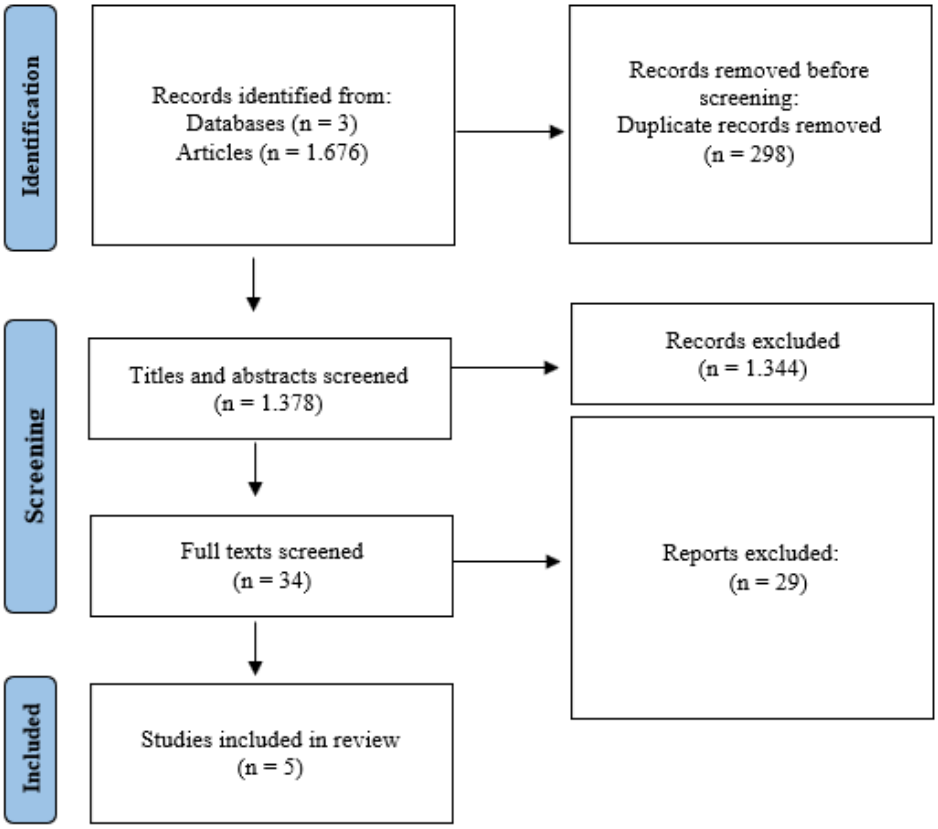
2.5 DATA ANALYSIS

The data were compiled, and the following information was extracted: author's name, year of publication, country of study, study design, description and size of the studied population, details of the intervention, and main results.

3 RESULTS

Through the search strategy applied in October 2017 and updated until September 2018, 1.676 articles were found in the three databases. After excluding duplicate articles, a quantitative of 1.378 articles remained. After analyzing the titles and abstracts of the studies, 34 articles remained that went to the phase of analysis of the full texts. Of these, five studies were included in this systematic review. The flowchart that shows selecting the studies is detailed in Figure 1.

Figure 1. Flowchart of the studies selection process



3.1 GENERAL CHARACTERISTICS OF STUDIES AND POPULATION

We included five Randomized Clinical Trials (RCTs),[17-21] totaling the participation of 617 adolescents. The studies were conducted in three countries: China (1),[21] Iran (1),[17] and Brazil (3). [18-20]

Five RCTs selected in this systematic review included a variety of characteristics of interventions with effects on NAFLD and MS, resulting in great heterogeneity regarding the diagnostic criteria evaluated, types of intervention, and period of studies (Table 1). Four studies evaluated interventions on NAFLD preponderantly [17-21] and one on MS.[17]

Table 1. Characteristics of the studies included in the final analysis.

