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EFFECT OF MAGNESIUM ADMINISTRATION ON URINARY ION EXCRETION IN HEALTHY SUBJECTS AND CANCER PATIENTS

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A b s t r a c t

Ion deficiency is a risk factor for any cancer patient. Magnesium is an intracellular ion that plays a key role in the intermediary metabolism. In this study we investigated whether an oral magnesium loading test had any effect on the concentration of ions in serum and their excretion by urine. The test included the administration of a total dose of 45 mmol magnesium, together with 5.4 mmol potassium, to a group of 17 women with ovarian cancer and to eight healthy women during a period of 12 h. In the control group, the loading test resulted in an increase in urinary magnesium excretion by 32 %, a decrease in sodium excretion by 17 % and a decrease in creatinine excretion by 16 % ($P < 0.05$). In cancer patients, there was no increase in urinary magnesium excretion after the test but sodium ion excretion decreased by 37 % , chlorine by 48 % and calcium by 29 % ($P < 0.05$). The results indicate that cancer patients have a deficit in magnesium and that its administration leads to a better saturation of tissues with Na^+, Ca^{2+} and Cl^- ions.

K e y w o r d s

Magnesium, Deficiency, Loading test, Cancer patient, Urine, Serum

INTRODUCTION

The cancer patient is at a higher risk of ion deficit that healthy persons. This is due to a reduced food intake, ions included, a decrease in intestinal resorption, an increased loss of ions, the effect of anti-cancer treatment, such as surgery, radiotherapy or chemotherapy, as well as due to accompanying factors of disease and treatment, such as anorexia, nausea or mucositis. In some patients several causes may be combined.

Magnesium is one of the intracellular ions and has a key role in the intermediary metabolism. It is involved in a number of enzymes and is also a component of the high-energy ATP-Mg^{2+} complex (*1*) that provides a universal form of energy for the organism. The presence of this complex is essential for kidney functioning. The kidneys maintain ion homeostasis in the organism by either an active or a passive resorption of ions by kidney tubules. Since the active transport depends on the ATP-Mg^{2+} complex, it is obvious that the presence of Mg^{2+} ions is of utmost importance for these processes.

The Czech population has been reported to receive less that the recommended daily allowances of magnesium. The aim of this study was to find out to what extent the daily magnesium intake was related to urinary ion excretion in both healthy subjects and cancer patients. The effect of an increased daily dose of magnesium in an oral loading test on both the serum and urinary levels of several ions was studied.

MATERIALS AND METHODS

The patient group consisted of 17 women (mean age ± SD, 53 ± 16 years) diagnosed with stage II or stage III ovarian cancer. The control group included eight healthy women aged 40 ± 12 years. Both groups received magnesium in the Magnosolv®-Granulat (ASTA Medica, Vienna, Austria) that contained 670 mg magnesium subcarbonate, 342 mg magnesium oxide and 500 mg potassium hydrogencarbonate in one dose. The net contents of magnesium and potassium in every dose were 365 mg (15 mmol) and 210 mg (5.4 mmol), respectively. Three doses of Magnosolv®-Granulat were administered during a 12-hour period to both the patient and the control group.

Serum levels of ions were determined in blood collected immediately before the test and then next morning. Urine samples were collected 24 h before the test and, from the beginning of the test, for 24 h.

The results were statistically evaluated by the Wilcoxon ranks test.

The study was approved of by the Ethic Committee of the Faculty of Medicine, Masaryk University, and informed consent was obtained from each participant.

RESULTS

The serum levels of ions in healthy women were within the physiological range and there were no significant differences in the ion levels before and after the test. The differences in Cl^- and Ca^{2+} concentrations, although evaluated as significant at the 5 % level, were only 3 % and 6 %, respectively (*Table 1*).

The patient group also had ion serum levels within the range of physiological values both before and after the loading test. The increase in chlorine concentration after the test, shown as significant, was only by 1 % (*Table 2*).

The urinary excretion of ions was markedly different from that before the test in the healthy women. Sodium excretion decreased by 17 %, magnesium excretion increased by 32 % and creatinine levels decreased by 16 % (*Table 3*). In the patient group, the levels of several ions excreted by urine were also significantly reduced, namely, sodium by 37 %, chlorine by 48 % and calcium by 29 % (*Table 4*).

