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ORIGINAL ARTICLE

Prevalence of non-nutritive sweeteners consumption in a population of patients with diabetes in Mexico

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Abstract

Objective: *To estimate the prevalence of non-nutritive sweeteners (NNS) consumption in a sample of patients with diabetes.* **Material and methods:** *We applied two questionnaires, one of food frequency adapted to products containing NNS and the other of beliefs related to NNS. The prevalence of NNS consumption was determined and correlated with the body mass index, energy and sugar consumption, waist circumference, glycated hemoglobin, triglycerides, diabetes type, education and socioeconomic status.* **Results:** *The prevalence of NNS consumption was 96%; the consumption was greater in men and in patients with type 1 diabetes. A negative correlation was found between the consumption and age and a positive correlation with glycated hemoglobin and education.* **Conclusions:** *The prevalence of NNS consumption is high due to the great availability of products in the market.* (Gac Med Mex. 2017;153:56-68)
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KEY WORDS: *Non-nutritive sweeteners. Diabetes. Prevalence. Consumption. Mexico.*

Introduction

In Mexico, more than 70% of the adult population suffers from overweight or obesity, and the proportion of people older than 20 years with a previous diabetes diagnosis increased to 9.2% in 2012[1,2]. This is mainly due to the nutritional transition phenomenon experienced by our country, as availability of processed foods and fast food with high amounts of fats, sugars and salt at low cost was increased[2,3].

Mankind has always shown a marked preference for sweet flavor by adding different types of sweeteners to its food and beverages[4]. Non-nutritive sweeteners (NNS), also known as non-caloric sweeteners, are substances that don not provide energy and offer a sweet flavor; they are used to completely or partially replace sugar added to food[5]. Their main benefits are that they don't have an effect on blood sugar and are an option to sweeten foods without the energy provided by conventional sweeteners, and are of great help for people with diabetes or obesity in the nutritional management of their condition[6,7].

Some organizations that have endorsed the safety of their consumption include the U.S. Food and Drug Administration (FDA)[8], the Joint FAO/WHO Expert

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Committee on Food Additives (JECFA)[9], the American Diabetes Association (ADA)[10,11], the Academy of Nutrition and Dietetics (AND)[12], the American Heart Association (AHA)[11] and the Ministry of Health in Mexico[13]. Non-caloric sweeteners currently approved by the FDA as safe for human consumption are: Aspartame, sucralose, potassium acesulfame (acesulfame K), stevia, saccharin, neotame, advantame and Luo Han Guo fruit extracts[8,10-12], although in Mexico practically only the first five are consumed. All have different characteristics in their structure and are obtained from various sources.

The ADA states that the use of NNSs is safe when consumed according to the levels established by the main regulatory bodies (FDA and JEFCA) as admissible daily intake (ADI), with these products being useful for the control of carbohydrate and energy consumption[10,12]. ADIs for non-caloric sweeteners are established in milligrams per body weight kilogram (mg/kg) and represent the amount that can be consumed everyday throughout life without any risk for health. Established ADIs are the following: Acesulfame K 15 mg/kg, aspartame 40 mg/kg, sucralose 15 mg/kg, saccharine 5 mg/kg, stevia 4 mg/kg, neotame 2 mg/kg and advantame 5 mg/kg[11,14].

Different studies conducted in Italy[15], Belgium[16], Sweden[17], Denmark[18], Chile[5], Portugal[19], England[16] and France[16], among others, have estimated NNS consumption mainly in children and adolescents due to the risk for exceeding their ADI, and in people with diabetes, since this is a population where high consumption would be expected. In general, these investigations reveal that NNS consumption prevalences are high but that ADIs are not exceeded[5,15,16], except for some cases in childen[17]. In Mexico, the consumption of sugar and high-fructose corn syrup has been estimated; however, NNS consumption has not been studied[20]. For this reason, the purpose of this study is to estimate the prevalence of NNS consumption in patients with diabetes in our country. On the other hand, the association between sweetener consumption and some relevant variables of the study population is intended to be explored. In addition, beliefs related to NSSs will be examined. The hypothesis is proposed that the prevalence of NNS consumption is elevated in the population with diabetes.