Author Year Location	N	Age in years	Sex (M/F)	Main Criteria Assessed	Intervention	Duration in weeks
Kelishadi *et al.* 2010 Iran	360	12-16	No description	CT, LDL, TG, HDL, CRP, fasting glucose, SBP, DBP	Nutritional Physical Activity Psychological	26
Campos *et al.* 2012 Brasil	40	15-19	NR	Liver fat (US), CT, LDL, TG, HDL, ALT, AST, blood glucose, Insulin, HOMA-IR, adiponectin, leptin	Nutritional Physical Activity Psychological	52
De Piano *et al.* 2012 Brasil	58	15-19	27/31	Liver fat (US), fasting glucose, lipid profile, liver enzymes, adiponectin, leptin, AgRP, MCH	Nutritional Physical Activity Psychological	52
De Lira *et al.* 2017 Brasil	107	13-18	44/63	CT, LDL, TG, HDL, ALT, AST, blood glucose, Insulin	Nutritional Physical Activity Psychological	12

Chan *et al.* 2018 China	52	14-18	No description	Liver fat (RM), fasting glucose, lipid profile, ALT, AST, serum insulin, BMI	Nutritional Physical Activity	68

US - Ultrasonography; AgRP - Agouti-related-protein; MCH - Melanin-concentrating hormone; TC - Total Cholesterol; LDL - Low density lipoprotein; HDL - High density lipoprotein; PCR - C-reactive protein; SBP - Systolic blood pressure; DBP - Diastolic blood pressure; MRI - Magnetic resonance imaging; ALT - Alanine aminotransferase; AST - Aspartate aminotransferase; BMI - Body Mass Index; TG - Triglycerides; NR - not reported.

Regarding the types of intervention, the selected studies were presented in a diversified way, through dietary programs, physical exercises, and psychological therapy generally applied simultaneously between the groups involved in the study (Table 2). In the end, three studies performed the evaluation and follow-up with endocrinologists.[18-20]

Table 2. Description of interventions and results of studies included in the final analysis.

Author Year Location	Groups	Dietetic intervention	Physical activity intervention	Physiological intervention	Results
Kelishadi *et al.* 2010 Iran	POMN (120) - obese adolescents with normal blood glucose, lipid profile and blood pressure PNMO (120) - normal-weight adolescents with at least 1 altered cardiometabolic risk factor POMA (120) - obese adolescents with MS criteria, that is, at least 3 of the 5 risk factors for MS	Nutrition education sessions. Diet with 30% fat, 15% protein and 55% carbohydrates	Aerobic activity classes were held 3 days/without. The sessions were composed of 15 minutes of orientation, followed by 40 minutes of physical training, and 20 minutes of fitness activities and 20 minutes of games and running	Behavioral modification sessions were performed by a psychologist	After 2 months, BMI, WC and mean body fat mass significantly decreased in the obese groups (POMN and POMA), while mean body fat mass decreased in all groups. CT, LDL, TG and CRP significantly decreased in the POMA and PNMO groups. After 6 months, mean WC and body fat mass, as well as LDL, TG, and CRP, increased significantly compared to the 2-month results, however, they remained below baseline

Campos *et al.* 2012 Brasil	With NAFLD (18) Without NAFLD (22)	All patients received a hypocaloric diet and were individually adjusted. Once a week, teenagers took dietary classes	During the 1-year therapy period, adolescents followed aerobic training plus resistance (TA + TR). The protocol was performed 3 times a week for 1 year and included 30 min of aerobic training plus 30 min of endurance training per session	Adolescents were followed weekly in the 1-year therapy support group and, if necessary, individual psychological therapy was recommended when behavioral changes were found	-
De Piano *et al.* 2012 Brasil	Aerobic training (29)	Weekly diet classes. Nutritional consultation during the intervention period	TA - 29 Adolescents performed a 60-minute session, 3 times a week, for 1 year	Adolescents held weekly group psychological support sessions	-
De Lira *et al.* 2017 Brasil	High intensity training (n=31) Low intensity training (n=31) Control Group (n= 45)	Nutritional counseling for 1 hour per week in small groups (9 participants). Participants were encouraged to follow a balanced diet	Aerobic training on a treadmill, 3 times a week, the exercise was performed with intensity corresponding to LV1. Aerobic training on a treadmill, 3 times a week, the exercise was performed with intensity 20% below LV1. No intervention report	Psychological counseling was held for 1 hour per week in small groups	Both high and low intensity trainings improved NAFLD-related biomarkers. The main results are: (a) a significant improvement in the lipid profile due to reductions in LDL, CT/HDL ratio, LDL/HDL ratio and increase in HDL, regardless of the intensity of aerobic training; (b) decrease of ALT and AST, suggesting a protective effect of exercise on hepatocytes; c) reduction of BMI and fat mass

