2014-07-15

The Use of Non-Nutritive Sweeteners in Establishing and Maintaining A Healthy Weight

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An evidence based scholarly paper submitted to the faculty of
Brigham Young University
in partial fulfillment of requirements for the degree of

Masters of Science

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College of Nursing

Brigham Young University

August 2014

ABSTRACT

The Use of Non-Nutritive Sweeteners in Establishing and Maintaining a Healthy Weight

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Obesity is an epidemic and continues to rise. The associated increased risk of mortality and co-morbid conditions is well documented. The use non-nutritive sweeteners (NNS) is a strategy being used to manage weight by reducing calorie intake. Research is inconclusive regarding the efficacy of NNS in weight management due to their inappropriate use and also the potential they may increase appetite. To most effectively manage weight, a comprehensive individualized plan must be devise of which proper use NNS may be a part.

Keywords: Nonnutritive sweetener; artificial sweetener; non-caloric sweeteners; sugar substitutes; obesity; weight; BMI; body mass index; appetite; sugar; aspartame; acesulfame potassium; sucralose; saccharin

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THE USE OF NON-NUTRITIVE SWEETENERS IN ESTABLISHING AND MAINTAINING A HEALTHY WEIGHT

Introduction

Obesity is an epidemic in America with over 35% of adults and 17% of children being obese [1]. The effects of obesity are well understood and found to contribute to such diseases as coronary heart disease, stroke, hypertension, diabetes, and dyslipidemia [1]. Obesity not only has major physical consequences on one's health, but it also impacts mental health and economic wellbeing [2]. It is estimated that Americans spend $147 billion dollars on obesity related care [3] with obese individuals spending $1,429 more on health care per year compared to those of normal weight [4]. Ultimately obesity contributes to poorer quality of life and adds to greater morbidity and mortality.

Although it is thought that many factors contribute to obesity, high sugar and fat intake are considered leading causes. This thinking has resulted in the increase production and use of non-nutritive sweeteners (NNS). The use of foods and beverages containing NNS has increased significantly in the past few decades and it is estimated that approximately 15% of the US population use NNS [5]. Results of the National Health and Nutrition Examination Survey which included data collected from 1999 to 2008 showed that the use of NNS beverages increased from 18.7% to 24.1% among adults [6].

The use of non-nutritive sweeteners (NNS) in diet drinks and in food is one way to reduce calorie intake. They provide the sweet taste that people desire without adding calories. Yet the danger is that some people choose to use artificial sweeteners as their only effort to manage weight because it requires minimal lifestyle changes. During the 1980's some began to suggest that rather than help in weight management that NNS may in fact have an adverse effect

on weight management by increasing hunger which may lead to increased food intake and weight gain [7]. Given the various perspectives on the efficacy of NNS with weight management, the purpose of this paper is to review of the scientific literature to determine the effects of NNS on weight including weight loss and maintenance and appetite level. Areas that will be discussed are physiological effects of NNS on weight and appetite level. Also position statements by profession organizations will be reviewed. Finally clinical recommendations will be made regarding the use of NNS.

Physiological Actions of Non-Nutritive Sweeteners

Non-nutritive sweeteners also referred to as sugar substitutes or artificial sweeteners have few or no calories or nutrition. They are derived from plants, herbs or sugar. They have a greater intensity of sweetness compared to sugar and require smaller portions to provide food and beverages a sweet taste. Generally they are not metabolized and pass through the gastrointestinal system unchanged.

Aspartame *AKA:* Equal, NutraSweet, NatraTaste.

Aspartame is one of the most studied artificial sweeteners. It is 200 times sweeter than sucrose necessitating small amounts to provide the sweet taste. It is found in beverages, cereals, yogurt, frozen gelatin desserts, and diet soda. Also it is used in vitamin supplements and laxatives. The US FDA has set the acceptable daily intake of aspartame at 50 mg/kg/day [8]. Generally the average daily aspartame intake is much less (2-5 mg/kg/day). If all of the sugar in an American diet were replaced by an equal sweetness load of aspartame it would only come out to 8.3 mg/kg/ day [9].

