



Trabajo Original

Epidemiología y dietética

Consumption of non-caloric sweeteners among pregnant Chileans: a cross-sectional study *Consumo de edulcorantes no calóricos en embarazadas chilenas: estudio transversal*

Fabiola Fuentealba Arévalo, Jonathan Espinoza Espinoza, Carolina Salazar Ibacache and Samuel Durán Agüero

Escuela de Nutrición y Dietética. Facultad de Ciencias para el Cuidado de la Salud. Universidad San Sebastián. Chile

Abstract

Introduction: consumption of non-caloric sweeteners (NCS) has increased worldwide in the last 35 years.

Objective: to determine the consumption of NCS among pregnant Chilean women and measure if consumption exceeded the acceptable daily intake.

Methods: we conducted a cross-sectional study of pregnant women from the two main cities in Chile. Women were interviewed to determine the consumption of NCS and socioeconomic level; anthropometry was measured.

Results: six hundred and one pregnant women were interviewed; 98% of pregnant women surveyed consumed NCS. The most consumed sweetener was sucralose (95.6%), followed by acesulfame k (80.6%), stevia (78.3%), aspartame (75.1%), saccharin (14.8%), and cyclamate (10%). We observed that consumption closest to the acceptable daily intake was reported for stevia (82.5%), followed by acesulfame k (44%). However, except stevia, which reached 12%, average values were under 5% of the acceptable daily intake. No pregnant woman in the sample exceeded the acceptable daily intake and there were no differences in sweetener consumption by trimester of pregnancy or by socioeconomic level.

Conclusions: a high prevalence of NCS consumption was observed, however, none of the pregnant women exceeded the acceptable daily intake.

Key words:

Pregnancy. Non-caloric sweeteners. Intake. Sucralose. Stevia. Aspartame.

Resumen

Introducción: el consumo de edulcorantes no calóricos (ENC) ha aumentado en todo el mundo en los últimos 35 años.

Objetivo: determinar el consumo de ENC en embarazadas chilenas y medir si el consumo excede la ingesta diaria admisible (IDA).

Métodos: realizamos un estudio transversal en embarazadas, proveniente de las dos principales ciudades de Chile. Se las entrevistó para determinar el consumo de ENC y nivel socioeconómico, además se realizó antropometría.

Resultados: se entrevistaron a 601 embarazadas; el 98% de las embarazadas encuestadas consumieron ENC. El edulcorante más consumido fue sucralosa (95,6%), seguido de acesulfamo k (80,6%), estevia (78,3%), aspartamo (75,1%), sacarina (14,8%) y ciclamato (10%). Observamos que el consumo más cercano a la IDA se reportó para la estevia (82,5%), seguido de acesulfamo k (44%). Sin embargo, excepto la estevia, que alcanzó el 12% de adecuación con respecto al IDA, los valores promedio estuvieron por debajo del 5% de la IDA. Ninguna mujer embarazada en la muestra excedió la IDA y no hubo diferencias en el consumo de ENC por trimestre del embarazo o por nivel socioeconómico.

Conclusiones: se observó una alta prevalencia de consumo de ENC, sin embargo, ninguna de las mujeres embarazadas excedió la IDA.

Palabras clave:

Embarazo. Edulcorantes no calóricos. Ingesta. Sucralosa. Estevia. Aspartamo.

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Correspondence:

Fabiola Fuentealba Arévalo. Escuela de Nutrición y Dietética. Facultad de Ciencias de la Salud. Universidad San Sebastián. General Cruz, 1577. Concepción, Chile
e-mail: fabiola.fuentealba@uss.cl

INTRODUCTION

Non-caloric sweeteners (NCS) are food additives that have the function of sweetening without adding calories (1). They can be of artificial (saccharin, cyclamate, aspartame, acesulfame potassium, sucralose) or natural origin (stevia, thaumatin) and are present in countless foods such as dairy products, beverages and dietary juices, cookies, breakfast cereals, and as a powder or liquid to sweeten tea, coffee or infusions. NCS must be approved for mass use. The organisms that regulate use at the international level are *Codex Alimentarius*, the Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) (2-4). According to the United States Academy of Nutrition and Dietetics, NCS are safe for use in the general population, including pregnant women (5).

