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COVER STORY

Sweet Debate

Do artificial sweeteners contribute to rather than combat obesity?

By Trout Lowen

Drink diet soda. Switch to low-fat or no-fat products. Cut down on or eliminate sugar. People who are overweight, have diabetes, or have metabolic syndrome hear advice like this all the time. But is it the right advice?

Some say it isn't. Results from several large-scale population studies suggest that regular consumption of artificial sweeteners such as aspartame and sucralose, particularly in diet soda, may actually contribute to rather than combat weight gain and type 2 diabetes.

No study so far has identified a direct causal link between artificial sweeteners and weight gain or diabetes, and proving one is difficult because there are so many confounding factors. But the positive association raises interesting questions: Do artificial sweeteners, most of which are hundreds of times sweeter than sugar, increase our desire for more and sweeter foods? Do diet soda drinkers overestimate the number of calories they're saving and then eat more? Do artificial sweeteners somehow disrupt or alter the body's processes in ways we don't yet understand? Or are those who are prone to weight gain or who have a family history of diabetes more likely than others to consume diet soda?

Of Mice and Man

In late June, epidemiologists and nutritional immunologists from the University of Texas Health Science Center at San Antonio presented the results of two new studies at the annual meeting of the American Diabetes Association (ADA). One study found that artificially sweetened soft drink consumption was associated with increased waist circumference in elderly people. The second found aspartame raised glucose levels in diabetes-prone mice.

The human study tracked diet soda consumption and waist measurement in 474 participants in the San Antonio Longitudinal Study of Aging at enrollment and at three follow-up exams over 10 years. As a group, participants who consumed artificially sweetened soft drinks saw a 178 percent greater increase in waist circumference compared with those who did not, and those who consumed two or more beverages containing artificial sweeteners per day saw a 500 percent (or almost three times greater) increase. "That's quite a statistically significant trend," says Sharon P. Fowler, M.P.H., co-author of the study.

That study reinforced the results of Fowler and colleagues' earlier analysis of San Antonio Heart Study data published in *Epidemiology* in 2008 that looked at the relationship between consumption of beverages containing artificial sweeteners and weight gain. That analysis showed that subjects who were 25 to 64 years old at baseline who consumed more than 21 artificially sweetened beverages per week almost doubled their risk for obesity over the next seven to eight years, compared with nonconsumers, and that their adjusted body mass indices increased 47 percent more than those of nonusers.

Both of the San Antonio studies support the findings of an earlier analysis of data from the Baltimore Longitudinal Study of Aging presented at the annual meeting of the Endocrine Society in 2009. That analysis found artificial sweetener consumers were younger and heavier, and had a higher body mass index than nonconsumers, although the number of calories and the amount of fat, carbohydrates, and protein consumed was the same in both groups. Three other studies published in *Circulation* and *Obesity* in 2007 and 2008 also showed an association between consumption of artificially sweetened soda and the development of obesity and metabolic syndrome.

In the mouse study presented at the ADA meeting, 40 diabetes-prone mice were divided into two groups. Both were fed a high-fat diet. Half of the mice were also fed high doses of aspartame. After three months, the mice that were given aspartame weighed the same or slightly less than the control mice, had better lipid and triglyceride levels, and their nonesterified fatty acids were much lower, Fowler says. But their fasting glucose values were 37 percent higher. In addition, 69 percent of the mice fed aspartame became hyperglycemic compared with 31 percent of the control group.

Fowler says having both lab and epidemiological studies strengthens the findings of each. "Having them together is so much more powerful to me than either separately." But she admits the results are preliminary. "How relevant these results would be for humans of different ages and diabetes risk levels is something that must be studied further."

Cause or Coincidence?

Fowler thinks there's compelling research suggesting a physiological explanation for why consuming artificial sweeteners might cause people to gain weight. As an example, she points to the work of Barbara Corkey, Ph.D., the most recent winner of the ADA's Banting Medal for Scientific Achievement, who was part of a team that looked at the effects of artifical sweeteners on the sweet taste receptor on the surface of pancreatic beta cells. Corkey and her colleagues found that in rats consumption of sucralose, aspartame, and saccharin increased insulin secretion.