After consumption, aspartame is metabolized into three components; aspartame, phenylalanine, and methanol. Studies have shown that consumption well above the average daily

intake of 2-5 mg/kg, (34-75 mg/kg/day of aspartame; 30 mg/kg/day of phenylalanine), does not result in the accumulation of either components in human plasma [9]. This suggests that the body is able to excrete the components in a timely manner. Also, the plasma methanol level is well below what one would normally get from a healthy consumption of vegetables, fruits, and juices [10]. In reviewing the effect of aspartame on blood glucose and insulin, Smeets et al. (2005) using functional magnetic resonance imaging to visualize the human hypothalamic response, investigated the effects of sweet taste and energy content on blood glucose and insulin concentrations. They found that both the sweet taste and energy content of glucose were necessary for hypothalamic response which resulted in an early rise in glucose levels and plasma insulin levels. No hypothalamic response and resultant effect on insulin and glucose levels was found with aspartame which was contributed to lack of energy content. There continues to be mixed reports regarding the safety of aspartame [11]. Shankar and colleagues (2013) in a systematic review, reported aspartame may cause headaches, Alzheimer's disease, attention-deficit disorders, birth defects, cancer, diabetes, and lupus. Aspartame remains a frequently used NNS, yet controversial.

Acesulfame Potassium (Sunett, Sweet One)

Acesulfame is 200 times sweeter than sugar and the recommended ADI is 15 mg/kg/day [8]. Studies have shown that acesulfame is not metabolized by the human or animal body and is instead excreted unmetabolized [8,12]. It is highly used and is found in over 5000 products. It is generally consumed in combination with other non-nutritive sweeteners and is often found in sugar free soda. The pharmacokinetics have also been studied and found that acesulfame is quickly excreted in the urine [8,12]. However, as it passes though the body, it is broken down into acetoacetamide, which can be toxic at high levels although the amounts found in food and

beverages are far below the amount needed to be toxic [8]. Tissue samples of animals and humans do not show accumulation after multiple doses of acesulfame [12]. Several studies have looked at the effects of acesulfame on blood glucose levels and found that acesulfame has no effect on insulin secretion or blood glucose [12] It is suggested that acesulfame does not pose a risk to safety [8].

Sucralose (Splenda)

Sucralose has been widely studied as an artificial sweetener. It is a chemical derivative of sucrose or table sugar. It is versatile and can replace sugar in cooking and is found in numerous low-calories foods and beverages. Numerous studies have shown it to be poorly absorbed by the human body [13]. About 85% of sucralose is unabsorbed and excreted unchanged. The amount that is absorbed is circulated throughout the body. However, there is no active transport across the blood-brain barrier, placenta, or into human milk [13]. It does not bind to proteins. [13]. The remaining 2-3% of consumed sucralose is turned into a water soluble solute that is non-toxic [13]. The half-life of this remaining sucralose is about 13 hours [13]. It lacks bioactivity as it is not lipid-soluble and so there is no bioaccumulation [8,13]

Studies have shown that sucralose does not affect human blood glucose levels, slow gastric empting, or alter insulin levels or HbA1c levels [13]. Some have suggested that sucralose may cause insulin resistance and thus weight gain, although studies have not found this to be the case [8]. In fact is has been recommended for patients with diabetes as there is no apparent effect on carbohydrate metabolism. Also it does not appear to affect appetite in healthy normal-weight adults [8]. As such sucralose is an accepted artificial sweetener by the American Diabetic Association[14]

Saccharin (Sweet'N Low)

Saccharin is one of the most recognized artificial sweeteners worldwide and the oldest having been on the market for over 100 years. It is 200-700 times sweeter than sugar. It is frequently used in soft drinks, salad dressings, dessert toppings, and jams [8]. Saccharin is not metabolized by the human body but is excreted in stool and urine [8,15]. As such, it does not affect blood insulin levels. Some has suggested that it has carcinogenic properties, yet evidence is not adequate to support it as a carcinogenic agent. Current research indicates that saccharin can be safely consumed as long as it is within the recommended ADI of 5 mg/kg/day [8].

Outcomes

Weight

A higher BMI is well established to cause a higher morbidity and mortality due to cardiovascular changes. The available studies that assess weight changes and NNS are conflicting. Several large retrospective and observational studies have found that those who use NNS are often overweight or obese [16-20] but it is unclear if it is a causal relationship.

Some studies have found that those who consume more NNS may also consumption more high calorie foods and beverages negating the calories saved by NNS. The National Health and Nutrition Examination Survey study (NHANES) (1999-2010), surveyed 23,965 individuals [20]. They found that overweight and obese individuals who drank diet drinks compared to high calorie drinks consumed similar amounts of total calories but they consumed more calories from solid foods at meals and also snacks. Normal weight individuals seemed to use diet-drink consumption as a method to maintain their healthy weight in that they ate 73 fewer kilocalories from solid foods on an average day in comparison to overweight and obese individuals who consumed 88 and 194 more kilocalories per day respectively.