In Chile, the Guide for Diabetes and Pregnancy created by the Ministry of Health, indicates that consumption of NCS such as aspartame, sucralose, acesulfame potassium, and stevioside in moderation during pregnancy can be allowed. In addition, the guide recommends preferring alternatives to saccharin, since it is eliminated more slowly from the fetus than from the adult (6).

However, there are some institutions, like the Institutes of Medicine, which indicate that there is not enough evidence, in order to recommend NCS (7).

Consumption of NCS has increased in the last 30 years, as shown by several studies conducted among adults and children (8-10), however, there are no studies showing intake during pregnancy.

The objective of the study was to determine the consumption of NCS in Chilean pregnant women.

METHODS

We conducted a cross-sectional study of pregnant women from Santiago and Concepción (center and south of the country). Women were interviewed in Family Health Centers (public sector) and private clinics during the second semester of 2016 and data was processed during the first half of 2017.

The sample size was calculated for each city from the Arcella study (11) with a confidence interval of 95%, a power of 90% and a precision calculated as the observed average-recommended value.

Inclusion criteria was attending one pregnancy check-up appointment. Diabetic pregnant women (type 1 and type 2), those who had a metabolic disease, and those who had not completed the forms were excluded; the subjects were chosen for convenience. A signed informed consent was obtained from each participant. The protocol was reviewed and approved by the Ethics Committee.

PROCEDURES

Food consumption surveys

Sampling of sweeteners and foods containing NCS was carried out in the commercial market, with a total of 187 foods containing

NCS (yogurt, prepared dessert, liquid flavored milk, cultured milk, flavored milk, jam, cereal for breakfast, milk caramel, flavored mineral water, soft drinks, fruit pulp juice, powdered juice, sweet cookie, ice cream, desserts, light sugar, biscuits, and liquid and powder NCS). The type and quantity of NCS was reported on food labels. We used a weekly Quantified Consumption Trend Survey. The survey was validated by experts to evaluate the intake of sweeteners (12). The portions were described as typical measurements used at home (drops, glass, cup, spoon, teaspoon, plate, etc.). This information was used to calculate the daily intake of each NCS. Surveys were administered by a trained nutritionist. The amount of NCS was obtained taking the consumption of 100 ml or 100 g of food per type of NCS in each product. Nutritional information was collected from content exhibited in the package of each product. This method is in accordance with the Chilean food regulation bureau, which indicates that all packed foods must indicate which NCSs are present and their amount per 100 g or ml and per portion. Following this step, the acceptable daily intake (ADI) value was obtained for each NCS.

Anthropometry

Weight, height and weeks of pregnancy were obtained from the medical record. Nutritional status was determined using body mass index (BMI) and weeks of gestation. The result was contrasted with the Nutritional Assessment Table published by Atalah et al. (13).

Socioeconomic level

The ESOMAR socioeconomic survey was applied to each pregnant woman. This method originated in Europe and is restricted to occupation and education variables. The survey has been validated in Chile and the results express social economic status (high class, upper middle class, middle class, lower middle class and low class) (14).

Statistics

Data were processed in an Excel spreadsheet with the statistical program SPSS 22.0. To evaluate the normality of the continuous variables (age, weight, height and intake of sweeteners) the Kolmogorov-Smirnov goodness of fit test was used. For comparisons between weeks of gestation, an ANOVA test with a Bonferroni post hoc was used. In all cases, a value of $p < 0.05$ was considered as statistically significant.