But Jennifer Nettleton, Ph.D., a nutritional epidemiologist and faculty member at the University of Texas at Houston, thinks the data associating artificial sweeteners with weight gain says more about human behavior than human chemistry. "I feel fairly strongly this is not a causal relationship. It's about behavior patterns," says Nettleton, who did her doctoral and postdoctoral research at the University of Minnesota.

Nettleton's views may surprise some, as she was the lead author on a paper published in *Diabetes Care* in 2009 that raised concern about artificial sweeteners and weight gain. The researchers examined data from the Multi-Ethnic Study of Atherosclerosis pertaining to diet soda consumption and the risk of metabolic syndrome and type 2 diabetes among 6,814 Caucasian, African-American, Hispanic, and Chinese adults (between the ages of 45 and 84 years) over six years. Nettleton and her colleagues found that people who consumed diet soda at least daily had a 36 percent greater relative risk of incident metabolic syndrome and a 67 percent greater relative risk of incident type 2 diabetes as compared with those who consumed no diet soda, after adjusting for demographic characteristics and energy intake. Those who consumed more than one daily serving of diet soda also were more likely to have a greater waistline circumference or higher fasting glucose levels than those who did not.

But in analyzing the data, Nettleton says she and the other researchers tried to rule out all of the other factors that could be responsible for the results. "We couldn't rule any of them out," she says. It isn't possible to conclude anything about the health effects of diet soda consumption from that research, Nettleton argues.

For that reason, she believes it is behavior, rather than diet soda consumption, that is the real culprit when it comes to weight gain. "When we focus on something like this, it really misses the bigger picture," she says, "which is people are overweight, people don't exercise, and people also eat an otherwise horrible diet.

"I just feel very strongly that it's just part of a larger behavior pattern," Nettleton adds. "But I do think, as it says in the paper, it is important to bring this up because a lot of studies have seen this association, and we need to figure out what is driving it. … If there is truly something, a biologically plausible mechanism by which those compounds increase your risk of diabetes or metabolic syndrome, or cause any kind of metabolic abnormality, we need to know about it."

Other Explanations

Isolating that mechanism, if there is one, will be difficult. A number of artificial sweeteners are on the market, and new ones are being developed all the time. Each has its own chemical signature and action when consumed. For example, saccharin, the first artificial sweetener used commercially, is not digested or absorbed into the body. Aspartame, one of the most widely used sweeteners under the trade names NutraSweet and Equal, is digested, and individuals who have the rare hereditary condition phenylketonuria are sensitive to phenylalanine, one of two amino acids that make up aspartame, must restrict their intake of aspartame. Sucralose, or Splenda, which is derived from sucrose, or sugar that has been chemically altered, is not digested. But a paper published in 2008 demonstrated that, in animal studies, it alters microflora in the gut.

One limitation of population-based studies is that they can't parse out which artificial sweetener participants are consuming, and most participants are likely ingesting several of them. "That to me makes it less likely that [artificial sweeteners] are the signal," Nettleton says. "It's a messy exposure. It's not just one artificial sweetener."

But could artificial sweeteners be changing human chemistry? Some researchers think they may increase consumers' desire for ever-sweeter tastes. As a group, artificial sweeteners are much sweeter than sugar—saccharine is 300 times sweeter than sugar, aspartame 180 times sweeter, and sucralose 600 times sweeter. Some experiments have shown that sweet taste, whether it's derived from sugar or artificial sweeteners, increases appetite. One study found drinking aspartame-sweetened water increased appetite in normal-weight adult males, but swallowing an aspartame capsule did not. In another study, aspartame, saccharine, and acesulfame potassium were all associated with an increased motivation to eat more.

Other research suggests that artificial sweeteners do not provide the same food reward that natural sweeteners do, and that may contribute to increased appetite and, as a result, weight gain.

There are also other variants on theories about behavior that may explain the study results. People may overestimate the calorie-saving benefits of artificially sweetened foods and eat more as a result. Study subjects may over-report their consumption of artificially sweetened soda when they are really drinking sugar-sweetened soda. Those mostly likely to drink diet

soda may already have difficulty maintaining weight or have a family history of obesity or diabetes.

