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Research Article

High Dietary Salt Intake in Pediatric Patients with Type 1 Diabetes Mellitus Not Related to Overweight and Obesity

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ARTICLE INFO

Article history:
Received: 21 April, 2020
Accepted: 4 May, 2020
Published: 29 May, 2020

Keywords:
Salt intake
type 1 diabetes mellitus
obesity
urinary sodium excretion
cardiovascular risk

ABSTRACT

Aim: People around the world are consuming much more sodium than is physiologically necessary. A number of studies suggest that dietary sodium intake is related to weight gain. The aim of our study was to evaluate in a population of children and adolescents with type 1 diabetes mellitus, possible correlations between the urinary sodium excretion (UNa24h), indirect marker of sodium intake, and both duration of diabetes and BMI z-score. Moreover, we also evaluated the correlation between UNa24h and duration of diabetes according with the presence/absence of overweight/obesity.

Research Design and Methods: Children and adolescents aged between 4 and 18 years with type 1 diabetes were consecutively enrolled from Regional Center for Pediatric Diabetes in Naples. Urinary sodium concentrations were tested in three 24 h urine samples of 68 individuals (204 tests).

Results: Mean UNa24h was 141.3±68.2 mmol/24h corresponding to 8.1±3.9 gr of NaCl intake. Seventy-five percent of subjects aged between 4 and 6 years, 95% of subjects aged between 7 and 10 years and 79.5% of subjects aged between 11 and 18 years consume more salt of the LARN's advice.

Urinary sodium excretion increased in relation to the increase of duration, in years, of diabetes (p=0.0027). No statistically significant relationship is between UNa24h (mmol/24h) and zBMI (p=0.705).

Conclusions: This study shows that young patients with type 1 diabetes have high levels of UNa24h. Given the close correlation between the UNa24h and salt intake we can conclude that they take more salt with their diet. High salt intake is not related to overweight but to diabetes duration.

Introduction

Type 1 Diabetes Mellitus increases the risk of cardiovascular diseases that are the main cause of morbidity and mortality in patients with diabetes [1, 2]. Also elevated sodium intake has been associated with hypertension, cardiovascular diseases and stroke, and decreasing sodium intake may reduce blood pressure and the risk of cardiovascular diseases (CVDs), leading cause of death in the world [3-5]. Recent data on sodium intake show that populations around the world are consuming much more sodium than is physiologically necessary [6]. Therefore, the World Health Organization (WHO) Member States have agreed on a voluntary global noncommunicable diseases (NCD) target for a 30% relative reduction in mean population intake of salt, with the aim of achieving a target of less than 5 g per day (approximately 2 g sodium) by 2025. The recommendations for children are adjusted for their energy requirements and age [7].

Recently, a number of studies have emerged which suggest that dietary sodium intake may be implicated in weight gain. Studies in children have reported positive associations between sodium intake and adiposity [8-10]. Several studies have analyzed association between salt intake and (early) microvascular complications in individuals with type 1 diabetes, with a higher prevalence of microalbuminuria, an association that was more pronounced in overweight individuals and with vascular

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http://dx.doi.org/10.31487/j.JICOA.2020.02.12

dysfunction (Glyceryl trinitrate mediated dilatation (GTN) related to sodium intake) [11-13]. At present, no studies analyzed the association between salt intake and duration of diabetes or BMI z-score in type 1 diabetes patients.

The aim of our study was to evaluate in a population of children and adolescents with type 1 diabetes mellitus, possible correlations between the urinary sodium excretion (UNa24h), indirect marker of sodium intake, and both duration of diabetes and BMI z-score. Moreover, we also evaluated the correlation between UNa24h and duration of diabetes according with the presence/absence of overweight/obesity.

Materials and Methods

The study was approved by the Ethics Committee of the University of the Study of Campania (Naples, Italy), and was conducted according to the Declaration of Helsinki.

