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Relationship between Sucralose Consumption and Serum Concentration of Glycosylated Hemoglobin in People with Type 2 Diabetes Mellitus without Complications

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ABSTRACT

People who live with diabetes consume sucralose to control their blood glucose, but there is a controversy about this topic. To evaluate the relationship between sucralose consumption and serum concentration of glycosylated hemoglobin in people with Type 2 Diabetes Mellitus without complications. Cross-sectional study. Universe of 27 214 people with Type 2 Diabetes Mellitus without complications, users of a primary care unit from the Instituto Mexicano del Seguro Social in the state of Jalisco, Mexico. Simple probabilistic sample, n = 194 (p = 0,05). Propositive sampling. Selection criteria: adults of any gender and education level who agreed to participate. Variables: sociodemographic, anthropometric, clinical and dietary. Data collection instruments: Sociodemographic questionnaire, Tanita Fitscan© 585 scale, Tanita Fitscan© HR-200 stadiometer, Body Flex© tape-measure, Slim Guide© plicometer, Afinion© AS100 analyzer, and Frequency of Food Consumption Questionnaire. Information sources: clinical files and Mexican System of Equivalent Foods. Analysis: descriptive and inferential statistics (p ≤ 0,05). 194 people. Mean age 60,23 ± 11,16, interval 28-93 years. 56,2% females and 43,8% males. Difference between glycosilated hemoglobin means: sucralose consumers 7,5% ± 1,7%, no sucralose consumers 8,1% ± 2,1% (p < 0,01). Association force "sucralose consumption/high glycosilated hemoglobin concentration" OR = 1,42 ($CI_{95\%}$ 0,63, 3,21). Lineal correlation "quarterly sucralose consumption/serum concentration of glycosylated hemoglobin" ρ = -0,754 (R^2 = 0,0057, p = 0,333). This results were partially consistent to the pre-existing literature. Studies with representative stratified samples and control of dietary variables are required for better results.

Key words: Diabetes Mellitus, Type 2; Non-nutritive Sweeteners; Hemoglobin A, Glycosylated; Cross-sectional Studies; Analytical Epidemiology

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INTRODUCTION

Type 2 Diabetes Mellitus is a global public health problem in terms of its prevalence, incidence, mortality and economic, and social costs [1]. In Mexico, is especially important because of the

genetic predisposition of its population due to their ethnic origin [2, 3]. Considering that this disease is currently incurable, the treatment's cornerstone is the glycemic control to delay the onset of its complications, which is achieved with an adequate diet, regular physical activity and pharmacological treatment [4]. In this context, diet is one of the most important elements because with the regulation of the intake of simple carbohydrates, we can reach the glycemic control [5], and because changing dietary habits has proven to be a great challenge in which most of the people fail [6]. So, the consumption of non-nutritive sweeteners, among which, sucralose is the most commonly used due to its physicochemical properties [7], has emerged as the most frequently used option, by these patients, to regulate their consumption of simple carbohydrates and their body weight, in an attempt to keep their blood glucose levels under control [8-10].

However, there is controversy regarding the consumption of sucralose and other non-nutritive sweeteners to achieve glycemic control. Although there are numerous studies in which their effects on human physiology have been explored [7-15], only some of these assess the possible relationship between sucralose consumption and serum glycosylated hemoglobin concentration as a gold standard to monitor glycemic control [9,10]. However, their results are inconclusive, so the controversy still persists today. Therefore, this study was conducted with the objective of assessing the relationship between sucralose consumption and serum glycosylated hemoglobin concentration in people with Type 2 Diabetes Mellitus without complications. This, with the ultimate purpose of strengthening scientific knowledge about this subject-matter, to provide new scientific evidence on the possible positive, negative or null influence of sucralose consumption on the blood glucose in people with Type 2 Diabetes.

MATERIALS AND METHODS

Design, site, temporality and universe

Applied, correlational, empirical and quantitative research [16], of analytical's cross-sectional design [17], achieved in the Unidad de Medicina Familiar No. 171 from the Instituto Mexicano del Seguro Social, in Jalisco state, México, from January 2016 to July 2017, in a universe of 27 214 people with Type 2 Diabetes Mellitus without complications of this disease.