Chan *et al.* 2018 China	Lifestyle Modification Intervention Group (GI) (n=26) Conventional Group (GC) n=26	Pediatric consultations with dietary advice were conducted every 16 weeks during phases I and II	Pediatric consultations with guidance on physical exercises were performed every 16 weeks during phases I and II	No intervention report	After the initial phase intervention, there was a greater reduction of intrahepatic fat in the IG (4.02%) than in the CG group (0.96%). At the end of initiation phase I, body weight, BMI, and body fat decreased significantly in IG. The reduction of the AST/ALT ratio was higher in the GI group but was not significant. At the end of the study in both groups, there was a 2-3% reduction in the intrahepatic fat content

PNMO - Phenotypically normal and metabolically obese; POMA - Phenotypically obese metabolically abnormal; POMN - Phenotypically obese metabolically normal; MS - Metabolic syndrome; BMI - Body Mass Index; CC - Waist circumference; LDL - Low density lipoprotein; TG - Triglycerides; TC - Total cholesterol; PCR - C-reactive protein; NAFLD - Non-alcoholic fatty liver disease; AT - Aerobic training; TR - Resistance training; AST - Aspartate aminotransferase; ALT - Alanine aminotransferase; BMI - Body Mass Index; LDL - Low density lipoprotein; TC - Total cholesterol; HDL - High density lipoprotein; LV 1 - Ventilatory threshold 1;

3.2 NUTRITIONAL INTERVENTION

All five studies have some degree of intervention in the dietary component, predominating the orientation of a healthy diet with individual follow-up or through groups.[17-21]

In the study by Kelishadi et al.,[17] nutritional education sessions were conducted by nutritionists. A balanced diet was recommended for participants, and guidance on saturated and trans-fat was provided, and encouragement of fruit and vegetable intake.

In the study by Campos et al,[18] all patients received a hypocaloric diet, adjusted by nutritionists according to individual habits. Every week, the adolescents held classes with information on the food pyramid, diet log, weight-loss diets, and fashion diets, food labels, dietetic, low-calorie, and non-fat foods, fats, fast food calories, and nutritional composition, good nutritional choices for special occasions, healthy sandwiches, shakes and products to promote weight loss, functional foods, and decisions about food choices.

In the study by De Piano et al.,[19] all groups received dietary classes once a week and nutritional consultations. The classes had similar content to that applied in the study by Campos et al.[18]

In the study by De Lira et al.,[20] all groups received weekly nutritional counseling, addressing subjects on healthy eating behavior, weight-loss diets, and notions about macro and micronutrients. Participants were encouraged to reduce total calorie intake and follow a balanced diet.

Chan et al.,[21] was the only one to present a differentiation in dietary orientation between intervention and control groups. One group was submitted in the initial phase to weekly consultations with a nutritionist and one consultation every two months in the maintenance phase. In the follow-up sessions, dietary practices were reviewed, and an individualized food plan was carried out. The guided diet was balanced, rich in fruits and vegetables, with a moderate amount of carbohydrates, low fat, low glycemic index, and products with low-calorie content. On the other hand, the other group underwent a conventional intervention, receiving dietary guidance throughout the study period, with pediatric consultations every 16 weeks, receiving guidance regarding the reduction of carbohydrate and animal fat intake.

