Brief report

Nutritional aspects in primary hypercalciuria

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Presentation of a clinical case

A 48-year-old businessman presented himself at our Stone Centre 6 years ago, subsequent to a recent recurring episode of right kidney colic followed by the expulsion of a calcium oxalate stone with traces of calcium phosphate.
The medical history of the patient revealed a pneumonia in his youth, cured without repercussions, a duodenal ulcer treated with ranitidine and antacids, and a history of bilateral kidney stones, with at least 5 episodes in 13 years, one of which was treated with ESWL for left ureteral stone. In that occasion a pyelography was performed and was found to be normal except for hydronephrosis due to the stone which was later broken up.
He had not been referred to a specialized Centre for stone disease and the only advice given had been to eliminate milk, yoghurt and cheese from his diet and to drink plenty. The patient had only partially followed these instructions due to problems connected with his intense and stressful lifestyle.
On occasions when his arterial blood pressure had been measured it had, he reported, been "a little" high, but no provisions were then taken.
He had approached our Centre following the advice of one of our patients whom he knew.
The family medical history was negative for kidney stones; the father, who had died as a result of a myocardial heart attack, had hypertension and was diabetic in his later years; the mother was in good health considering her age.
The objective examination did not show any pathology except a high arterial blood pressure (170/110 mmHg) and he was slightly overweight (87 kg) with BMI of 26.8.
The patient was subjected to our screening protocol for the recurring kidney stones which involved: 1) a 3-day dietary diary together with an investigation into the frequency of consumption of food substances over a period of 6 months; 2) renal echography and pyelography (if not already carried out); 3) a blood sample to study the levels of glucose, urea, creatinine, uric acid, sodium, potassium, chloride, bicarbonate, calcium, phosphorus, parathormone, cholesterol, triglycerides; and 4) a collection of the urine over 24 hours in order to determine the urinary stone risk profile on a free diet and with the advice not to change dietary habits or lifestyle.
The investigation of the diet showed a high consumption of meat, dressed-pork products, sugar (in the numerous coffees), a poor intake of fruit and vegetables and a moderate excess of alcohol.
The echography was negative and the blood sample showed high levels of uric acid (7.7 mg/dl), cholesterol (252 mg/dl) and triglycerides (268 mg/dl).
The urinary stone risk profile, which is shown in detail in Table I (not shaded), highlighted, above all, hypercalciuria (520 mg/day) and a high saturation level for calcium oxalate (15.36) and for calcium phosphate (3.40), together with a modest hypocitraturia (340 mg/day), hyperoxaluria (37 mg/day) and hyperuricosuria (720 mg/day).

Table I - Urinary stone risk in the patient on free diet and after a week of "antilithogenic" diet.

	Free diet	"Antilithogenic" diet
Volume, ml/day	1240	2100
Creatinine, mg/day	1914	1820
Sodium, mEq/day	306	34
Potassium, mEq/day	41	62
Chloride, mEq/day	290	32
Calcium, mg/day	520	210
Phosphorus, mg/day	1112	960
Magnesium, mg/day	73	88
Urea, g/day	35	22
Sulphate, mmol/day	28	21
Uric acid, mg/day	720	605
Oxalic acid, mg/day	37	22
Citrate, mg/day	340	480
Cystine, mg/day	60	44
Ammonium, mmol/day	52	38
pH, 24 hours	5.92	6.12
Ca Ox saturation	15.36	4.12
Ca P saturation	3.40	0.96
Uric acid saturation	2.69	0.99
Struvite saturation	0.059	0.037

