Obesity

Low-Calorie Sweeteners: Exploring Underutilized Database Resources to Understand Dietary Patterns and Obesity

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The use and impact of low-calorie sweeteners (LCS) in relation to the national challenges of overweight and obesity are complex and controversial. Most research on LCS have focused on the prevalence of consumption of LCS in beverages. The 2015 Dietary Guidelines Advisory Committee emphasized dietary patterns and health rather than a focus on specific nutrients or foods. The committee took this approach to shift the national emphasis onto the context of total rather than individual nutrient consumption. A broader research paradigm is needed to elucidate the actual exposure to LCS and how they are consumed within dietary patterns in the US population. National-level databases exist that can be used to broaden scientific understanding of the effects of LCS and health outcomes. These databases are underutilized, and they provide potential tools for grasping a fuller picture of LCS in the US diet.

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Introduction

The food industry is exploring ways to reduce the sugar content of foods and beverages in order to meet guidelines set by health and regulatory bodies such as the World Health Organization (WHO) or the US Dietary Guidelines for Americans (1,2). One method with the potential to decrease sugar content is to use low-calorie sweeteners (LCS) as a substitution. However, the use of LCS has subsequently led to questions regarding the intake of these ingredients. For example, the role of LCS in weight management is a topic of considerable controversy. While randomized controlled trials have consistently found LCS to be of modest benefit in weight loss programs (3,4), some epidemiological studies have shown that LCS consumption is associated with higher body weight (5,6).

The amount, frequency, and pattern of LCS consumption are also areas of debate. Some studies have reported that LCS consumption is increasing dramatically (7), but these results are based on the percent of the population that consumes any LCS and does not reflect an increase in the amount of LCS consumed across the population. Sales data show that diet soft drink consumption, which accounts for nearly half of total LCS usage globally, has been declining precipitously (8). US Department of Agriculture (USDA) data suggests total available tonnage of LCS is increasing but at rates considerably less steep than reports based on population percentages (7,9). In addition, Ng et al. (10,11) performed an analysis of 85,451 uniquely formulated foods purchased during 2005 to 2009 and found that 1% of food items contained LCS alone and an additional 6% contained both LCS and nutritive sweeteners.

Martyn et al. (12) examined global trends in the use of aspartame, acesulfame-K, saccharin, sucralose, cyclamate, thaumatin, and steviol glycosides from 2008 to 2018 and found that the data did not support a shift in exposure over time, with several studies indicating a reduction in intake. While these authors acknowledged that there may be an increase in the number of consumers (i.e., percent of the population) of LCS, they considered the lack of increase of exposure levels more salient and recommended that future research should consider a more standardized approach to monitoring changes in exposure. Thus, focusing on the percent of the population that consumes LCS may not give an accurate picture of the extent, level, or pattern of LCS consumption. The important questions are whether the consumption of LCS leads to decreased sugar and calorie intake as well as the issue of how best to address these questions.

These questions about the quantity of LCS consumed as well as on what eating occasions they are consumed need considerably more exploration. The fundamental purpose of LCS consumption is to reduce both overall sugar and calorie intake. However, there is concern about whether LCS are in fact useful tools for controlling body weight or to permit sweet-tasting foods without elevating blood glucose for people with diabetes. Given these fundamental factors driving the consumption of LCS, it is critically important to understand the differences in

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consumption patterns among people with normal weight, overweight, and obesity.

Evidence suggests that LCS consumption in adults is associated with healthier eating patterns. For example, LCS consumption tracks with higher Healthy Eating Index (HEI) scores as well as more recreational physical activity and less smoking (13). However, the relationship of LCS consumption to dietary consumption patterns is complex; this study also found that while LCS consumers had better HEI subscores for intake of vegetables, whole grains, and low-fat dairy, they had worse subscores for intake of saturated fat and sodium compared with nonconsumers of LCS. In this study, trend patterns did not differ between consumption of LCS beverages, tabletop sweeteners, or LCS foods.

