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IM - REVIEW

Cardiovascular risk and dietary sugar intake: is the link so sweet?

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Abstract Soft drinks and sugar-sweetened beverages have been targeted as one of the primary culprits in the escalating rates of obesity and diabetes and reduction of added sugars is considered between the goals to achieve in order to promote cardiovascular health and to reduce deaths from cardiovascular causes. Many reliable mechanisms, such as dislypidemia, inflammation and enhanced oxidative stress, have been proposed to support a causal link between sugar sweetened beverages intake and cardiovascular risk, but the ultimate underlying pathways remain to be determined in adequately designed studies. Furthermore, while epidemiological evidence strongly supports an association between sugar sweetened beverages consumption and obesity, type 2 diabetes mellitus or cardiovascular risk, incongruous findings yielded by clinical trials, or formal meta-analyses make difficult to draw firm conclusions in this regard. Further and rigorous studies are needed to better understand the role of sugar sweetened beverages in the etiology of cardiovascular diseases and to better address the warnings and decisions of regulatory authorities on public health worldwide.

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Introduction

Obesity is becoming a global epidemic, and in the past 10 years in the western countries, particularly in the US, dramatic increases in obesity incidence have occurred in both children and adults. Over the past two decades, a huge increase in the number of people with the metabolic syndrome (MetS) has taken place all around the globe. However, the uncertainty about its pathogenesis has brought some doubt with regard to whether the MetS is a syndrome or an independent cardiovascular disease (CVD) risk factor. Nevertheless, MetS may be associated with the global epidemic of obesity and diabetes—reported in Zimmet et al. [1] as "diabesity".

It is well known that obesity is associated with an increased mortality and morbidity for CVD [2], and that adipose tissue is recognized as an important player in obesity-mediated CVD. Although overweight and obesity affect all subpopulations, the burden is particularly striking among adolescents compared to younger children. This implies, on the one hand, that pediatric populations experience weight-related chronic diseases previously seen only in adults, and, on the other hand, that the epidemic of obesity and its downstream consequences including type 2 diabetes and CVD are increasing exponentially. Correlated with economic, social and lifestyle changes, obesity represents a common condition of different populations living in environments characterized by abundant calorie-rich food and low physical activity (International Obesity Task Force 2005, http://www.iotf.org/). The current environment, including restaurants, food markets, schools in

industrialized countries, has been regarded as "obesogenic", in that it drives unhealthy habits such as large portion sizes, sneaking away-from-home meals, and consumption of sugar-sweetened beverages (SSBs).

In the setting of a pandemic of obesity and related chronic diseases, the American Heart Association has recently released scientific recommendations to reduce added-sugar intake to no more than 100–150 kcal/day for most Americans [3]. Given the elevated risk of not only diabetes but also CVD from obesity and the MetS, strategies to stop the emerging global epidemic of obesity are urgently needed.

This review will focus on the epidemiology of SSBs consumption, its contribution to the epidemic of obesity, type 2 diabetes and CVD, possible biological mechanisms underlying this link, methodological pitfalls affecting clinical studies on this subjects, and clinical implications and perspectives.

Obesity, diabetes and cardiovascular risk

Both obesity and diabetes are associated with an increased mortality and morbidity for CVD [1, 2]. Low-grade inflammation, oxidative stress, and platelet/coagulative activation appear as the mechanisms underlying the features of the MetS, including obesity and diabetes [4].