Sample size and sampling method

A simple probabilistic sample of n = 194 people with Type 2 Diabetes Mellitus without complications of this disease was studied, which was obtained using the "statistical formula for calculating the sample size in studies to associate two quantitative variables" [18] $n = [((Z\_1 - \alpha/2) + \ 〚(Z〛\ \_1 - \beta))/(1/2\ ln[(1 + r)/(1 - r)]\ )]\hat{}2 + 3$, for which a confidence level of 95% (Z = 1,96), a power of 80% (α = 0,05, β = 0,20), and an estimated Pearson's correlation coefficient of 0,2 (r = 0,02) obtained from a pilot test were considered. After an open invitation, to patients with Type 2 Diabetes Mellitus at the selected medical unit waiting room, a purposive sampling was carried out, in which those who satisfied the selection criteria were included in this study.

Inclusion and exclusion criteria

People aged 18 years or older, with Type 2 Diabetes Mellitus without complications of this disease, users of the medical unit, literate or illiterate with a literate caregiver, and those who agreed to participate in the study, through a signed informed consent letter, were included. At the same time, the subjects who fulfilling the inclusion criteria, had any of the following conditions were excluded: endocrinopathy, (hypothyroidism, Cushing's disease, etc), pregnancy, anemia, splenectomy, blood transfusion during the last three months prior to their participation in the study, or treatment with corticosteroids. No elimination criteria were formulated, since they do not apply in cross-sectional studies [19].

Variables

Sociodemographic, anthropometric, clinical and dietetic variables were studied. The sociodemographics were: age, sex, education level, occupation, family type, marital status and monthly family income. The anthopometrics were: weight, height, body mass index, nutritional status according to body mass index, waist circumference, hip circumference, tricipital skin fold, bicipital skin fold, subscapular skin fold, suprailiac skin fold and body fat percentage. The clinics were: years from diagnosis, control of the disease, treatment, physical activity, glycosylated hemoglobin, glucose, total colesterol, triglycerides, creatinine and glomerular filtration rate. The dietetics were: average daily percentage of

carbohydrates, average daily percentage of proteins, average daily percentage of lipids, and quarterly, average monthly and average daily of calories, non-nutritive sweeteners, sucralose, aspartame, acesulfame-K and steviosides. For statistical inferences purposes, the independent variable was sucralose consumption during the three months measured, the dependent was serum concentration of glycosylted hemoglobin, and the rest were considered sample's descriptors.

Information sources, instruments and procedures

The sociodemographic, anthropometric and clinical data were collected in a self-made questionnaire, which was not validated by its descriptive-compilation nature [20]. The information sources or instruments used, as well as the procedures followed by the variables measurement during the study, are shown in Table 1. Additionally, it is necessary to point out that the "Frequency of Food Consumption Questionnaire" estimates the individual food intake according to the number of times a specific type of food is eaten during a defined period [21], in this study, such instrument consisted of 24 items divided into two sections, one of 16 items with the food groups according to their classification in the Mexican System of Equivalent Foods [22], and other of 8 items which listed the main foods containing non-nutritive sweeteners according to their label. These procedures were achieved with prior authorization of the study, after which identification of potential participants was carried out with the help of the medical assistants, who provided daily lists of patients to identify those who atended a control appointment for Type 2 Diabetes Mellitus. Once identified the candidates, it was confirmed that they satisfied the selection criteria and they were invited to participate in the study. Those who agreed to participate signed the informed consent letter, from there on, data collection was initiated according to the procedures described (Table 1). The anamnesis was performed in the waiting-room, while physical examinations and reviews of clinical files were completed in a medical office designated by the clinic manager. On each occasion, the participants were given a monthly appointment, to have a second and third "Frecuency of Food Consumption Questionnaire". These procedures were routinely performed to cover the estimated sample size.

Statistical analysis plan

The statistical analysis was carried out in four stages: descriptive, comparative, associative and correlational. In the descriptive analysis, frequency and central tendency and dispersión measures were obtained for the qualitative and quantitative variables, respectively. In the comparative analysis, two groups were established, sucralose' consumers and non-consumers, based on which the rest of variables were compared, for wich Z test (z) was used to compare two proportions, Ji squared (χ^2) to compare more tan two proportions, and Student´s T test (t) to compare two means, according to each case [23]. In the associative analysis, the association force "sucralose consumption/uncontrolled Type 2 Diabetes Mellitus" was measured considering "uncontrolled Type 2 Diabetes Mellitus" as a high percentage of glycosylated hemoglobin, using an odds ratio (OR) with 95% confidence interval ($p \leq 0,05$), for which the "Case" as uncontrolled Type 2 Diabetes Mellitus, the "Control" as controlled Type 2 Diabetes Mellitus, the "Exposed" as sucralose intake and the "Not exposed" as sucralose no-intake were defined. Finally, in the correlational analysis, the correlation between quarterly sucralose consumption and serum concentration of glycosylated hemoglobin was determined by mean of Pearson's (r) or Spearman's (ρ) correlation coefficient according to the distribution type of independent variable, determined with Kolmogórov-Smirnov test (K-S) [24]. This test was given a 95% confidence ($p \leq 0,05$), using SPSS© 20 for the Microsoft© Windows© Operative System.