3.3 INTERVENTION IN PHYSICAL ACTIVITY

The five selected studies have interventions in physical activity, ranging from general orientation to specific training with different intensity degrees.[17-21]

The study by Kellishadi et al.,[17] was applied to all participants for two months, often three times a week. The events combined aerobic physical activity aimed at physical fitness and recreational activities, including guidance on the benefits of being active, overcoming barriers, strategies to maintain a healthy lifestyle, and reducing sedentary activities.

In the study by Campos et al.,[18] for one year, adolescents underwent aerobic training sessions (AT) plus resistance exercises three times a week. Participants were instructed to reverse the order of the exercises in each training session. AT consisted of running on a motorized treadmill at a heart rate intensity representing ventilatory threshold I (4 bpm), which was determined by the results of an initial oxygen consumption test

De Piano et al.[19] intervened in a group of 29 adolescents, with AT under supervision, three times a week, for one year. The intensity was established by a workload corresponding to a ventilatory threshold of 1 (LV1), corresponding to 50 to 70% of the oxygen consumption test. At the end of six months, aerobic tests were performed to assess physical capacity, and the intensity of physical training was adjusted for everyone. The other group, with 29 adolescents,

received AT combined with resistance training (RT), with a frequency of three sessions per week for one year, also under supervision. AT consisted of running on a treadmill with a heart rate within the LVI (4 bpm), as determined by an initial oxygen consumption test for aerobic exercise. The RT consisted of exercises directed to each of the main muscle groups.

In the study by De Lira et al.,[20] participants in the high-intensity training group performed personalized training on the treadmill three times a week. In this group, adolescents exercised in intensity corresponding to LV1. However, the other group performed the same training with an intensity 20% below the LV1. The exercise sessions were isocaloric, with an energy expenditure of 350 Kcal, recommended for weight loss in children and adolescents (1,050 kcal/week), estimated by indirect measurement.

In the study by Chan et al.,[21] in the group that underwent lifestyle modifications, an exercise instructor assessed the levels of physical activity before the intervention and devised an individualized exercise program for adolescents to practice at home or any convenient place, according to the level of physical conditioning and medical history of each participant. Adolescents were encouraged to undergo an AT twice to three times a week. The other group, who underwent a conventional intervention, had pediatric consultations every 16 weeks during phases I and II and were encouraged to exercise for 30 minutes, two to three times a week.

3.4 PSYCHOLOGICAL INTERVENTION

Of the five studies selected, four included psychological intervention.[17-20] In the study by Kelishadi et al.,[17] behavioral modification sessions were conducted by psychologists. In the study by Campos et al.,[18] adolescents were followed weekly in the therapy group for one year, and when necessary, individual psychological therapy was recommended.

In the study by De Piano et al.,[19] adolescents participated in weekly sessions of group psychological support when subjects related to body image and eating disorders, such as bulimia, anorexia nervosa, and binge eating, were discussed. Individual psychological therapy was recommended when individuals with nutritional and behavioral problems were found. In the study by De Lira et al.,[20] psychological counseling sessions were held in groups with nine people. Subjects related to body image, eating disorders, the relationship between eating and feelings, family and social problems, mood, anxiety, and depression were also addressed.

3.5 EFFECTS ON NONALCOHOLIC FATTY LIVER DISEASE

Four selected studies focused mainly on evaluating the impact of interventions on NAFLD, with the following main interventions: diet, physical and psychological activity.[18-21]

In the study by CAMPOS et al.,[18] participants were divided into two groups, one with NAFLD and the other without NAFLD. The diagnosis of NAFLD was made by ultrasonography. In the group with NAFLD, after one year of interdisciplinary intervention, the prevalence of NAFLD decreased from 100 to 33%, with a significant reduction in BMI and fat mass. In the group without NAFLD, a significant reduction in BMI and body fat was also observed, similar to the trend observed in the group with NAFLD. In addition, it resulted in a significant increase in the concentration of HDL, lean body mass. However, there were no significant changes in the liver enzymes analyzed. Then, as can be observed in this study, after one year of interdisciplinary intervention, changes in the metabolic profile of obese adolescents with and without NAFLD were observed.