Obesity

Obese adipose tissue is characterized by inflammation and progressive infiltration by macrophages as obesity develops, and has the capacity to secrete biologically active mediators [5]. Adiponectin, an adipokine with proved anti-atherogenic and anti-inflammatory properties, which is inversely related to insulin resistance, has been recently shown to act as an endogenous antithrombotic factor, since its over expression attenuates thrombus formation in mice [6]. In addition, the increase of circulating leptin, in obese women, is associated with markers of the hemostatic system [5]. The proinflammatory state coupled with oxidative stress induces insulin resistance, which promotes further inflammation through an increase in free fatty acids (FFA) concentration and interference with the anti-inflammatory effect of insulin [5]. Moreover, FFA release from adypocytes induces endothelial dysfunction due to an increased reactive oxygen species (ROS) generation and oxidative stress [7]. Insulin resistance is the *core* abnormality that may account for most of the features predisposing to atherothrombosis in obesity. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral obesity, and decreases insulin sensitivity in obese humans [8]. Resistance to the metabolic and vascular actions of insulin [9], leads, in turn, to a further pro-inflammatory state, and a significant association exists between insulin resistance and the markers of inflammation and thrombin generation [10]. Moreover, we characterized low-grade inflammation and lipid peroxidation with higher isoprostane formation as putative biochemical links between obesity and platelet activation [11]. Successful weight loss due to caloric restriction is associated with a statistically significant reduction in both platelet activation and oxidative stress, suggesting that in abdominal obesity, low-grade inflammation may trigger thromboxane-dependent platelet activation mediated, at least in part, through enhanced lipid peroxidation [12]. Furthermore, insulin resistance per se is a major determinant of an increased platelet activation in obesity, independent of underlying inflammation [12]. Successful weight loss or the insulin-sensitizer pioglitazone, are associated with a concomitant improvement in insulin sensitivity and platelet activation [12]. Moreover, diet-induced body-weight reduction restores platelet sensitivity to the physiological antiaggregating effect of nitric oxide (NO) and prostacyclin, and reduces platelet activation and insulin resistance in subjects affected by visceral obesity [13]. Finally, diet-induced improvement in insulin sensitivity may partly be mediated by upregulation of adiponectin: exercise alone and in combination with a diet-induced weight loss enhances the mRNA expression of adiponectin receptors in adipose tissue and skeletal muscle, whereas a pronounced hypocaloric-induced weight loss is necessary to increase circulating adiponectin in obese subjects [14]. Nevertheless, leptin, but not adiponectin, has been recently recognized as a reliable biomarker of diet-induced weight loss in humans [15].

Diabetes

The abnormal metabolic state that accompanies diabetes, including insulin resistance, hyperglycemia and excess FFA release, activates various adverse systems, such as oxidative stress, advanced glycation end products (AGE)/receptor for AGE (RAGE) system, endothelial dysfunction, eventually leading to inflammation, vasoconstriction and thrombosis [16]. The expression of proinflammatory cytokines and other mediators, including adhesion molecules, suggests that inflammatory processes may contribute to vascular disease in diabetes [5]. Enhanced oxidative stress in the hyperglycemic milieu accelerates the non-enzymatic glycoxidation of proteins and lipids to generate AGEs, resulting in hyperactivation of their receptor (RAGE) [16]. Consistent with this, a significant inverse association is reported between metabolic control as assessed by hemoglobin A1c, and circulating levels of the soluble decoy RAGE in type 2 diabetic subjects [17].

Hyperglycemia may induce ROS production directly via glucose metabolism and auto-oxidation and indirectly through the formation of AGE and their receptor binding. In addition to increased ROS production, enhanced peroxidation of arachidonic acid to form biologically active isoprostanes may represent an important biochemical link between impaired glycemic control and persistent platelet activation both in type 1 and type 2 diabetes [16, 18].

In fact, we initially demonstrated enhanced thromboxane biosynthesis in type 2 diabetes, and provided evidence for its platelet origin and its reduction in response to tight metabolic control [19]. Improvement of metabolic control in these patients is accompanied by a significant reduction in 11-dehydro-TXB_2 excretion. Thus, changes in the rate of arachidonate peroxidation to form biologically active isoeicosanoids, such as 8-*iso*-$PGF_{2\alpha}$, may represent an important biochemical link between altered glycemic control, oxidant stress and platelet activation in type 2 diabetes [18–20].

Sugar-sweetened beverages consumption in the general population

A healthy and well-balanced diet contains natural sugars, such as monosaccharides (glucose, fructose and galactose) and disaccharides (sucrose and lactose) that are integral components of fruit, vegetables, dairy products, and many cereals. However, deleterious health effects may occur when sugars are consumed in large amounts over time [3].

