Sugar-Sweetened Beverage and Vascular Function
Not So Sweet After All
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Sugar-sweetened beverages (SSBs) are some of the most commonly consumed beverages around the world. Sweeteners used in these beverages include sucrose, fruit juices, and high fructose corn syrup. Increased consumption of these beverages has been causally linked to obesity, diabetes mellitus/metabolic syndrome, hypertension, gout, and cardiovascular disease.1–5 On the basis of a comparative risk analysis model, Micha et al6 concluded that, in 2012 in the United States, ≈45% of 702,308 deaths attributed to heart disease, stroke, and type 2 diabetes mellitus were associated with consumption of 10 dietary factors, with consumption of SSB accounting for 7.4% of cardiometabolic deaths. The consumption of SSB accounted for 10.8% of deaths from coronary heart disease and 14.8% of type 2 diabetes mellitus–related deaths.4

These adverse effects of SSB consumption may be mediated through increased glycemic load, obesity, insulin resistance, type 2 diabetes mellitus, increased oxidative stress, inflammation, and vascular dysfunction.1–5 Endothelial dysfunction is considered to be one of the potential mediators of adverse cardiovascular effects of SSB.6 Normal healthy vascular endothelium mediates vasodilation, exhibits an antithrombotic/profibrinolytic phenotype, and inhibits inflammation by its antiadhesive properties against circulating leucocytes, thereby maintaining vascular health. Endothelial dysfunction is often a precursor of and is associated with atherosclerotic cardiovascular disease. Although previous studies have shown that endothelial dysfunction can be induced by acute hyperglycemia,7 detailed examination of the acute effects of consuming an SSB on microvascular and large vessel function has not been systematically performed.4

In this issue of Arteriosclerosis, Thrombosis, and Vascular Biology, Loader et al8 report the acute effects of consuming an SSB on micro- and macrovascular vasomotor function in 12 healthy volunteers in comparison with a placebo using a randomized single-blind crossover design. The authors used laser speckle contrast imaging to measure cutaneous microvascular blood flow at baseline and during a vasodilator stimulus provided by iontophoretically delivered acetylcholine (an endothelium-dependent vasodilator) and sodium nitroprusside (an endothelium-independent direct smooth muscle relaxant and vasodilator). Macrovascular function was assessed using ultrasonographic monitoring of brachial artery diameter changes in response to both transient arterial occlusion followed by release (reactive hyperemia, an endothelium-dependent vasodilator stress) and nitroglycerin (an endothelium-independent direct vasodilator stimulus).

Furthermore, the authors conducted additional in vivo and ex vivo experiments in rats given intraperitoneal sucrose to simulate an SSB load, and they examined vascular vasodilator function at baseline and in response to endothelium-dependent and endothelium-independent vasodilators. The authors also examined the role of oxidative stress in the adverse effects of sugar load on vascular function by measuring reactive oxygen species and evaluating the effects after pretreatment with the antioxidants N-acetylcysteine and the NADPH inhibitor apocynin.8

Overall, the results of these investigations and experiments showed that acute hyperglycemic load, triggered by consumption of SSB, rapidly leads to impaired endothelium-dependent microvascular and macrovascular vasodilation compared with placebo in human subjects, with similar results observed in rats given intraperitoneal sucrose loads.9 In contrast, direct smooth muscle relaxation (endothelium-independent vasodilator effect) was not significantly affected by SSB consumption. Furthermore, in rats, pretreatment with antioxidants prevented the adverse effects of SSB on endothelium-dependent vasodilator response in vivo and in vitro, implicating acute oxidative stress in the vascular dysfunction caused by the acute sugar load. The authors went on to show that in rats, the nitric oxide bioavailability was reduced by the sucrose-induced acute oxidative stress, contributing to reduced endothelium-dependent vasodilator response. However, no change in vascular eNOS or phosphorylated eNOS levels was noted in response to sucrose loading in rats.

Overall, the authors provide fairly compelling evidence to support their conclusions that acute glycemic load induced by SSB consumption in man impairs acute endothelium-dependent vasodilator responses in the microvasculature, as well as in large arteries. The experiments with rats indicate that this effect is likely to be related to acute oxidative stress impairing nitric oxide bioavailability.

However, some limitations of the study should be pointed out. First, only male volunteers were included, making it difficult to know whether similar effects would have been observed in females as well. Vascular function may vary based on racial/ethnic origin, and therefore, results cannot necessarily be extrapolated to all racial/ethnic groups. The authors used a short-term randomized trial design, and it is unclear...
whether longer-term cumulative exposure would cause a more permanent vascular dysfunction that outlasts the actual duration of hyperglycemic exposure. The authors only studied the vasomotor component of vascular function, and it remains unclear whether other aspects of endothelial function, such as thrombogenicity or leukocyte-endothelial adhesiveness, could have been altered as well. How hyperglycemic load creates oxidative stress was not explored in this study. Furthermore, it is conceivable that habitual consumption of SSB may produce additional adverse vascular effects such as structural vascular remodeling that would not necessarily be observed in short-term single exposure experiments as reported by Loader et al.8

Notwithstanding these limitations, the authors provide a significant contribution to the field of vascular biology by investigating the potential mechanisms by which SSB consumption could directly affect vascular function at the level of both large arteries and the microcirculation. The increased cardiovascular risk associated with SSB consumption is likely multifactorial (increased weight gain, dyslipidemia, increased risk of insulin resistance and type 2 diabetes mellitus, hypertension, gout, inflammation) but also could be attributed, in part, to direct vascular effects, such as endothelial dysfunction, as described by Loader et al.8 (Figure).

Increased awareness of the cardiometabolic health hazards of SSB consumption is warranted, particularly considering the high consumption of SSB around the world and the potential for risk mitigation with reduced consumption of SSB. The good news is that in the United States, between 2002 and 2012, population-adjusted cardiometabolic deaths dropped by 26.5%, which was in part associated with and potentially attributable to reduced consumption of SSB.5 Public health efforts to discourage consumption of SSB and potentially replace them with more healthy beverages, such as coffee and tea (without added sugar or cream), as suggested by Malik and Hu,6 may be warranted. SSBs may not be so sweet after all.

Disclosures

None.

References


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