Ethical considerations

According to Mexican federal legislation on health research valid at the time of the study [25], the study was classified as a minimum risk for participants by the National Commissions of Ethics and Scientific Research of the Instituto Mexicano del Seguro Social, who approved the research protocol, granted the federal registry number R-2015-785-045, and authorized the use of institutional resources to perform glycosylated hemoglobin tests to meet study's objectives.

Table 1: Sources of information, instruments and procedures for measuring variables

Groups of variables	Variables	Information sources or instruments	Measurement procedure
Sociodemographic	Age, sex, education level, occupation, family type, civil status and monthly family income	Direct anamnesis to the person or indirect anamnesis throught the caregiver	This data was obtained through direct questioning of the patient, or indirectly to their primary caregiver in the waiting room of the medical unit. This questionnaires took place after the screening of the candidates and the acceptance to participate in the study, as well as the signing of the informed consent letter
Anthropometric	Weight	Tanita Fitscan© 585 scale	This was carried out on a stable and flat floor. The participants were instructed to remove everything from their feet, get on the scale with one foot on each side, to remain steady, to look forward and keep their arms on either side of the body during the measurement
	Height	Tanita Fitscan© HR-200 stadiometer	Subjects were asked to be barefoot, without hats or high hairstyes. They were asked to look forward, with their feet together, heels against the stadiometer and straight knees. The slide was lowered until it contacted the participants head and they were asked to take a deep breath and stand straight
	Waist circumference	Body Flex© tape-measure	Each subject was measured with the clothes raised to uncover the skin, at the end of a normal exhalation, with the arms relaxed on each side. The perimeter was obtained between the middle axillary line and the point between the lower part of the last rib and the highest part of the hip
	Hip circumference	Body Flex© tape-measure	This was measured on bare skin, with the arms relaxed on each side. The perimeter was obtained in the widest place above the glutes
	Arm circumference	Body Flex© tape-measure	This was measured on the uncovered skin, with the arms relaxed on each side, from behind the subject, on the dominating arm, at the midpoint between the lower part of the olecranial process of the ulna and the acromial process of the scapula
	Tricipital skinfold	Slim Guide© plicometer	This was measured from behind the subject with the arm flexed at 90°, the elbow close to the side in the dominant arm, in the posterior region of this arm, at the midpoint between the lower part of the olecranon process of the ulna and the acromial process of the scapula, pulling out the skinfold with the thumb and index finger of the left hand, to then place the plicometer
	Bicipital skinfold	Slim Guide© plicometer	This was measured next to the participant, with the arm in extension and the elbow near the side, in the anterior region of the dominant arm, on the biceps muscle, in the middle circumference of the arm, pulling out the skinfold over the midpoint of the arm where the plicometer was placed.
	Subescapular skinfold	Slim Guide© plicometer	This was measured behind the subject, one centimeter below the lower angle of the scapula, with the dominant arm of the participant behind the back, pulling out the skinfold diagonally over a 45° angle, the calipers of the plicometer were applied one centimeter away from the position
	Suprailiac skinfold	Slim Guide© plicometer	This was measured facing the subject, locating a point on the anterosuperior iliac crest and the median axillary line, a diagonal skinfold was pulled out on the highest point of this arc
Clinical	Years from diagnosis, control of the disease, treatment, physical activity, glucose, total colesterol, triglycerides, creatinine and glomerular filtration rate	Clinical files	They were obtained by reviewing the clinical records of the participants, through the Electronic Clinical File System, accessing from a computer located inside one of the offices in the medical unit where the study was conducted
	Glycosylated hemoglobin	Afinion© AS100 analyzer	This was obtained by a blood sample analysis, at the beginning of the study and after three months of follow up. The blood sample was obtained and processed in the clinical laboratory of the medical unit, as a separated batch of the blood samples taken and routinely carried out during a usual day of the department
Dietetic	Daily percentage of carbohydrates, proteins, lipids and calories	Frequency of Food Consumption Questionnaire and Mexican System of Equivalent Foods	They were obtained in the corresponding units for each case, performing arithmetically the conversion of the equivalent units obtained with the "Frequency of Food Consumption Questionnaire", according to the equivalents described in the Mexican System of Equivalent Foods. For the convertions, a spreadsheet was prepared with Microsoft© Excel© version 2016 for Microsoft Operating System© Windows©, licensed for particular use
	Non-nutritive sweeteners intake	Frequency of Food Consumption Questionnaire and food labels	They were obtained in the corresponding units for each case, performing arithmetically the conversion of the units obtained in the "Frequency of Food Consumption Questionnaire", according to the amounts of non-nutritive sweetener described in the labels of the reported foods. For the convertions, a spreadsheet was prepared with Microsoft© Excel© version 2016 for Microsoft Operating System© Windows©, licensed for particular use

