Fructose-Rich Beverage Intake and Central Adiposity, Uric Acid, and Pediatric Insulin Resistance

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Objective To determine the association between sugar-sweetened beverage (SSB) consumption with biomarkers of insulin resistance (IR) and investigate whether/how this relates to obesity and serum uric acid in adolescents.

Study design Adolescents (n = 1454, aged 12-16 years) were assessed in a study conducted to monitor Multilevel Risk Profiles for Adolescent Metabolic Syndrome in Taiwan. Detailed information about demographics, diet, physical, anthropometric, and clinical variables was collected. An original homeostatic model assessment of IR (HOMA1-IR), updated nonlinear homeostatic model assessment of IR (HOMA2-IR) model, and several IR markers were measured.

Results Adolescents who consumed a greater amount of SSBs were more likely to have elevated fasting serum insulin, HOMA1-IR, and HOMA2-IR (*P* for trends, ≤.028). Compared with SSB nondrinkers, those with >350 mL/d intake of heavy high-fructose corn syrup-containing SSBs had a 0.52 and 0.30 higher multivariate-adjusted HOMA1-IR and HOMA2-IR, respectively. Waist circumference and serum uric acid were correspondingly found to explain 25.4% and 23.6%, as well as 23.2% and 20.6%, of the increases in the 2 IR markers. Both the elevations of HOMA1-IR and HOMA2-IR for high-fructose corn syrup-rich SSB intake were strengthened among obese adolescents (*P* for interaction, ≤.033).

Conclusions Fructose-rich SSB intake is associated with elevated levels of IR, and this relationship may be partially mediated by central adiposity and serum uric acid. Obesity may modify the effect of this type of SSB consumption in intensifying the elevation of IR in adolescents. *(J Pediatr 2016;171:90-6)*.

Insulin resistance (IR), which promotes atherosclerosis and increases one's risk of developing diabetes and cardiovascular disease in adulthood, can occur in childhood, and may persist into adulthood.[1-3] Consumption of sugar-sweetened beverages (SSBs) and the fructose they contain has risen sharply in recent decades.[4,5] In a cross-national analysis of 75 countries, soft drink intake was estimated to have globally increased from 9.5 to 11.4 gallons per capita per year between 1997 and 2010.[4] SSB consumption was found to be associated with an elevated IR among adults.[6,7] Data from dietary trials have revealed that fructose ingestion induces hepatic de novo lipogenesis, leading to increased visceral fat accumulation.[8] Such fat accrual has been associated with IR.[9] School age children and young adults have been documented to consume the largest quantity of fructose-rich SSB.[10]

The concentration of SSB shops and convenience stores in Taiwan is among the highest in the world, with 1 shop/store in the community for every 2300 people.[11] Bubble tea-derived hand-shaken beverages, made instantly using high-fructose corn syrup (HFCS) as the only added sugar, are a fructose-rich SSB that is usually consumed by adolescents in Taiwan.[12] According to a market research report,[13] this type of SSB was recently developed in the United Kingdom and has been spread across Europe and the Middle East. In previous decades (1980-1996), the prevalence of obesity among schoolchildren in Taiwan had gone up by 27.7% among girls and 25.8% for boys.[14] In addition, according to Taiwan Nutrition and Health

BMI	Body mass index	HOMA2-%B	HOMA2 of percentage beta cell function
BSD	Bottled sugar-containing drink	HSD	Hand-shaken sugar-containing drink
FPG	Fasting plasma glucose	IR	Insulin resistance
FSI	Fasting serum insulin	MET	Metabolic equivalent task
HFCS	High-fructose corn syrup	mRP-aMS	Multilevel risk profiles for adolescent metabolic syndrome
HOMA	Homeostatic model assessment	QUICKI	Quantitative insulin sensitivity check index
HOMA1	Original HOMA	SSB	Sugar-sweetened beverage
HOMA1-IR	HOMA1 of IR	WC	Waist circumference
HOMA1-%B	HOMA1 of percentage beta cell function		
HOMA2	Updated nonlinear HOMA		
HOMA2-IR	HOMA2 of IR		

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Survey (1993-1996), the prevalence of hyperuricemia for male and female teenagers was reported to be as high as 59.8% and 30.3%, respectively.[15] The chief purpose of our study, then, has been to determine the association between SSB consumption, particularly fructose-rich SSBs, with biomarkers for IR, and to determine whether, and/or how this association is related to adiposity and serum uric acid among adolescents in Taiwan.

