EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Lifestyle interventions for the treatment of non-alcoholic fatty liver disease in adults: A systematic review

Christian Thoma[1,2,3], Christopher P. Day[1,2], Michael I. Trenell[1,2,3,*]

[1]*Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK;* [2]*NIHR Biomedical Research Centre for Ageing & Age-related Disease, Newcastle University, Newcastle upon Tyne, UK;* [3]*MRC Centre for Brain Ageing & Vitality, Newcastle University, Newcastle upon Tyne, UK*

Non-alcoholic fatty liver disease is a serious and growing clinical problem. Despite lifestyle modification, i.e. diet and physical activity, being the recommended therapy, there are currently no systematic evaluations of its efficacy. This review applies a systematic approach to evaluating lifestyle modifications studied to date.

Medline (Pubmed), Scopus, and the Cochrane Controlled Trials Register were searched for studies and study groups assessing the effect of diet, physical activity, and/or exercise modification in adult populations with non-alcoholic fatty liver disease. The outcome markers of interest were indicators of steatosis, histological evidence of inflammation and fibrosis, and glucose control/insulin sensitivity.

We identified 23 studies for inclusion; seven had control groups, but only six were randomised. Eleven groups received diet-only interventions, two exercise-only, and 19 diet and physical activity/exercise. Studies consistently showed reductions in liver fat and/or liver aminotransferase concentration, with the strongest correlation being with weight reduction. Of the 5 studies reporting changes in histopathology, all showed a trend towards reduction in inflammation, in 2 this was statistically significant. Changes in fibrosis were less consistent with only one study showing a significant reduction. The majority of studies also reported improvements in glucose control/insulin sensitivity following intervention. However, study design, definition of disease, assessment methods, and interventions varied considerably across studies.

Lifestyle modifications leading to weight reduction and/or increased physical activity consistently reduced liver fat and improved glucose control/insulin sensitivity. Limited data also suggest that lifestyle interventions may hold benefits for histopathology.

Published by Elsevier B.V. on behalf of the European Association for the Study of the Liver.

Keywords: Non-alcoholic fatty liver; Liver fat; Systematic review; Lifestyle modification; Exercise; Physical activity; Diet; Weight reduction.

Received 1 February 2011; received in revised form 23 June 2011; accepted 27 June 2011

* Corresponding author. Address: MoveLab; 4th Floor William Leech Building, Newcastle University, Newcastle upon Tyne, NE4 6BE, UK. Tel.: +44 191 222 6935.

E-mail address: m.i.trenell@ncl.ac.uk (M.I. Trenell).

Abbreviations: NAFLD, non-alcoholic fatty liver disease; IHTAG, intrahepatic triacyglycerol concentration; ^{1}H-MRS, proton magnetic resonance spectroscopy; CT, computed tomography; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Introduction

Non-alcoholic fatty liver disease (NAFLD) encompasses liver conditions ranging from hepatic steatosis through steatohepatitis to cirrhosis [1]. Its prevalence has been estimated at between 20% and 33% of the adult population depending on criteria and country [2]. Prevalence increases with degree of obesity [3] and the condition is very common in those with type 2 diabetes [4,5]. Rising prevalence of obesity and Type 2 diabetes, particularly in younger people, will ensure that NAFLD remains a growing clinical concern for the future [3].

Elevated intrahepatic triacyglycerol concentration (IHTAG) is the first step in the development of steatohepatitis, liver fibrosis, liver cirrhosis, and hepatocellular carcinoma [1]. Excess liver fat is also linked to insulin resistance [6], and is an independent risk factor for Type 2 diabetes [7] and cardiovascular disease [8]. Liver lipid is part of the early adaptive response to stress, and as such, is a biomarker of NEFA flux, oxidative-, ER- and cytokine-mediated stress that result in steatosis and progressive liver damage. Lifestyle modification, encompassing diet, physical activity, and/or exercise related behaviours, is the primary recommended therapy for NAFLD [9], especially in the absence of approved pharmaceutical agents.

Although reviews with NAFLD disease as their focus abound, few have reported using a systematic approach to study selection or reporting, and none, to date, have applied this approach to examining the efficacy or effectiveness of lifestyle management. This systematic approach is necessary to provide clinical care teams with the information to determine whether lifestyle therapy should be used, and if so, what aspects are key to achieving success. Our objective was to perform a systematic assessment of lifestyle interventions in adults with NAFLD to: (i) Define the efficacy of different lifestyle interventions in reducing IHTAG and/or liver aminotransferases; (ii) assess the effect of lifestyle interventions on histological parameters; and (iii) establish the efficacy of different lifestyle interventions on glucose control/insulin sensitivity (Fig. 1).