Source: Compiled by authors

RESULTS

194 subjects with Type 2 Diabetes Mellitus without complications were studied. Their qualitative and quantitative characteristics are shown in Tables 2 and 3, respectively, in which it is observed that, the sample's majority was composed of elderly women, married, with elementary educational level, housewives, nuclear family and medium socioeconomic level, with unhealthy anthropometric characteristics, mostly overweight, with approximately 10 years as carryng the disease. This disease was controlled according to concentration of glycosylated hemoglobin, but with high seric levels of glucose and triglycerides, with pharmacological treatment, based on oral hypoglycemic agents and light physical activity, with a balanced diet within normal limits and a daily intake of non-nutritive sweeteners within the recommended limits.

Table 2: Frequency distribution of qualitative characteristics of the participants

Group	Variables	Characteristics	Frequency	Percentage (%)
Sociodemographic characteristics	Sex	Female	109	56,2
		Male	85	43,8
	Age	Young adults	84	43,3
		Older adults	110	56,7
	Civil status	Single	11	5,7
		Never married	11	5,7
		Married	131	67,5
		Widowed	28	14,4
		Divorced	4	2,1
		Separated	9	4,6
	Educational level	Illiterate	12	6,2
		Literate	38	19,6
		Elementary school	47	24,2
		Secondary school	35	18,0
		High school	25	12,9
		Technical career	6	3,1
		Degree	28	14,4
		Postgraduate degree	3	1,5
	Ocupation	Housewife	85	43,8
		Employee	27	13,9
		Pensioner	27	13,9
		Any	12	6,2
		Professional	6	3,1
		Retired	6	3,1
		Worker	30	15,5
		Religious minister	1	0,5
	Family type	Nuclear	101	52,1
		Single-parent	10	5,2
		Extensive and composed	22	11,3
		Extensive	58	29,9
		Live alone	3	1,5
Antrophometric characteristics	Nutritional status	Normal weight	34	17,5
		Overweight	81	41,8
		Obesity class I	47	24,2
		Obesity class II	18	9,3
		Obesity class III	14	7,2
Clinical characteristics	Controled Type 2 Diabetes Mellitus	No	79	40,7
		Yes	115	59,3
	Treatment	Hypoglycemic agents	132	68,0
		Insulin	21	10,8
		Diet	8	4,1
		Hypoglycemic agents and insulin	33	17,0
	Physical activity	Any	9	4,6
		Light	166	85,6
		Moderate	19	9,8

Source: Compiled by authors with data collected

Table 3: Central tendency and dispersion measures of quantitative characteristics of the participants

