Nutrition 32 (2016) 338–348

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Effects of different dietary approaches on inflammatory markers in patients with metabolic syndrome: A systematic review and meta-analysis

Nico Steckhan M.Sc. [a,b,*], Christoph-Daniel Hohmann M.D. [a,b], Christian Kessler M.D. [a,b], Gustav Dobos M.D. [c], Andreas Michalsen M.D. [a,b], Holger Cramer Ph.D. [c]

[a] Institute of Social Medicine, Epidemiology and Health Economics, Charité-University Medical Centre, Berlin, Germany and Immanuel Hospital Berlin

[b] Immanuel Hospital Berlin, Department of Internal and Complementary Medicine, Berlin, Germany

[c] Department of Internal and Integrative Medicine, Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany

ARTICLE INFO

Article history:
Received 1 June 2015
Accepted 16 September 2015

Keywords:
Metabolic syndrome
NCEP ATP III
Nutrients
Diets
Inflammation
Systematic review
Meta-analysis

ABSTRACT

Objective: Chronic low-grade inflammation has been associated with insulin resistance, diabetes, atherosclerosis, obesity, and metabolic syndrome (MetS). A proinflammatory environment contributes to several metabolic disturbances and possibly the development of MetS. Dietary approaches have defined impact on immune function and putative antiinflammatory effects. The aim of this study was to assess the effects of different dietary approaches on markers of inflammation in patients with MetS. Further effects on weight loss and fasting insulin were analyzed.

Methods: Medline/PubMed, Scopus, and the Cochrane Library were screened in September 2014 for randomized controlled trials (RCTs) on different dietary approaches for participants with MetS as defined by National Cholesterol Education Program Adult Treatment Panel III. Primary outcomes were markers of the immune system. Secondary outcome was body weight and fasting insulin. Standardized mean differences (SMD) and 95% confidence intervals (95% CIs) were calculated.

Results: Thirteen randomized controlled trials with a total of 2017 patients were included. Low-fat diets (29 ± 2% energy from fats) decreased C-reactive protein compared with control diets (SMD: −0.98; 95% CI: −1.6 to −0.35; $P = 0.002$). Low-carbohydrate diets (23 ± 10% energy from carbohydrates; SMD: −0.33; 95% CI: −0.63 to −0.03; $P = 0.004$) and multimodal interventions (SMD: −1.02; 95% CI: −1.97 to −0.07; $P = 0.04$) were able to induce significant weight loss. Low-carbohydrate diets were able to decrease insulin (SMD: −0.33; 95% CI: −0.63 to −0.03; $P = 0.03$).

Conclusions: C-reactive protein; however, this effect is also dependent on weight loss. Furthermore, low-carbohydrate diets have beneficial effects on insulin and body weight. Dietary approaches should mainly be tried to reduce macronutrients and enrich functional food components such as vitamins, flavonoids, and unsaturated fatty acids. People with MetS will benefit most by combining weight loss and anti-inflammatory nutrients.

Introduction

Metabolic syndrome (MetS) is a major health issue of Western and westernized modern societies [1]. Here, lifestyle is often characterized by stress, fast food, and little exercise. The World Health Organization states obesity and overweight as the fifth leading risk for global deaths [2]. MetS is defined by the simultaneous occurrence of at least three of the following criteria: central obesity, elevated blood pressure, elevated plasma glucose, and dyslipidemia [3]. Obesity is common among patients suffering from MetS, which is associated with serious comorbidities [3]; obesity is a critical risk factor for cardiovascular diseases, diabetes mellitus 2, and arterial diseases [4].

* Corresponding author. Tel.: +49(0)30 80 505 663; fax: +49(0)30 80 505 692.
E-mail address: nico.steckhan@charite.de (N. Steckhan).

http://dx.doi.org/10.1016/j.nut.2015.09.010
0899-9007/

These symptoms of MetS interact with and exacerbate each other.

The primary mediators of Mets may be excess accumulation of abdominal fats and mature adipocytes [5]. Insulin resistance correlates with a state of chronical subclinical inflammation and endothelial dysfunction. Furthermore, MetS is thought to be a low-grade inflammatory disease [5].

Adipose tissue itself can be seen as an endocrine organ that plays a critical role in the immune homeostasis. It produces and releases a variety of adipokines and cytokines, including leptin, adiponectin, resistin, and visfatin, as well as tumor necrosis factor (TNF)-α, interleukin (IL)-6, and others [6,7]. Proinflammatory molecules produced by adipose tissue have been implicated as active participants in the development of metabolic disease [5]. Furthermore, adipose tissue macrophages are a prominent source of proinflammatory cytokines, which can block insulin action in adipose tissue, skeletal muscle, and liver autocrine/paracrine signaling and cause systemic insulin resistance via endocrine signaling, providing a potential link between inflammation and insulin resistance [6]. Dietary approaches are thought to positively influence the immune responses by decreasing its predominant proinflammatory milieu [8].

Several trials and reviews have documented the potential benefits of different dietary approaches on immune functions [5, 8–11]. However, just a few studies about different dietary approaches for patients with MetS were conducted.