In the research of De Piano et al.,[19] two groups and four sub-groups were formed; one group received AT and the other AT plus RT, and both groups were subdivided into two others, one with NAFLD and the other without NAFLD. The diagnosis of NAFLD was by ultrasonography. The prevalence of NAFLD in both groups was 48.3% at the beginning of the treatment. After one year of intervention, there was a significant reduction to 38% in the AT group and 17.2% in the group with AT plus RT. The group without NAFLD, which followed the AT plus RT protocol, presented lower insulin values, homeostasis model Assessment - Insulin Resistance (HOMA-IR), and very-low-Density lipoprotein (VLDL) compared to the group with only AT. The group with NAFLD, which followed the AT plus RT protocol, presented lower values of insulin, HOMA-IR, and alanine aminotransferase (ALT) after the long-term intervention compared to AT. It was also found that there was a greater magnitude of alteration in subcutaneous fat, blood glucose, total cholesterol (TC), LDL, ALT, and adiponectin in the group submitted to AT plus RT. Based on the data of adipokines and neuropeptides, it was found that all patients, with and without NAFLD submitted to AT plus RT, exhibited significantly higher adiponectin and leptin after long-term therapy compared to the AT group.

The study by De Lira et al.,[20] consisted of three groups, one received high-intensity training, the second low-intensity training, while the third was the control group. Authors analyzed the effect of the two types of aerobic exercise on serum biomarkers of NAFLD in obese adolescents. A significant improvement in the lipid profile was observed, regardless of aerobic training intensity. There was also a decrease in serum level of liver enzymes, suggesting a protective effect of exercise on hepatocytes and a reduction in BMI and fat mass.

In the study by Chan et al.,[21] participants were divided into two groups, one group underwent lifestyle modification (GI) intervention, and another group received conventional

follow-up (CG). Magnetic resonance imaging (presence of hepatic steatosis with a fat content of 5% or more) was used as the diagnostic method for NAFLD. In the beginning, GI and CG had 13.1% and 13.5%, respectively, of hepatic steatosis. After the initial phase, there was a greater reduction of intrahepatic fat (4.02%) in the GI than in the CG (0.96%). At the end of the maintenance phase, a similar rate of intra-hepatic fat reduction was documented in both groups (-3.81% GI and -2.07% CG). Ten of the 52 subjects, six from the GI and four from the CG, had complete remission from the NAFLD at the end of the first phase, and 16 from the 52 participants, eight from the GI and eight from the CG, in the maintenance phase. At the end of the initial phase, body weight, BMI, and total body fat content decreased significantly in GI. At the end of the maintenance phase, the mean BMI z-score in the GI returned to 2.2, while in the CG, there was a modest reduction of 0.07 in the BMI z-score. The percentage of body fat was significantly lower in the GI than in the CG at the end of the initial phase. At the end of the initial phase, laboratory variables, including the AST/ALT ratio, serum insulin, and HOMA-IR index, improved significantly in GI compared to baseline. At the end of the maintenance phase, all biochemical markers showed no change concerning the baseline values of the two groups, and the activity levels in both groups were similar to baseline levels.

3.6 EFFECTS ON METABOLIC SYNDROME

In the study by Kelishadi et al.,[17] the authors considered as a diagnostic criterion the presence of at least three of the following risk factors: triglycerides 150 mg/dl, HDL < 40 mg/dl, fasting glycemia 100 mg/dl, systolic blood pressure 130 mmHg or diastolic blood pressure 85 mmHg, being called POMA group (phenotypically obese metabolically abnormal). Overall, 94.7% of the adolescents enrolled completed the two-month test, and 87.3% of them (82.7% of the total sample enrolled) returned to the six-month study. The frequency rate of sessions ranged between 72 and 78%, with no significant difference between groups.[17]