Group	Variables	Average	Standard Deviation	Minimum value	Maximum value
Sociodemographic characteristics	Age (years)	60,23	11,16	28	93
	Monthty family income (USD)*	383,81	376,77	75,72	2 163,47
Anthropometric characteristics	Weight (Kg)	78,7	16,3	47,5	129,0
	Height (m)	1,6	0,1	1,39	1,95
	Body mass index (Kg/m^2)	29,9	5,6	18,7	49,7
	Waist circumference (cm)	102,1	12,7	73,3	144,0
	Hip circumference (cm)	109,8	12,2	88,0	159,0
	Middle arm circumference (cm)	32,9	4,3	18,0	50,0
	Tricipital skinfold (mm)	18,8	7,5	6,0	55,0
	Bicipital skinfold (mm)	11,5	6,0	3,0	33,5
	Subescapular skinfold (mm)	22,2	7,2	8,0	45,0
	Suprailac skinfold (mm)	20,0	6,0	7,0	40,0
	Body fat percentage (%)	34,2	6,3	18,6	45,4
Clinical characteristics	Time from diagnosis (años)	10,4	8,8	1	60
	HbA_{1c} in young adults (%)†	7,8	2,0	4,8	13,5
	HbA_{1c} in older adults (%)†	7,4	1,5	5,0	12,8
	Seric glucose (mg/dl)	162,6	75,1	70	500
	Cholesterol (mg/dl)	195,2	41,2	96	334
	Triglycerides (mg/dl)	191,9	133,1	49	1,177
	Creatinine (mg/dl)	0,8	0,2	0,3	1,9
	Glomerular filtration rate (ml/min/1.73m^2)	95,0	14,4	57,6	136,8
Dietetic characteristics	Carbohydrate intake (%)‡	58,3	9,3	29,6	78,6
	Protein intake (%)‡	18,3	4,5	10,5	36,6
	Lipid intake (%)‡	22,3	6,7	6,4	43,4
	Daily calorie intake (cal)‡	1 466,0	647,4	579,7	3 827,2
	Monthly calorie intake (cal)§	43 981,2	19 421,8	17 391,5	114 816,3
	Quarterly calorie intake (cal)	131 943,6	58 265,4	52 174,5	344 448,9
	Daily NNS intake (mg)‡	44,8	94,7	0,0001	657,3
	Monthly NNS intake (mg)§	1 344,1	2 842,3	0,0040	19 719,2
	Quarterly NNS intake (mg)	4 032,2	8 527,0	0,0120	59 157,5
	Daily sucralose intake (mg)‡	2,7	7,8	0,0001	77,7
	Monthly sucralose intake (mg)§	80,8	233,7	0,0020	2 329,7
	Quarterly sucralose intake (mg)	242,3	7 001,0	0,0060	6 989,0
	Daily aspartame intake (mg)‡	39,5	58,2	0,0018	313,9
	Monthly aspartame intake (mg)§	1 185,7	1 747,2	0,0530	9 417,9
	Quarterly aspartame intake (mg)	3 557,2	5 241,7	0,1590	28 253,6
	Daily acesulfame-K intake(mg)‡	33,9	56,8	0,0012	328,5
	Monthly acesulfame-K intake (mg)§	1 017,4	1 704,3	0,0350	9 853,9
	Quarterly acesulfame-K intake (mg)	3 052,2	5 112,9	0,1050	29 561,6
	Daily steviosides intake (mg)‡	0,3	1,7	0,0003	12,0
	Monthly steviosides intake (mg)§	8,6	51,3	0,0080	360,0
	Quarterly steviosides intake (mg)	25,9	154,0	0,0240	1 080,0

*****Data collected in Mexican pesos (MXN), converted into US dollars (USD) according to the exchange rate of January 27, 2018. †Upon completion of the investigation. ‡Daily average. §Monthly average. **NNS =** Non-Nutritive Sweeteners. **Source:** Compiled by authors with data collected.

Table 4: Comparison of qualitative characteristics between sucralose consumers and non-consumers

