Original Paper

NEPHRON

Nephron 1996;73:569–572

Hypertension in Kidney Stone Patients

Adamasco Cupisti
Ester Morelli
Mario Meola
Vincenzo Cozza
Massimo Parrucci
Giuliano Barsotti

Istituto Clinica Medica I,
Università di Pisa, Italy

Abstract

The prevalence of arterial hypertension (HT) was investigated in 258 patients (171 m, 87 f, 22–68 years) with a history of primary stone disease. HT was detected in 64 patients (24.8%), with no difference between males (25.7%) and females (23.0%). The prevalence of HT by age was very similar to that of a general population, especially in the calcium stone group. The discriminant analysis demonstrated that the composition of stones, other than the age and body weight of the patients, were the main factors associated with HT.

As far as the different kind of stone is concerned, the prevalence of HT was higher in patients with uric acid (17/37, 45.9%) and struvite stones (11/27, 40.7%) than in calcium stone formers (35/188, 18.6%) (χ^2 16.31, $p < 0.001$). The prevalence of hypercalciuria was higher in the calcium stone group than in uric acid or struvite stone patients (36.4 vs. 9.7 vs. 13.7%; χ^2 10.35, $p < 0.01$). Furthermore, the hypercalciuria showed a trend to be more prevalent in the untreated (47.0%) than in the treated (31.2%) hypertensives, or normotensives (35.1%). Uric acid stone formers were older, heavier and with higher triglycerides and uric acid plasma levels than calcium or struvite patients. Also the struvite stone formers were older than the calcium stone ones.

Our data suggest that the prevalence of HT in kidney stone patients and particularly in calcium stone formers is similar to that of a general population. The role of hypercalciuria as the link for HT-urolithiasis association seems quite uncertain. Struvite and uric acid stone formers have higher risk for HT than calcium stone formers, probably due to the old age or to the associated metabolic abnormalities.

Key Words
Hypertension
Hypercalciuria
Nephrolithiasis

Introduction

An independent clinical association between arterial hypertension (HT) and kidney stone disease was recently described [1, 2]. In fact, studies performed on a general population showed that a history of kidney stones was approximately 2 or 3 times more frequent in hypertensive than in nonhypertensive subjects [1]. Since urinary calcium excretion is increased in hypertensives [3–5], the hypercalciuria was regarded as the pathogenetic link between HT and urolithiasis.

Conversely, to our knowledge, data concerning the prevalence of HT in stone patients, as well as the differences related to the stone composition, are not available in the literature.

In our opinion, it is of great importance that the analysis of the relationship between urolithiasis and HT takes into account the different chemical stone composition

KARGER

E-Mail karger@karger.ch
Fax + 41 61 306 12 34
http://www.karger.ch

0028–2766/96/0734–0569$10.00/0

Prof. Giuliano Barsotti
Clinica Medica I, Università di Pisa
via Roma 67
I–56100 Pisa (Italy)

Accepted:
September 13, 1995

Table 1. Age, body weight, serum biochemistry and urinary urea excretion in hypertensive (HT) and in nonhypertensive (non-HT) stone patients, by gender

	Males		Females	
	44 HT	127 non-HT	20 HT	67 non-HT
Age, years	51 ± 10[a]	42 ± 12	49 ± 11[c]	42 ± 13
Body weight, kg	81.8 ± 10.5[b]	75.9 ± 10.2	63.8 ± 11.2	61.8 ± 11.0
Serum creatinine, mg/dl	1.0 ± 0.2	1.0 ± 0.2	0.8 ± 0.1	0.8 ± 0.1
Serum uric acid, mg/dl	5.5 ± 1.6	5.2 ± 1.3	4.5 ± 1.0	4.3 ± 1.2
Total cholesterol, mg/dl	215 ± 40	197 ± 38	202 ± 43	202 ± 45
Triglycerides, mg/dl	176 ± 82[c]	144 ± 90	136 ± 83[c]	103 ± 48
Serum potassium, mEq/l	3.9 ± 0.4	3.8 ± 0.4	3.9 ± 0.4	3.9 ± 0.4
Serum sodium, mEq/l	139 ± 2	139 ± 3	139 ± 2	139 ± 4
Urinary urea, g/24 h	24.8 ± 7.6	22.4 ± 5.8	17.3 ± 8.9	17.0 ± 4.5

[a] $p < 0.001$; [b] $p < 0.01$; [c] $p < 0.05$ vs. non-HT.

because (1) it is often associated with epidemiological and clinical features that can influence the risk of HT, and because (2) the hypercalciuria is a well-known risk factor for calcium urolithiasis [6–8], but not for the other types of kidney stones.