Binkley and Golub took a different approach to examine the characteristics of LCS consumers' diets; they demonstrated that those who consume LCS included better overall nutrition choices in their grocery purchases, including fewer desserts and other foods sweetened with caloric sweeteners, compared with nonconsumers of LCS (14). These studies, while demonstrating that those consuming LCS have higher HEI and make some food choices that would be considered preferable, do not look at specific dietary patterns reflecting the consumption of LCS.

Evaluating Dietary Patterns

Recent dietary guidance has shifted the focus from identifying specific shortfall nutrients and food categories in dietary intake to an emphasis on the importance of understanding dietary patterns that contribute to better overall health (1). The 2015 Dietary Guidelines Advisory Committee (DGAC) report focused on dietary patterns because "the totality of the diet—the combinations and quantities in which foods and nutrients are consumed—may have synergistic and cumulative effects on health and disease." Specifically, the DGAC reported that their review of the literature found a strong body of evidence linking specific dietary patterns to obesity and health outcomes (1).

The dietary pattern research cited in the 2015 DGAC report primarily incorporated prevalence of intake of types of foods as they were associated with health status. Assessing actual sequential dietary intake patterning coupled with other food-related behaviors may provide additional information to build upon what is known about the relationship between diet patterns and health outcomes. In particular, the DGAC report addressed the relationship between healthy diet and reduction in overweight and obesity. It should be noted, however, that there is considerable risk of confounding when using observational data. Moreover, current methods also involve issues with accurate measurement of food intake (15).

Eating frequency has been associated with higher energy intake (16,17), although the reported relationship between eating frequency and BMI has been inconsistent. Some have reported an inverse association of meal frequency and BMI (17-19), while others have found a direct relationship (16,20,21). Little is known about the patterns of LCS consumption by humans, and thus human studies are warranted to compare the relationship between intake of LCS, eating frequency, and BMI. One way to gather this information is to use national-level databases.

Levels of Analysis Using National Databases

A number of national-level databases exist that can be used to conduct much-needed research in this area. These resources can provide more information on the role of sequential dietary patterning and health in the United States. These databases, while often used for population-level analysis, are underutilized for determining dietary pattern analysis, and yet they have the potential to provide a wealth of information. Specifically, there is potential to add information on the sequential patterning of Americans' diets using the Eating and Health Module of the American Time Use Survey (ATUS) and the National Health and Nutrition Examination Survey (NHANES). The ATUS Eating and Health Module database has information on time use patterns and can provide insight into economic behaviors associated with eating patterns as well as the diet and health status of individuals. Knowing more about eating patterns, grocery shopping, and meal preparation, as well as understanding the patterns of both participants and nonparticipants in food and nutrition assistance programs, is important for future research (22). It is also possible to include and understand the related economics of food selection, by use of the USDA National Household Food Acquisition and Purchase Survey (FoodAPS) (23). The FoodAPS survey provides detailed information about purchases and acquisitions of food items intended for consumption at home and away from home. This database also provides information about factors that affect food purchase decisions, such as the number and characteristics of people in the household and their available resources, including those on food assistance programs such as the Supplemental Nutrition Assistance Program.

The most studied database is the NHANES dietary assessment. NHANES is a multistage, stratified area design that, after correction, is representative of the civilian, noninstitutionalized US population. There is oversampling of certain groups, such as specific age groups including young children and minority populations, in order to correct for bias that might exist in the original data set (24). The NHANES dietary assessment includes an in-person, interview-based 24-hour dietary recall as well as a second telephone interview-based 24-hour recall, followed by a 30-day food frequency questionnaire that is initiated 3 to 10 days following the interview-based assessments. The data produced can be analyzed at the individual, food, and eating occasion levels, which allows for analysis of the time of day and amount of foods consumed, as well as identification of eating occasions, including meals and snacks.