DISCUSSION

The daily allowance of magnesium for an adult person is recommended to be, in relation to age, gender and physical activity, between 300 and 400 mg/day (*2, 3, 4, 5*). However, several observations have indicated that the proportion of the general population still taking this daily amount is progressively growing smaller (*6*). There are several reasons for this. In industrialised countries, drinking water, the major source of all ions, is treated and technologically processed with the

Table 1

Serum levels of ions, glucose, urea and creatinine in the healthy subjects (n = 8)

Ions	Before loading test (mmol/l)	After loading test (mmol/l)	*P*
Na^+	144.5 ± 2.07	145 ± 2.93	ns
K^+	4.83 ± 0.51	4.55 ± 0.26	<0.05
Cl^-	109.17 ± 4.11	109.83 ± 4.91	ns
Ca^{2+}	2.31 ± 0.06	2.24 ± 0.10	<0.05
Phosphates	0.97 ± 0.14	0.95 ± 0.16	ns
Mg^{2+}	0.96 ± 0.03	0.95 ± 0.04	ns
Glucose	5.20 ± 0.46	5.40 ± 0.48	ns
Urea	4.03 ± 1.10	4.18 ± 2.07	ns
Creatinine	93.50 ± 17.14	89.83 ± 14.13	ns

Values are expressed as mean ± SD; *P* level of significance; ns, non-significant.

Table 2

Serum levels of ions, glucose, urea and creatinine in the cancer patients (n = 17)

Ions	Before loading test (mmol/l)	After loading test (mmol/l)	*P*
Na^+	141.90 ± 4.40	143.00 ± 2.70	ns
K^+	4.20 ± 0.50	4.50 ± 0.30	ns
Cl^-	108.60 ± 5.30	109.50 ± 4.70	<0.04
Ca^{2+}	2.28 ± 0.21	2.34 ± 0.27	ns
Phosphates	1.10 ± 0.27	1.10 ± 0.20	ns
Mg^{2+}	0.92 ± 0.10	1.01 ± 0.07	ns
Glucose	5.24 ± 0.73	5.50 ± 0.66	ns
Urea	4.23 ± 2.14	4.23 (1.53	ns
Creatinine	79.90 ± 8.53	79.90 ± 8.52	ns

Values are expressed as mean ± SD; *P,* level of significance; ns, non-significant.

Table 3

Urinary excretion of ions, urea and creatinine in the healthy subjects (n = 8)

Ions	Before loading test (mmol/24 h)	After loading test (mmol/24 h)	*P*
Na^+	227.57 ± 128.85	195.29 ± 84.16	<0.01
K^+	71.89 ± 89.00	59.59 ± 15.05	ns
Cl^-	229.71 ± 96.74	175.43 ± 76.04	ns
Ca^{2+}	3.20 ± 1.49	3.64 ± 1.59	ns
Phosphates	11.32 ± 5.93	8.56 ± 3.81	ns
Mg^{2+}	3.18 ± 1.06	4.21 ± 1.15	<0.02
Urea	312.61 ± 107.32	272.36 ± 97.72	ns
Creatinine	11.50 ± 2.40	9.63 ± 1.80	<0.02

Values are expressed as mean ± SD; *P,* level of significance; ns, non-significant.

Table 4

Urinary excretion of ions, urea and creatinine in the cancer patients (n = 17)

Ions	Before loading test (mmol/24 h)	After loading test (mmol/24 h)	*P*
Na^+	229.30 ± 121.40	142.94 ± 64.27	<0.03
K^+	56.87 ± 36.20	49.36 ± 23.23	ns
Cl^-	238.10 ± 137.70	124.00 ± 55.33	<0.004
Ca^{2+}	5.44 ± 2.91	3.87 ± 2.17	<0.02
Phosphates	18.14 ± 10.54	13.09 ± 4.81	ns
Mg^{2+}	2.59 ± 1.11	3.08 ± 1.82	ns
Urea	248.51 ± 92.90	211.53 ± 83.36	ns
Creatinine	9.50 ± 4.00	8.65 ± 2.83	ns

Values are expressed as mean ± SD; *P,* level of significance*;* ns, non-significant.

results that it is eventually deprived of ions, magnesium including. Intensive farming also leads to a reduction in ion concentration in soil either due to field cultivation methods or a natural loss of ions by washing out without adequate supplementation. The present-day cooking habits, such as frying, roasting or baking, also contribute to diminished amounts of magnesium in our daily meals. In addition, in individuals suffering from various chronic diseases, medication may significantly alter ion balance and increase ion urinary excretion, for instance diuterics in hypertonic subjects or cytostatic drugs in cancer patients (*2, 4, 7*).

