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Urinary loss of micronutrients in diabetic patients attending a tertiary hospital service

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Abstract

Background/aims: **micronutrient deficiency may contribute to a poorer control of diabetes. Thus, the objective of the present study was to assess the urinary excretion of micronutrients in patients with type 2 diabetes mellitus.**

Methods: **patients with diabetes and controls were assessed regarding food intake, anthropometry, urinary loss of micronutrients and compared by the nonparametric Mann-Whitney test ($p<0.05$).**

Results: **nine diabetic volunteers (52±14 years, BMI 30±11 kg/m² and abdominal circumference (AC) of 99±25 cm) and 9 control individuals (51±16 years, BMI 26±5 kg/m² and AC of 90±13 cm) were studied. Higher iron excretion was observed in the diabetic group and higher magnesium excretion in the control group.**

Conclusions: **the type 2 diabetic patients here studied did not show increased micronutrient excretion in urine when compared to controls.**

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Key words: *Type II diabetes mellitus*. *Micronutrients*.

PÉRDIDA URINARIA DE MICRONUTRIENTES EN PACIENTES DIABÉTICOS ATENDIDOS EN UN HOSPITAL DE TERCER NIVEL

Resumen

Introducción/objetivos: **la deficiencia de micronutrientes puede contribuir a un menor control de la diabetes. El objetivo de este estudio fue evaluar la excreción urinaria de micronutrientes en pacientes con diabetes mellitus tipo 2.**

Métodos: **los pacientes con diabetes y los controles fueron evaluados por la ingesta de alimentos, la antropometría, la pérdida urinaria de micronutrientes y comparados por Mann Whitney no paramétrico ($p<0,05$).**

Resultados: **fueron evaluados nueve sujetos diabéticos (52±14 años con un IMC de 30±11 kg/m² y la circunferencia de la cintura (CC) de 99±25 cm) y nueve sujetos control (51±16 años, IMC 26±5 kg/m² y CA total de 90±13 cm). La excreción de hierro más alta se observó en el grupo diabético y la mayor excreción de magnesio en el grupo de control.**

Conclusiones: **el tipo 2 de pacientes diabéticos estudiados aquí no mostraron un aumento en la excreción de micronutrientes en la orina en comparación con los controles.**

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Palabras clave: *Diabetes mellitus tipo II*. *Micronutrientes*.

Introduction

The world prevalence of diabetes mellitus (DM) is 171 million people and it is estimated to reach approximately 299 million in 2025 (WHO, 1997; 2000). According to the estimates of the Ministry of Health, about 11 million people with diabetes live in Brazil[1,2]. The Brazilian Multicenter Study[3] has reported that the prevalence of type 2 diabetes mellitus (DM2) and of glucose intolerance among the adult Brazilian population is 7.6% and 7.8%, respectively. The annual cost for the treatment of these patients has been estimated at R$ 3963/patient[4].

Diabetic patients are more predisposed to the development of atherosclerotic diseases, dyslipidemia,

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hypertension, hyperuricemia, renal failure, retinopathy and neuropathy compared to the geneal population[5]. In addition, these patients may show urinary loss of nutrients such as iron, copper, selenium, chromium and zinc and some authors have suggested that this change in micronutrient levels may contribute to the worsening of glucose homeostasis[6,7,8]. Other studies have suggested that increased excretion of some nutrients such as zinc, calcium and protein may be associated with changes in renal function in these patients[10,11,12]. These losses are believed to possibly lead to the development of complications such as atherosclerotic disease, dyslipidemia and osteoporosis, among others.

Thus, the objective of the present study was to investigate whether type 2 diabetic patients excrete higher amounts of micronutrients in urine when compared to controls.

Methods

Patients

This was a cross-sectional study conducted in the Diabetes Mellitus Outpatient Clinic of the University Hospital, Faculty of Medicine of Ribeirão Preto (HCFMRP/USP). The study was approved by the Research Ethics Committee of HCMRP/USP (Protocol nº6228/2009) and did not interfere at any time with the clinical course of the patients or with the ambulatory routine.

