Effect of Artificial Sweets on Neurologic Disorders

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ABSTRACT

Background: Sugar- and artificially-sweetened beverage consumption have been connected to cardio metabolic hazard factors, which rise the danger of cerebrovascular illness and dementia.

Purpose: We studied whether sugar or artificially sweetened beverage intake was related with the prospective dangers of incident stroke or dementia. **Materials and methods:** We studied 361 members aged more than 45 years for incident stroke (mean age 61 [SD, 10] years; 163 men) and 185 participants aged >60 years for incident dementia (mean age 68 [SD, 7] years; 85 men). Beverage consumption was computed using a food-frequency questionnaire at cohort studies. We quantified latest consumption at investigation 7 and cumulative intake by averaging across examinations. Surveillance for incident events commenced at examination 7 and continued for 5 years. We observed 12 cases of incident stroke (10 ischemic) and 10 cases of incident dementia (8 consistent with Alzheimer's disease). **Results:** After modifications for age, gender, education (for analysis of dementia), caloric consumption, diet feature, physical activity, and smoking, higher recent and higher cumulative consumption of artificially sweetened soft drinks were related with an increased risk of ischemic stroke, all-cause dementia, and Alzheimer's disease dementia. When comparing day-to-day aggregate consumption to 0 per week (reference), the risk ratios were 2.87 (95% confidence interval, 1.24–6.89) for ischemic stroke and 2.91 (95% confidence interval, 1.15–6.99) for Alzheimer's disease. Sugar-sweetened beverages were not associated with stroke or dementia. **Conclusions:** Artificially sweetened soft drink consumption was allied with a higher risk of stroke and dementia.

Keywords: Artificial Sweets, Soft Drinks, Dementia, Stroke, Sugar.

INTRODUCTION

Sugar-sweetened beverages are linked with cardio metabolic illnesses [1,2], which can increase the danger of stroke and dementia [3,4]. Limited prior findings recommend that sugar and artificially sweetened beverages are both linked with an improved risk of occurrence stroke [5], even though contradictory findings have been reported [6]. To our knowledge, studies are yet to examine the relations between sugary beverage intake and the risk of occurrence dementia. Therefore, we studied whether sugar or artificially sweetened soft drinks were linked with the 5-year risks of occurrence stroke and dementia. We furthermore studied total sugary beverages, which combined sugar-sweetened soft drinks with noncarbonated high sugar beverages, for instance, fruit juices and fruit drinks.

MATERIALS AND METHODS

We estimated the 5-year risk of both incident stroke and dementia beginning from the 4th examination cycle. For the study of stroke in relation to beverage intake, we excluded people with prevalent stroke or other significant neurological disease at baseline and those less than 45 years. For investigating the occurrence of dementia, we excluded people with prevalent dementia, mild cognitive impairment, or other significant neurological disease at baseline and those less than 60 years. These age cutoffs are consistent with our prior work in this area. There were 361 and 185 participants available for analysis of occurrence stroke and new-onset dementia, respectively. Participants completed the Harvard semi quantitative food-frequency questionnaire (FFQ) at examination cycles 2. The FFQ provides a validated measure of dietary intake over the past 12 months [7]. Participants replied according to how frequently they consumed 1 glass, bottle, or can of each sugary beverage item, on average, across the previous year. The FFQ included 3 items on sugar-sweetened soft drink, 4 items on fruit juice, 1 item on noncarbonated sugar-sweetened fruit drinks, and 3 items on artificially sweetened soft drinks. Each item was scored according to 9 responses spanning from never or <1 per month to 6+ per day. Intake of soft drinks using the FFQ has been validated against dietary records (correlation coefficients of 0.81 for Coke/ Pepsi) and is reliable when re-administered after 12 months (correlation coefficients of 0.85 for Coke/Pepsi) [8,9]. We combined FFQ items to create variables reflecting consumption of total sugary beverages (combining sugar-sweetened soft drinks,

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fruit juice, and fruit drinks); sugar-sweetened soft drinks (high-sugar carbonated beverages, such as cola); and artificially sweetened soft drinks (sugar-free carbonated beverages, such as diet cola). We created new intake categories to ensure that an adequate number of participants were retained in each intake group across each variable. Cut points were determined before conducting the main analyses based on the relative distribution of consumption for every variable. Total sugary beverage consumption was studied as 2 per day; sugar-sweetened soft drink intake was examined as 0 per week (reference), ≤3 per week, and >3 per week; and artificially sweetened soft drink intake was examined as 0 per week, ≤6 per week, and ≥1/d. We used FFQ data acquired from examination cycle 4 as a measure of recent consumption. We related beverage consumption to the 5-year risk of stroke and dementia. Surveillance commenced from examination cycle 4 to the time of incident event over a maximum of 5 years or until last known contact with the participant. We defined stroke as the rapid onset of focal neurological symptoms of presumed vascular origin, lasting >24 hours or resulting in death.