At the end of the screening, all of the results were shown to the patient and he was given detailed information concerning the meaning of the urinary stone risk profile. He was given an in-depth "lesson" on the importance of diet for the prevention of his kidney stones and more in general for his health, and he was given a written dietary prescription, whose nutritional composition is shown in Table II.
After a week of this diet, the urinary stone risk profile risk was repeated, the results are shown in Table I. Significant changes in the excretion of many substances may be seen, all of which are positive in the "antilithogenic" sense. In particular, there is a normalization of urinary calcium, a reduction in oxalate and uric acid, an increase in citrate and, above all, a net reduction in the saturation levels for calcium oxalate and calcium phosphate.
In terms of nutritional markers, there was a drastic reduction in sodium, chloride, urea and sulphate and an increase in potassium.
The patient was impressed by these changes. Among other things, he refers to the almost "euphoria-inducing" effect of the diet: he had lost 2 kg in weight, his arterial blood pressure was almost in the normal range (145/90 mmHg) and he said that he felt "lighter".
He left the outpatients clinic convinced of what he had been recommended, with the undertaking to continue with the diet and to return every year for the check-up which formed part of our follow-up, and which included the renal echography and the urinary stone risk profile. This he did for the five years that followed.
In the 5 years of follow-up he no longer experienced renal colic, the echography was always negative, the calciuria was always less than 300 mg/day, oscillating between 230 and 270 mg/day, the urinary sodium, urea and sulphate showed values

Table II - Composition of the "antilithogenic" diet prescribed for the patient.

Daily Intake	Value*
Total calories (Kcal)	2500
Total protein (g)	93 (372 Kcal, or approximately 15% of total calories)
From meat or fish	21
From milk and derivatives	31
From bread, pasta and vegetables	41
Lipids (g)	93 (837 Kcal, or approximately 33% of total calories)
Carbohydrates (g)	333 (1332 Kcal, or approximately 52% of total calories)
Fibers (g)	40
Sodium chloride (mEq)	50
Potassium (mEq)	120
Calcium (mg)	1200
Phosphorus (mg)	1512
Magnesium (mg)	348
Oxalate (mg)	Approximately 200
Water in foods (ml)	1550

* The date were obtained from the composition tables issued in 1989 by the Italian National Institute for Nutrition. The values are based on direct chemical analyses of the foods available in Italian markets.

of 100 mEq/day, 25 g/day and 23 mmol/day respectively, thus showing a fair adherence to the diet.
His arterial blood pressure remained stable between the values 140-150/80-90 mmHg and his body weight fell still further to about 80 kg.

Discussion

This man has the typical clinical and laboratory characteristics that are often found in recurrent formers of calcium kidney stones and a significant idiopathic hypercalciuria was particularly evident.
The diet to which he was subjected we define as "antilithogenic" because it takes into consideration all of the nutritional factors which are known to provoke or promote a high calcium excretion level.
Calcium nephrolitiasis is a disease which effects a high percentage of people in industrialized nations and idiopathic hypercalciuria (calcium excretion in excess of 300 mg/day in men and 250 mg/day in women) is the most frequent urinary stone risk factor.
There are various nutritional factors that act together for its genesis and all must be taken into consideration in order to obtain its correction, and to help in the prevention of stone recurrences.
It has been known for some time that there is a positive relationship between body weight and the excretion of calcium, so much so that some authors have proposed that calciuria be expressed in relation to body weight, considering in this case a value of 4 mg/kg for both sexes as the limit used in the definition of hypercalciuria. We too have seen in our patients (data not published) that even a modest increase in body weight is accompanied by a significant increase in calciuria and viceversa. But the proof that excess weight is an independent factor in stone risk was supplied in 1998 by Curhan et al. (1). These Authors subdivided 51,529 men into 5 categories in relation to their body weight and found that the percentage of stone formers increased with the increase in BMI: in particular, with BMI between 21 and 22.9 the percentage of stone formers was 7.1% and with a BMI greater than 32 the figure was 9.8% (a relative risk of 1.38). The same data were investigated in 89,376 women: with BMI of 21-22.9 the percentage of stone formers was 2.5%, with BMI > 32 the percentage of stone formers was 4.4% (a relative risk of 1.76). It is known that being overweight is often accompanied by arterial hypertension, as was the case with our patient, and it is possible that the two elements acting together explain the fact that the hypertensive subjects suffer from kidney stones more often, as first demonstrated by Tibblin in 1967 (2). In keeping with this epidemiological survey, various authors have found that hypertensive subjects have a higher level of calcium excretion, compared to normotensive subjects, and a considerable percentage of them had marked hypercalciuria (3). We too have confirmed this data also demonstrating, in a five-year follow-up, that hypertensive subjects have a much higher risk of stone formation than normotensive ones (4). Therefore, an overweight hypertensive subject has a higher probability of being hypercalciuric and he should reduce his body weight to the normal level and treat any hypertension, if necessary, with anti-hypertension drugs which reduce urinary calcium, such as thiazides or indapamide.
Various Authors have shown that hypercalciuric stone formers have a high intestinal absorption of calcium (5) and this was the basis for the habit of recommending a low-calcium diet (about 400 mg/day) with the removal of milk and its derivatives. However, over the years it has been observed that the low-calcium diet can lead to an increase in urinary oxalate (6) and a negative calcium balance, with the consequent risk of osteo-