Added or extrinsic sugars refer to sugars and syrups added to foods during their preparation, processing, or at the table. They have not been a significant component of the human diet until the advent of modern food-production methods. Since then, the intake of sugar has risen steadily. SSBs which include the full range of soft drinks, fruit drinks, energy drinks, and vitamin water drinks, are the primary source of added sugars in Americans' diets and around the globe [3, 21]. National representative estimates from the US show a steady increase in per capita calories from SSBs in both children and adults starting from the mid 1960s [22]. At the same time, while juice consumption has remained relatively stable across all age groups, there is a decrease in calories consumed from milk, particularly among children [22]. The most recent data show that children and adults consume about 172 and 175 kcal per day, respectively, from SSBs [22]. Particularly, among 2- to 18-year-olds, SSBs are reported to be the largest contributor to "empty" calories, representing the sum of energy from solid fat and added sugars. Moreover, among both boys and girls aged 9–13 and 14–18 years, the empty calories consumed from soda and fruit drinks exceed the discretionary calorie allowance, which ranges from 8 to 20% of total energy consumed [23]. This trend has raised concerns about the possible role of SSBs in displacing or diluting nutrients in the diet, and contributing to the epidemic of obesity in developed countries.

High-fructose corn syrup (HFCS), the most frequent sugar used as a sweetener in many SSBs, is manufactured by hydrolyzing corn starch into glucose, which then is partly isomerized into fructose by enzymatic measures. In fact, while "common table sugar", also known as sucrose, contains sequimolar amounts of fructose and glucose linked to form a disaccharide, HFCS contains about 5% more fructose than glucose, and both sugars are present as monosaccharides. This "free fructose" is preferred by food and soft drink manufacturers because it exerts a significantly increased perception of sweetness. Furthermore, HFCS confers a long shelf-life, and its low cost has contributed to a very rapid increase in its consumption at the expense of sucrose [21]. In the US, HFCS consumption has continuously increased over the past three decades, and accounts for 42% of total caloric sweetener consumption in any age group, including young children [24]. In addition, total energy intake has increased by 18% and total carbohydrate intake by 41% during the same period, while the contribution of fructose to carbohydrate intake has remained nearly constant despite increased consumption of free fructose [24]. Although there are no available data, it is probably true that free fructose consumption has undergone a similar increase in most parts of the world. Thus, one can speculate that free fructose consumption is the main item responsible for cardiovascular risk associated to SSBs and soft drinks worldwide, and that potentially their adverse metabolic effects are related to their fructose over glucose fraction [25].

Recently, SSB is emerging as an indicator of the quality of lifestyle habits. In a recent cross-sectional analysis, examining the dietary and activity correlates of SSB consumption among girls and boys from a population-based sample of children in Texas, "unhealthy" foods (meats, fried snacks, desserts) are unequivocally associated with SSBs. Vegetable and fruit consumption increases with the level of noncarbonated flavored and sports beverage (FSB) consumption, but decreases with the level of soda consumption. Sedentary measures (hours spent watching television, using the computer, and playing video games) increases in general with both soda consumption and FSB consumption [26].

Sugar-sweetened beverages intake and cardiovascular risk

Recently, the American Heart Association has published a statement on dietary sugar intake and cardiovascular

Table 1 Biases affecting the feasibility of randomized controlled studies (RCTs), and the validity and transferability of their findings

Heterogeneity in the outcome measure	Changes of plasma lipid levels and anthropometric measures, increase of cardiovascular risk biomarkers, weight gain, metabolic syndrome, occurrence of type 2 diabetes mellitus and cardiovascular events could variably and heterogeneously reflect the impact of SSB consumption on health status.
Intervention intensity and study design	Type, number and frequency of SSB intake in the general population is hardly measured and difficult to emulate in the setting of a clinical trial.
Misclassification of SSB intake	The wide range of SSBs (soft drinks, fruit drinks, energy drinks, vitamin water drinks) that differ in sugar added, especially in fructose and glucose amount, may have a different impact on outcome measures.
Compliance	It may vary with type, number and frequency of SSB intake and decrease with increasing study length.
Study duration	Results from short-term trials are difficult to extrapolate to dietary alterations of longer durations because significant changes in body composition and metabolic structure accounting for cardiovascular risk occur slowly over time. Thus, a sufficient follow-up time is needed to effectively evaluate the causal role of SSBs to occurrence of cardiovascular diseases.
Confounding by lifestyle factors affecting total energy intake	Incomplete adjustment for neglected or imperfectly measured lifestyle factors may overestimate the strength of the association between SSB consumption and the outcome measures.
Publication biases	Industries may be prone to not publish significant results supporting a strong association, and non-industry researchers may be prone to not publish non-significant findings.

health, and has recommended a reduction in the intake of added sugars to be not more than 80 calories for a daily energy consumption of 1,800 calories for an average adult woman, and not more than 144 calories for a daily energy consumption of 2,200 calories for an average adult man [3]. Furthermore, the reduction of added sugars is considered between the goals to promote cardiovascular health and to reduce mortality from CVD by 20% by the year 2020 [27]. These recommendations stem from several epidemiological and interventional data supporting a link between dietary sweetened beverages intake and the occurrence of metabolic and cardiovascular disorders.