Patient sampling was non-probabilistic, by convenience and on a voluntary basis[13], with recruitment of patients who were willing to participate in the study and who satisfied the inclusion criteria. In addition to the diabetic patients, healthy individuals on the hospital staff were invited to participate in the study as controls and were also recruited by the same sampling method.

The inclusion criteria for diabetic patients were: 1) to have DM and to be under treatment at the Diabetes Mellitus Outpatient Clinic of HCMRP/USP, and 2) to be older than 18 years.

Only patients with chronic renal disease were excluded.

The inclusion criteria for control subjects were: 1) to have similar weight and height and to be of similar age as the diabetic patients. To this end, the diabetic patients were first recruited and when their group was complete the controls were recruited for appropriate pairing. 2) To be older than 18 years. Subjects with DM and chronic renal diseases were excluded.

Experimental design

The study was first explained to the possible participants and the patients willing to participate gave written informed consent. Next, four 1-liter demineralized flasks containing 10 ml hydrochloric acid were delivered to each participant for collection of 24 hour urine. Also at this first meeting, the food record was delivered and explained to the subjects, who were instructed to fill it out on the day of urine collection, and who also received instructions for urine collection. The food record consisted of the foods, preparations and quantities ingested and the times of ingestion. On the day scheduled for return, the patients delivered the flasks and the food record and were submitted to anthropometric measurements of weight, height and abdominal circumference (AC).

The control subjects were submitted to the same evaluation as the diabetic group. They received four flasks for 24-hour urine collection, recorded the food ingested on the day of urine collection and signed the term of consent. They were also submitted to the anthropometric measurements of weight, height and AC.

The patients' medical records were also reviewed for information about age (years), time of evolution of DM (years), type of treatment (insulin, hypoglycemic drugs and diet), presence of micro- and macrovascular complications related to DM, and the presence of associated comorbidities.

Anthropometry

Weight, height, body mass index (BMI) and AC were determined as described by Lohman et al.[14] and were compared to the values recommended by the World Health Organization (WHO)[15]. AC was measured around the midpoint between the costal margin and the iliac crest during expiration.

Evaluation of food intake

Food intake on the day of urine collection was evaluated by means of the food record and calculated using the *Nutwin®* software, which provided the nutritional composition of the various foods.

The recommended percentage of macronutrientes in relation to the total calorie value was calculated with respect to the baseline energy expenditure obtained by the Harris & Benedict formula (1919)[16], being 15%, 25% and 60% of the basal energy value, respectively. The value, in grams, of these nutrients was obtained by dividing the calculated amount by 4l, 9 and 4 kcal, respectively.

The intake of the remaining nutrients was compared to the dietary recommendations of the Dietary Reference Intakes (DRIs)[17,18,19] according to patient age.

Preparation of the flasks for urine collection

The flasks and their lids were immersed in nitric acid for 24 hours. The acid was then removed by

simple washing with Milli-q water, with the process being repeated at lest ten times. Next, the flasks and lids were removed from the acid solution and completely dried in an oven. Finally, the duly demineralized and labeled flasks containing 10 ml 50% hydrochloric acid were delivered to the volunteers.

Micronutrient determination

Urinary strontium, calcium and zinc concentrations were determined with a Shimadzu AA-6200 atomic absorption spectrophotomer. Nitrogen was determined by pyrochemiluminescence using an Antek – 720 instrument.

Statistical analysis

Data were treated with descriptive statistics and are reported as frequency, mean and standard deviation. The nonparametric Mann-Whitney test was used to compare the diabetic and control groups. The Pearson correlation coefficients were calculated in order to determine the association beween the urinary and dietary values of the minerals analyzed. The Statistica® software version 8.0 was used for all analyses.

Results

Eighteen volunteers, 12 women (66%) and 6 men (33%), participated in the study. The DM group consisted of 9 volunteers; the mean (±SD) age of this group was 52±14 years, BMI was 30±11 kg/m², AC 99±25 cm, and mean time of disease evolution was 11.3±7 years. Regarding complications, arterial hypertension was observed in 5 patients (28%) and dyslipidemia and obesity in 4 (22%).