Intra-group comparisons showed that after two months, BMI and waist circumference (WC) decreased significantly in obese participants, i.e., in the POMA and POMN groups (phenotypically obese metabolically normal) while the average body fat mass decreased in all groups.[17]

In the last stage of the study, six months after the initial survey, the mean WC and body fat, as well as serum levels of LDL, TG, and PCR, increased significantly compared to the results of two months. However, they remained below baseline values. After two months, the decrease in mean body fat, serum levels of TC, LDL, TG, CRP, and SBP was higher in the POMA than in the POMN group. At six months, the decrease of these variables, except for

body fat, remained significantly higher in the POMA than in the POMN group. Both at two and six months, the average decrease in BMI, WC and body fat, serum TG level, and SBP was higher in the POMA group than in the PNMO (phenotypically normal metabolically obese).[17]

3.7 RISK OF BIAS OF INCLUDED STUDIES

All studies were controlled and randomized, but four do not detail how randomization was performed.[17-19,21] None of the studies detailed allocation concealment.[17-21] Regarding blinding, there was blinding of the doctor or technician who performed the imaging exam in three studies.[18,19,21] All studies reported specific results and the loss of patients.[17-21]

4 DISCUSSION

Despite the limited number of randomized controlled trials available, this systematic review showed that guidelines on healthy eating habits together with physical exercise and psychological support result in positive outcomes on the parameters of NAFLD and MS. Concerning nutrition, it was observed that the studies carried out interventions mainly in the implementation of a healthy, low-calorie diet and focused on nutritional education fundamentally seeking a change in eating habits.[17- 21]

Regarding the practice of physical exercise, in the study by Chan et al.,[21] adolescents were guided and encouraged to perform physical activities at home or anywhere convenient, a situation closer to most adolescents' reality. An important aspect is to emphasize the importance of public policies that encourage young people to perform physical activity and a greater offer of public areas to practice sports. Psychological interventions were present in most selected studies, showing that it is of fundamental importance to improve adherence and achieve good results.

In the study by De Piano et al.,[19] it was demonstrated that the exercise protocols associated with interprofessional action effectively improved metabolic and hormonal profiles in all patients analyzed. In the study by Chan et al.,[21] the GI that was focused on the patient presented a significant rebound effect concerning some parameters. In the CG, the parents participated most of the time, and the adolescents maintained a reduction, even if modest, until the end of the study.

A limitation of the studies included in this review is that none of them performed liver biopsy as a diagnostic method of NAFLD. However, the imaging and laboratory diagnostic methods used were able to detect and monitor changes related to NAFLD, as well as control

throughout the study. Another important aspect of being stressed is that some of the results found may have happened independently of the interventions.

Although we did not identify another systematic review with the same inclusion criteria, the review carried out by Gibson et al.,[23] concluded that the lifestyle modification, aiming at weight loss through reduced energy consumption and increased physical activity, should remain the first line of treatment for NAFLD in pediatrics until additional high-quality evidence is available. In the review conducted by Pacífico et al.,[24] that addresses the management of MS in children and adolescents, the authors concluded that lifestyle changes, with increased physical activity and changes in diet, are the basis of MS treatment. And that behavioral modification in overweight children reduces body weight, improves body composition, and positively modifies many MS components.

Some limitations of this systematic review should be recognized, it only contemplated the published literature, and publication bias cannot be excluded. The selected studies have a high degree of heterogeneity, such as intensity and types of interventions, which made it impossible to perform a meta-analysis. The included studies have a limited methodological quality due to the risks of bias identified. Therefore, this reinforces the need for more well-designed, controlled, and randomized clinical studies to avoid bias. The studies showed positive results regarding the effect of interventions on NAFLD and MS during adolescence.

This systematic review showed that the selected studies performed their interventions in more than one component,[17-21] being applied simultaneously by professionals from different areas, highlighting the importance of comprehensive and interdisciplinary care. However, more controlled and randomized studies are needed to enable more consistent systematic reviews that can provide more evidence on the real impact of interventions on adolescents' lifestyles in NAFLD and MS, mainly concerning the long term.

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