RESULTS

Six hundred and one pregnant women were interviewed and they all answered the interview; 98% of them consumed NCS daily: 80.6% acesulfame k, 14.8% saccharin, 10% cyclamate,

95.6% sucralose, 78.3% stevia and 75.1% aspartame. Nearly 7% reported consuming these five NCS at the same time. Table I shows the descriptive statistics of the sample. Age and weeks of gestation were 27.1 ± 5.7 years and 26.4 ± 4.5 weeks, respectively.

Table II shows a significantly lower consumption of cyclamate for the third compared to the second trimester. For the other NCS, consumption was similar by week of gestation.

Table III presents the intake data by socioeconomic level. No significant differences were observed.

Table IV shows average consumption by ADI. Consumption closest to ADI was observed for stevia (82.5%), followed by acesulfame K (44%); however, average values were under 5% of the ADI, except for stevia, which reached 12%. No pregnant woman in the sample exceeded the ADI.

Table I. Descriptive statistics of the sample (n = 601)

	Average	SD	Minimum	Maximum
Age (years)	27.1	5.7	16.0	47
Weight (kg)	71.3	12.4	43.5	170.0
Height (m)	1.60	0.06	1.45	1.77
BMI (kg/m ²)	27.6	4.5	17.2	62.4
Gestational age (weeks)	26.4	4.5	1	41
Acesulfame K (mg/kg/weight)	0.48	0.63	0	6.6
Aspartame (mg/kg/weight)	0.91	1.4	0	14.9
Saccharin (mg/kg/weight)	0.07	0.11	0	0.85
Cyclamate (mg/kg/weight)	0.16	0.21	0	0.82
Sucralose (mg/kg/weight)	0.54	0.57	0	3.69
Stevia (mg/kg/weight)	0.50	0.53	0	0.001
<i>Education</i>				
Primary school (number/%)	16 (2.6)			
Secondary (number/%)	230 (38.2)			
College (technical/university) (number/%)	355 (59.0)			
<i>Nutritional status</i>				
Underweight (number/%)	61 (10.1)			
Normal weight (number/%)	283 (47.0)			
Overweight (number/%)	173 (28.7)			
Obesity (number/%)	84 (13.9)			
<i>Physical activity (> 150 min/week)</i>				
Yes (number/%)	128 (21.2)			
No (number/%)	473 (78.7)			
<i>Socioeconomic level</i>				
Low (number/%)	121 (20.1)			
Medium (number/%)	371 (61.8)			
High (number/%)	109 (18.1)			
<i>Pregnancy care</i>				
Public system (number/%)	241 (41.0)			
Private (number/%)	195 (32.4)			
Mixed (number/%)	165 (27.4)			
<i>Smokers</i>				
Yes (number/%)	18 (2.9)			
No (number/%)	583 (97.0)			
<i>Who recommended to use NCS?</i>				
Nutritionist (number/%)	112 (18.6)			
Doctor (number/%)	40 (6.6)			
Another professional (number/%)	16 (2.6)			
Friends/Family (number/%)	35 (5.8)			
No one (number/%)	398 (66.2)			

Table II. Comparison of anthropometry and sweetener consumption by pregnancy trimester

Variables	First trimester (n = 80)	Second trimester (n = 265)	Third trimester (n = 256)
Age (years)	26.6 ± 5.7	26.8 ± 5.5	27.5 ± 6.0
Weight (kg)	65.5 ± 10.8*†	68.5 ± 10.5*	76.1 ± 13.1†
Height (m)	1.61 ± 0.05	1.60 ± 0.05	1.60 ± 0.06
BMI (kg/m ²)	24.9 ± 3.7*†	26.6 ± 3.8*†	29.3 ± 4.8†‡
Gestational age (weeks)	11.7 ± 2.5*†	23.3 ± 3.7*†	34.2 ± 2.9†‡
Acesulfame k (mg/kg/weight)	0.40 ± 0.55	0.5 ± 0.6	0.44 ± 0.69
Aspartame (mg/kg/weight)	0.68 ± 0.99	1.02 ± 1.56	0.86 ± 1.50
Saccharin (mg/kg/weight)	0.05 ± 0.05	0.08 ± 0.09	0.07 ± 0.15
Cyclamate (mg/kg/weight)	0.13 ± 0.16	0.24 ± 0.25*	0.08 ± 0.15*
Sucralose (mg/kg/weight)	0.58 ± 0.62	0.56 ± 0.56	0.52 ± 0.05
Stevia (mg/kg/weight)	0.49 ± 0.45	0.53 ± 0.52	0.47 ± 0.57

