Is Sucralose Ingestion Acceptable Before ^{18}F-FDG PET/CT Imaging?

A 2009 international survey of 128 PET/CT technologists revealed that 58% of them administered oral contrast agents as part of their protocol for "some or most patients" (*1*). Among those using oral contrast agents, iodine-based contrast material was administered 35% of the time. An artificially sweetened beverage is commonly used to dilute the iodinated contrast and improve palatability. Sucralose, a nonnutritive sweetener often known by its trade name, Splenda (McNeil Nutritionals, LLC), is present in most sugar-free, noncarbonated, ready-to-drink beverages commercially available in the United States. The European Association of Nuclear Medicine procedure guidelines for tumor PET imaging suggest that patients not consume any food or sugar for at least 6 h before the start of the injection of ^{18}F-FDG and that patients have plasma glucose levels less than 120 mg/dL (*2*). To achieve the desired plasma glucose levels, many imaging centers ask their patients to consume a low-sugar diet the day before their examination. Imaging centers vary in their stance regarding the consumption of sucralose as part of a low-sugar diet before PET/CT imaging. A search of the Internet revealed at least 4 U.S. imaging center Web pages that specifically mention sucralose as an acceptable part of a low-sugar diet before PET imaging and at least 2 centers that specifically restrict the use of sucralose but not the use of other artificial sweeteners.

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Why would there be concern about the consumption of sucralose before PET/CT imaging, as distinguished from other artificial sweeteners? One of McNeil Nutritionals' prior advertising slogans for Splenda was "Made from sugar so it tastes like sugar." Indeed, sucralose is made from sugar in a 5-step process that selectively substitutes 3 atoms of chlorine for 3 hydroxyl groups in the sucrose (sugar) molecule (*3*). Is there any scientific evidence that demonstrates what effect, if any, sucralose ingestion has on the uptake of ^{18}F-FDG tracer in PET/CT imaging? The answer is no, for a literature search revealed essentially no scientific research regarding the effects of sucralose on PET imaging. Cheng et al. reported the use of a sucralose-based beverage as a vehicle for high-quantity fat administration 1 h before ^{18}F-FDG administration (*4*). However, their study did not independently evaluate the effects of the sucralose beverage. Williams and Kolodny instructed patients in their study to avoid sucralose, stating that "Although sucralose. . .is not known to have carbohydrate properties, whether it would affect myocardial FDG uptake was unknown because its chemical structure. . .is similar to that of glucose" (*5*). Because sucralose is present in many sugar-free foods and beverages, it would be helpful to determine whether sucralose ingestion should be avoided before ^{18}F-FDG PET scanning. In view of the lack of scientific evidence on the actual effects of ingested sucralose on ^{18}F-FDG tracer uptake in tissues, an effort was made to determine whether there is a science-based reason for why sucralose might have an effect.

Sucrose is broken down into glucose and fructose, which are completely absorbed within the small bowel. In the body, nearly all of the absorbed glucose and fructose is used as an energy source. Unlike sucrose, about 84% of the ingested sucralose passes through the digestive tract without absorption and is excreted unchanged in the feces (*6,7*). Sucralose does not serve as a substrate for colonic bacteria (*7*). The remaining 16% of the ingested sucralose is absorbed from the small bowel by passive diffusion and excreted into the urine. Most of the urine-excreted material is unchanged sucralose. However, about 20% of the absorbed sucralose undergoes glucuronide conjugation to form 2 metabolites. The 2 metabolites are excreted unchanged in the urine and are not used as an energy source (*6,7*). Unlike sucrose, the glycosidic linkage of sucralose is unavailable to the enzymes that cleave it, and hydrolysis of sucralose into chlorinated glucose and fructoselike molecules thus does not occur. Therefore, sucralose does not act as a source of energy (*8*).

Sucralose has a sweetness intensity 600 times that of sucrose and is therefore used in extremely small quantities. In addition, it is often used in conjunction with other artificial sweeteners to achieve a more balanced sweetness profile. Therefore, by my calculations, sucralose may be found in concentrations of 80–150 mg/L in most artificially sweetened beverages. Assuming an ingested dose of 150 mg of sucralose in 1 L of beverage and the absorbance data previously described, one can calculate that on average 126 mg will be excreted unchanged in the feces, 19 mg will be excreted unchanged in the urine, and 5 mg will be excreted in the urine as nonnutritive metabolites.

Several articles have demonstrated the lack of effect of sucralose on glucose homeostasis (*8–11*). Ma et al.

found that 800 mg of sucralose in 500 mL of normal saline delivered by gastric infusion did not stimulate the release of insulin, glucagonlike peptide–1, or glucose-dependent insulinotropic polypeptide (*9*). The latter 2 compounds are incretin hormones that stimulate glucose-dependent insulin release. Sims et al. demonstrated that rats given high concentrations of sucralose for more than 18 mo did not show metabolic adaptation of gut microflora or mammalian enzymes, suggesting that sucralose metabolism is unchanged despite long adaptation periods (*10*).

Sucralose in its pure, concentrated form is used in ready-to-drink commercial beverages. In contrast, single-serving individual packets of sucralose contain dextrose (glucose) and maltodextrin (a polymer of repeating glucose units) as carriers/fillers. These carriers are used to improve delivery of the sucralose product, which otherwise would be of such small quantity that the packet would appear "empty." A 1-g single-serve packet of sucralose (Splenda; McNeil Nutritionals, LLC) has the sweetening equivalent of 2 teaspoons of sucrose; this packet contains greater than 99% dextrose and maltodextrin. Glucose and maltodextrin are completely absorbed and utilized as energy sources by the body. Artificially sweetened, flavored beverage powders usually contain maltodextrin or a similar carbohydrate to serve as carriers and dissolution aids for the other powdered ingredients. Whether the amount of glucose or maltodextrin in the sweetener packets or powdered beverage mixes is sufficient to affect ^{18}F-FDG has not been studied. However, Brown et al. administered a 355-mL beverage sweetened with 6 g of Splenda (sucralose, glucose, and maltodextrin) to fasting subjects and demonstrated no significant change in plasma glucose, insulin, or glucagon levels at 30 and 60 min after consumption (*11*).

In conclusion, sucralose is used in minute quantities because of its high sweetness intensity and most of the small amount ingested is excreted unchanged. Sucralose is not metabolized as a source of energy, and therefore ingestion of large quantities of sucralose has not been proven to have any significant effect on plasma glucose or insulin levels. As such, there does not appear to be a scientific basis for why sucralose should interfere with ^{18}F-FDG PET imaging or for why it should be treated differently from other artificial sweeteners. Nonetheless, the lack of scientifically reasonable evidence for a potential effect does not exclude the possibility that an effect might exist. A definitive answer awaits further evaluation via a controlled experiment.

DISCLOSURE

No potential conflict of interest relevant to this article was reported. The author has a licensing agreement with Beekley Medical, the makers of Breeza, a sucralose-containing beverage used to dilute iodinated contrast material.

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