The control group also consisted of 9 subjects, 3 males (33%) and 6 females (66%). Mean age was 51±16 years, mean BMI was 26±5 kg/m² and mean AC 90±13 cm. In this group, the prevalence of arterial hypertension was 33%, the prevalence of obesity 22%, and the prevalence of dyslipidemia 11%. There was no significant difference in age or in the anthropometric variables between groups (Table I).

The food recall was obtained only from 16 of the 18 participants since two patients dd not agree to record these data. The results are shown in Table II.

It can be seen that the diabetic patients showed excessive protein intake and insufficient calcium and magnesium intake. Conversely, they showed greater meal fractionation along the day and greater fiber intake (fruits and vegetables). The energy intake of most patients was below the basal expenditure. Some inadequacies were also observed in the control group,

Table I
Nutritional composition of the food record corrected for 1000 kcal

Nutrients	*Diabetes Group*			*Control Group*			
	Median	*Minimum*	*Maximum*	*Median*	*Minimum*	*Maximum*	*p-value*
Energy (kcal/day)	1206	1015	1651	2407	1061	4380	0.008*
Protein (g/day)	64	42	139	55	26	243	0.354
Lipid (g/day)	33	23	44	40	25	111	0.004*
Carbohydrate(g/day)	141	97	223	159	105	602	0.015
Calcium (mg/day)	515	90	913	548	381	1920	0.037*
Phosphorus (mg/day)	822	563	1551	785	496	2989	0.105
Iron (mg/day)	8	6	12	7	4.17	30	0.298
Sodium (mg/day)	570	131	1035	1062	441	8232	0.011*
Potassium (mg/day)	2505	1087	3920	1429	642	4355	0.820
Riboflavin (mg/day)	1.03	0.61	1.65	0.90	0.52	3.73	0.018*
Saturated fat (g/day)	7	0.77	14	13	5.75	46	0.002*
Cholesterol (mg/day)	130	45	357	119	16	534	0.728
Folate (mcg/day)	222	109	412	172	57	555	0.355
Zinc (mg/day)	6	2.70	10	6	2.59	27	0.083
Strontium (mg/d)[a]	-[a]	-[a]	-[a]	-[a]	-[a]	-[a]	-
Magnesium (mg/day)	217	130	301	213	102	772	0.083

[a]Not available in nutritional composition tables; *Statistically significant difference between groups.

Table II
Urinary loss of micronutrients

Nutrients	*Diabetes Group*	*Control Group*	*p-value*
Strontium (μg/total volume)	425 ± 216	485 ± 192	>0.05
Iron (μg/total volume)	790 ± 233	545 ± 382	0.012[a]
Magnesium (mg/total volume)	103 ± 93	242 ± 204	0.038[a]
Zinc (μg/total volume)	575 ± 195	489 ± 245	>0.05
Calcium (mg/total volume)	18 ± 9	10 ± 5	>0.05
Nitrogen (g/total volume)	12 ± 6	17 ± 12	>0.05

[a] Statistically significant difference between groups; [b] Not determined.

such as insufficient calcium and magnesium intake and increased lipid, carbohydrate and protein intake. In contrast to the diabetic group, most of the control subjects showed energy intake above the basal expenditure.

The groups differed significantly in terms of the intake of energy (p = 0.008), lipids (p = 0.004), calcium (p = 0.037), sodium (p = 0.011), riboflavin (p = 0.018) and saturated fat (p = 0.02), which was higher in the control group.

Table II presents the results or urinary nutrient loss. The diabetic group showed a significantly higher iron loss compared to control, whereas the control group excreted more magnesium. When the intake of these nutrients was correlated with their excretion, no correspondence was detected between them.

Discussion

The objective of the present study was to determine the urinary excretion of micronutrients in diabetic patients followed up at a university hospital.

The excess weight of the diabetic group agreed with the data reported by Blackburn in 2002[20], showing a high prevalence of obesity in patients with DM2. The high AC value detected in the diabetic group is representative of the accumulation of fat in this region, which is intimately related to insulin resistance[21,22].