Methods

This study is a phase II investigation with participants randomly selected from the phase I investigation conducted to monitor multilevel risk profiles for adolescent metabolic syndrome (mRP-aMS) in southern Taiwan during 2007 and 2009.[12,16,17] As described in detail elsewhere, the mRP-aMS investigation is a large-scale representative cross-sectional study comprised of 2727 multistage randomly selected adolescents aged 12-16 years with fasting blood samples from 36 junior high schools.[12,16] In 2011, to evaluate the impact of SSB consumption on pediatric IR, in phase II of our investigation, we performed fasting serum insulin (FSI) assays for 1454 participants (a random sample selected from the participants in the mRP-aMS study). Because of funding limitations, only 53.3% of the original samples were examined. However, the distribution of sex, age, body mass index (BMI), and SSB consumption among those selected, and all participants, were comparable ($P > .05$ for all disparities). This investigation was performed after the research protocol was reviewed and approved by the institutional review board of Kaohsiung Medical University Hospital. All adolescent participants and their guardians/caretakers offered written informed assent or consent prior to being involved.

Dietary Assessment

A semiquantitative food frequency questionnaire was employed to measure the daily dietary pattern for the 23 food groups commonly consumed among adolescents in Taiwan during the previous month for each participant. The national Food and Drug Administration established a Food and Nutrient Databank based on the analysis of nutrients with respect to all Taiwanese food as a whole.[18] In order to estimate the total daily calories according to individual food consumption data, this nutrient information was applied to each participant. Participants who consumed at least 1 serving of any type of SSBs per week over the prior month, including sweetened teas, soft drinks, and fruit drinks, were determined to be SSB drinkers. The total SSB consumption per day was calculated and, according to a typical serving size in Taiwan, participants were divided into nonintake and consumption of 1-350, 351-750, and ≥750 mL/d. These adolescents consumed 2 types of SSBs: hand-shaken sugar-containing drinks (HSDs) and bottled sugar-containing drinks (BSDs). HSDs are sweetened completely with HFCS (mainly, HFCS-55), and BSDs are sweetened mainly with sucrose (granulated sugar), a handful with HFCS, or a mixture of HFCS and sucrose. We referred to HSDs as HFCS-rich SSBs and BSDs as mixed-sweetener SSBs. HSDs are instantly made SSBs sold in hand-shaken beverage shops. Commonly ingested HSDs consist of pearl or boba milk teas, bubble black tea, and green tea. Of these, pearl/boba milk teas are made up of a tea base that is mixed/shaken with a milk or fruit flavor, and chewy tapioca balls (small- and marble-sized black tapioca balls are referred to as pearl and boba, respectively) and/or fruit jellies are frequently added. HSD shops provide various HFCS-containing beverages for their consumers, such as slight, half, and heavy HFCS-sweetened HSDs. A 750-mL beverage that is slightly, half, and heavily sweetened bubble black or green tea, respectively contain approximately 17, 25, and 50 mL (22, 34, and 68 g) HFCS.[12] Though, in BSDs, the added sugar is a constant, the manufacturers determine how much of this is added.

Physical Activity Assessment

The participants' physical activity, both on weekdays and during the weekend, was evaluated using 9 groups of questions. The data for each activity was translated to a metabolic equivalent task (MET)-minutes per week according to the formula: (MET level of activity) × (the minutes of the activity per day) × (the number of days per week).[19] The overall MET-minutes per week were calculated by accumulating all of the MET-minutes for the activities that the adolescents practiced. Participants were categorized into 3 groups according to the tertiles of their total MET-minutes.

Anthropometric Measurement

Information on height, weight, waist circumference (WC), hip circumference, and body fat were collected by trained research workers using a standardized process. Body fat percentage was evaluated using a body impedance system (the BF-800, by Tanita Corporation, Tokyo, Japan). The BMI [(weight in kg)/(height in m)^2] was used to determine overweight for each participant. According to the adult BMI criteria as defined by the Department of Health in Taiwan, adolescents with BMI values of ≤23.9, 24-26.9, and ≥27 kg/m^2 were defined as normal weight, overweight and obesity, respectively.[14]

Clinical and Laboratory Data

Blood specimens from the participants were obtained in schools during the morning after a 10-hour overnight fast. In the mRP-aMS investigation, the agreement rate for clinical specimen collection was 72.1%.[12] Fasting plasma glucose (FPG) was measured via a modified hexokinase enzymatic method, and serum uric acid was assessed using an enzymatic colorimetric assay (TBA-c16000 automatic analyzer, Toshiba, Tokyo, Japan). The presence of hyperuricemia was defined as an individual who had a serum uric acid level of ≥7 mg/dL in

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