What about Sugar?
Although there is concern that artificial sweeteners may contribute to obesity and the diseases associated with it, there's clear evidence that sugar, particularly as it's consumed in sweetened beverages, is a major contributor to weight gain and the development of metabolic syndrome and type 2 diabetes. A recent meta-analysis of studies involving nearly 20,000 people in four countries published in *Diabetes Care* in 2010 found sugar consumption was associated with development of both metabolic syndrome and type 2 diabetes. In a lecture made popular on YouTube, Robert H. Lustig, M.D., professor of pediatrics in the division of endocrinology at the University of California, makes the case that sugar consumption is the main cause of obesity and diabetes and that it ought to be considered a toxin. Yet multiple studies have shown consumption of sugar-sweetened beverages including soft drinks, fruit drinks, ice teas, and energy and vitamin water drinks is rising in the United States and around the world. Sugar-sweetened beverages are now the primary source of added sugars in this country.

Advice for Physicians
Whether consumption of sugar or artificial sweeteners is more likely to contribute to obesity and its byproducts—metabolic syndrome and diabetes—misses the bigger picture, according to Nettleton. She says the real issue in terms of preventing weight gain and development of metabolic syndrome and diabetes is simply overconsumption. From a public health perspective, preventing weight gain is more important than any single component of diet. "The elephant in the room is you're 250 pounds and you should weigh 160 pounds," she says. "So let's not worry about how many grams of sugar are in that candy bar. Let's worry about why you're eating a candy bar."

She says physicians would be better off counseling patients about diet, exercise, and maintaining a healthy weight, and connecting them with someone who can help them develop an eating plan that works for them, rather than discussing consumption of artificial sweeteners. "We try to make the message too complicated. Like 'you need to eat more of this and less of that,' and really it's just 'eat less and do more.'" **MM**

Trout Lowen is a Minneapolis freelance writer.

Sweet choices

Artificial Sweeteners First developed in the late 19th century, artificial sweeteners appear under a variety of trade names. The Food and Drug Administration (FDA) has approved five for general consumption: Saccharin (Sweet'N Low, Necta Sweet, and others) is the original artificial sweetener. It was discovered in 1879 by a chemist working on coal tar derivatives. It is 300 times sweeter than sugar, has no calories, and is not digested or absorbed by the body.

Aspartame (Equal, NutraSweet, others) is made up of the amino acids phenylalanine and aspartate, plus methanol. It has been used in foods since 1981 and in diet sodas and other beverages since 1983. Unlike most other artificial sweeteners, it can be metabolized; but it

has effectively no caloric impact because it is used in such small quantities. It is 180 times sweeter than sugar.

Acesulfame potassium or acesulfame K(Sunett, Sweet One) was approved by the FDA in 1988. It is used in cooking and baking because it retains its sweetness when heated. It is 200 times sweeter than sugar and is not metabolized by the body.

Sucralose (Splenda) is a chlorinated hydrocarbon derived from sugar that is chemically altered by substituting chlorine for three of its hydroxyl groups. It was first approved by the FDA for limited use in 1999 and for general use in 2008. It's 600 times sweeter than sugar and has no caloric impact.

Neotame is the most potent sweetener on the market. It is 7,000 to 13,000 times sweeter than sugar. Foodfacts.com lists neotame as an ingredient in 23 products including Tang breakfast drink. (In contrast, aspartame is listed in 1,396 products, sucralose in 2,015, acesulfame potassium in 1,752, and saccharin in 64.)

Sugar Alcohols Sugar alcohols are used in a broad range of products including ice cream, chocolate, candy, cookies, desserts, chewing gum, toothpaste, and mouthwash. They occur naturally in certain fruits and vegetables and can be manufactured. Unlike artificial sweeteners, sugar alcohols are not sweeter than sugar; in fact, some are less sweet than sugar. Sugar alcohols usually replace sugar in equal measure. They contain about two calories per gram, less than regular sugar, which has four calories per gram. As with artificial sweeteners, the FDA regulates the use of sugar alcohols. Approved sugar alcohols include the following:

Erythritol
Hydrogenated starch hydrolysates
Isomalt
Lactitol
Maltitol
Mannitol
Sorbitol
Xylitol

"Natural" Options Stevia, a South American plant, is one of the newest no-calorie sweeteners to enter the marketplace. The FDA has not permitted the use of whole-leaf stevia or crude stevia as a food additive, although it has approved highly refined forms of stevia (Truvia, Pur Via) for use in food products.

Just Like Sugar. The marketers of this product claim it is the safest new sweetener on the market. Its promoters say it's an all-natural product that contains calcium, vitamin C, chicory root, and orange peel and has no calories.—**T.L.**