The most commonly studied level of analysis using NHANES is the proportion of individuals in the US exhibiting a specific health status. For example, this level of analysis was used by Sylvetsky et al. to examine the proportion of individuals consuming LCS (25). Their analysis determined the percent of the population consuming LCS by use of the National Nutrient Database for Standard Reference (26). The Standard Reference provides product descriptions that indicate whether or not that product contains LCS. However, Sylvetsky and colleagues then identified foods containing LCS by searching for all food items containing the terms "low-calorie" or "sugar-free." This methodology thus might exclude many food items that are not identified in this way but contain LCS, such as Fiber One™ Cereal or some yogurts. Also, as noted by the authors, because LCS are classified as food additives, there is no requirement to provide information regarding the quantity of LCS contained in these foods. As mentioned previously, this level of analysis does not permit understanding total use or dietary patterns.

Analysis at the food level has been undertaken much less frequently. Food-level analysis examines both the distribution of foods and the nutrient content of the foods. In this type of analysis, the number of food products containing specific nutrients can be analyzed and used to estimate quantity when assed in combination with food frequency questionnaires (27).

In addition, NHANES' 24-hour dietary recall includes information on the timing of consumption and thus allows analysis of patterning of intake throughout the 24-hour period to enable analysis at the eating episode level (28). The NHANES interviewer captures the time of the beginning of each eating or drinking event and the respondent's "identification" of that intake event as a specific meal, snack, or a beverage without any accompanying food items.

LCS Consumption in the Context of Dietary Patterns

Few studies have examined how LCS consumption relates to dietary patterns and intake of other nutrients. Piernas et al. (29) used the NHANES database and purchased data from the Nielsen Homescan longitudinal data set from 2000 to 2010. However, they focused solely on LCS in beverages and thus did not account for more than half of LCS consumption (in foods, food and beverage additions, and tabletop sweeteners (30)). In their analysis of LCS in beverages, they grouped eating patterns into four groups: prudent, breakfast, ready-to-eat/fast food, and prudent/snacks/LCS desserts. They found that consumers of any sweetened beverage, whether sweetened with LCS, caloric sweeteners, or a combination of the two, were less likely to follow either prudent or breakfast food-purchasing and consumption patterns. By adhering to the less healthful patterns, those consuming sweetened beverages consumed overall more calories. However, those consuming LCS beverages were more likely than those consuming calorically sweetened beverages to adhere to the breakfast or prudent patterns. Therefore, consumption of LCS may serve as an indirect indicator of behavior or intent to actively pursue lower-calorie consumption and/or dietary patterns more closely aligned with the US Dietary Guidelines. In addition, Duffey et al. (31) examined the interplay between dietary patterns and diet beverage consumption and found that while nonconsumers of diet beverages following a so-called "prudent" diet had the lowest health risks, those following the prudent diet were more likely to consume diet beverages. They concluded that "a Prudent dietary pattern is consistently associated with lower risk and being a diet beverage non-consumer sometimes, but not always, additionally lowers that risk" (31).

There are also few studies examining how LCS consumption fits into the patterns of daily life. We have recently undertaken an analysis of NHANES data to describe eating patterns as reported by US adults by defining eating episodes and examining LCS consumption within that context (32). We sought to assess whether individuals consuming LCS exhibit different eating patterns from non-LCS consumers and whether those patterns were consistent with animal studies demonstrating over-consumption of calories in rodents exposed to LCS (33-35). We have also undertaken an analysis that compares macronutrient intake per eating episode and daily energy and macronutrient intake by LCS use and BMI.