Group	Variables	Characteristics	Sucralose consumers	Sucralosa non-consumers	p value
Sociodemographic characteristics	Sex	Female	98 (58,7%)	11 (40,7%)	0,081*
		Male	69 (41,3%)	16 (59,3%)	
	Age	Young adults	72 (43,1%)	12 (44,4%)	0,897*
		Older adults	95 (56,9%)	15 (55,6%)	
	Civil status	Single	9 (5,4%)	2 (7,4%)	0,728†
		Not married	10 (6,0%)	1 (3,7%)	
		Married	111 (66,5%)	20 (74,1%)	
		Widowed	26 (15,6%)	2 (7,4%)	
		Divorced	4 (2,4%)	0 (0%)	
		Separated	7 (4,2%)	2 (7,4%)	
	Educational level	Illiterate	10 (6,0%)	2 (7,4%)	0,949†
		Literate	32 (19,2%)	6 (22,2%)	
		Elementary school	40 (24,0%)	7 (25,9%)	
		Secondary school	30 (18,0%)	5 (18,5%)	
		High school	23 (13,8%)	2 (7,4%)	
		Technical career	5 (3,0%)	3 (11,1%)	
		Degree	25 (15,0%)	1 (3,7%)	
		Postgraduate degree	2 (1,2%)	1 (3,7%)	
	Ocupation	Housewife	74 (44,3%)	11 (40,7%)	0,932†
		Employee	23 (13,8%)	4 (14,8%)	
		Pensioner	24 (14,4%)	3 (11,1%)	
		Any	10 (6,0%)	2 (7,4%)	
		Professional	5 (3,0%)	1 (3,7%)	
		Retired	6 (3,6%)	0 (0%)	
		Worker	24 (14,4%)	6 (22,2%)	
		Religious minister	1 (0,6%)	0 (0%)	
	Family type	Nuclear	87 (52,1%)	14 (51,9%)	0,546†
		Single parent	7 (4,2%)	3 (11,1%)	
		Extended composited	20 (12,0%)	2 (7,4%)	
		Extended	50 (29,9%)	8 (29,6%)	
		Live alone	3 (1,8%)	0 (0%)	
Antropometric characteristics	Nutritional status	Normal weight	30 (18,0%)	4 (14,8%)	0,552†
		Overweight	66 (39,5%)	15 (55,6%)	
		Obesity class I	42 (25,1%)	5 (18,5%)	
		Obesity class II	17 (10,2%)	1 (3,7%)	
		Obesity class III	12 (7,2%)	2 (7,4%)	
Clinical characteristics	Controlled T2DM	No	66 (39,5%)	13 (48,1%)	0.397*
		Yes‡	101 (60,5%)	14 (51,9%)	
	Treatment	Hypoglycemic agents	115 (68,9%)	17 (63,0%)	0.586†
		Insulin	19 (11,4%)	2 (7,4%)	
		Diet	7 (4,2%)	1 (3,7%)	
		Hypoglycemic agents and insulin	26 (15,6%)	7 (25,9%)	
	Physical activity	Any	3 (1,8%)	6 (22,2%)	0.000†
		Light	148 (88,6%)	18 (66,7%)	
		Moderate	16 (9,6%)	3 (11,1%)	

*****According to Z test (z). †According to Ji square test (χ^2). ‡Young adults with $HbA_{1c} \leq 7\%$ and older adults with $HbA_{1c} \leq 8\%$. **T2DM =** Type 2 Diabetes Mellitus. **Source:** Compiled by authors with data collected.

Table 5: Comparison of quantitative characteristics between sucralose consumers and non-consumers

Group	Variables	Sucralose consumers (n = 167; $\tilde{x}$ ± s)	Sucralose non-consumers (n = 27; $\tilde{x}$ ± s)	p* value
Sociodemographic characteristics	Age (years)	60,46 ± 11,20	58,78 ± 11,04	0,000
	Monthty family income (USD)†	390,19 ± 390,38	336,97 ± 258,15	0,000
Antropometric characteristics	Weight (Kg)	78,8 ± 16,4	77,8 ± 15,6	0,000
	Height (m)	1,62 ± 0,11	1,67 ± 0,10	0,000
	Body mass index (Kg/m^2)	30,17 ± 5,68	28,20 ± 4,94	0,000
	Waist circumference (cm)	101,6 ± 12,7	106,7 ± 11,6	0,000
	Hip circumference (cm)	109,7 ± 12,3	110,7 ± 11,6	0,000
	Middle arm circumference(cm)	33,0 ± 4,3	31,9 ± 4,8	0,000
	Tricipital skinfold (mm)	18,9 ± 7,7	17,6 ± 6,1	0,000
	Bicipital skinfold (mm)	11,4 ± 5,7	12,4 ± 8,4	0,000
	Subescapular skinfold (mm)	22,2 ± 7,3	22,7 ± 7,0	0,000
	Suprailiac skinfold (mm)	20,1 ± 5,8	19,3 ± 7,5	0,000
	Body fat percentage (%)	34,5 ± 6,2	31,2 ± 6,8	0,000
Clinical characteristics	Time from diagnosis (years)	10,4 ± 8,8	11,1 ± 9,0	0,000
	HbA_{1c} in the entire sample (%)‡	7,5 ± 1,7	8,1 ± 2,1	0,000
	HbA_{1c} in young adults (%)‡	7,64 ± 1,91	8,71 ± 2,61	0,093
	HbA_{1c} in older adults (%)‡	7,31 ± 1,53	7,68 ± 1,60	0,389
	Seric glucose (mg/dl)	160,3 ± 71,9	176,7 ± 93,2	0,000
	Cholesterol (mg/dl)	193,5 ± 40,0	207,6 ± 48,0	0,000
	Triglycerides (mg/dl)	192,2 ± 137,9	190,6 ± 92,8	0,000
	Creatinine (mg/dl)	0,74 ± 0,19	0,90 ± 0,35	0,000
	Filtration glomerular rate (ml/min/1.73m^2)	94,9 ± 14,6	96,1 ± 13,7	0,000
Dietetic characteristics	Carbohydrate intake (%)§	57,9 ± 9,3	58,5% ± 15,5%	0,000
	Protein intake (%)§	18,5 ± 4,6	16,1% ± 5,0%	0,000
	Lipid intake (%)§	22,4 ± 6,6	20,6% ± 8,6%	0,000
	Daily calorie intake (cal)§	1 457,9 ± 631,5	1 525,0 ± 766,6	0,000
	Daily NNS intake (mg)§	46,0 ± 95,9	3,5 ± 3,9	0,000