The authors gave several reasons why over weight and obese people that drink diet beverages also consumed more calories from solid food. They suggested that the sweet taste of NNS activates the brain's reward center which then is no longer able to accurately gauge energy consumption. Also they indicated that the higher amount of calories from solid food could be from the body trying to maintain the current body weight. They concluded that both NNS and sugar sweetened beverages (SSB) drinks may encourage sugar cravings leading to increased snacking [20].

The San Antonio Heart Study also examined the relationship between "artificially sweetened beverages" (ASB) use and long-term weight gain. This study followed height, weight and ASB use in 5,158 adult residents [16]. They found at 7 to 8 year follow-up that 47% (3,682 survivors) who used artificial sweeteners (AS) had an overall increased BMI compared to nonusers [16]. Also a significant positive dose-response relationship emerged between baseline ASB consumption and all outcome measures adjusted for baseline BMI and demographic characteristics. For example among 1,250 individuals who were normal weight at baseline and who consumed >21 ASBs/per week versus none were almost-twice the risk of becoming overweight and obese and double the risk for developing obesity if their baseline BMI was less than $30 kgm^2$. However, they were cautious to indicate that there was no causal relationship between AS use and weight gain. Possible explanations included that AS use may simply be a marker for those already on a weight gain trajectory which continued even with switching to AS. Another explanation supported by the study is that sugar consumption results in a sense of satiety and without it there may be over compensation in the form of increased fat and protein intake. They did find that the percent of calories from total and saturated fat did rise proportionately with ASB consumption. Also suggested was that consumers of AS overestimate caloric savings

and may overcompensate elsewhere in their food intake. Another alternative explanation is AS may result in a short-term caloric deficit and lower the resting metabolic rate resulting in a long-term weight gain. Finally most AS are significantly sweeter than sugar which may lead to taste distortions and increased appetite for sweet high caloric foods [16].

Another study found a relationship between the use of artificial sweeteners in coffee/tea and BMIs compared to those who did not use artificial sweeteners. The study included 3,823 participants who were part of the 2003-2004 National Health and Nutrition Examination Survey. They found that those who used artificial sweeteners in their tea or coffee were associated with a higher BMI ($p \leq 0.05$) compared to those who did not [17].

Another study proposed that the optimal replacement for sweetened caloric beverages (SCB) to lower total energy intake, was not necessarily non-caloric diet beverages but rather water [21]. They suggested that with non-caloric beverages there is often a compensatory increase in other food or beverages negating the reduced calorie intake. The results of this study found that the caloric benefit connected with replacing SCBs with non-caloric beverages was 30% smaller than that associated with drinking water. They proposed that beverages that contain more calories or sweeteners, although controversial, my actually stimulate appetite.

Other studies have found the use of NNS may be helpful in weight loss, weight maintenance and energy intake. A meta-analysis examined 16 studies [22], to determine the effect of substituting sugar with either aspartame alone or aspartame in combination with other intense sweeteners on energy intake and bodyweight. Nine studies evaluated weight loss as an outcome. Findings revealed both a reduction energy intake and a weight loss of about 0.2kg/week for a 75-kg adult and was attributed to the replacement of sugar with aspartame and other intense sweeteners. Of benefit, this meta-analysis attempted to quantify the caloric substitution needed

for meaningful weight loss. They estimated that a weight loss of 0.2kg/wk could be obtained from an approximate energy deficit of 220-kcal per day. Two studies in this analysis evaluated weight loss maintenance and followed participants for up to three years. One study showed that weight maintenance was better in men who consumed more aspartame products over the follow-up period but no difference was found for women. The other study found that weight gain was significantly less in those using aspartame-sweetened products and after three years had maintained a weight loss of 5.1 kg compared with those in the no-aspartame group who had regained all their previous weight lost.

Other studies have provided evidence the most successful approach in weight loss and weight maintenance is to use multiple dietary strategies one of which may be NNS. In a retrospective study evaluating the dietary strategies in a weight loss group who had maintained ≥ 10% weight loss for 11.5 years compared to an always normal weight group, they found the weight loss group used more stringent dietary practices. To be eligible for the study the weight loss maintainers had to be overweight or obese (body mass index (BMI) ≥25kgm $^{-2}$) at some point in their life, currently normal weight (BMI 18.5-25kg m^{-2}), and must have lost ≥10% of the maximum body weight and kept the weight off for at least 5 years. Their diet consisted of less sugar and fat, greater percentage of modified dairy and modified dressings and sauces than the always normal weight group. Also they were found to consume three times more daily servings of artificially sweetened soft drinks, significantly fewer daily servings of sugar-sweetened drinks, and more daily servings of water, than those who have never been overweight [23].