We used NHANES from 2007 to 2012 for US adults aged ≥19 years with an adjusted sample of $n=15,610$, which represented a weighted population sample of $N=213,245,729$. We defined an eating episode as a single unique episode in which some food and/or beverage items were consumed and in which all food or beverage items were consumed within 15 minutes of one another over the first 24-hour recall period of the NHANES data sample. Importantly, we examined all food, beverage, and food and beverage addition items consumed, which included 5,464 unique items, and coded them by type of item and LCS content. Thus, all food, beverage, or food and beverage addition items were coded as containing LCS, caloric sweeteners, neither, or both. We then assessed the frequency and type of eating episodes and nutrient intake by both LCS content and BMI category (32). It should be noted that no differentiation of LCS type (e.g., aspartame, sucralose, etc.) was made, as the type of sweetener in food items changes frequently due to manufacturing decisions and this data was therefore not available. We were also able to group eating episodes by the type of items consumed. We analyzed the episodes by foods alone, beverages alone, or food and beverages consumed together. Thus, by using the information in the NHANES 24-hour recall, we were able to assess dietary patterning of use of LCS. We believe these 24-hour samples of sequential intake within the NHANES data are a highly underutilized source of information of the dietary patterns of the US population.

When LCS are consumed in isolation without other caloric substances added, they do not provide the same postingestive consequences, such as raising blood glucose or releasing insulin, as caloric sweeteners (36), leading to the hypotheses that LCS can lead to weight gain by disrupting the normal physiological responses that lead to the sensation of fullness when consuming sweet-tasting foods (33-35). The experimental designs used to support the theory of dissociation of sweet taste and caloric response leading to weight gain have been tested only in rodents with highly controlled exposure to LCS (34). The proposed explanation is that these postingestive consequences serve as unconditioned stimuli in a classic Pavlovian learning scheme, while the sweet taste associated with LCS serves as the conditioned stimulus. For Pavlovian conditioning to occur, the necessary and sufficient conditions include consistent pairing of, or signaling for, the unconditioned stimulus with the conditioned stimulus. In the case of LCS, for this learning to occur there would need to be consistent pairing or signaling of LCS with no or lessoned caloric consequences.

In work for which we have published preliminary results as an abstract, we defined an eating episode using NHANES data as a single unique consumption episode in which some food and/or beverage items were consumed and in which all food or beverage items were consumed within 15 minutes (37). In this way we were able to determine the number of episodes in which only foods were consumed, only beverages were consumed, and when foods and beverages were consumed together. Through this analysis we found that consuming foods and beverages together was the most frequent type of eating episode accounting for not quite half of all episodes, while beverages alone or foods alone were closer to each other in frequency and made up the remainder of the episodes. In terms of LCS consumption, only in the beverages alone episodes is it possible for LCS to be dissociated from calories. That is, it is only in this condition that there can be sweet taste with no caloric consequences. Of the eating episodes in which only beverages were consumed, we found that those episodes in which LCS was the sole sweetener made up a very small percent of eating episodes. Our analysis of eating episodes suggests that in the US diet, the pairing of sweet taste with no postingestive consequences is rare and thus makes such Pavlovian conditioning unlikely. Thus, our preliminary analysis of reported human LCS consumption does not support suggestions from animal studies that LCS consumption increases energy intake.

Conclusion

Studies conducted to determine the exposures to and effects of LCS have used widely different methods. There are several national-level databases through which the data can be explored in different ways. Clearly, alternate approaches to data interrogation can lead to different conclusions. For example, examination at the population level suggests LCS exposure is increasing (7), while examination at the exposure level suggests a decline (12). In addition, analysis of eating episodes, food items, and dietary patterns can suggest either association of greater LCS intake with higher body weight or with lower overall caloric intake and specific decrements in sugar and carbohydrates. Future research should consider a more standardized analytic approach to allow the consistent monitoring of potential changes in LCS consumption, in specific population cohorts (e.g., overweight, obesity, people with diabetes, etc.) and to focus on outcomes such as sugar reduction and body weight. We contend that several national-level databases, such as ATUS, the USDA Economic Research Service's National Household FoodAPS (23), and NHANES that are highly underutilized but provide the potential for achieving a better understanding of the dietary patterns of the US population.**O**

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