A diagnosis of dementia was made in line with the Diagnostic and Statistical Manual of Mental Disorders, 4th edition [10]. A diagnosis of Alzheimer's disease dementia was based on the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association for definite, probable, or possible Alzheimer's disease [11].

The study was done according to the ethical board of King Abdulaziz university.

Statistical analysis

We utilized SAS software to appraise Cox relative risks regression models (after confirming the assumption of proportionality of risks). Recent consumption and cumulative consumption of total sugary beverages, sugar-sweetened soft drinks, and artificially sweetened soft drinks were related independently to the danger of all stroke, ischemic stroke, all-cause dementia, and AD dementia. Hazard ratios (HR) are presented accompanied by 95% confidence intervals (CIs). We first performed minimally adjusted statistical models, which included adjustments for age, gender, education (for analysis of dementia only), and total caloric intake. Then, we stepped in adjustments for lifestyle factors, incorporated the Dietary Guidelines Adherence Index (a variable quantifying adherence to the 2005 Dietary Guidelines for Americans), as a measure of overall diet quality [12], self-reported physical activity [13], and smoking status. A third statistical model incorporated the adjustments outlined, as well as additional cardiometabolic variables that can be affected by sugary beverage consumption [14, 15] or connected with an expanded danger of stroke or dementia. We performed mediation analyses to examine if any of the following covariates mediated the observed associations between cumulative intake of artificially sweetened soft drink and the outcomes: prevalent hypertension, prevalent cardiovascular disease, prevalent diabetes mellitus, waist-to-hip ratio, total cholesterol, and high-density lipoprotein cholesterol.

RESULTS

Table 1 shows cohort characteristics classified by total sugary beverage and artificially sweetened soft drink intake for the larger stroke study sample. Total caloric consumption increased across categories of total sugary beverage but not artificially sweetened soft drink intake categories. The pervasiveness of cardiovascular disease and diabetes mellitus decreased with more frequent consumption of total sugary beverages but increased with greater consumption of artificially sweetened soft drink.

Table 1: Cohort demographics for the stroke sample

	Total sugary beverages			**Artificially sweetened soft drinks**		
	<1/d	1–2/d	>2/d	0/wk	1–6/wk	≥1/d
N	165	138	58	168	128	65
Age	60	62	62	63	63	61
Male	67	65	31	72	57	34
No high school degree	7	5	2	8	4	2
Treatment for hypertension	57	48	18	51	47	25
Diabetes mellitus	23	16	5	12	18	14
Indicates atrial fibrillation	5	7	2	6	5	3
Prevalent cardiovascular disease	20	16	6	17	16	9
Smoker	23	14	7	26	11	7
Apolipoprotein E	36	30	13	36	28	15
Total caloric intake, Cal/d	1648	1840	2260	1842	1769	1871

Greater recent intake of artificially sweetened soft drink was linked with an increased danger of stroke, with the strongest relations witnessed for ischemic stroke. Higher cumulative intake of artificially sweetened soft drink was also associated with an increased risk of ischemic stroke. Neither intake of total sugary beverages nor intake of sugar-sweetened soft drink was linked with the risks of stroke.

When examining cumulative beverage consumption, daily intake of artificially sweetened soft drink was associated with an increased risk of both all-cause dementia and AD dementia. Neither total sugary beverages nor sugar-sweetened soft drink was associated with the risks of dementia. We did not see any interactions with waist-to-hip ratio, diabetes mellitus status, or the presence of the apolipoprotein E allele with intake of any beverage examined.

Prevalent diabetes mellitus status was identified as a potential mediator of the association between artificially sweetened beverage intake and the risk of both incident all-cause dementia and AD dementia. When repeating the primary analysis excluding those with prevalent diabetes mellitus and adjusting, daily intake of artificially sweetened beverages (versus no intake) remained a significant predictor of both incident all-cause dementia (HR, 2.40; 95% CI, 1.05–5.57) and AD dementia (HR, 3.19; 95% CI, 1.18–8.48). Therefore, diabetes mellitus was a partial but not full mediator of the association between artificially sweetened beverage intake and incident dementia. Prevalent hypertension was a potential mediator of the association between artificially sweetened beverage intake and incident all-stroke, but not ischemic stroke. After excluding people with prevalent hypertension, and after adjustment, the association between artificially sweetened beverage intake and incident all-stroke was attenuated (0 per week, reference; >0–6 per week: HR, 1.49; 95% CI, 0.55–4.08; ≥1 per day: HR, 1.47; 95% CI, 0.44– 5.15). No other mediation was recognized. When comparing day-to-day aggregate consumption to 0 per week (reference), the risk ratios were 2.87 (95% confidence interval, 1.24–6.89) for ischemic stroke and 2.91 (95% confidence interval, 1.15–6.99) for Alzheimer's disease. Sugar-sweetened beverages were not associated with stroke or dementia.