Several prospective cohort studies have provided robust evidence for a link between SSBs consumption and weight gain, risk of obesity, type 2 diabetes mellitus and the MetS among adults. For example, in women followed for 8 years, a higher consumption of SSBs is associated with weight gain while those people consuming one serving of SSBs per day have an 83% greater risk of developing diabetes compared to those consuming one serving SSB per month (RR 1.83, 95% CI, 1.42–2.36; $P < 0.001$) [28]. Furthermore, based on data from Malik and coworkers in a study with over 300,000 participants, the individuals in the highest quantile of SSB intake (most often 1–2 servings per day) have a 26 and 20% greater risk of developing type 2 diabetes and the metabolic syndrome, respectively, than those in the lowest quantile (none or <1 serving per month) [29].

Findings from the Framingham Offspring Study on about 6,000 subjects show that individuals who consume more than one soft drink per day have about 40% greater risk of developing obesity or the MetS during the course of a 4-year period compared to non consumers, and in addition, a 22% higher incidence of hypertension [30]. Regarding lipid profile, in this study, daily soft drink consumers have a 22% higher incidence of hypertriglyceridemia and low HDL cholesterol compared with non-consumers [30]. These data are in accord with a recent cross-sectional study from the National Health and Nutrition Examination Survey (NHANES) 1999–2006 that shows a statistically significant correlation between dietary added sugars and blood lipid levels among US adults and adolescents [31]. Particularly, added sugar consumption is inversely correlated with HDL cholesterol and positively associated with LDL cholesterol and triglycerides. In addition, among adolescents who are overweight or obese, added sugar intake is positively correlated with the homeostasis model assessment of insulin resistance (HOMA-IR) [31].

Furthermore, a recent prospective study addresses for the first time, the relation between SSBs intake and the incidence of clinical coronary heart disease (CHD) events. In women aged 34–59 years without previously diagnosed CHD, stroke, or diabetes followed for over two decades, a regular consumption of SSBs is positively associated with a higher risk of CHD [32]. This relation remains significant even after adjustment for a multitude of dietary and lifestyle factors. Additional adjustment for the BMI and energy intake score has somewhat attenuated this association, which suggests that excess calorie intake and obesity mediate the association [32].

A recent meta-analysis supports the same relationship between SSBs and weight gain or obesity in children and adolescents as in adults [33]. However, a longitudinal study with Finnish children and adolescents aged 3–18 years followed up for 21 years, shows that the increase of SSBs consumption from childhood to adulthood is directly

associated with BMI into adulthood in women ($b = 0.45$, $P = 0.0001$), but not in men [34]. A recent systematic review and meta-analysis of randomized experiments, incorporating 12 studies lasting at least 3 weeks and including an adiposity indicator as an outcome, consistently shows no effect of SSB consumption on BMI, with a suggestion of a benefit in overweight subjects. This paradoxical effect may be explained by the heterogeneity of studies, and the limited number of participants included in this meta-analysis, thus future ad hoc studies are warranted [35].

Finally, some studies have provided limited and uncertain data on habitual SSBs consumption and blood pressure both in adults [30] and in children [36]. In particular, a positive association has been observed between SSBs intake, fasting plasma glucose and diastolic blood pressure in Mexican school-age children [36]. In addition, in a recent interventional trial, subjects who have reduced their daily SSBs intake are found to have significantly lower values of diastolic and systolic blood pressure [37], thus suggesting that SSBs consumption may be an important dietary strategy to lower blood pressure.

Potential mechanisms by which soft drinks promote obesity and related diseases

Several mechanisms have been proposed to explain the effects of SSBs on health (Fig. 1). Mainly, it is thought that they lead to weight gain by decreasing satiety, and by incomplete compensatory reduction in energy intake at subsequent meals following intake of liquid calories. This evidence stems from several short-term feeding trials comparing SSB consumption to non-caloric artificially sweetened beverages.