porosis (7), and without any clear advantage in terms of calcium oxalate saturation levels. There are no long-term studies that have really shown that the low-calcium diet prevents relapses, but neither have they proved to be of no value. However, we have demonstrated in a randomized prospective 5-year study that the traditional low-calcium diet is less effective in the prevention of relapses in patients with hypercalciuria, in comparison with a normal-calcium, low-sodium, low-protein and high-potassium diet (8). In this study we were able to ascertain that the calciuria is reduced with both of these treatments, but those that follow the low-calcium diet will always have a higher oxaluria than those following the other type of diet. In addition, Curhan et al., in two large epidemiological studies, one on men (9) and the other on women (10) were able to demonstrate that the prevalence of kidney stones is lower in people who consume more than 1 g dietary calcium per day. Therefore, bearing in mind what is currently known, the low-calcium diet should not be considered as the gold standard for the treatment of idiopathic hypercalciuria.

In our diet, protein is the principal source of non-volatile, so-called fixed acids, which are eliminated via the kidneys, through the production of ammonium ions and titratable acidity. Their acidifying effect is linked to the metabolism of sulphate aminoacids (methionine and cysteine) which produce H+ and generate an increase in the renal excretion of calcium through the direct tubular mechanism and, when in excess, via a giving up of bone calcium. This is the metabolic basis that explains the well-documented hypercalciuria when the diet contains an excess of protein, particularly of animal origin (11). On the other hand, it is known that, also in stone formers, the reduction in animal protein is able to significantly reduce the excretion of calcium (12). This knowledge is consistent with the epidemiological data showing that an intake of animal protein in excess of 76 g/day is able to increase by 33% the risk of forming kidney stones (9). The calciuretic effect of proteins is partly reduced by the contemporary administration of alkaline salts such potassium bicarbonate or potassium citrate so in dietary terms, in addition to a reduction in proteins, it could be important to increase the intake of alkaline potassium via an adequate consumption of fruit and vegetables. It is also necessary to consider that the proteins of vegetable origin (soya, chickpeas, French beans, broad beans, peas, lentils) have a lower sulphur aminoacids content and are therefore preferable for hypercalciuric subjects.

As already mentioned, the alkaline potassium found in fruit and vegetables is important for reducing the calciuretic effect of proteins, but not only for this reason. A depletion of potassium in itself is accompanied by an increase in calciuria and, on the other hand, its addition in the form of potassium citrate or potassium bicarbonate can reduce the calciuria significantly (13). The mechanism could be linked to the variations in intracellular pH in the acidic sense when there is potassium depletion, and in the alkaline sense when there is high potassium availability. Also in this case there is strong epidemiological evidence in both men and women a high potassium intake (greater than 103 mEq/day) reduces the risk of stone formation by more than 50% in comparison with a low intake (9,10). Therefore, an important recommendation in idiopathic hypercalciuria is also that of consuming a reasonable quantity of fruit and vegetables on a regular basis, taking care to choose products with a relatively low oxalate content to avoid increases in oxaluria. One cannot ignore the fact that some fruit juices have been shown to significantly increase the urinary citrate, which is a very good inhibitor of calcium oxalate crystallization.