Material and methods

This was a descriptive, cross-sectional study. One-hundred and fifty patients of the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán* (INCMNSZ) diabetes outpatient clinic were recruited. Sample size calculation was made using the formula for prevalence studies. The research was approved by the INCMNSZ Ethics Committee and informed consent was obtained from all participants.

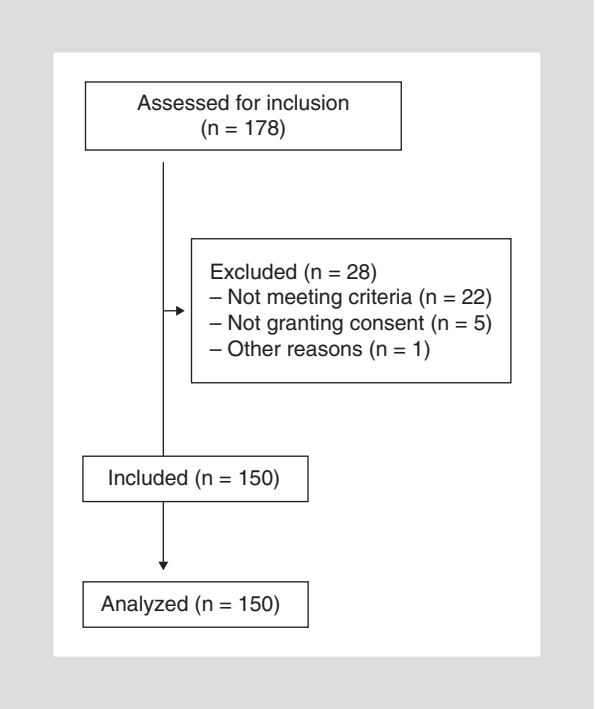

Figure 1. *Participants' flow chart.*

A consecutive sampling strategy was used considering all subjects who met the inclusion criteria until the estimated sample size was completed. Inclusion criteria were the following: Patients from both genders, older than 18 years, with either type of diabetes, attending the Nutrition-Diabetes consultation for the first time, and accepting to participate in the study. The following were regarded as exclusion criteria: Not being in conditions to undergo anthropometric assessment, existence of any impairment to adequately answer the questionnaire or refusal to participate in the study. The only censoring criterion that was considered was not correctly and/or adequately answering the questionnaire. Figure 1 shows the participants' flow chart.

Anthropometric measurements were performed using a SECA® model 700 mechanical scale with stadiometer, with 220 kg capacity and 50 g precision for weight, and 60 to 200 cm measurement range for height. For waist circumference measurement, a 2-m long LUFKIN® Executive Thinline metal measuring tape

Table 1. General characteristics of the study population of patients with diabetes of the INCMNSZ (n = 150)

Characteristic	Value
Age (years)	56.5 (44-65)
Weight (kg)	67.75 (60.07-79.62)
BMI (kg/m^2)	27.03 ± 4.37
Waist (cm)	
Men	95 ± 11.76
Women	90.05 ± 11.74
Energy consumption (kcal)	1644.75 (1413.5-1940.0)
Simple carbohydrate consumption (g)	45 (30-75)
HbA1c (%)	8.25 (7.1-9.3)
Triglycerides (mg/dL)	134 (88-183)
Total cholesterol (mg/dL)	179.29 ± 40.2
HDL cholesterol (mg/dL)	
Men	42 (38-47.5)
Women	52 (41-59)
LDL cholesterol (mg/dL)	101 (84-123)
Consumed products	4 (2-5)

Data expressed as means ± standard deviation or median and (interquartile interval), according to their distribution.
BMI: body mass index; HbA1c: glycated hemoglobin; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

model W606PM was used. The technique employed to measure the waist was the abdominal perimeter just in the midpoint between the lower lateral costal margin and the upper part of the iliac crest, perpendicular to the trunk longitudinal axis and after an expiration of patient, according to the Mexican Official Standard NOM-043-SSA2-2012[21]. The measurements were performed by a nutritionist with kinanthropometry international level I ISAK certification.