A cross-over trial shows that individuals drinking aspartame-sweetened beverages for 3 weeks lose weight while those drinking HFCS-sweetened beverages have a small weight gain [38]. Moreover, after 10 weeks of supplementation with either sucrose- or artificially sweetened beverages and foods, individuals in the sucrose group compared to the control group significantly increase body weight, energy intake and blood pressure [39]. These short-term studies raise the possibility that sucrose or high-fructose sweetened beverages added daily to calories from other foods may lead to an energy unbalance and weight gain over the course of a few years.

A study comparing the effects of liquid or solid isocaloric loads shows that individuals assigned to 450 kcal/day soft drink consumption significantly increase their weight and caloric intake from other foods as compared to subjects consuming the same amount of sucrose energy as jelly beans [40]. Thus, sweetened liquid beverages may not suppress solid food intake to the level needed to maintain energy balance, and hypothetically sugar solutions may fail to trigger satiety in the same way that solid preparations do. However, the physiologic mechanisms have not been fully determined [40].

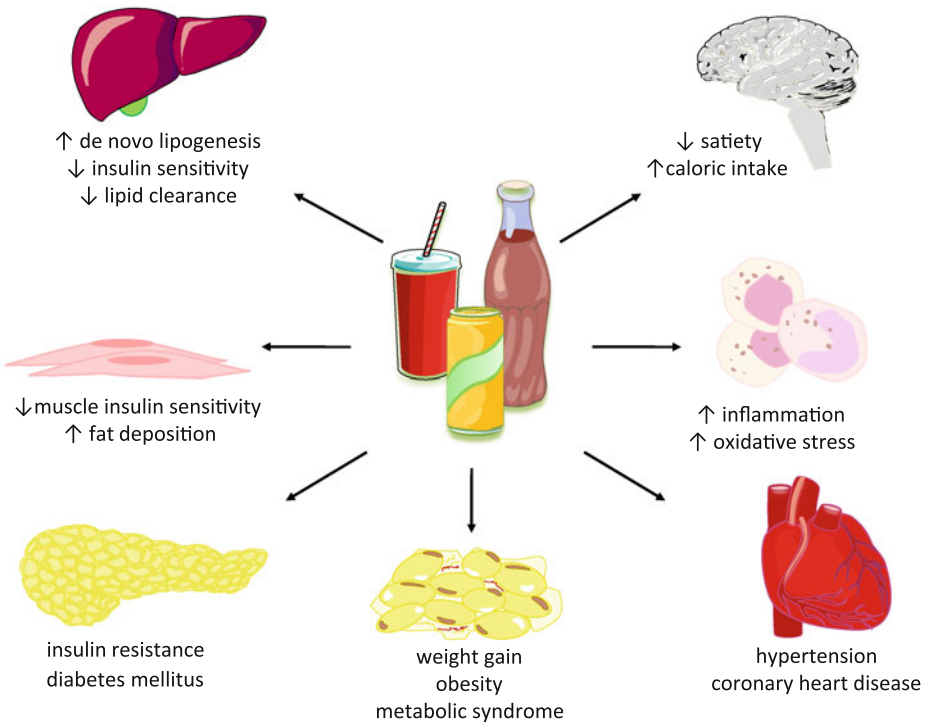

Fig. 1 Putative links between sugar sweetened beverages (SSBs) consumption and cardiovascular risk

SSBs may also affect body weight through other behavioral mechanisms. Whereas the intake of solid food is characteristically coupled to hunger, people may consume SSBs in the absence of hunger, simply to satisfy thirst or for social reasons [22]. Furthermore, the sensory properties of foods are important in affecting our nutrition. In fact, sugars add desirable sensory effects to many foods, and a sweet taste promotes enjoyment of meals and snacks. Persons, especially children, who habitually consume SSBs rather than water may find foods (such as vegetables, legumes, and fruits) that are more satiating but less sweet to be unappealing or unpalatable, thus leading to poor quality diets [22]. Importantly, repeated exposures to selected foods in early infancy are associated with acceptance, and then preference of these foods [41]. Moreover, food choices in childhood have long-term influence on dietary intake later in life. In this regard, although innate preferences for sweet tastes have been described from early infancy, and genetic propensities toward certain food groups have been shown in twin studies, familial (parental model eating behavior from birth onward) and environmental factors (e.g. exposure to mass-media) are the most important determinants in the development of taste preferences, leading to overeating of these foods and potentially contributing to excessive weight gain [41].