Values expressed as mean ± SD. Anova and Bonferroni post hoc test. Same symbols indicate significant differences (p < 0.05).

Table III. Comparison of sweetener consumption by socioeconomic group

Variables	High (n = 120)	Medium high (n = 126)	Medium (n = 142)	Medium-low (n = 120)	Low (n = 93)
Acesulfame k (mg/weight)	28.2 ± 42.0	37.8 ± 52.9	37.8 ± 63.7	37.9 ± 49.4	24.7 ± 23.8
Aspartame (mg/weight)	50.8 ± 52.9	67.8 ± 114.8	63.1 ± 117.8	65.9 ± 109.2	43.6 ± 50.4
Saccharin (mg/weight)	0.9 ± 3.0	0.3 ± 1.2	1.4 ± 1.9	0.4 ± 1.8	1.5 ± 2.3
Cyclamate (mg/weight)	0.9 ± 4.1	0.6 ± 2.3	0.3 ± 2.5	0.4 ± 2.7	2.2 ± 4.3
Sucralose (mg/weight)	36.6 ± 36.6	43.8 ± 36.5	46.9 ± 48.0	47.9 ± 48.1	44.7 ± 47.0
Stevia (mg/weight)	30.6 ± 41.9	33.3 ± 40.4	75.8 ± 36.7	20.8 ± 27.4	17.0 ± 14.6

Values expressed as mean ± SD. Anova and Bonferroni post hoc test.

Table IV. Average and maximum consumption, crude and as percentage of ADI

	ADI	Maximum consumption	Average consumption	Maximum/ADI %	Average/ADI %
Acesulfame k (mg/kg/weight)	15	6.6	0.48	44%	3.2%
Aspartame (mg/kg/weight)	40	14.9	0.9	37.2%	2.2%
Saccharin (mg/kg/weight)	5	0.8	0.07	16.0%	1.4%
Cyclamate (mg/kg/weight)	7	0.8	0.16	11.4%	2.2%
Sucralose (mg/kg/weight)	15	3.6	0.54	24.0%	3.6%
Stevia (mg/kg/weight)	4	3.3	0.50	82.5%	12.5%

ADI: acceptable daily intake.

Figure 1 shows that NCS consumption can vary by food type. Acesulfame k, aspartame and table sweetener are prevalent in drinks and juices, saccharine and cyclamate in preserves and marmalades, and sucralose and stevia in dairy (especially yogurt).

DISCUSSION

In our sample, NCS consumption was almost universal, however, no pregnant woman exceeded the ADI for any sweetener,

also without any major differences in relation to social economic status and trimester of pregnancy.

In our study, a high prevalence of NCS consumption was observed (98%), however, when we evaluated only intake of beverages with NCS, consumption decreased to 41.2%, a result much higher than that reported in other studies. In a sample of Danish pregnant women, 13% of NCS consumption came from beverages (15,16).