The Quetelet index was used to assess the participants' nutritional status, and they were grouped according to the World Health Organization (WHO) BMI classification[22] as low weight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2) and obesity (≥ 30 kg/m^2). To indicate the presence of abdominal obesity, a waist circumference ≥ 80 cm was taken as a cutoff point for women and ≥ 90 cm for men using the International Diabetes Federation (IDF) criteria for Central and South-Americans[23]. To assess dietary intake, a 24-hour reminder was applied.

A food-consumption frequency questionnaire was developed, adapted to NNS-containing products commercially available in Mexico, which included the most common NNS-containing products (appendix 1). It comprises a total of 119 products grouped in 10 categories: sugar substitutes, beverages, yoghurts, gelatins, chewing gums and breath mints, flavored drink mixes, biscuits, jams, desserts and others. For prevalence calculation, consumption of these products was enquired, and those participants consuming at least one NNS-containing at least once during the month prior to the assessment were considered. The number of consumed products, the consumption of each NNS in mg contained by each product and the total sum of consumed NNSs in mg regardless of the type were quantified. The ADI percentage consumed by each participant for each NNS was calculated according to the previously mentioned criteria.

In addition, a questionnaire about beliefs on NNS was created with 9 questions in order to assess the participants' beliefs with regard to NNS (appendix 2). For the answers, a Likert-type scale was employed with the following options: 1) completely agree, 2) agree, 3) don't agree or disagree, 4) disagree and 5) completely disagree.

Both questionnaires were validated by being assessed by a group of nutriology expert. In addition, the questionnaires were applied to a patient pilot group in order to assess if the questions were clearly understood, as well as to find out if they were easy to apply. Finally, the questionnaires were reviewed and approved by the INCMNSZ Ethics Committee.

Patients' complementary data such as socioeconomic status (scale from 1 to 7 according to the INCMNSZ classification), level of education, type of diabetes and most recent biochemical analyses (lipid profile and HbA1c) were extracted from the medical record. The biochemical variables that were considered were determined in a time period of ± 3 months with regard to when the assessment was carried out.

For statistical analysis, data were collected, stored and analyzed with the Statistical Package for the Social Sciences (SPSS®) for Windows®, version 19.0. Continuous variables distribution was analyzed using the Shapiro-Wilk test. According to their distribution, continuous variables description was made using means and standard deviations or medians and interquartile ranges for parametric and non-parametric variables, respectively. Categorical variables were described using percentages and proportions. Sweetener consumption was determined and correlation analysis was

made (using Pearson's or Spearman's coefficients, as appropriate) with BMI, waist circumference, HbA1c, triglycerides, energy consumption, simple carbohydrate consumption, age and socioeconomic status. For the analysis of consumption according to subgroups, Student's t-test, Mann-Whitney's U-test, one-way ANOVA or Kruskal-Wallis test were used, as appropriate. In all cases, a p-value < 0.05 was considered to be significant.

Results

Study population

The population was comprised by 83 women (55.3%) and 67 men (44.7%), out of which 73.3% had type 2 diabetes mellitus (DM2), 22% type 1 diabetes mellitus (DM1), 3.3% latent autoimmune diabetes in adults (LADA) and 1.3% had monogenic diabetes (maturity-onset diabetes of the young, MODY).

According to their level of education, the participants were classified in 6 categories, with 6% having no education at all, 14.7% having concluded primary school, 16% secondary school, 18.7% high school, 42% having a college degree and only 2.7% having postgraduate studies.

According to BMI, the majority was found to have overweight (40%), 32.7% had normal weight, 24.6% had obesity and 2.7% of participants had low weight. Abdominal obesity according to the waist circumference (≥ 80 cm in women and ≥ 90 cm in men) was found in 76% of the population.

General characteristics of the population with regard to anthropometrics, dietary assessment and biochemical analyses are presented in table 1.

