Research Article

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Community-based lifestyle modification programme for non-alcoholic fatty liver disease: A randomized controlled trial

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Background & Aims: Healthy lifestyle is the most important management of non-alcoholic fatty liver disease (NAFLD). This study aimed at assessing the efficacy of a community-based lifestyle modification programme in the remission of NAFLD.

Methods: This was a parallel group, superiority, randomized controlled trial. 154 adults with NAFLD identified during population screening were randomized to participate in a dietitian-led lifestyle modification programme at 2 community centres or receive usual care for 12 months. The primary outcome was remission of NAFLD at month 12 as evidenced by intrahepatic triglyceride content (IHTG) of less than 5% by proton-magnetic resonance spectroscopy.

Results: 74 patients in the intervention group and 71 patients in the control group completed all study assessments. In an intention-to-treat analysis of all 154 patients, 64% of the patients in the intervention group and 20% in the control group achieved remission of NAFLD (difference between groups 44%; 95% CI 30–58%; p <0.001). The mean (SD) changes in IHTG from baseline to month 12 were −6.7% (6.1%) in the intervention group and −2.1% (6.4%) in the control group (p <0.001). Body weight decreased by 5.6 (4.4) kg and 0.6 (2.5) kg in the two groups, respectively (p <0.001). While 97% of patients with weight loss of more than 10% had remission of NAFLD, 41% of those with weight loss of 3.0–4.9% could also achieve the primary outcome.

Conclusions: The community-based lifestyle modification programme is effective in reducing and normalizing liver fat in NAFLD patients.

Keywords: Obesity; Weight loss; Non-alcoholic steatohepatitis; Transient elastography; Magnetic resonance spectroscopy.

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Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; GI, glycaemic index; HDL, high density lipoprotein; ^{1}H-MRS, proton-magnetic resonance spectroscopy; IHTG, intrahepatic triglyceride content; LDL, low density lipoprotein; NAFLD, non-alcoholic fatty liver disease.

Introduction

Non-alcoholic fatty liver disease (NAFLD) affects 15–40% of the general adult population and is the most common cause of abnormal liver biochemistry worldwide [1,2]. Some patients with NAFLD run a progressive clinical course and may develop cirrhosis and hepatocellular carcinoma [3–6].

Lifestyle modification is the cornerstone of the management of NAFLD [7]. Weight reduction by dietary intervention and/or exercise is associated with decrease in liver enzymes [8–11], reduced liver fat [12–15], and improvement in liver histology [16,17]. However, 2 important questions remain unanswered. First, the majority of NAFLD patients are seen at the primary care setting. Reported intervention programmes were invariably conducted in expert centres. The implementation and efficacy of lifestyle modification programmes at the community setting are unclear. Second, many reported interventions involved tightly controlled diet over short periods ranging from several weeks to months. It is unlikely that patients can adhere to such diets for a long time. The optimal intervention with good efficacy and sustainability for patients with NAFLD is currently unknown.

This study tested the hypothesis that a community-based lifestyle modification programme is superior to usual care in normalizing hepatic steatosis in patients with NAFLD.

Patients and methods

Trial design

This was a parallel group, superiority, single-blind randomized controlled trial comparing a community-based lifestyle modification programme with usual care in NAFLD patients.

Study population

NAFLD patients were recruited from a population screening project in Hong Kong. Details of the project have been described previously [2,18]. In brief, a list of local citizens was randomly generated from the government census database. They were invited to undergo screening with proton-magnetic resonance spectroscopy (^{1}H-MRS).

Subjects found to have NAFLD were then invited to enter this intervention trial. The specific inclusion criteria were age 18–70 years; fatty liver by ^{1}H-MRS, defined as intrahepatic triglyceride content (IHTG) of 5% or above; and plasma alanine aminotransferase (ALT) above 30 IU/L in men and 19 IU/L in women. Subjects tested positive for hepatitis B surface antigen or anti-hepatitis C virus antibody, or anti-nuclear antibody titer above 1/160 were excluded. Other exclusion criteria were alcohol consumption above 20 g per day in men and 10 g per day in women; liver decompensation; and terminal illness and cancer including hepatocellular carcinoma. All patients provided written informed consent. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, was approved by the Clinical Research Ethics Committee of The Chinese University of Hong Kong, and was registered at ClinicalTrials.gov (NCT00868933).

Trial procedures

Patients fulfilling the inclusion and exclusion criteria were randomized in 1:1 ratio to participate in the lifestyle modification programme or receive usual care. Randomization was performed through the use of a computer-generated list of random numbers in blocks of 6 by a nursing officer. Treatment assignments were concealed in consecutively-numbered sealed envelopes, which were opened sequentially upon patient enrollment. Clinicians and radiographers who analyzed ^{1}H-MRS results were blinded to the treatment assignment.