Adverse and undesiderable metabolic consequences from this "energy unbalance" are inevitable. In rodents, high sucrose or a high-fructose diet cause obesity, dyslipidemia and diabetes, with decrease in both liver and muscle insulin sensitivity, body fat distribution changes, and ectopic lipid deposition in liver and muscle [42] (Fig. 1).

In humans, the adverse metabolic effects of fructose are less clearly documented, and the results from clinical studies are sometimes conflicting. For example, there is evidence that high-fructose diet causes an increase of plasma triglyceride levels through a hepatic de novo lipogenesis and a decrease of hepatic insulin sensitivity [42]. On the contrary, another study demonstrates that a hypercaloric high-fructose diet leads to ectopic fat deposition in hepatic and skeletal muscle cells, but does not cause insulin sensitivity decrease in healthy subjects [42]. However, the different amounts of fructose consumption assigned and the different duration of treatment may partially explain the conflicting results of these two studies on healthy individuals.

Fructose intake also increases several of the biomarkers of risk for cardiovascular disease, such as ApoB levels, LDL cholesterol, small dense LDL (sdLDL), oxidized LDL-cholesterol, remnant lipoprotein triglyceride, and apoB/apoA1 ratio, as well as glucose and insulin excursions during an oral glucose tolerance test, fasting insulin concentrations, and insulin-sensitivity index as assessed by deuterated glucose disposal. Thus, de novo hepatic lipid synthesis, lipid clearance reduction, and reduced insulin sensitivity are the main fructose-induced alterations [25].

However, it is difficult to draw unequivocal conclusions from such underpowered, uncontrolled and short-term studies and extrapolate results to dietary alterations of longer durations, since especially in non-healthy individuals, significant changes in body composition and metabolic structure occur over time, and account for the cardiovascular risk.

Fructose can also increase blood uric acid concentrations [43] (Fig. 2), and high consumption of soft drinks produces hyperuricemia and increases the incidence of gout [43], a condition commonly associated with hypertension, the metabolic syndrome, CHD, cerebrovascular disease, vascular dementia, preeclampsia, and kidney disease [43]. Experimental data support a relationship between fructose intake, hyperuricemia, and blood pressure values. In fact, rats fed with fructose develop hyperuricemia, hypertension, and a metabolic-like syndrome with renal hemodynamic and histologic changes very similar to those observed with hyperuricemia [43]. In experiments with cultured vascular smooth-muscle cells, uric acid induces cellular proliferation, inflammation, oxidative stress, and activation of the local renin–angiotensin system [43] (Fig. 2). Furthermore, the production of uric acid in the liver by xanthine oxidase may reduce endothelial NO [43] (Fig. 2). Thus, one might speculate that fructose-induced hyperuricemia may have a role in the increased prevalence of hypertension worldwide, as shown by recent data [37].

Although oxidative stress and inflammation have been proposed as mechanisms responsible for adverse metabolic effects of fructose, this issue remains controversial. In fact, in healthy subjects, the intake of 300 kcal as orange juice or fructose, unlike equivalent caloric intake of glucose (75 g), is not associated with an enhanced reactive oxygen species (ROS) generation by mononuclear cells (MNC) and polymorph nuclear cells (PMN) [38].

Observational studies find positive associations between SSBs consumption and markers of inflammation, such as C-reactive protein (CRP) [44]. Finally, an exaggerated intake of AGEs generated during the heating and cooking of foods [45] may induce low-grade inflammation, enhanced oxidative stress, and promote atherosclerosis [16]. In this regard, cola-type soft drinks contain a high amount of AGEs produced during the process of sugar caramelization, and a direct association exists between dietary AGE intake and markers of systemic inflammation such as serum CRP both in healthy and in diabetic subjects [45]. Moreover, in type 2 diabetic patients, urinary 8-iso-$PGF_{2\alpha}$, a marker of oxidative stress, is inversely correlated with soluble RAGE (sRAGE) (Fig. 3). This soluble form, acting as a decoy domain receptor, decreases AGEs cellular