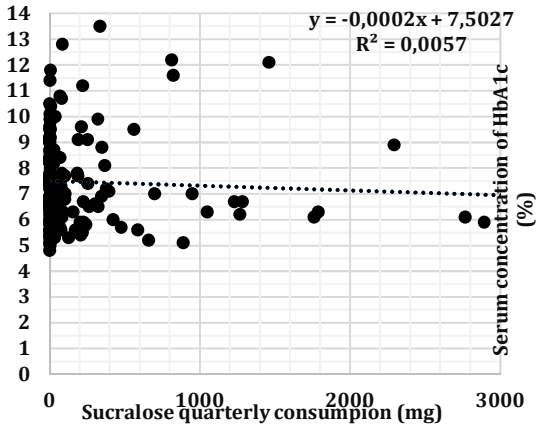
n = Sample size. $\tilde{x}$ **=** Sample's arithmetic mean. **s =** Sample's standard deviation. *According to T test (*t*). †Data collected in Mexican pesos (MXN), converted in US dollars (USD) according to the exchange rate of January 27, 2018. ‡Upon completion of the investigation. §Daily average. NNS: Non-nutritive sweeteners. **Source:** Compiled by authors with data collected.

Tables 4 and 5 show the comparative analysis of qualitative and quantitative sample characteristics respectively, in which it is observed that, in terms of qualitative characteristics, only a statistically significant difference was found (p < 0,05) regarding to physical activity, which was more frequently practiced among sucralose consumers. In regard to the quantitative characteristics, statistically significant differences were found (p < 0,05) in practically all attributes in sucralose consumers which had greater age, greater monthly family income, weight and body mass index, and had a greater arm circumference average, and a greater tricipital and suprailiac skinfold, body fat percentage, serum level of triglycerides and daily consumption of proteins, lipids and non-nutritive sweeteners. At the same time, they had been disease carriers for a shorter time since their diagnosis, although, they were shorter, had a smaller waist and hip circumference, a lower bicipital and subescapular skinfold as well as serum glucose level, cholesterol, creatinine, glomerular filtration rate, daily carbohydrate and calories intake.

It was found that mean serum level of glycosylated hemoglobin was significantly lower (p < 0,05) in sucralose consumers compared to non-consumers, however, when stratifying this analysis based on the age group, no statistically significant differences were found (p < 0,05) comparing young and older adults, sucralose consumers and non-consumers.

The measurement of the association force "sucralose consumption/high glycosylated hemoglobin concentration" obtained an OR = 1,42 ($CI_{95\%}$ 0,63, 3,21).

Finally, Figure 1 shows the linear correlation "quarterly sucralose consumption/glycosylated hemoglobin serum concentration", where a negative correlation is observed, but this was not statistically significant (ρ = -0,754, R^2 = 0,0057, p = 0,333), the independent variable (quarterly sucralose consumption) didn't follow a normal distribution (K-S = 4,715, p = 0,000).



Source: Compiled by authors

Figure 1: Linear correlation "sucralose quarterly consumption/serum concentration of glycosylated hemoglobin"

DISCUSSION

This is the first study known by the authors in which the relationship between sucralose consumption and seric concentration of glycosylated hemoglobin has been evaluated in people with Type 2 Diabetes Mellitus without complications. Several studies exist about sucralose effects over humans [7-15], only a few evaluate the possible relationship between its consumption and seric concentration of glycosylated hemoglobin [9-10]. However, these include populations with any diabetes' type, with and without complications, so the comparison of characteristics of these studies with ours is limited. In this context, the population's sociodemographic of this study and referents [9-10] are similar in age and gender, but there are no references aganinst to compare education level, occupation, family type, marital status and family monthly income, hence we can discuss little about it, beyond the fact that sociodemographic sample's profile is consistent with the national [2,3] and worldwide reports [1,7-15].