I Participants

A total of seventy-one children and adolescents aged between 4 and 18 years with type 1 diabetes, consecutively attending Regional Center for Pediatric Diabetes (University of the Study of Campania, Naples) between 2 May 2018 and 2 May 2019, was informed about this study. Sixty-eight of them were enrolled and included in the analysis. Patients with diabetic nephropathy, other renal disease and in therapy with natriuretic drugs were excluded. Written informed consent was obtained from all participants and their parents or legal guardians prior to enrolment in the study.

II Methods

The years of disease were calculated from the day of the diagnosis of diabetes mellitus. The z score of the BMI (zBMI) was calculated based on WHO charts. Subjects with zBMI values greater than 1.28 were considered overweight [14]. Urinary sodium concentrations (mmol/24h) were tested in three 24 h urine samples of 68 individuals (204 tests). The urinary sodium excretion was measured using an immunochemical methodology (Abbott Architect c4000).

A recent meta-analysis found that approximately 93% of dietary sodium is excreted in urine [15]. Therefore, sodium excreted (gr/day) is equivalent to the sodium ingested, approximately. To estimate the dietary salt intake (in gr/day) we multiplied 24 h urinary sodium excretion (converted in gr/day) by 2.5. In fact, sodium chloride (NaCl) contains, by weight, 40% of sodium. Salt intake in the sample was compared with Recommended Energy and Nutrient Intake Levels of Italian Population (LARN) for age [16] (4-6 years <1.2 gr/day; 7-10 years <1.5 gr/day; 11-18 <2 gr/day).

III Statistical Analysis

A linear regression analysis was performed to assess the relationship between UNa24h (mmol/24h) and years of diabetes, UNa24h (mmol/24h) and BMI z-score and between UNa24h (mmol/24h) and years of diabetes according with presence/absence of overweight/obesity. Statistical analyses were performed using Stat-Graph XVII software for Windows. p values < 0.05 were considered significant.

Results

I Participants

A total of 68 participants (47 boys, 21 girls), with a mean (± SD) age of 11.8± 3.2 years were recruited: their baseline characteristics are summarized in (Table 1).

Table 1: Baseline demographic and clinical characteristics (n=68).

Age (years)	11.8 ± 3.2
Gender (male/female)	47/21
	(69%/ 31%)
Body mass index (BMI: kg/m^2)	20,5 ± 3.4
BMI Z-score	0.76 ±1.08
HbA_{1c}	8.0 ± 1.1 %
	(63.8± 12.2 mmol/mol)
Years after the onset	5.1 ± 3.5

Data presented as mean ± SD, or as n (%).

Table 2: Gender specific 24h Sodium urinary excretion and corresponding salt intake.

	Sodium urinary excretion mmol/24h	**Salt (NaCl) g/dL**
Patients (n=68)	141.3 ± 68.2	8.1 ± 3.9
Male (n=47)	149.2 ± 70.4	8.6 ± 4
Female(n=21)	123.7 ± 60.7	7.1 ± 3.5

Data presented as mean ± SD.

Table 3: Subjects, in the sample, with higher sodium consumption than the LARN recommendations for age.

	Recommended Sodium intake gr/day	**Subjects n (%)**
4-6 years	< 1.2	3/4 (75%)
7-10 years	< 1.5	19/20 (95%)
11-18 years	< 2	35/44 (79.5%)

Data presented as mean ± SD, or as n (%).

II Urinary Sodium Excretion (UNa24h) and Salt Intake (NaCl)

Table 2 shows urinary sodium concentrations (mmol/24h) in the sample, expressed as mean (± SD), and the corresponding average value (± SD) of salt intake (NaCl) in gr/day. Urinary sodium concentrations in the sample is 141.3 ± 68.2 mmol/24h (8.1±3.9 gr of NaCl intake). Urinary sodium concentrations in males is 149.2 ± 70.4 mmol/24h (8.6±4 gr of NaCl intake) and in females is 123.7 ± 60.7 mmol/24h (7.1±3.5 gr of NaCl intake). Table 3 still shows salt intake (gr/24h) in the sample compared with LARN recommendations for age. 75% of subjects, aged between 4 and 6 years, 95% of subjects, aged between 7 and 10 years and 79.5% of subjects aged between 11 and 18 years consume more salt of the LARN's advice.