Several studies have evaluated whether the intake of NCS exceeds the ADI in both children and adults (8-11,17,18). Other studies have shown high levels of cyclamate and saccharin con-

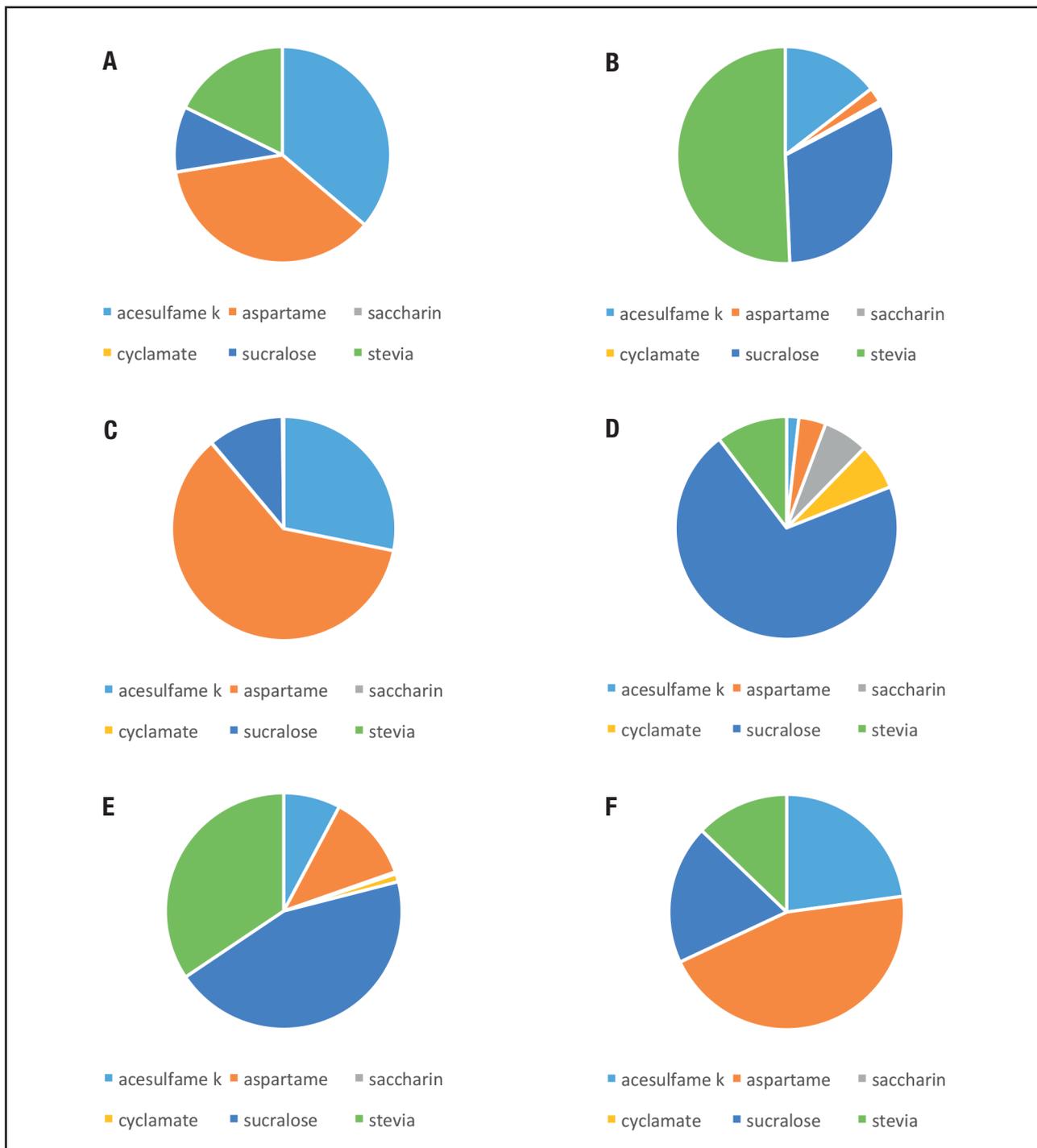


Figure 1. Presence of non-caloric sweeteners in different food groups. A. Breakfast cereal. B. Dairy products. C. Sodas and juices. D. Cookies and ice cream. E. Jams. F. Table sweetener.

sumption (19,20), however, a relatively low consumption of those NCS was observed in our study.

