International Urology and Nephrology 10 (2), pp. 147—152 (1978)

Seasonal Variations in Urinary Excretion of Calcium and Magnesium in Healthy Subjects and Patients with Renal Calculus and Chronic Renal Failure

J. GŁUSZEK, B. RASZEJA-WANIC, S. GRAJEK, Z. KWIAS, T. RATAJCZAK, C. SMARSZ

Department of Internal Diseases, Department of Cardiology and Department of Urology, Medical Academy, Poznan, Poland

(Received March 12, 1977)

Renal excretion of calcium in healthy subjects and in patients with renal stones increases in the summer, as compared to the winter values. In patients with chronic renal failure calciuria shows no seasonal variations. No essential difference in the monthly excretion of magnesium in 24-hour urine has been found between healthy persons and patients with renal stones.

Calciuria in healthy persons depends among others on the age, sex, and calcium, sodium and magnesium intake [3, 4]. Recently, Robertson et al. [13, 14] have stated that 24-hour calciuria tends to be higher in the summer than in the winter (both in healthy subjects and in patients with renal stones). We have evaluated the dependence of calcium ion excretion on the seasons of the year and compared it with the excretion of another bivalent ion, i.e. magnesium.

Material and methods

Twenty-four-hour urinary calcium and magnesium excretion was studied in 323 persons aged 18 to 74 years. Three groups were set up. Group I comprised 119 patients (61 women and 58 men) who had no apparent or demonstrable renal disease, nephrolithiasis, cirrhosis of the liver, neoplasm, or changes in bones and joints. The majority stayed at the Clinic for cardiological reasons, e.g. angina pectoris, or valvular heart disease – except for patients with chronic circulatory failure, and there were also convalescents from pneumonia and patients with neurosis. The precondition of testing any person was that calcium, magnesium and phosphorus in blood, and urinary calcium should not exceed the normal levels, i.e. 250 mg/day for women and 300 mg/day for men. Thus in Group I there was no pathological calcium, phosphorus and magnesium homeostasis. These persons are called conventionally "healthy". In the 2nd and 3rd quarters of the year 62, and in the 1st and 4th, 57 subjects were tested.

Group II consisted of 144 subjects, aged 18 to 72 years, with nephrolithiasis diagnosed on the basis of case history characterized by clinical symptoms, first of all by positive urographic findings. They were otherwise healthy and had no

primary hyperparathyroidism and renal tubular acidosis. In the 2nd and 3rd quarters of the year 97, and in the other two 47 persons were tested.

Finally, Group III was made up of 60 patients (32 men and 28 women) with chronic renal failure. In 27 patients we found chronic glomerulonephritis, in 23 chronic pyelonephritis, and in 10 systemic lupus erythematosus, diabetic glomerulosclerosis, polyarteritis nodosa or renal polycystic degeneration. The values of GFR varied between 2 ml/min and 30 ml/min (mean: 15.1 ml/min). In the 2nd and 3rd quarters 23, and in the 1st and 4th 37 persons were tested.

The above-mentioned tests were carried out in such a way that the age of the patients in both compared halves of the year was similar, and the number of women and men in these two periods should not differ significantly in the χ^2 test. Considering the fact that calciuria is conditioned by the glomerular filtration rate and is reduced in chronic renal failure, patients were selected in such a way that their mean glomerular filtration rate would not show any significant variations during the two halves of the year in the Student test.

All tested subjects were kept on a hospital diet containing 720 mg of calcium, 294 mg of magnesium and 1286 mg of phosphorus in December, and 743 mg calcium, 328 mg magnesium and 1401 mg phosphorus in June. The patients did not get vitamin D_4, calcium and magnesium preparations, or diuretic drugs. In every patient the calcium, magnesium, and phosphate concentration and the fractions in serum and excretion of these electrolytes in 24-hour urine samples were tested. The concentration of calcium was determined by the method of Bett and Fraser [1], and magnesium was checked according to Orange and Rhein [7]. Ultrafiltration without air access made it possible to determine the ultrafiltrable calcium and magnesium [15]. The concentration of creatinine was determined by the Papper method [8]. The mean urinary calcium and magnesium excretions in 24-hour urine samples collected from April to September were compared with those obtained from October to March.

Results

The mean 24-hour calcium and magnesium urinary excretion in each particular month of the year in healthy persons is shown in Fig. 1. Maximum urinary calcium excretion was recorded in July (224.1 mg/day) and the minimum (122.3 mg/day) in December. Comparative tests showed that these values were statistically significantly higher in June ($p < 0.01$), July ($p < 0.01$) and August ($p < 0.02$) than in December. There were significant seasonal variations in the daily excretion of magnesium which tended to increase slightly in the summer, but this was not significant. Table 1 shows a comparison between the 24-hour mean excretion of calcium and magnesium in the 2nd to 3rd, respectively the 1st and 4th quarters of the year. In the first period calcium excretion was higher (184 ± 66.5 mg/day), while in the rest of the year it decreased to 137.7 mg/day. Magnesium excretion in the corresponding periods did not change essentially.