The food intake of the diabetic group showed various inadequacies such as excessive protein consumption and insufficient calcium and magnesium intake, although these patients showed greater fractionation of the meals and greater consumption of fruits and vegetable which, however, was still below recommended levels[23]. These results agree with data reported by Mayer-Davis et al[24] and Overby et al[25]. Other diabetic populations have shown inappropriate food consumption, such as mean protein intake above recommended values and percent carbohydrate contribution to the caloric value of the diet below ADA recommendations[23] in both Brazilian and international studies[26,27,28,29].

Regarding the urinary excretion of micronutrients, the only nutrient excreted in larger quantities by the diabetic group was iron. This nutrient is believed to generate oxidative stress, understood as an increase in the steady state concentration of reactive oxygen and nitrogen species[30,31].

These species cause several types of cell damage including impairment of proteins that regulate and/or limit extracellular iron uptake. As a consequence of oxidative stress, cell injury occurs (lipid peroxidation) with possible destruction of the membrane and cell death, in parallel to an increased risk to develop DM2[32,33]. Besides, oxidative stress has also been shown to contribute to poor glycemic control and to the macro and microvascular complications of diabetes[34]. We therefore speculate that increased iron urinary excretion could be a defense mechanism against oxidative stress in type 2 diabetes mellitus.

As is the case for most clinical investigations, the present study had some methodological limitations such as a small sample size. However, to the best of our knowledge, few studies have investigated the loss of various micronutrients in urine by diabetic patients.

Conclusion

We concluded that diabetic patients excrete more iron in urine when compared to non-diabetic subjects.

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Disclosure

The authors have no potential conflicts of interest relevant to this article.

Author´s contributions

Andressa Feijó da Silva Santos: research project writing, recruitment of the volunteers, data collection and analysis, manuscript writing.

Roberta Deh Souza Santos: recruitment of the volunteers, data collection and analysis, manuscript writing.

Maria Cristina Foss-Freitas: research project writing, recruitment of the volunteers, data collection and analysis, manuscript writing.

Júlio Sérgio Marchini: data analysis, manuscript writing.

Vivian Marques Miguel Suen: research project writing, data analysis, manuscript writing.