Having a wide variety of NCS in the market makes it difficult to exceed the ADI, since its use is diversified. Not all NCS can be used in all products, for example, aspartame degrades at high temperatures (21), which makes its use impossible in cooked foods.

Regarding saccharin, this NCS crosses the human placenta (22). In a study carried out in rhesus monkeys, the elimination of saccharin from the fetus was much slower than on the mother's side, suggesting that repeated maternal ingestion of saccharin could lead to saccharin accumulation in the mother and fetus (23). Data from animals reporting exposure at doses of 100 to

400 times the human ADI do not suggest a risk of malformations (24). A case-control study reports no increased risk of spontaneous abortion in women who consumed saccharin (25).

Participants consumed the lowest amounts of saccharin and cyclamate. Less than 15% of pregnant women indicated eating foods containing these NCS, probably because the foods that contain them (e.g., jams and preserved fruits) are less massively consumed. In relation to cyclamate, this NCS also crosses the placental barrier, approaching the amniotic fluid in a proportion of one quarter of the concentration in maternal blood, and thus reaches fetal tissues (26). Currently, cyclamate is approved by *Codex Alimentarius* and EFSA, but not by the FDA.

Like saccharin and cyclamate, acesulfame k crosses the placental barrier (26). Acesulfame k is absorbed in the small intestine and is excreted by the kidney in less than 24 hours without being metabolized, so it does not produce oxidative energy (27).

Sucralose, the NCS with the highest prevalence of consumption in the sample, cannot be easily absorbed by the digestive tract. Approximately 85% is eliminated in feces and the remaining 15% is passively absorbed and cannot be metabolized for energy purposes (28).

A study conducted in humans found that aspartame degradation products cross the placenta (30). However, a dose of 200 mg/kg of aspartame (four to five times the ADI) did not lead to toxicity, such as methanol poisoning or increase of phenylalanine in fetal blood to levels associated with mental retardation in the offspring (29). Based on available data, the consumption of aspartame during pregnancy is not expected to be a concern while consumption does not exceed recommended levels (30).

The NCSs most consumed by pregnant women according to the results of this study were sucralose and stevia, present mainly in beverages, juices, and dairy and table sweeteners.

It is interesting to note that NCS consumption did not present differences by trimester of pregnancy, nor by socioeconomic level, which contrasts with findings from the National Food Survey, where consumption and education are positively related (31).

Stevia glycosides (stevioside, rebaudioside A, rebaudioside D, rebaudioside M, steviol glycosides) are considered as "generally recognized as safe" by the FDA. However, the FDA has not allowed the use of stevia leaf or the raw leaf extract.

We observed that the consumption closest to the ADI was for stevia (82.5%), followed by acesulfame k (44%). Average values, however, were under 5% of the ADI, except for stevia, which reached 12%.

A recent study shows that the consumption of NCS during pregnancy may increase the risk of overweight in children (32).

Research on NCS has focused mainly on artificially sweetened beverages for several reasons: their consumption has increased over the past 30 years and they are the largest contributor to total NCS intake. A study that evaluated maternal consumption of beverages with NCS and infant weight gain suggests that when oral or intestinal receptors are exposed to artificial sweeteners, hormonal signals between the intestine and the brain can stimulate appetite and lead to weight gain (33).

In a Canadian cohort study, 3,033 pregnant women were followed until their child turned one year old. The study concluded

that more than a quarter of women (29.5%) consumed beverages with NCS during pregnancy, including 5.1% who reported daily consumption. In comparison with no consumption, the daily consumption of beverages with NCS is associated with an increase of 0.20 units in BMIz for infants (adjusted 95% CI, 0.02-0.38) and two times higher risk of overweight at one year of age (adjusted OR: 2.19, 95% CI, 1.23-3.88). These effects were not explained by maternal BMI, diet quality, total energy intake or other obesity risk factors (34).