Table 1

Seasonal variations of calcium and magnesium excretion in healthy persons

Excretion (mg/24 h)	Months		Significance
	IV–IX	X–III	
Calcium	185.3	135.6	$p < 0.001$
Magnesium	128.2	122.2	N.S

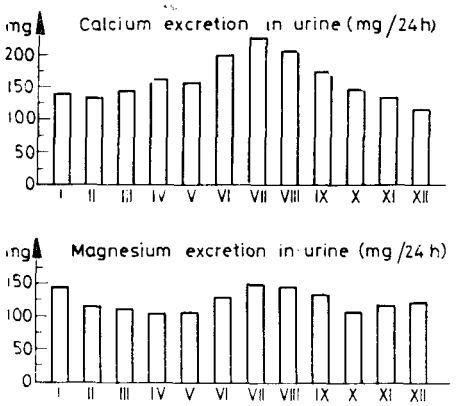

Fig. 1

It was found in patients with kidney stones that the highest 24-hour calcium excretion takes place in summer. Although the standard deviation of the mean of calciuria and magnesiuria in each particular month was much higher than in the controls, we found that the 24-hour urinary calcium excretion in July was 2.3 times higher than in January. In July, 24-hour urinary calcium excretion was 320 mg/day, in January 137 mg/day, as compared to 89.6 mg/day and 81 mg/day of magnesium, respectively.

Table 2

Seasonal variations of calcium and magnesium excretion in patients with renal calculi

Excretion (mg/24 h)	Months		Significance
	IV–IX	X–III	
Calcium	220.5	186.2	$p < 0.01$
Magnesium	86.5	82.0	N.S

Table 2 contains the results of the mean 24-hour urinary calcium and magnesium excretions in patients with renal calculi during the 2nd and 3rd as well as the 1st and 4th quarters. Calcium excretion was higher in the first period while magnesium excretion did not differ significantly in the two periods. In both halves of the year calciuria in patients with kidney stones was higher than in the group of controls.

Table 3

Seasonal variations of calcium and magnesium excretion in patients with chronic renal failure

Excretion (mg 24 h)	Months		Significance
	IV–IX	X–III	
Calcium	125.1	119.8	N.S.
Magnesium	89.6	87.4	N.S.

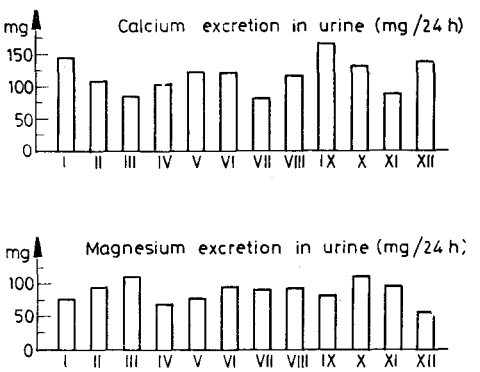

Fig. 2

In patients with chronic renal failure no characteristic seasonal rhythm of calcium in 24-hour urine was found (Fig. 2, Table 3). Calcium and magnesium excretion was lower in the two halves of the year than in the healthy persons.

Discussion

Our results confirm the reports of Robertson et al. [13, 14] on the increase of 24-hour urinary calcium excretion in summer in relation to winter and, moreover, in both healthy persons and patients with kidney stones. While explaining

the phenomenon described above, we must take into consideration first of all the increased dietary calcium and magnesium intake in the summer. Yet, at our clinic, the dietary calcium and magnesium ion intakes were similar in the two halves of the year. According to Peacock et al. [10] only a 3 times higher dietary intake of calcium increases calciuria by 120–150 mg/day.

The increased activity of vitamin D_3 in summer is postulated by many authors who showed that the concentration of the active metabolite of vitamin D_3, i.e. 25-hydroxycholecalciferol, in serum increases in summer [6, 16]. The increase of 25-hydroxycholecalciferol does not correlate with calcium concentration in serum because the level of calcium in serum does not show seasonal variations. The data shown here may suggest that there is a causal relation between the increased calciuria and intensified activity of vitamin D_3. On the basis of present knowledge about the transformation of vitamin D_3 we cannot prove which of its metabolites has an important influence on the changes discussed here. McLaughlin et al. [6] showed that an extreme hydroxycholecalciferol activity in serum is found in September, whereas according to Robertson et al. [13, 14] and our own experience it is the highest in July. Brickman et al. [2] proved that another metabolite of vitamin D_3, i.e. 1,25-dihydroxycholecalciferol, increases calciuria in healthy persons, without changing the serum calcium concentration. Reduced supply of vitamin D_3 in the diet and/or reduced synthesis of its active metabolites might be factors responsible for the absence of seasonal variations in calciuria in chronic renal failure, because these patients rarely stay in the open and insolated places. According to Parry and Lister [9], at least ten days of exposure to insolation are required to cause hypercalciuria in healthy persons.

Kodicek [5] has reported that the biological synthesis of the active metabolite, 1,25-dihydroxycholecalciferol, takes place in the renal cortex. So it seems probable that the lack of seasonal changes in calciuria may be connected first of all with the very reduced synthesis of this metabolite of vitamin D_3. Although the direct estimation of the concentration of 1,25-dihydroxycholecalciferol concentration in each particular season of the year has not been done yet, it can be stated that this substance increases calciuria in healthy subjects. Under the influence of the analogy of this substance 1-alpha-hydroxycholecalciferol excretion of calcium in urine increases in thyreoparathyroidectomized animals [11] and there is also a tendency to hypercalciuria in patients with chronic renal failure [2, 17].

In the light of the data described above it seems possible that in patients with chronic renal failure, as a result of reduced synthesis of 1,25-dihydroxycholecalciferol, there is no increased excretion of calcium with urine in summer. This interpretation suggests at the same time that in healthy persons an increased synthesis of 1,25-dihydroxycholecalciferol in summer may be responsible for the increased calcium excretion. Contrary to the behaviour of calciuria, the urinary excretion of magnesium in each particular month in healthy subjects and in patients with renal stones varies only insignificantly. In the summer, patients with renal stones and healthy subjects show a tendency of increased magnesium

excretion in comparison to winter months, but without significant difference the small variations in magnesiuria suggest that in the kidney this ion exerts probably a lesser influence of metabolites of vitamin D_3 than calcium ions.

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