Appetite

The topic of whether or not NNS affects appetite levels has been the subject of much debate across several disciplines. Mattes and Popkin (2009) in their critical review of the

literature suggested that when NNS are added to non-energy-yielding products that appetite may increase. However when NNS are ingested in conjunction with other energy sources such as food, this was not observed [5]. Later studies examined the effects of hunger when NNS were consumed with food and found no change in hunger, appetite, food intake, and/or weight changes [5,8,24-27]. This suggests that a person's appetite might increase when NNS are ingested without a calorie yielding food or drink due to the sweet and palatable taste. However, appetite levels do not change when NNS are consumed with food. A recent controlled cross-over trial also found that NNS, specifically aspartame, in soft drinks did not increase appetite or total calories consumed [28].

Statement of Professional Organizations on NNS's

Several national associations have reviewed the effects of NNS on human health according to their association's perspective. The following are their official statements.

The most recent official recommendation from the American Diabetes Association states that "Sugar alcohols and nonnutritive sweeteners are safe when consumed within the daily intake levels established by the Food and Drug Administration" [29(pS64)].

A joint scientific statement from the American Heart Association and the American Diabetes Association reads, "The evidence reviewed suggests that when used judiciously, NNS could facilitate reductions in added sugars intake, thereby resulting in decreased total energy and weight loss/weight control, and promoting beneficial effects on related metabolic parameters. However, these potential benefits will not be fully realized if there is a compensatory increase in energy intake from other sources" [19(p517)].

The official position of the American Dietetic Association is that, "…consumers can

safely enjoy a range of nutritive and nonnutritive sweeteners when consumed in a diet that is guided by current federal nutrition recommendations, such as the Dietary Guidelines for Americans and the Dietary References Intakes, as well as individual health goals" [30(p256)].

Clinical Recommendations

Obesity is at epidemic proportions in the United States and is impacting health in a major way resulting in reduced quality of life and increased health care costs. High sugar intake has been suggested as a major contributing factor. Many strategies are being used to reverse the upward trends in obesity rates with the focus being on reducing energy intake and increasing energy expenditures. One way to reduce energy intake is the use of non-nutritive sweeteners in food and beverages which provide palatable options while reducing energy intake and enabling weight loss and maintenance. Though NNS have been established as safe when federal nutrition guidelines are followed and recommended by major professional organizations, to obtain optimal outcomes they must be used in the proper way.

Results of this review suggest that although NNS have the potential to assist in establishing a healthy weight, the optimal results are not always accomplished in that patients do not always know how to correctly use NNS. Some research has shown that those who use NNS actually consume more solid foods and snacks negating the calorie reduction of NNS resulting in weight gain. This may be due to the fact that patients often justifying themselves in eating a high caloric meal or snack because they are using NNS. Also others have suggested that they do not provide the satiety that sugary foods do resulting in increased food intake. In addition some have indicated that when NNSs are added to non-energy-yielding products that appetite may be increased whereas when they are ingested with other energy sources such as food this was not

observed. In fact when taken in conjunction with food, no changes in hunger, appetite, food intake or weight changes were noted.

Evidence further suggests that the most effective way to establish and maintain a healthy weight is to use multiple dietary strategies of which NNS may be a part. Those patients who were able to lose weight and maintain weight for a significant period of time were found to use more stringent dietary strategies such as less sugar and fat, a greater percentage of modified dairy, sauces and dressings and increased use of NNS and water. Also some have proposed that the optimal replacement of sweetened caloric beverages is not necessarily NNS, but rather that of water which appears to exceed the positive outcomes of NNS.

In summary, in counseling patients who are attempting to lose or maintain weight, multiple dietary strategies including the use of NNS should be used with the ultimate goal to decrease energy intake. The use of diet programs or smart phone applications may be effective tools for some patients in tracking energy intake. Also patients need to be taught regarding the proper use of NNS reminding them that although they can reduce calories through their use, they must then be cautious not to increase calorie intake through additional foods and snacks.

Conclusions

Epidemiological data continues to demonstrate that obesity is at epidemic levels. The use of NNS in beverages and foods has been suggested as one strategy to reduce energy intake resulting in weight loss and maintenance. The literature continues to be controversial regarding the efficacy of NNS in weight loss and weight maintenance. Most studies are observational in nature limiting the ability to establish causality. When NNS are properly used and in combination with other effective dietary strategies, there is supporting evidence that they can be

helpful in losing and maintaining weight. More rigorous and longitudinal designs are needed to establish the efficacy of NNS's in healthy weight management.

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