Prevalence of NNS consumption

Based on the food consumption frequency questionnaire adapted to NNS-containing products commercially available in Mexico, the prevalence of NNS consumption in this population of patients with diabetes was found to be 96%.

The percentages of patients who consumed each one of the different NNSs, as well as the consumption percentages of each one of the product categories can be appreciated in figure 2. Of the 119 NNS-containing products enquired, the highest number of consumed products was 13.

When the consumption of each NNS-containing group of products was analyzed, sucralose-containing products were found to be mainly consumed among sugar substitutes (45.3%), followed by those containing stevia (16.7%), with the least consumed being those containing the aspartame plus acesulfame K mixture (5.3%). In the group of beverages, the highest consumption was for "light" cola soft drinks (43.3%), followed by prepared flavored drinks and sugar-free teas (20%), "light" soda of varied flavors (16.1%) and "light" fruit juices (5.4%). In the category of desserts, the most highly consumed is chocolate (4.7%). In the others' group, which included various products, a higher consumption was observed of sugar-free instant oatmeal (16.7%), probiotics (15.3%), sugar-free granola (10.6%), reduced-calorie pancake mix (8%) and "light" honey (4.7%).

ADI estimation

ADI was calculated according to body weight in 44% of patients. ADI calculation was not possible in the entire sample because many products contain aspartame or sucralose mixtures with acesulfame K and do not specify the precise amount of each substance on the label. No subject exceeding ADI 100% was identified. Highest calculated ADIs were: 67.3% for saccharine, 66.9% for stevia, 34.9% for sucralose, 17.1% for acesulfame K and 9.7% for aspartame.

Association between NNS consumption and variables of interest

In order to be able to correlate NNS consumption with the rest of the participants' characteristics, a variable accounting for total mg per day of any NNS consumed by the patient, either alone or mixed, was created.

Men were observed to consume higher amounts of NNS in comparison with women (p = 0.013) (Fig. 3). Higher NNS consumption was also documented in patients with DM1 in comparison with those with DM2 (p = 0.041).

A positive correlation was found between NNS total consumed amount and HbA1c (p = 0.023) (Fig. 4). This correlation continued to be significant after being adjusted for gender, type of diabetes, age, energy intake and BMI. When the population was divided according to glycemic control considering a HbA1c cutoff point of 7%, the group of participants with HbA1c higher than 7% had a NNS consumption significantly higher than the group with HbA1c lower than 7% (91.3 [24.9-227.3] vs. 52.0 [20.1-89.1] mg/day; p = 0.023). When NNS consumption was explored according to the type