Regarding anthropometric characteristics, only one reference explores them [10], it is limited to body mass index and waist circumference, reporting means of 27,03 Kg/m^2 and 92,75 cm, respectively, which were lower than those found in this study, where population was obese, whereas referred only as overweight [10], without referring to other anthropometric measures of this research that support this conclusion. When it came to clinical characteristics, only one group of authors consulted explored them [10], and they reported a glycosylated hemoglobin mean of 8,25% (without distinguishing between young and older adults), total cholesterol of 179,3 md/dl, and triglycerides of 134 mg/dl, in contrast to a glycosylated hemoglobin mean of 7,8% ± 2,0% for young adults and 7,4% ± 1,5% for older adults, total cholesterol of 195,2 mg/dl, and triglycerides of 191,9 mg/dl, without cases of renal failure in this study, so that there are no important clinical differences in blood chemistry between populations, beyond inclusion [10] or exclusion (this study) of people with chronic renal failure or other diabetes complications.

In regards to dietary characteristics, only one reference compiled information of this type [10], they only reported daily caloric consumption and simple carbohydrates, of 1 644,8 cal/day and 45 g/day, respectively, in contrast to 1 466 cal/day and 58,3 g/day in this study. Therefore, it can be argued that the diet in this study was better compared with the one in question.

Finally, referring to consumption of non-nutritive sweeteners, Grotz [9] reports a daily intake of sucralose of 667 mg/day, while Romo-Romo [10] reports a daily average intake of non-nutritive sweeteners of 80 mg/day, in contrast to means of 2,7 mg/day of sucralose and 44,8 mg/day of general non-nutritive sweeteners obtained in this study, so, both daily average consumptions were lower in the population of this study. On the other hand, regarding the possible relation between sucralose consumption and serum glycosylated hemoglobin concentration in the population with diabetes, with respect to differences between glycosylated hemoglobin levels according to whether sucralose was consumed or not, Grotz [9] reported a statistically significant difference (p = 0,020) between sucralose consumers and non-consumers, in favor of the first, after 13 weeks of diet, which was corroborated in this study in the general population, but the observation didn't persist when stratified by age groups.

Meanwhile, in terms of correlation between sucralose consumption level and serum glycosylated hemoglobin concentration, Romo-Romo [10] reported a statistically significant positive correlation (p = 0,023) between the general level of non-nutritive sweetener consumption (the majority was sucralose) and the serum concentration of glycosylated hemoglobin, while in this study, a negative correlation was observed without statistical significance between

the level of sucralose consumption (in particular) and the serum concentration of glycosylated hemoglobin. While there were no references that measured the association force "consumption of sucralose/high glycosylated hemoglobin concentrations" or another similar one, since, in this study, an association was obtained without statistical significance. In this ideas' order, the differences observed between the findings in this research and what was reported by the consulted authors [9,10], could be explained by the methodological differences of these studies, such as the general comparison without considering the age group, the inclusion of people with any type of Diabetes Mellitus and with complications of this disease. Another difference is the application of a single measurement of the consumption of non-nutritive sweeteners, which could imply an overestimation of the average daily consumption of these substances.

Finally, it should be considered that the results of this study may be influenced by memory bias of its participants, since it is recognized that dietary surveys may imply underrreporting due to the Hawthorne's effect. Therefore, sucralose and food consumption should be controlled in future studiesin order to obtain free measurements of this bias. At the same time, the results are limited by the heterogeneity of the sample studied, so in future studies it is suggested to study homogeneous samples, stratified according to variables with influence on glycaemia, as age, evolution time, resistance to insulin, among others for which it is recommended to conduct multicentric studies.

CONCLUSIONS

It can be concluded that, in general terms, in this study, a statistically significant relationship between sucralose consumption and serum glycosylated hemoglobin concentration in people with Type 2 Diabetes Mellitus without complications was not found. Prospective studies with control of dietary variables and representative stratified homogeneous samples are required to obtain better conclusions about this subject-matter.

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