Nutrition 30 (2014) 503–510

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

Association of fructose consumption and components of metabolic syndrome in human studies: A systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 21 June 2013
Accepted 17 August 2013

Keywords:
Fructose
Blood glucose
Triglycerides
Lipoproteins
HDL
Blood pressure

ABSTRACT

Objective: The aim of this study was to review the current corpus of human studies to determine the association of various doses and durations of fructose consumption on metabolic syndrome.
Methods: We searched human studies in PubMed, Scopus, Ovid, ISI Web of Science, Cochrane library, and Google Scholar databases. We searched for the following keywords in each paper: *metabolic syndrome x, insulin resistance, blood glucose, blood sugar, fasting blood sugar, triglycerides, lipoproteins, HDL, cholesterol, LDL, blood pressure, mean arterial pressure, systolic blood pressure, diastolic blood pressure, hypertens*, waist circumference, and fructose, sucrose, high-fructose corn syrup, or sugar.*
Results: Overall, 3102 articles were gathered. We excluded studies on natural fructose content of foods, non-clinical trials, and trials in which fructose was recommended exclusively as sucrose or high-fructose corn syrup. Overall, 3069 articles were excluded. After review by independent reviewers, 15 studies were included in the meta-analysis. Fructose consumption was positively associated with increased fasting blood sugar (FBS; summary mean difference, 0.307; 95% confidence interval [CI], 0.149–0.465; $P = 0.002$), elevated triglycerides (TG; 0.275; 95% CI, 0.014–0.408; $P = 0.002$); and elevated systolic blood pressure (SBP; 0.297; 95% CI, 0.144–0.451; $P = 0.002$). The corresponding figure was inverse for high-density lipoprotein (HDL) cholesterol (−0.267; 95% CI, −0.406 to −0.128; $P = 0.001$). Significant heterogeneity existed between studies, except for FBS. After excluding studies that led to the highest effect on the heterogeneity test, the association between fructose consumption and TG, SBP, and HDL became non-significant. The results did not show any evidence of publication bias. No missing studies were identified with the trim-and-fill method.
Conclusion: Fructose consumption from industrialized foods has significant effects on most components of metabolic syndrome.

Introduction

Fructose is a monosaccharide that naturally exists in fruits, honey, and some vegetables. These days, however, fructose is mostly ingested from industrial and commercial products such as soft drinks, sweetened beverages, and high-fructose corn syrup (HFCS) [1,2]. Natural foods that contain fructose, such as fruits and vegetables, only contain small amounts; moreover their fructose is absorbed slowly. Thus, after consuming these foods, the rise in serum fructose concentration is negligible [3]. The use of HFCS in beverages and soft drinks is increasing by food manufacturers because of its low cost compared with sucrose, and the ease with which it can be added to food products [4]. Actually, the consumption of fructose through manufactured products is concerning. The average daily intake of total fructose in the United Stated increased 12 g/d between 1978 (37 g/d) and 2004 (49 g/d) [5,6].

Fructose is more lipogenic than other carbohydrates, and unlike glucose it can be converted to glycerol-3-phosphate (required for tri-acylglycerol synthesis) without passing from the phosphofructokinase pathway, which is an important rate-limiting pathway of glycolysis. Therefore, high-fructose consumption can be the cause of triglyceride (TG) synthesis from

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http://dx.doi.org/10.1016/j.nut.2013.08.014

Table 1
Search strategy for PubMed, Scopus, Ovid, ISI Web of Sciences, Cochrane library and Google Scholar databases

No.	Search terms
1	"Metabolic syndrome x" [Mesh] OR "insulin resistance" [Mesh] OR "blood glucose" [Mesh] OR "blood sugar"[tiab] OR "FBS" [tiab] OR "Triglycerides" [Mesh] OR "Lipoproteins, HDL" [Mesh] OR "Cholesterol, HDL" [Mesh] OR "Lipoproteins, LDL" [Mesh] OR "Cholesterol, LDL" [Mesh] OR "Blood Pressure" [Mesh] OR "mean arterial pressure" [tiab] OR "BP" [tiab] OR "SBP" [tiab] OR "DBP" [tiab] OR "hypertens*"[tiab] OR "Waist Circumference"[Mesh]
2	"Fructose" [Mesh] OR "Sucrose" [Mesh] OR "high fructose corn syrup" [tiab] OR "sugar"[tiab]
3	1 AND 2

unchecked pathways [7]. According to animal studies, consumption of a 60% total energy diet with fructose can induce obesity and some components of metabolic syndrome (MetS) such as insulin resistance, dyslipidemia, and hypertension [8–10].