III Urinary Sodium Excretion (UNa24h) and Years of Disease

There is a statistically significant relationship between UNa24h (mmol/24h) and duration of diabetes (p=0.027). With increasing of duration in years of diabetes, urinary sodium excretion enhances (Figure 1).

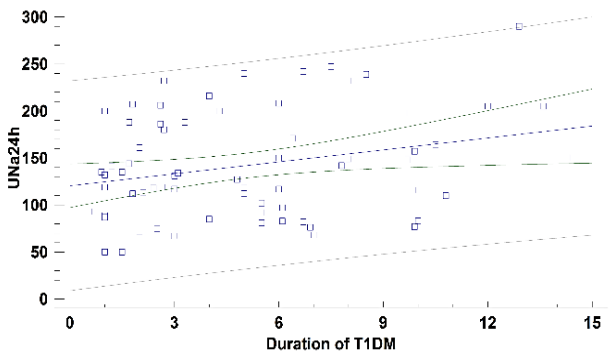

Figure 1: Regression analysis describing the relationship between UNa24h and duration of diabetes (years).
Model r^2=7.18; p=0.027. The regression is described by the equation y= 120,448 + 4,23612 * x. P value for intercepts was <0.001, p value for the slopes was 0.027.

IV Urinary Sodium Excretion (UNa24h) and zscore-BMI

There was no statistically significant relationship between UNa24h (mmol/24h) and zBMI (p=0.705) (Figure 2). The regression analysis describing the relationship between UNa24h (mmol/24h) and duration of diabetes according with presence/absence of overweight/obesity did not show any significant difference (Figure 3).

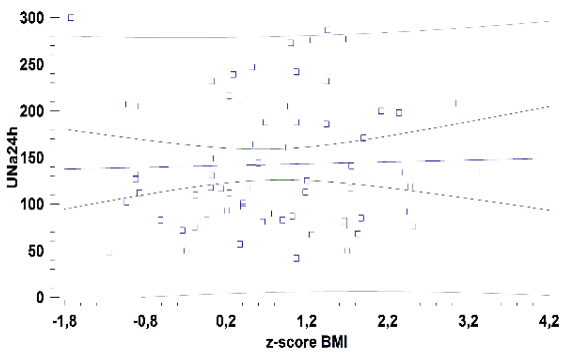

Figure 2: Regression analysis describing the relationship between UNa24h and BMI z-score.
Model r^2=0.217; p=0.705. The regression is described by the equation y = 138,655 + 2,95233*x.
P value for intercepts was <0.001, p value for the slopes was 0.70.

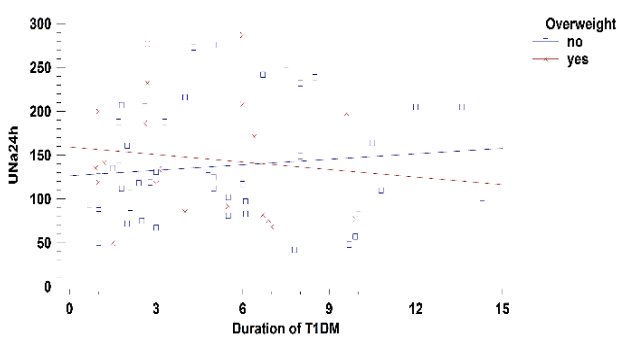

Figure 3: Regression analysis describing the relationship between UNa24h and duration of diabetes(years) according with presence/absence of overweight/obesity.
Model r^2=1.18; p=0.76. Y = 126,515 + 2,08114*x + 32,7982*(presence of overweight) 4,94615*x*(presence of overweight).
P value for intercepts was .0.56, p value for the slopes was 0.41.