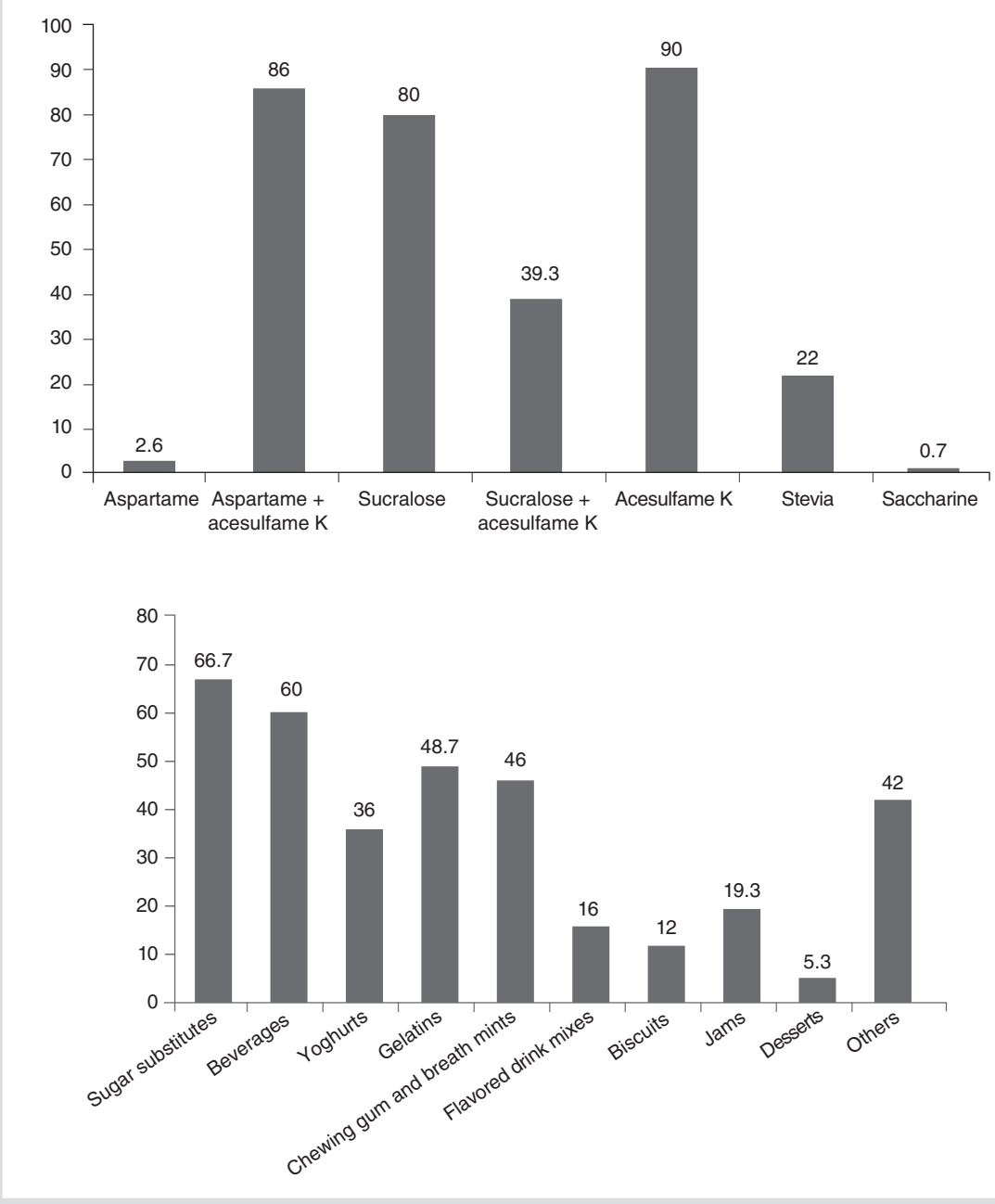

Figure 2. *Consumption percentage of different non-nutritive sweeteners during the last month* **(A)** *and consumption percentage of the different product categories during the last month* **(B)** *in INCMNSZ the population of patients with diabetes.*

of received treatment (metformin, sulfonylureas or DPP-4 inhibitors), no significant differences were found in the amount of consumed NNS between patients with or without treatment at each drug category. Additionally, no associations were found between the amount of consumed NNS and body weight, BMI, waist circumference, daily energy intake, amount of simple carbohydrates consumed per day or triglyceride levels. These results are shown in table 2.

When the number of consumed products was compared in the different education level categories was compared, an increase in the number of consumed products became evident with higher education levels ($p = 0.001$). No difference was found in the number of

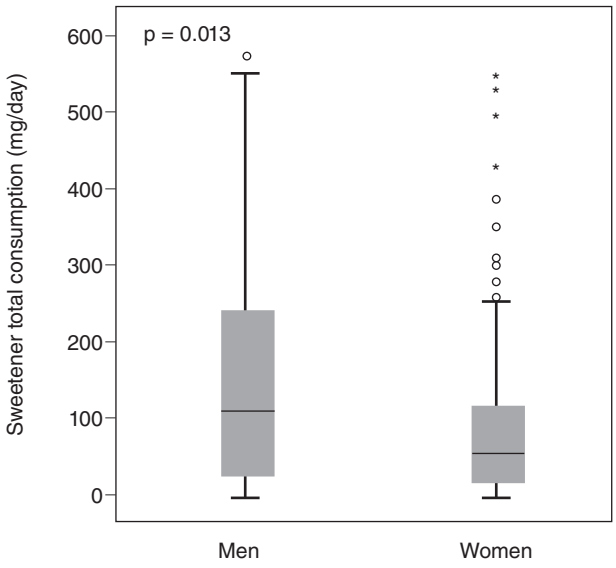

Figure 3. *Non-nutritive sweeteners total consumption according to gender in the INCMNSZ population of patients with diabetes.*