A primary goal of low-carbohydrate diets is weight loss. Weight loss leads to reductions in inflammatory biomarkers in overweight men [12]. Experimental studies have provided evidence that, independent from weight gain, high intake levels of refined or simple carbohydrates are associated with proinflammatory effects [13].

Low-fat diets may simultaneously change macronutrient intake and quality that can increase intake of natural anti-inflammatory foods, such as fruits and vegetables, which may ultimately lower C-reactive protein (CRP) [14]. Another proposed mechanism involves low-fat foods limiting postprandial glucose response, thereby inhibiting cytokine release into the bloodstream [15] and subsequent CRP release from the endothelium [16].

Refined grains are able to induce short-term acute hyperglycemia and thus trigger proinflammatory cytokines. Switching to a diet rich in whole grains may decrease circulating levels of free radicals and proinflammatory cytokines, such as IL-6, IL-18, and TNF-α [8]. Intervention studies found a decrease in markers of inflammation in subjects with MetS who consume Mediterranean diets and/or adhere to national dietary guidelines [9]. By contrast, diets high in refined starches, sugars, and saturated and trans-fatty acids and poor in natural antioxidants and fiber from fruits, vegetables, and whole grains may cause an activation of the innate immune system. This is most likely caused by the excessive production of proinflammatory cytokines associated with a reduced production of anti-inflammatory cytokines. Thus, it seems likely that dietary adjustments have the potential to mediate a major effect on different components of MetS.

This systematic review was conducted to assess whether dietary interventions can positively modulate the immune system in MetS and help to improve favorable conditions, thus reducing the severity of the metabolic disorders in MetS.

Methods

This review was constructed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses [17] and the recommendations of the Cochrane Collaboration [18].

Eligibility criteria

To be eligible, studies had to meet the following conditions:

1. Types of studies. Only randomized controlled trials (RCTs) and randomized crossover studies were eligible. Crossover studies were only eligible if data of the first active treatment phase were available. Studies were eligible only if they were published as full-text articles in peer-reviewed scientific journals. No language restrictions were applied.
2. Types of participants. Studies of adult (older than 18 y) patients with MetS were eligible. There are slightly different definitions of MetS, because 41.3% of the patients were Caucasians. In general, MetS was defined as the presence of at least three of five risk factors defined by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) [19] and WHO-Asia Pacific (WHO Expert Consultation, 2004): increased waist circumference (>90 cm in men and >80 cm in women), hypertriglyceridemia (>150 mg/dL [1.7 mmol/L]), low levels of high-density lipoprotein cholesterol (HDL-C; <40 mg/dL [1 mmol/L] in men and <50 mg/dL [1.3 mmol/L] in women), elevated blood pressure (≥130/85 mm Hg or use of antihypertensive medication), and elevated fasting plasma glucose (≥110 mg/dL [6.105 mmol/L] or treatment for diabetes mellitus).
3. Types of interventions. Studies that compared interventions with main focus on diets with conventional diets or no treatment were eligible. Studies were excluded if they intervened only with supplements (multivitamins) such as certain nutritional or phytopharmacological drugs, such as n-3 fatty acids or antidiabetics. If studies supplemented beside a dietary regime, those studies were also eligible. Articles dealing only with postprandial effects of a dietary or meal intervention were excluded. No further restrictions were made regarding dietary approaches or length of the intervention. Multimodal interventions of diet combined with exercise and behavior training or other lifestyle interventions were also eligible.
4. Types of outcome measures. Studies were eligible if they assessed at least one immunologic and atherosclerotic outcome. Outcomes of interest were important immunologic factors such as CRP, IL-6, TNF-α, nuclear factor kappa B, interferon-gamma, and intercellular adhesion molecule 1, to name a few. (For more details, see search strategy, Supplementary File 1.) Secondary outcomes were body weight, blood pressure, HDL, low-density lipoprotein, triacylglycerols, insulin, glucose, and glycated hemoglobin.

Search strategy and study selection

Three electronic databases were searched: Medline/PubMed, Scopus, and the Cochrane Library. Searches were undertaken in September 2014. All articles published until September 2014 were considered for this review. References of included studies and key review and guideline reports were checked for additional studies.

The literature search was constructed around the search terms “diet” and “metabolic syndrome” with main focus on inflammatory markers. Search strategy was adapted for each database as necessary. The complete search strategy for PubMed can be found in Supplementary File 1.

Additionally, reference lists of identified original articles and reviews were searched manually. Abstracts of identified records were screened and the full articles of potentially eligible studies were retrieved.

Data extraction and management

C.-D.H. and N.S. independently extracted data on characteristics of the studies (e.g., trial design, randomization, and blinding), characteristics of the patient population (e.g., sample size, age, and diagnosis), characteristics of the intervention and control condition (e.g., type, program length, frequency, and duration), dropout rates, outcome measures, follow-ups, results, and safety. Discrepancies were rechecked with a third reviewer and consensus was achieved by discussion. Table 1 is organized by date.

Risk of bias in individual studies

Risk of bias was assessed by two authors independently using the Cochrane risk of bias tool. This tool assesses risk of bias on the following domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias [18]. Trial authors were contacted for further details if necessary. Studies with high risk of attrition bias were not excluded from meta-analyses.