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Review

Effect of fructose on postprandial triglycerides: A systematic review and meta-analysis of controlled feeding trials

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ABSTRACT

Background: In the absence of consistent clinical evidence, concerns have been raised that fructose raises postprandial triglycerides.
Purpose: A systematic review and meta-analysis was conducted to assess the effect of fructose on postprandial triglycerides.
Data sources: Relevant studies were identified from MEDLINE, EMBASE, and Cochrane databases (through September 3, 2013).
Data selection: Relevant clinical trials of ≥7-days were included in the analysis.
Data extraction: Two independent reviewers extracted relevant data with disagreements reconciled by consensus. The Heyland Methodological Quality Score (MQS) assessed study quality. Data were pooled by the generic inverse variance method using random effects models and expressed as standardized mean differences (SMD) with 95% confidence intervals (CI). Heterogeneity was assessed (Cochran Q statistic) and quantified (I^2 statistic).
Data synthesis: Eligibility criteria were met by 14 isocaloric trials ($n = 290$), in which fructose was exchanged isocalorically for other carbohydrate in the diet, and two hypercaloric trials ($n = 33$), in which fructose supplemented the background diet with excess energy from high-dose fructose compared with the background diet alone (without the excess energy). There was no significant effect in the isocaloric trials (SMD: 0.14 [95% CI: −0.02, 0.30]) with evidence of considerable heterogeneity explained by a single trial. Hypercaloric trials, however, showed a significant postprandial triglyceride raising-effect of fructose (SMD: 0.65 [95% CI: 0.30, 1.01]).
Limitations: Most of the available trials were small, short, and of poor quality. Interpretation of the isocaloric trials is complicated by the large influence of a single trial.

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Conclusions: Pooled analyses show that fructose in isocaloric exchange for other carbohydrate does not increase postprandial triglycerides, although an effect cannot be excluded under all conditions. Fructose providing excess energy does increase postprandial triglycerides. Larger, longer, and higher-quality trials are needed.
Protocol registration: ClinicalTrials.gov identifier, NCT01363791.

Contents

1. Introduction

Postprandial lipids were first associated with atherogenesis in 1979 by Zilversmit [1]. Several studies have demonstrated that non-fasting trigycerides, in particular peak postprandial triglycerides, are better predictors of cardiovascular risk than fasting triglycerides. The Copenhagen City Heart Study demonstrated an association between increased nonfasting triglycerides and myocardial infarction and death with postprandial triglycerides 4 h after the last meal (within the peak range) the strongest predictors of cardiovascular events [2]. In the Women's Health Study, non-fasting triglyceride levels were more strongly correlated with cardiovascular disease incidence than fasting triglycerides, which lost significance after adjustment for total and HDL cholesterol [3]. Based on these data, the American Heart Association has proposed an initial lipid screen for non-fasting triglycerides with a cut point of 200 mg/dL (2.26 mM) [4].

Dietary factors which contribute to raised postprandial triglycerides have become a focus of concern. Particular attention has been focussed on the role of fructose. Highly reproducible animal models of fructose overfeeding have shown raised triglycerides secondary to increases in triglyceride secretion [5], impaired VLDL clearance, and enhanced fatty acid esterification [6]. Whether these findings hold true in humans under "real-world" intake patterns is unclear. Earlier systematic reviews and meta-analyses of controlled feeding trials have suggested a dose threshold for triglyceride-raising effects of fructose with increases in fasting triglyceride seen only at doses >60-g/day in type 2 diabetes [7] and ≥100-g/day across different metabolic phenotypes [8]. The threshold appears to be even lower for postprandial triglycerides with increases seen only at ≥50-g/d [8], a threshold roughly equivalent to the average fructose intake in the US [9]. This effect of fructose on postprandial triglycerides, however, is derived largely from acute, single-bolus studies [8]. The effect of fructose on postprandial triglycerides under chronic feeding conditions needs further investigation.

To assess the effects of longer-term fructose intake on postprandial triglycerides, we conducted a systematic review and meta-analysis of controlled feeding trials.

2. Methods

We followed the Cochrane Handbook for Systematic Reviews of Interventions for the planning and conduct of this meta-analysis [10]. The reporting followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [11]. The review protocol is available at ClinicalTrials.gov (registration number: NCT01363791).

2.1. Study selection

We searched Ovid MEDLINE (1946 through September 3, 2013), Embase (1980 through September 3, 2013) and The Cochrane