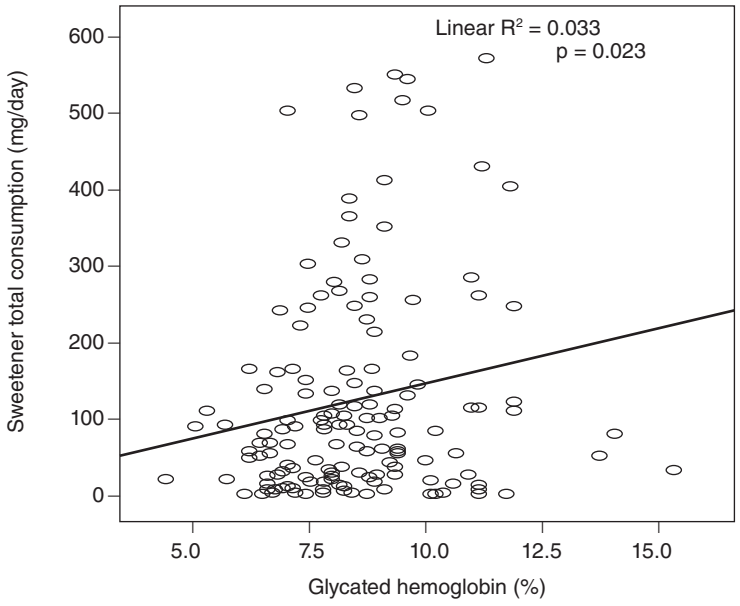

Figure 4. *Correlation between non-nutritive sweeteners total consumption per day and glycated hemoglobin levels in the INCMNSZ population of patients with diabetes.*

Table 2. Correlations between variables of interest and non-nutritive sweetener total consumption

Variable	ρ	p
HbA1c	0.187	0.023
Age (years)*	–0.186	0.024
Weight (kg)	0.128	0.119
BMI (kg/m^2)	–0.092	0.264
Waist circumference (cm)	–0.065	0.426
Energy consumption (kcal/day)	–0.033	0.689
Simple carbohydrate consumption (g/day)	–0.089	0.285
Triglycerides (mg/dL)	-0.083	0.318

*Correlation with the number of consumed products.
HbA1c: glycated hemoglobin; BMI: body mass index.

consumed products between socioeconomic status categories (p = 0.240).

Similarly, correlations were made between the number of consumed products and different variables, with a negative correlation being found with the participants' age (p = 0.024).

Beliefs about NNS

In the questionnaire on beliefs with regard to NNS (appendix 2), most the population (62.7%), answered to know what NNSs are. It was found that the higher the level of education, the higher the number of patients who answered knowing NNSs (p = 0.004).

When the participants were asked if they used NNS in any "light" or sugar-free product mentioning the product categories, 75.3% answered they did consume them; however, this does not represent the consumption prevalence. With regard to information patients believe they have about NNSs, 46.6% consider the information they have on the subject to be insufficient. When asked if any healthcare professional has recommended the consumption of NNS, 51.3% answered yes; and, subsequently, 53.3% referred NNSs had been recommended by some relative or friend had or that they consumed them by own choice, which reflects that the decision to NNS consume is not necessarily made based on the recommendation of a healthcare professional.

With regard to NNS safety, 46.6% think they are safe for health, while 30% consider they are not safe, and 23.3% do not agree or disagree about their safety.

Sixty-eight percent agreed that they don't cause discomforts such as nausea, headache or others. Finally, 54.7% considered their taste to be pleasant. This might reflect general acceptance of NNS consumption in this population. However, 58.7% considered their price to be elevated and this might be a limitation for their consumption. No differences were found between the different socioeconomic levels and the answer about NNS prices.