Intervention group

Patients randomized to the intervention group participated in a dietitian-led lifestyle modification programme for 12 months. All patients received individual education. The programme was held at 2 urban centres that are open to the public for the management of obesity and related disorders. The programme is based on a strategy of increasing energy expenditure and reducing caloric intake using lifestyle behavioral change to achieve long-lasting impact. The patients attended dietary consultation sessions weekly in the first 4 months, and monthly in the following 8 months. At the first session (about 1 h), the dietitian carried out a complete behavioral assessment, covering important areas such as the patient's current eating and lifestyle patterns, specific eating-related behaviors, knowledge of risks associated with current eating patterns, and concerns and feelings about specific lifestyle changes. The dietitian also discussed the expected duration and specific dietary and lifestyle advices to achieve a desirable weight status with the patients.

In the follow-up sessions (about 20 min), the dietitian reviewed the patient's dietary practice and provided recommendations. Each patient was given an individualized menu plan. The dietary component and portion sizes of the menu plan were based on the recommendations of the American Dietetic Association [19]. A varied balanced diet with an emphasis on fruit and vegetables, and moderate-carbohydrate, low-fat, low-glycaemic index (GI) and low-calorific products in appropriate portions was encouraged. The diet resulted in a relative increase in energy consumption from proteins, which also promoted satiety. Each patient was provided with two booklets, one for food portion size exchange and tips for eating out, and another listing the low-GI food options and meal plans (GI <55). Moreover, techniques for coping at-risk situations such as parties and festival celebrations were taught. Recipes were also provided to the patients to encourage healthy cooking. Adherence to dietary intervention was assessed by calculating the percentage attendance to the intervention sessions and evaluating the dietary intakes and meal patterns using a weekly food record.

Besides, patients were encouraged to see an exercise instructor at least once during the lifestyle modification programme. During the first exercise consultation (about 30 min), the exercise instructor reviewed the patient's medical history and exercise habits, and designed a suitable exercise regime for the patient. The patients were first instructed to do moderate intensity aerobic exercise for 30 min, 3 to 5 days a week and encouraged to increase daily physical activities. During subsequent appointments, the exercise instructor evaluated the patient's exercise progress on aerobic exercise and stretching during follow-ups. When patients were able to develop a routine exercise habit, they were instructed to perform resistance training to increase their muscle endurance and strength for better aerobic performance and liver fat reduction [20]. The intensity of exercise was gradually increased to 30 min every day. The target was a reduction of body mass index (BMI) towards 23 kg/m^2.

Control group

Patients in the control group received routine care at the medical clinic of the Prince of Wales Hospital, Hong Kong. At baseline, a clinician explained the laboratory test results and the natural history of NAFLD to the patients. The patients were encouraged to reduce carbohydrate and fat intake, and to exercise for at least 3 times per week, 30 mins per session.

Follow-up assessments

The patients attended the clinic at months 3, 6, 9, and 12 for metabolic assessment, and received further advice from a clinician at months 6 and 12. During each visit, new symptoms and drug intake were monitored by history and territory-wide computer prescription record. Anthropometric measurements, liver biochemistry, fasting glucose and lipids were assessed. BMI was calculated as body weight (kg) divided by body height (m) squared. Waist circumference was measured at a level midway between the lower rib margin and iliac crest with the tape all around the body in the horizontal position. Physical activities were recorded as the total duration of active exercise (min) per week.

At baseline and month 12, ^{1}H-MRS and liver stiffness measurement were performed to assess hepatic steatosis and fibrosis, respectively. IHTG was measured by ^{1}H-MRS using a whole-body 3.0T scanner with a single voxel point-resolved spectroscopy sequence and an echo time of 40 ms and repetition time of 5000 ms as described previously [21]. Liver stiffness measurement was performed by transient elastography (Fibroscan, Echosens, Paris, France) by experienced operators who had performed at least 50 measurements prior to this study, according to the manufacturer's instructions [22]. Ten liver stiffness measurements were performed on each patient. The median of 10 measurements reflected the liver stiffness, while the interquartile range was used to estimate the variability of measurements. Cases with less than 10 successful acquisitions or an interquartile range-to-median ratio of 0.3 or more were considered to have unreliable measurements and were excluded from analysis.

Study outcomes

The primary outcome was remission of NAFLD at month 12 as evidenced by IHTG of less than 5% by ^{1}H-MRS. Secondary outcomes were reduction in IHTG and changes in liver stiffness by transient elastography, anthropometric measurements, liver biochemistry, fasting glucose, and lipids.

Statistical analysis

A large observational study in Japan showed that 16% of patients had spontaneous remission of NAFLD within 1–2 years [23]. Assuming that 45% of patients in the intervention group and 20% of patients in the control group would have remission of NAFLD, a sample size of 62 patients per group would achieve 80% power to detect the difference at a 5% significance level using the Chi-squared test. Assuming that 20% of the patients would be lost to follow-up, a total sample size of 155 patients was required.

Continuous variables were expressed in mean (SD) unless otherwise specified and were compared between the treatment groups using unpaired *t* test. Categorical variables were compared using χ^2 test or Fisher exact test as appropriate. Intention-to-treat analysis was performed for each outcome. Missing values were treated using the last-observation-carried-forward method and were considered failure for that outcome. A two-sided *p* value of less than 5% was taken as statistically significant. All statistical tests were performed with IBM SPSS Statistics version 20 (IBM Corporation, Armonk, NY).