Table 2: Cohort demographics for the dementia sample (N=185)

	Total sugary beverages			**Artificially sweetened soft drinks**		
	<1/d	1–2/d	>2/d	0/wk	1–6/wk	≥1/d
N	79	77	29	85	72	28
Age	68	68	69	69	69	67
Male	33	36	16	37	33	15
No high school degree	4	4	1	5	3	1
Treatment for hypertension	35	34	12	34	34	13
Diabetes mellitus	14	12	3	7	14	7
Indicates atrial fibrillation	3	5	2	4	4	2
Prevalent cardiovascular disease	16	13	5	13	15	6
Smoker	7	6	2	9	4	2
Apolipoprotein E	17	16	7	17	16	7
Total caloric intake, Cal/d	1658	1802	2150	1833	1743	1779

DISCUSSION

In our community-based cohort, higher intake of artificially sweetened soft drink was linked with an increased danger of both stroke and dementia. Neither total sugary drinks nor sugar-sweetened soft drink intake was linked with the dangers of stroke or dementia. The Nurses Health Study and Health Professionals Follow-Up Study reported that greater intake of sugar and artificially sweetened soft drinks was each independently associated with a higher risk of incident stroke over 28 years of follow-up for women (N=84,085)

and 22 years of follow-up for men (N=43,371) [5]. Another study, a population-based multiethnic cohort (N=2,564), reported that everyday consumption of artificially sweetened soft drink was related with a higher risk of combined vascular events but not stroke when studied as an independent outcome [6]. Our study provides more indication to link intake of artificially sweetened drinks with the risk of stroke, mainly ischemic stroke. Our study reports a link between daily intake of artificially sweetened soft drink and an increased threat of both all-cause dementia and dementia because of AD. Our observation that artificially sweetened, but not sugarsweetened, soft drink consumption was allied with an increased risk of stroke and dementia is intriguing. Sugarsweetened beverages deliver a high dose of added sugar, leading to a rapid spike in blood glucose and insulin [16], providing a plausible mechanism to connect consumption to the improvement of stroke and dementia risk factors. Like sugar-sweetened soft drinks, artificially sweetened soft drinks are linked with threat factors for stroke and dementia, even though the mechanisms are moderately understood, and changeable findings have been reported [17]. Earlier studies connecting artificially sweetened beverage intake to negative health outcomes have been questioned based on worries concerning residual confounding and reverse causality, whereby sicker individuals drink diet beverages as a means of negating an additional deterioration in health [18]. Indeed, in our study, diabetes mellitus—a known risk factor for dementia was more prevalent in those who frequently consumed artificially sweetened soft drinks [19].

Diabetes mellitus status furthermore partially mediated the relationship between artificially sweetened soft drink consumption and incident dementia. As our study was observational, we are unable to determine whether artificially sweetened soft drink intake increased the risk of incident dementia through diabetes mellitus or whether people with diabetes mellitus were simply more likely to consume diet beverages. Some studies have provided evidence for the former. Artificial sweeteners have been shown to cause glucose intolerance in mice by altering gut microbiota and are connected with dysbiosis and glucose intolerance in humans [20]. A systematic review and meta-analysis stated that artificially sweetened beverage intake was linked with incident diabetes mellitus, even though publication bias and residual confounding were considered possible [15]. Clinical trials are required to start whether the consumption of artificially sweetened beverages is causally linked to dementia or alternate end points, for example, cognitive decrease or brain atrophy. In our study, dominant hypertension, the single most vital stroke risk factor, decreased the link between artificially sweetened beverage consumption and incident all-stroke, even though not ischemic stroke. Prospective cohort studies, for example, the Nurses Health Study, have revealed relations between higher consumption of artificially sweetened beverages and an increased threat of hypertension occurrence [21]. Nonetheless, it remains imprecise whether artificial sweeteners cause hypertension or whether diet beverages are preferred by those most at risk. Given that clinical trials linking stroke end points are large and costly, clinical trials ought to investigate whether artificially sweetened drinks are linked with vital stroke risk factors, such as high blood pressure.

Limitations of the study comprise the observational nature of our study that prevents us from assuming causal links between artificially sweetened beverage intake and the risks of stroke and dementia; the utilization of a self-report FFQ to get dietary consumption data might be subject to recall bias, consequently, introducing error into our estimated models; even though we addressed confounding in many ways, we cannot ignore the likelihood of residual confounding; finally, we did not adjust for multiple comparisons meaning that some findings might be attributable to chance.

CONCLUSION

Artificially sweetened soft drink consumption was connected with an increased risk of stroke and dementia. Sugar-sweetened beverages were not linked with an increased risk of such consequences. As the consumption of artificially sweetened soft drinks is growing [22], along with the prevalence of dementia [23] and stroke [24], future research is needed to replicate our findings and to examine the mechanisms underlying the described associations.

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