Since participants with DM1 and DM2 almost represented the entire population, only both these types of diabetes were taken into account to compare the differences between diabetes types. Patients with DM1 were found to answer more often having knowledge about NNS in comparison with patients with DM2 (p = 0.001); however, there were no significant differences with regard to the other beliefs between diabetes types.

Associations between the answers obtained in the questionnaire about NNS-associated beliefs and NNS total consumption per day, with a significant correlation being found between consumption and the following beliefs: 1) knowing about NNS (ρ = 0.215, p = 0.009); 2) the belief of having sufficient information on NNS (ρ = 0.175, p = 0.033); 3) recommendation of NNS consumption by healthcare personnel (ρ = 0.190, p = 0.021); 4) belief that they are safe for health (ρ = 0.255, p = 0.002); 5) belief that they don't cause discomfort (ρ = 0.268, p = 0.001) and, finally, 6) if they are considered to have a pleasant taste (ρ = 0.360, p < 0.0001). A linear regression model was constructed (R^2 = 14.9, F = 4.10, p = 0.001), including NNS total consumption in mg/day as a dependent variable and the above-mentioned beliefs that were significantly associated with NNS consumption as independent variables. Only the perception that NNSs have a pleasant taste was significantly associated with NNS total consumption (p = 0.004), while the belief of having sufficient information was also associated with consumption, although without statistical significance being reached (p = 0.068).

Discussion

The results of this study show an elevated prevalence of NNS consumption (96%), i.e., almost the entire study population consumes NNS in some type of product. When the ingested amount of each sweetener was assessed, consumption could be appreciated to be low, since no case was recorded where the ADI was exceeded.

The most highly consumed NNSs include acesulfame K, sucralose and aspartame with similar percentages, with acesulfame K being at first place, since it is found in a large number of products in combination either with aspartame or sucralose. Following acesulfame K appears aspartame, which is rarely used as the only NNS in a product. In third place, sucralose is consumed, which is commonly individually found. The consumption of stevia was found to follow, which is a relatively new NNS and, finally, saccharine was consumed in practically negligible amounts by the study population.

Owing to the recent epidemic of obesity and diabetes, strategies have been sought to reduce food energetic content by using ingredients such as NNS. However, when NNS-containing products were collected, many were found not to mention being "light", sugar-free or low-calorie products on their labels, and some individuals therefore ignore they consume NNSs.

The results obtained for consumption prevalence are similar to those that have been reported in studies conducted in other countries with different populations[5,15,16,24].

The positive association between the NNS consumed amount and HbA1c, even after adjusting for confounders such as gender, age, BMI, energy consumption and type of diabetes, should motivate future studies aimed at assessing NNS effect on glucose metabolism, since this association does not indicate causality.

Interestingly, a positive correlation was found between the NNS-containing products consumed amount and the participants' level of education, as well as a negative correlation with age. One possible explanation is the higher level of exposure to NNS-containing products in more educated and younger groups.

The questionnaire on beliefs revealed that 20.7% of the population is not aware that they consume NNS-containing products, since while they denied consumption in the beliefs questionnaire, the NNS-containing food consumption frequency questionnaire revealed consumption of at least one NNS-containing product in the last month. Possibly this occurred because, since there are so many options in the market, it is difficult for patients to identify all NNS-containing products.

Almost half the surveyed patients considered not having sufficient information about NNS, which should motivate healthcare professionals involved in the treatment of patients with DM to address the subject. Regarding the belief on NNS consumption safety, great variability was found, since while half considers them to be safe, the other half doesn't think so, or has doubts. Currently, NNS consumption is considered to be safe and has been endorsed by different organizations; however, not all surveyed patients know this information. As for other assessed beliefs about NNS, they are thought not to cause discomfort when consumed and to have a pleasant taste, although their price is considered to be high.