Symptoms indicating an insufficient magnesium content in the organism are many but they are not specific (*4, 7*). In many cases, they are missed, underestimated or associated with other clinical entities or diseases. The routine diagnosis of magnesium deficit is reduced to a determination of magnesium levels in serum. However, the finding of a physiological value for serum magnesium levels does not provide evidence of a sufficient magnesium content in tissues because serum contains only less than 1 % of the total amount of magnesium in the organism (*2, 3, 4, 7*). In order to improve this situation, loading tests have been introduced in clinical practice. They determine what proportion of the total amount of the substance administered has been excreted in urine and, therefore, how much has been retained by tissues in the organism. Indirectly, they also allow us to asses what is the degree of the organism's deficit in this substance (*8, 9, 10*).

In the loading test, urinary magnesium ion levels are assessed before and after administration of the known amount of magnesium. The difference between the levels indicates the extent to which the organism is saturated with magnesium ions. If the difference is small or non-existent, it suggests that the organism has used up the magnesium ions in order to compensate for magnesium deficit in tissues.

The most simple form of this test is oral administration of magnesium. If more than 10 % of the magnesium dose administered is retained, it is evident that the organism has a deficit in magnesium (*11*).

In this study, physiological values for serum magnesium levels, which did not differ much before and after the loading test, were found in both the patient and the control group. On the assumption that the dose administered in the loading test was three times that of the daily magnesium allowance, it could be expected that an organism sufficiently saturated with magnesium would remove its excess by urinary excretion (*10, 11, 12, 13*). An increase in urinary magnesium excretion was found only in the healthy subjects at a level much lower than it would have corresponded to the state of magnesium saturation. The fact that a high dose of orally administered magnesium did not result in either increased serum levels of magnesium or its increased urinary secretion can have one explanation only: the magnesium ions have been transported to tissues that suffer from the lack of magnesium.

In the healthy women, the loading test led to a slight decrease in calcium serum levels; this drop was only by 3 % and was not associated with any

significant changes in urinary calcium excretion. In the cancer patients, there were no marked differences in calcium serum levels before and after the test but, at 24 h, there was a significant decrease in calcium urinary excretion. This suggests an increased resorption of calcium by the kidney after the test. The decrease in calcium urinary excretion was accompanied by a decrease in excretion of sodium and chlorine, which indicates an increase in active transport of ions in kidney tubules due to the loading test. This may be explained by the role of these ions in Na/K^+ -ATPase and Ca^{2+} - ATPase- mediated ion resorption in kidney tubules (*14*).

It is obvious that, in cancer patients, magnesium administration is very important (*2,3,15*), even if its physiological levels in serum indicate normomagnesiemia, because an overall deficit of magnesium in tissues cannot be excluded. Magnesium administration results not only in a reduced loss of ions by urinary excretion due to improved resorption of these ions by the kidney, but also in promotion of other metabolic processes that are associated with the Mg^{2+} presence (*1,2,4,5,15*).

Although the effect of a long-term administration of magnesium to cancer patients has not been investigated yet, we suggest, on the basis of our results, that magnesium supplements to the diet of cancer patient are important.

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VLIV PODÁNÍ HOŘČÍKU NA EXKRECI IONTŮ U ZDRAVÝCH JEDINCŮ A U ONKOLOGICKÝCH PACIENTŮ

S o u h r n

Onkologický pacient je zvýšeně ohrožen deficitem iontů. Klíčovým orgánem v regulaci iontové rovnováhy jsou ledviny, kde dochází k jejich zpětné resorpci aktivním i sekundárně aktivním transportem. Tento transport je vázán přímo i nepřímo na complex ATP-Mg^{2+}. Zajímalo nás, zda podání hořčíku v dávce 3 x 15 mmol/12 hodin p.o. může změnit vylučování iontů močí.

Výsledky: podání p.o hořčíků vedlo ke zlepšení zpětné resorpce iontů a jejich nižšího vylučování do moči za 24 hodin u kontrol pouze u Na^{+} 229,71 ± 96,74 vs 195,29 ± 84,16 mmol/24 hod, u onkologicky nemocných pak u Ca^{2+} 238,1 ± 137,7 vs 124 ± 55,33 mmol/24 hod, Na^{2+} 229,3 ± 121,4 vs 142,94 ± 64,27 mmol/24 hod, Cl^{-} 238,10 ± 137,70 mmol/24 hod)

Velmi malé ztráty hořčíku po zátěžovém perorálním testu u kontrol a nesignifikantní ztráty hořčíku u onkologicky nemocných svědčí o tom, že se jak u zdravých tak onkologicky nemocných s nejvyšší pravděpodobností jedná o celkový deficit hořčíku při současné normomagnesemii. Celkový deficit hořčíku v organismu se tak může významně podílet na změněné homeostáze iontů kontrol i onkologicky nemocných.