The escalating trend in the prevalence of chronic diseases in industrialized and developing countries [11] and the increase in fructose consumption in the population's diet is of concern. Researchers have proposed an association between fructose consumption and chronic diseases [12]. Therefore, many experimental and human studies are being conducted to assess the relationship of fructose consumption with the development of chronic diseases such as diabetes and MetS [4].

Studies of young healthy individuals have shown that fructose consumption (250 g/d) compared with the same amount of glucose significantly decreased insulin sensitivity [7]. There are fewer studies on the long-term effects of fructose consumption on human health than on the effects of glucose [3]. The adverse short-term effects of fructose seem to be dose-dependent. Short-term consumption of fructose in humans did not have adverse effects on health status, unless consumed in excessive amounts. Long-term consumption of fructose is associated with an increase in adiposity, dyslipidemia, and insulin resistance [3,7].

Findings about fructose and health status are controversial. Some studies supported the hypotheses that fructose consumption leads to an increase in chronic disorders such as MetS [13–16], whereas others did not confirm the positive association of fructose with the components of the disease [17–20]. Some reasons may be suggested for the differences between the findings of various studies. Low fructose dose, for instance < 20 g/d, mostly showed improved or no effect on MetS parameters; however, high doses of fructose mostly increased the features of MetS [16,20]. Different forms of fructose such as natural fructose, fructose alone, or fructose bonded with glucose in the form of sucrose, showed various findings [3]. Race, study design, animal or human studies, and different characteristics of participants such as sex, age, and body weight are other factors that influence differences in the findings obtained in various studies.

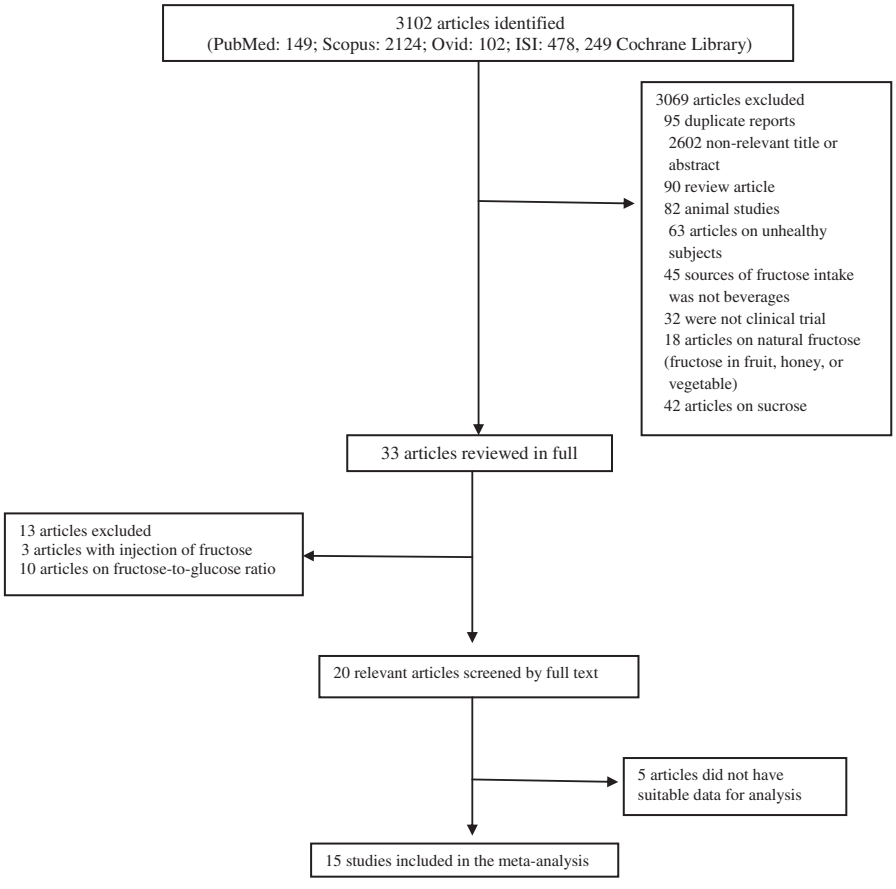

Fig. 1. Flowchart of the literature search.