One of the limitations of the study is that the NNS consumption frequency questionnaire is retrospective, and consumption could therefore be under-reported. It should be considered that intake percentage could not be assessed in comparison with ADI in 100% of participants, since some products do not specify the contained NNS mg on the nutrimental label or only mention total amount contained by mixture, without the amount of each substance being specified. However, in those patients in whom the ADI percentage could not be estimated, a calculation was made based on all NNS total mg daily consumed and an average ADI of all assessed NNSs of 1.78 mg/day. When the consumed percentage of this ADI was assessed, no participants were found to exceed it. In addition, the applied instruments should be used in future studies, in order to reproduce their usefulness. Finally, the included sample belongs to a tertiary care health center, and the obtained results are therefore not necessarily applicable to the entire population of Mexicans with diabetes.

Conclusion

The prevalence of NNS consumption in this population of individuals with diabetes was elevated, with the ADI not being exceeded for any NNS in the assessed percentage. A positive association was found between the amount of consumed NNSs and HbA1c levels. In addition, a positive correlation was found between the number of consumed products and education levels, and a negative correlation between the number of consumed products and age. We consider that NNS detailed study is necessary with new technologies that include relevant aspects such as their effects on glucose metabolism and gut microbiota. Furthermore, we consider important that patients receive sufficient, evidence-based information on NNS, particularly those with diabetes or obesity, in which NNSs are an alternative within their nutritional treatment.

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Appendix 1. Questionnaire on beliefs about NNS

1. Do you know what NNSs such as aspartame, sucralose, stevia, acesulfame K or saccharine are?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

2. Do you use NNS as sugar substitute to sweeten your food or products containing them such as, for example: "light" sodas, "light" yoghurts, "light" gelatins, sugar-free jams, sugar-free chewing gum?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

3. Is the information you have about NNSs enough?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

4. Do you consume any NNS by recommendation of a healthcare professional such as a physician, nutritionist and/or nurse?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

5. Do you consume any NNS by recommendation of some relative or friend and/or by your own decision?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

6. Do you consider NNS consumption to be safe for health?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

7. Do you consider NNS price to be elevated?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

8. Do you consider that NNS consumption cause discomforts such as, for example: headache, nausea and/or others?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

9. Do you consider NNSs have a pleasant taste?
   a. Completely agree
   b. Agree
   c. Don't agree or disagree
   d. Disagree
   e. Completely disagree

Appendix 2. Questionnaire about food consumption frequency adapted to NNS-containing products available in the Mexican market

Group	No.	Amount	g/mL	Daily frequency	Weekly frequency	Monthly frequency
Sugar substitutes	1					
	2					
	3					
	4					
	5					
	6					
	7					
	8					
	9					
	10					
	11					
	12					
	13					
	14					
	15					
	16					
	17					
	18					
	19					
	20					
	21					
	22					
	23					
	24					
Beverages	25					
	26					
	27					
	28					
	29					
	30					
	31					
	32					
	33					
	34					
	35					
	36					
	37					
	38					
	39					
	40					
	41					
	42					
	43					
	44					
	45					
	46					
	47					
	48					
	49					
	50					

(Continue)

Appendix 2. Questionnaire about food consumption frequency adapted to NNS-containing products available in the Mexican market (Continued)

Group	No.	Amount	g/mL	Daily frequency	Weekly frequency	Monthly frequency
Drinks	51					
	52					
	53					
	54					
	55					
	56					
	57					
	58					
Yoghurts	59					
	60					
	61					
	62					
	63					
	64					
	65					
	66					
	67					
	68					
	69					
Jellies	70					
	71					
	72					
	73					
	74					
	75					
	76					
	77					
	78					
	79					
bubble gum and pills	80					
	81					
	82					
	83					
	84					
	85					
	86					
	87					
water flavorings	88					
	89					
	90					
	91					
	92					
	93					
	94					

(Continue)

Appendix 2. Questionnaire about food consumption frequency adapted to NNS-containing products available in the Mexican market (Continued)

Group	No.	Amount	g/mL	Daily frequency	Weekly frequency	Monthly frequency
Others	95					
	96					
	97					
	98					
	99					
	100					
	101					
	102					
	103					
	104					
	105					
	106					
	107					
	108					
	109					
	110					
	111					
	112					
	113					
	114					
	115					
	116					
	117					
	118					
	119					

(Continue)