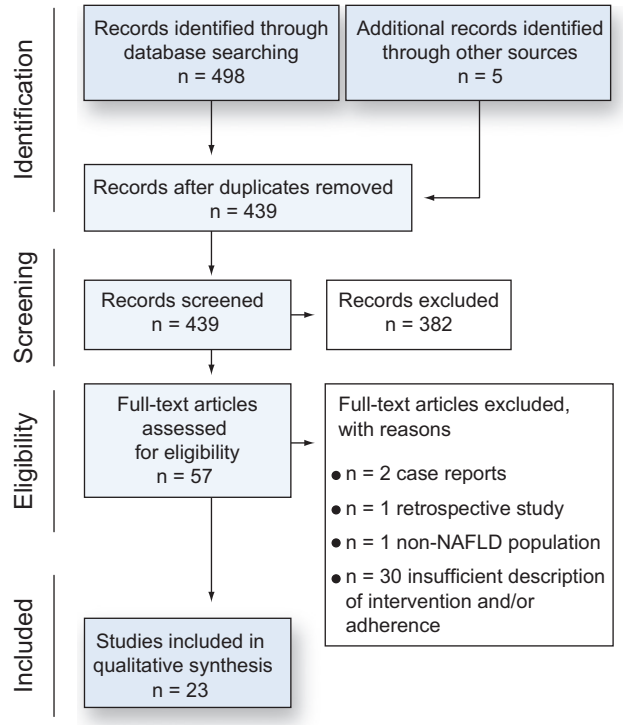

Fig. 1. Flow diagram of study selection.

Methods

Eligibility criteria

The review is restricted to published prospective interventions reporting the effects of lifestyle modification on IHTAG, liver enzymes, and/or insulin sensitivity in adults ($\geqslant$19 years) with NAFLD, including non-alcoholic steatohepatitis but not late stage liver diseases i.e. cirrhosis or hepatocellular carcinoma. Eligible publications included: randomised controlled trials or specific arms thereof, and non-randomised interventions. Only full reports were considered to provide sufficient information to allow critical evaluation.

No specific criteria defining NAFLD were set as the methods of diagnosis and cut-offs vary between studies. It was considered sufficient for reports to provide their own diagnostic criteria based on one or more of the following in order of preference: (1) histological examination of biopsies; (2) proton magnetic resonance spectroscopy (^{1}H-MRS); (3) computed tomography (CT); (4) ultrasound; and/or (5) blood concentrations of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST).

Lifestyle modification could include general recommendations or specific diet, physical activity, and/or exercise prescription. Studies or study arms designed to test pharmaceuticals, dietary supplements, or herbal preparations were excluded. Study arms in which pharmaceutical agents were used as part of standard treatment and where participants were receiving these prior to the study, without a reported increase in dose during the study, were eligible for inclusion.

The primary outcomes of interest were changes in IHTAG assessed by liver biopsy, ^{1}H-MRS, CT, or ultrasound, and histological indicators of inflammation and fibrosis. Blood ALT and/or AST concentrations were also considered. The secondary outcome was glucose tolerance and/or insulin sensitivity as assessed directly by insulin clamp techniques or oral glucose tolerance tests, or inferred by validated formulae.

Only studies that clearly described or appropriately referenced their intervention, and that provided some direct indicators of protocol adherence, or those conducted under very close supervision, e.g. inpatient protocol delivery, were eligible for inclusion.

Search strategy and study selection

The following databases were searched: Medline (Pubmed), Scopus, and the Cochrane Controlled Trials Register. The search of Scopus, the most comprehensive of the three databases, was done in duplicate by two authors (CT and MT), whereas the other databases were searched by one author (CT). The last search of all three databases was done on June 26, 2010. However, automatic updates of the Scopus search were reviewed up to October 18, 2010. A medical librarian assisted with the selection of the search strategies.

The selected search terms and related MESH headings were: (NAFLD or "non-alcoholic fatty liver" or "nonalcoholic fatty liver" or "non-alcoholic steatohepatitis" or "nonalcoholic steatohepatitis" or "non-alcoholic steatosis" or "nonalcoholic steatosis" or "non-alcoholic liver steatosis" or "nonalcoholic liver steatosis" or "non-alcoholic hepatic steatosis" or "nonalcoholic hepatic steatosis") AND (lifestyle or exercise or "diet$*$" or diet or training or behaviour or behavior or nutrition or sport or "physical activity" or "weight reduction" or "weight loss" or "energy restriction"). These were restricted to title, abstract, and keyword (Scopus only). The database permitting, the following were excluded: reviews; letters; editorials; commentaries; animal studies; and studies in those aged under 19 years. Review of articles was restricted to those published in English.

Titles and abstracts of studies identified were evaluated against eligibility criteria. Studies appearing eligible based on their abstract were read in full. The decision to exclude any of these studies was made by the consensus of two authors (CT & MT).

Data items

The items of interest from each report included: study type/design; diagnostic criteria for NAFLD; inclusion and exclusion criteria; blinding; similarity of groups at baseline; sex; age; definition of participant adherence; treatment protocol, including professions involved and contact time; reported adherence; criteria for dealing with medication; methods used to assess diet and physical activity; loss to follow-up; intention-to-treat or per-protocol analysis; IHTAG; measures of glucose control; ALT and/or AST concentration.

Data extraction

Relevant data from included reports were recorded in itemised tables. Results were converted to SI units or otherwise standardised and changes from baseline converted to percentages to facilitate comparison across studies. Where liver fat is given as a percentage, a change from 10% fat to 5% fat is referred to as an *absolute* reduction of 5% (10–5%) and a *relative reduction* of 50%.

Download English Version:

https://daneshyari.com/en/article/6105326

Download Persian Version:

https://daneshyari.com/article/6105326

Daneshyari.com