Discussion

This study has shown that young patients with type 1 diabetes have high levels of urinary sodium concentrations. Given the close correlation between the urinary sodium concentration and salt intake with the diet, in absence of renal disease or natriuretic drugs therapy, we can conclude that they take more salt with their diet. Urinary sodium concentrations in whole population is 141.3 ± 68.2 mmol/24h (8.1±3.9 gr of NaCl intake). It is clear that the sample consumes more salt than WHO recommendations for adults. Furthermore, if we compare the sodium intake with the LARN recommendations for age, they consume more sodium than the indications. These data are comparable to those of a recent Italian survey [17].

Despite a number of studies suggested that dietary sodium intake may be implicated in weight gain, we have shown no correlation between urinary sodium concentrations and overweight (p= 0.7056). This data shows that the high dietary sodium intake is not related to overeating. We tried to assess whether the high urinary sodium concentrations were related to the duration of diabetes, and we have shown a strong correlation between these two parameters (p=0.0316).

This study has some strengths and limitations. A first strength is the lack of association between high salt consumption and overweight in young people with type 1 diabetes. It is well known that an increasing prevalence of overweight and obesity was reported in youth with type 1 diabetes, likely due to the intensive insulin treatment and/or an unhealthy lifestyle [18-22]. The addition of sodium chloride (salt) increases the palatability of many foods and encourages greater energy intake [23]. Moreover, it has been suggested that salt may act as a vehicle that drives intake of dietary fat. This is supported by reports which show that attraction to salty-and-fatty foods are associated with higher total daily energy intakes in adults, uncontrolled eating and overweight in children [24-27].

A second strength is the association between years of the disease and urinary sodium concentrations. This data may suggest following other factors in the increase of renal sodium excretion different from diabetic nephropathy. High urinary sodium levels could be explained by the increase in dietary intake due to lack of perception of the taste of salty. It is possible that the first manifestation of diabetic neuropathy may be the alteration of the sense of taste [28-30].

Conversely, the absence of a control group limits the possibility for generalizing the findings and may be considered as a limitation of the study. However, the high statistical significance of the results may justify this lack. Another limitation could be the number of patients. However, each patient performed three urine tests (samples collected on three different days) for a total of 204 tests. This increases the sample's significance. Finally, we preferred not to compare the data on renal sodium excretion with patients' HbA1c because glycated hemoglobin was tested only at the time of delivery of urine samples as a single value and does not represent the metabolic control of the patients.

In conclusion, this study demonstrated that young patients with type 1 diabetes have high levels of urinary sodium concentrations and so it means that they take more salt with their diet. Since this high renal sodium excretion is not related to overweight, it is possible to hypothesize other factors in high salt intake in young type 1 patients, like

the lack of sensitivity to the taste of salt as an early sign of diabetic neuropathy. Further studies will be performed to confirm our results.

Acknowledgments

The authors thank all the children who participated in the study, and their parents.

Author Contributions

All authors reviewed and provided feedback on manuscript drafts. In addition, authors had the following responsibilities: A.Z. conceived the study, wrote the manuscript and contributed to the discussion. P.M. and S.C. analyzed data and wrote the manuscript. L.S., A.S.R., V.T., M.G.G., A.P., F.C., St. Cu. and G.O. collected, analyzed data, and contributed to the discussion. E.M.G reviewed the manuscript. D.I. conceived the study, wrote the manuscript, and contributed to the discussion. A.Z. and D.I. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Disclosure

This research did not receive any specific grant from funding agencies in the public, commercial or not-for- profit sectors.

Conflicts of Interest

Dr. Testa reports personal fees from Medtronic, outside the submitted work. All other authors have no financial or other relationships that could lead to a conflict of interest.

Data Share Statement

Data described in the manuscript, code book, and analytic code will be made available upon request pending application and approval.

Clinical Trial Registry Number

NCT04256447

Abbreviations

UNa24h: Urinary sodium excretion by 24 hours
BMI: Body mass index
zBMI: Body mass index z-score
NaCl: Sodium chloride
LARN: Recommended energy and nutrient intake levels for italian population
CVDs: Cardiovascular diseases
WHO: World health organization
NCD: Noncommunicable diseases
GTN: Glyceryl trinitrate mediated dilatation
HbA1c: Glycated hemoglobin

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