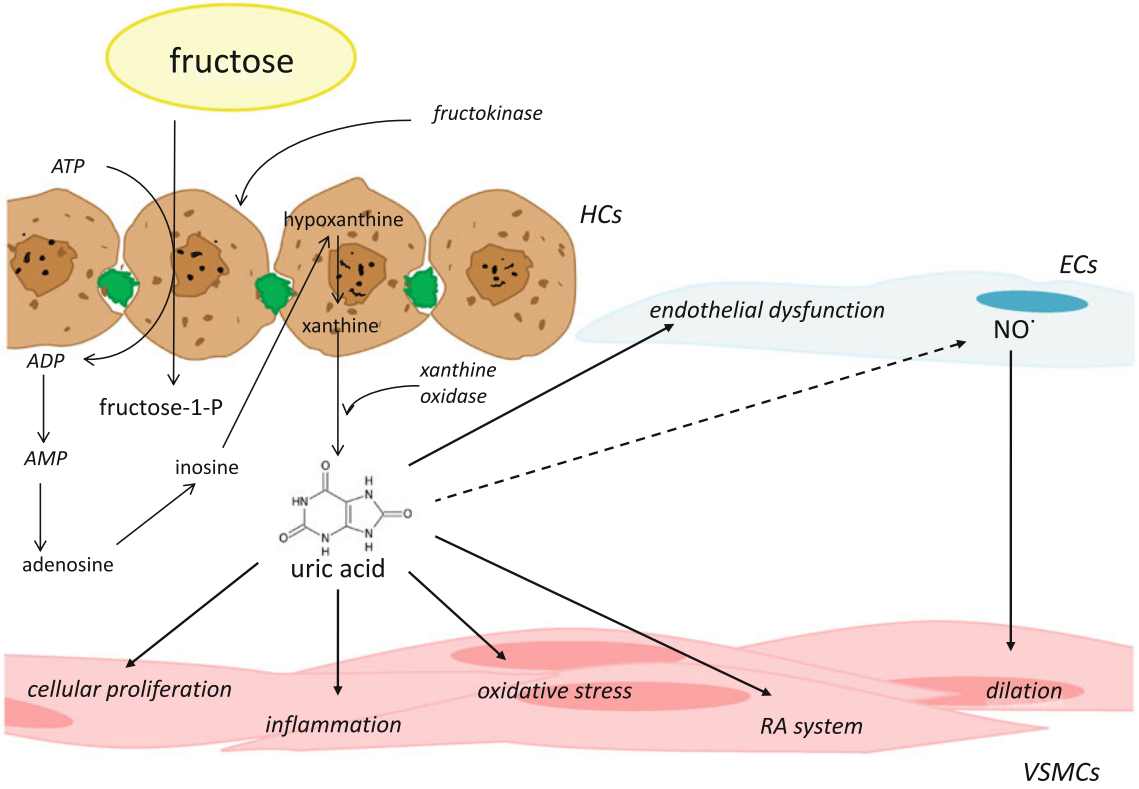

Fig. 2 Possible mechanism linking fructose intake and uric acid-mediated hypertension. Excessive intake of fructose by sugar sweetened beverages may determine chronic hyperuricemia, a condition associated with a wide variety of clinical conditions at high cardiovascular risk, including hypertension. Fructose is converted in fructose-1-phosphate (fructose-1-P) by fructokinase and induces increasing ATP degradation to ADP, a uric acid precursor. The accompanying phosphate depletion limits regeneration of ATP from ADP and AMP, which in turn serves as a substrate for uric acid formation. Uric acid generated may induce cellular proliferation, inflammation, oxidative stress in vascular smooth-muscle cells (VSMCs), and activate the renin–angiotensin (RA) system, contributing to renal and systemic vasoconstriction and thus increasing blood pressure. Moreover, in endothelial cells (ECs) it causes dysfunction and nitric oxide (NȮ) reduction, limiting its vasodilatating effect. In hepatic cells (HCs), xanthine is also usually converted to uric acid by xanthine oxidase. *Dotted lines* represent inhibition way

binding, and, thus, may improve AGE-mediated diabetic vascular complications. Improvement in metabolic control results in a significant increase in sRAGE and concurrent decrease in oxidative stress in this setting [17].