It is not possible to measure with accuracy the salt consumption of a person, but given that dietary sodium chloride is almost completely absorbed in the intestine and eliminated in the urine, its consumption can be easily deduced by measuring its renal excretion. Kleeman et al. were the first to demonstrate that the increase of sodium chloride in the diet of normal subjects provoked an increase in the excretion of calcium (14). Various authors then confirmed the existence of a strict relationship between the intake of sodium chloride and calciuria, in both normal and hypercalciuric subjects, and some experiences have been indicated where idiopathic hypercalciuria was corrected with the simple restriction of salt in the diet. Also on the epidemiological level, it could be detected that when the consumption of sodium exceeded certain levels, the risk of forming kidney stones increased (10). Many authors, when speaking of salt, make reference to sodium. But to be more exact, it should be said that it does not appear that the sodium ion is responsible for the increase in calciuria, but rather the chloride ion. A study to clarify the situation was performed by Muldowney et al. in 1994 (15). These Authors indicated that when supplementing the diet with a certain quantity of sodium chloride there was a marked increase in calciuria, but when the same diet is supplemented with an equimolecular quantity of sodium bicarbonate, the increase in calciuria is not produced. Finally, it should also be remembered that the calciuretic effect of sodium chloride is summed with that of animal proteins (16) and, vice versa, when sodium chloride is removed from the diet, the calciuretic effect of the potassium depletion is prevented (17). So the consumption of table salt or the intake of excessive quantities of foods which, because of their nature or industrial processing, contain a lot of salt should be strongly limited in hypercalciuric subjects. In addition, those same mechanisms through which the sodium chloride increases the calciuria, in other words the expansion of the extracellular volume and the tubular competition of the two cations for their reabsorption, also seems to cause an increase in arterial pressure in salt-sensitive subjects.

Therefore, the limitation of salt could be decisive also for reducing the blood pressure of patients similar to the subject that we presented.

The above-mentioned epidemiological study has also identified the influence of sucrose on stone risk (10). Subdividing the population under investigation in relation to the use of sucrose, it was seen that increasing quantities of sugar are accompanied by increasing risk levels, double the risk being reached with an intake greater than 56 g/day. An explanation of this fact would seem to lie in the well-known effect that sugars have on the secretion of insulin. Every time that there is a dietary load of sugars, especially simple sugars, there is a blood-insulin peak which is proportional to the load and, in some so-called insulin-resistant subjects, it is exaggerated with respect to the load. A high proportion of overweight and/or hypertensive people are seen to have this metabolic anomaly which is described as insulin-resistance. Holl and Allen, in 1987 (18), published results showing a strict positive correlation between the levels of insulin in the serum, caused by a sugar load, and an increase in urinary calcium. It is probable than insulin acts directly on the renal tubule reducing its capacity to reabsorb calcium. This fact explains the various studies that have indicated a constant and significant increase in calciuria in conditions of oral intake of simple sugars (19,20). This phenomenon, which is repeated intermittently during the day, could generate peaks of calcium oxalate supersaturation in the urine which are responsible for an increased lithogenic risk. Therefore, the limitation in the daily consumption of sugars, especially simple sugars, must also enter into the dietary norms which concern idiopathic hypercalciuria.

The principal dietary norms that are useful for the prevention of idiopathic hypercalciuria are summarized in Table III.

It is not easy to maintain with constancy, and over a long period of time, a good adherence to the type of diet recommended, but the results convince both the doctor and the patient to make a concerted effort.

Table III - Norms for the prevention of idiopathic hypercalciuria.

– Reduce any excess body weight.
– Reduce the arterial pressure if high, with thiazides or indapamide associated with potassium-sparing drugs or with supplements of alkaline potassium (citrate or bicarbonate).
– Maintain a normal intake of dietary calcium and avoid calcium supplements between meals.
– Reduce the intake of protein, above all of animal origin.
– Increase the intake of alkaline potassium (fruit and vegetables with low oxalate content).
– Reduce the intake of sodium chloride.
– Limit the intake of sugars, especially simple sugars.

For the compliance of the patient, it is very important that the doctor spend some time explaining the importance of diet in this area and educating the patient in a primary prevention activity which does not rely on the use of drugs.

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