A study that included 59,334 Danish pregnant women evaluated the association between the consumption of drinks sweetened with sugar or NCS and preterm birth. The study found a positive association between consuming beverages with NCS and prematurity; the adjusted OR for those who drank > 1 serving/day was 1.11 (95% CI = 1.00-1.24) (15).

Another prospective longitudinal study in Danish pregnant women, which included 60,466 women, evaluated the association between beverages with NCS, childhood asthma and allergic rhinitis. Mothers who consumed beverages with NCS were more likely (OR = 1.23, 95% CI = 1.13-1.33) to report a diagnosis of asthma in their children, compared to women who drank beverages sweetened with sugar. Similarly, mothers who consumed beverages with NCS were more likely to have a child diagnosed with asthma at seven years (OR = 1.30, 95% CI = 1.01-1.66) (16). Although the association was stronger for drinks sweetened with sugar, the authors concluded that they could not determine whether this risk is due to the effect of these beverages or other associated dietary or socioeconomic factors.

A study conducted on 20 breastfeeding mothers determined the presence of NCS in human milk and found saccharin, sucralose and acesulfame k (35). The finding of sucralose is controversial since the absorption is very low < 15%, and it is mostly eliminated in feces (36).

However, a recent systematic review and meta-analysis concludes that there is limited and inconsistent evidence of the long-term effects of metabolic exposure of NCS during pregnancy, lactation and childhood. Further research is needed to support recommendations for the use of NCS in this sensitive population (37).

On the other hand, the highest quality evidence, systematic reviews and meta-analysis, show that NCS consumption is a safe and effective option that can help reduce the number of calories we eat and drink (38,39), and can be a tool to limit excessive weight gain during pregnancy.

The food and additive safety, including NCS safety, is based on animal studies as required by the FDA approval process. The appropriate use of animal models is consistent with the International Conference on harmonization of protocols, which allows testing with large amounts of food additives that would not be allowed in human subjects (5). On the basis of the available data, it is not possible to identify any benefit or draw conclusions regarding the risks related to the consumption of intense sweeteners during pregnancy, in terms of maternal health, obstetric parameters or the health of the newborn.

Among the strengths of the study, it must be noted the use of a validated and adapted survey to quantify the consumption of

sweeteners in this group and not of nutrients. In addition, pregnant women of different socioeconomic levels were considered. Only Chile and Mexico require the type and quantity of NCS be reported on food labels, which makes our data more reliable. Among the weaknesses, the cross-sectional nature of our study and that results depend on the reliability of the nutritional labels should be considered.

CONCLUSIONS

As far as we have found in research, this is the first study evaluating NCS intake in pregnant women. A high prevalence of consumption was found; however, despite massive consumption, no NCS exceeded the ADI. More studies of this type are required, especially cohort studies, to evaluate possible health risk of this food additive.

NCS are widely consumed in the population, in replacement of sugar, to reduce the consumption of total calories. However, there are no long-term studies of NCS consumption among pregnant women that guarantee safety.

When reviewing the guidelines from the Ministries of Health from different countries, the recommendations for NCS consumption are scant. In Chile, the Ministry of Health suggests moderate consumption during pregnancy of aspartame, sucralose, acesulfame potassium, and steviol glycosides. Alternatives to saccharin are also suggested, since it is removed more slowly from the fetus.

Further studies involving the use of NCSs in pregnant and nursing mothers are required to understand their effects on energy consumption, appetite, satiety, weight control, biochemical parameters such as insulin, glucose, leptin, cortisol and preference for sweet flavors.

Pregnancy is a time of special attention. Given the current obesity epidemic and the widespread use of NCS, more research is justified to confirm our findings and investigate underlying biological mechanisms. Special populations, such as pregnant women, should limit their consumption of NCS.

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