Methodological pitfalls

Epidemiological evidence supports an association between SSB consumption and obesity, type 2 diabetes mellitus or cardiovascular risk, whereas discrepant findings are yielded by clinical trials, critical reviews or formal meta-analyses. Randomized controlled studies (RCT) have the potential to adequately address the unanswered questions since they can control for both known and unknown confounders. Unfortunately, a number of biases affect the feasibility of RCTs, and the validity and transferability of their findings. Variability in the choice of the outcome measure (weight gain, cardiovascular events), intervention intensity,

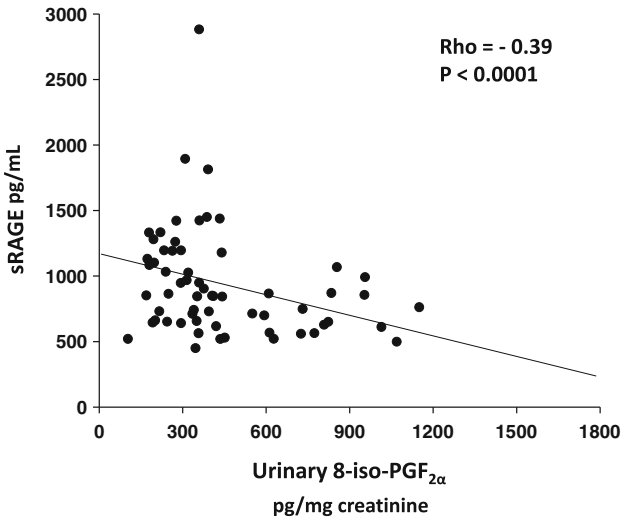

Fig. 3 Correlation between plasma levels of sRAGE and urinary 8-*iso*-$PGF_{2\alpha}$ in 85 type 2 diabetic patients (modified from Devangelio et al. [17])

misclassification of SSB intake, compliance, waning with increasing study duration, and confounding by other lifestyle factors affecting total energy intake, altogether limit the interpretation of their results (Table 1). Incomplete adjustment for neglected or imperfectly measured lifestyle factors may be responsible for overestimation of the strength of the association between SSB consumption and the outcome measures. Finally, industries may be prone to not publish significant results supporting a strong association, and non-industry researchers may be prone to not publish non-significant findings, driving publication biases in both cases. Ad hoc RCTs appropriately designed to answer the question whether reducing SSB consumption may improve obesity and cardiovascular risk will support and enforce the plausibility drawn from observational, animal and behavioral studies [46].

Clinical implications

The association between SSB consumption and obesity, type 2 diabetes mellitus and cardiovascular risk claims an urgent need for strategies to limit their consumption as a pivotal preventive measure. Epidemiological evidence can help address the population and specific strategies who may better revert this detrimental cascade. In USA, the highest consumers of SSBs are adolescents aged 12–19 years (13% total calories), particularly males, non-Hispanic blacks and Mexican-Americans, those who are low-income, or obese (14–16% total calories) [47]. Several social and environmental factors have been linked to the purchase and consumption of SSBs, including advertising and promotion, increased portion sizes, fast food consumption, television watching, permissive parenting practices, parental SSB consumption, and increased access to SSBs in the home and school [48].

Research indicates that consumption of SSBs is a modifiable behavior, and that reducing consumption can result in a decrease in weight, a measure commonly used to assess excess body fat [49]. Strategies to reduce SSB consumption have been identified for each of the priority settings for obesity prevention. These include communities (including homes), schools (including child care facilities), worksites, and medical care settings. The USA Center for Disease Control (CDC) has recently (March 2010) published a Guide to Strategies for Reducing the Consumption of Sugar-Sweetened Beverages. Recommended strategies discussed in the document include: ensure ready access to potable drinking water; limit access to SSBs, promote access to and consumption of more healthful alternatives to SSBs; limit marketing of SSBs and minimize marketing's impact on children; decrease the relative cost of more healthful beverage alternatives through differential pricing of SSBs; include screening and counseling about SSB consumption as part of routine medical care; expand the knowledge and skills of medical care providers to conduct nutrition screening and counseling regarding SSB consumption.

Such a multifactorial intervention strategy starting from childhood and including all the social environment around this issue, is a hard and ambitious goal but has the potential to become a powerful means to prevent the downstream effects on cardiovascular health.

European Countries are adhering more and more consistently to US lifestyle and dietary habits, but the awareness of their detrimental consequences is at present underestimated by the European scientific and medical community as well as by the social environment surrounding SSB consumption. The first reports addressing this issue have been published in the past few years [35, 50], but specific initiatives targeting SSB intake in children or in the general population are limited and of uncertain effectiveness until now. Efforts should be undertaken to fill this potentially dangerous gap between the size of the problem, and its sharp rate of increase towards US standards, and the magnitude of the interventions planned to stem this emerging and underestimated healthcare problem.

Conflict of interest None.

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