References

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995- 2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998;21:1414-31.
2. Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Diabetes Mellitus/Ministério da Saúde, Secretaria de Atenção à Saúde, Departamento de Atenção Básica. Brasília: Ministério da Saúde 2006. 64p. il. (Cadernos de Atenção Básica, n. 16) (Série A Normas e Manuais Técnicos).
3. Malerbi DA, Franco LJ. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in urban Brazilian population aged 30-69 years. *Diabetes Care* 1992; 15:1509-16.
4. Bahia LR, Araujo DV, Schaan BD et al. The costs of type 2 diabetes mellitus outpatient care in the Brazilian public health system *Value Health* 2011;14(5 Suppl 1):S137-40.
5. Beletate VE Dib R, Atallah AN. Zinc supplementation for the prevention of type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2007; 24(1): CD005525.
6. Uusitupa MI, Mykkanen L, Siitonen O et al. Chromium supplementation in impaired glucose tolerance of elderly: effects on blood glucose, plasma insulin, C-peptide and lipid levels. *Br J Nutr* 1992; 68(1): 209-16.
7. Yamada Y, Fushimi H, Inoue T et al. Effect of eicosapentaenoic acid and docosahexaenoic acid on diabetic osteopenia. *Diabetes Res Clin Pract* 1995; 30(1): 37-42.
8. Chausmer, AB. Zinc, insulin and diabetes. *J Am Coll Nutr* 1998; 17(2): 109-15.
9. Danascu LG, Levy S, Levy J. Vitamin D and diabetes mellitus. *Endocrine* 2009; 35(1): 11-7.
10. Gebre-Medhin M, Kylberg E, Ewald U et al. Dietary intake, trace elements and serum protein status in young diabetics. *Acta Paediatr Scand Suppl* 1985; 320: 38-43.
11. Heisse CC, King JC, Costa FM et al. Hyperzincuria in IDDM women: relationship to measures of glycemic control, renal function, and tissue catabolism. *Diabetes Care* 1988; 11(10): 780-6.
12. Melichar B, Malír F, Tichý M. Urinary zinc excretion in patients with different disorders: the acute phase response in the kidney. Sb Ved Lek Fak Karlovt Univerzity Hradci Kralove 1993; 36(4-5): 325-35.
13. Silva EP. Plano de amostragem utilizado no estudo de reprodução humana no distrito de São Paulo. *Rev Saude Publica* 1968; 2(1): 10-22.
14. Lohaman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. *Abridged* 1991.
15. Organização Mundial de Saúde (OMS). Physical status: The use and interpretation of anthropometry technical report series. *Genebra: OMS* 1995. p. 854.
16. Harris JA, Bnedict FG. A biometric study of basal metabolism in man. Pub nº279, Washington, DC, Carnegie Institute of Washington.
17. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: for energy, carbohydrate, fiber, fatty acids, cholesterol, protein, and amonoacids. Washingtn, DC, 2002, The National Academies Press.
18. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: for calcium, phosphorous, magnesium, vitamin D, and fluoride. Washingtn, DC, 1997, The National Academies Press.
19. Institute of Medicine, Food and Nutrition Board: Dietary reference intakes: for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washingtn, DC, 2001, The National Academies Press.
20. Blackburn GL. The obesity epidemic: prevention e treatment of the metabolic syndrome. Págs 1-4. Available at:<http://www.medscape.com>. Accessed September/2011.
21. Grecco AV, Mingrone G, Giancaterini A. . Insulin resistance in morbid obesity: reversal with intramyocellular fat depletion. Available at:<http://www.medscape.com>. Accessed September/2011.
22. Cnop M, Landchild MJ, Vidal J et al. The concurrent accumulation of intra- abdominal and subcutaneous fat explains the association between insulin resistance and plasma leptin concentrations distinct metabolic effects of two fat compartments. *Diabetes* 2002; 51(4):1005-15.
23. American Diabetes Association (ADA). Nutrition recommendations and principles for people with diabetes mellitus (position statement). *Diabetes Care* 1997; 20 (17).
24. Batista MCR, Priore SE, Rosado, LEFPL et al. Avaliação dietética dos pacientes detectados com hiperglicemia na "Campanha de Detecção de Casos Suspeitos de Diabetes" no município de Viçosa, MG. *Arq Bras Endocrinol Metabol* 2006. 50(6): 1041-6.
25. Lodefalk M, Aman J. Food habits, energy and nutrient intake in adolescents with Type 1 diabetes mellitus. *Diabet Med* 2006; 23(11): 1225-32.
26. Mayer-Davis EJ, Nichols M, Liese AD et al. Dietary intake among youth with diabetes: the SEARCH for Diabetes in Youth Study. *J Am Diet Assoc* 2006; 106(5): 689-97.
27. Overby NC, Margeirsdottir HD, Brunborg C et al. The influence of dietary intake and meal pattern on blood glucose control in children and adolescents using intensive insulin treatment. *Diabetologia* 2007; 50(10): 2044-51.
28. Philippi ST, Latterza AR, Cruz ATR et al. Pirâmide alimentar adaptada: guia para escolha dos alimentos. *Rev Nutr* 1999; 12(1): 65-80.
29. Robertson RP. Oxidative stress and impaired insulin secretion in type 2 diabetes. *Curr Opin Pharmacol* 2006; 6(6): 615–9.
30. Simmons RA. Developmental origins of diabetes: the role of oxidative stress. *Free Radic Biol Med* 2006; 40(6):917–22.
31. Puntarulo S. Iron, oxidative stress and human health. *Mol Aspects of Med* 2005; 26: 299-312.
32. Choi SW, Benzie IF, Ma SW et al. Acute hyperglycemia and oxidative stress: direct cause and effect? *Free Radic Biol Med* 2008; 44(7):1217–31.
33. Robertson RP. Oxidative stress and impaired insulin secretion in type 2 diabetes. *Curr Opin Pharmacol* 2006; 6(6): 615–9.
34. Goyal R, Singhai M, Faizy AF. Glutathione peroxidase activity in obese and nonobese diabetic patients and role of hyperglycemia in oxidative stress. *J Midlife Health* 2011; 2(2):72-76.