The aim of this study was to evaluate the prevalence of HT and of hypercalciuria in a cohort of patients with well-documented kidney stone disease, having the purpose to look for the differences associated with the stone composition.

Table 2. Prevalence of HT in calcium, uric acid or struvite stone formers

Stone composition	Calcium		Uric acid		Struvite	
	n	%	n	%	n	%
Males	26/129	20.1	14/29	48.3*	3/9	33.3
Females	9/59	15.2	3/8	37.5	8/18	44.4*
Total	35/188	18.6	17/37	45.9**	11/27	40.7*

** $p < 0.01$; * $p < 0.05$ vs. calcium (χ^2 test).

Patients and Methods

Only patients with a definite history of kidney stone disease (stones passed or removed by surgery, urological maneuvers or ESWL, or detected by sonography or X-ray methods) were considered for the study.

Stone patients aged <20 or >70 years, with serum creatinine >1.2 mg/dl, hypercalcemia, bone diseases, primary hyperparathyroidism, diabetes, polycystic kidney disease, obstructive nephropathy, or with clinical or laboratory signs of secondary HT were excluded.

Two hundred and fifty-eight stone patients (171 males and 87 females, aged 22–68 years) were selected; calcium stone disease was the most frequent (72.8%), followed by uric acid (14.3%), struvite (10.5%) and cystine (2.3%). The patients having a diastolic blood pressure >95 mm Hg on at least three measurements performed in different days, as well as the patients having a previous diagnosis of essential HT and for this already on antihypertensive treatment at the time of observation, were classified as hypertensives.

Blood pressure was measured by a physician, using a mercury sphygmomanometer, after 5 min of rest with the patient in an upright position. Data regarding age, body weight, plasma levels of creatinine, electrolyte, total cholesterol and triglycerides, urinary calcium and urea excretion, were collected at the time of the first visit in our stone clinic. All the assays were performed using the standard laboratory procedures. Hypercalciuria was defined as daily urinary calcium excretion >4 mg/kg b.w. The results have been expressed as mean ± SD.

Statistical evaluation was performed using Student's t test for unpaired data, analysis of variance (one-way ANOVA), χ^2 test, discriminant analysis (by software 'SOLO' BMDP); p values <0.05 were regarded as statistically significant.

Results

Hypertension was present in 64 out of the 258 stone patients (24.8%). Thirty-two of them were untreated hypertensives, whereas 32 have been taking antihypertensive drugs for more than 6 months. The drugs employed were angiotensin-converting enzyme (ACE) inhibitors (12 patients), calcium channel blockers (10), clonidine (6) and β-blockers (5); in 8 patients thiazides were used in association with ACE inhibitors, clonidine or β-blockers. The prevalence of HT was similar in males (25.7%) and in females (23.0%), as well as in the recurrent (26.4%) or in the single (19.4%) stone formers.

Table 3. Age, sex and serum biochemistry in patients affected by calcium, uric acid or struvite stone disease

Stone composition	Calcium	Uric acid	Struvite	ANOVA
Males/females	129/59	29/8	9/18	
Age, years	41.7±11.9	50.9±11.2^{++}	53.6±11.4^{++}	<0.001
Body weight, kg	71.3±12.5	80.0±13.1***	65.0±9.0^{+}	<0.001
Triglycerides, mg/dl	127±68	198±131**	136±52	<0.001
Total cholesterol, mg/dl	199±39	210±44	211±44	NS
Uric acid, mg/dl	4.8±1.3	5.8±2.0*	4.6±1.1	<0.05

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ vs. calcium and struvite. $^{+}$ $p < 0.05$; $^{++}$ $p < 0.001$ vs. calcium group.

Data regarding hypertensive and normotensive patients are shown in table 1. In the former, age, body weight and triglyceride plasma levels were significantly higher than in the latter. In our series, discriminant analysis showed that HT mainly correlated with the composition of stones (specificity 86%, sensitivity 42%), followed by the age and body weight of the patients. The highest values of specificity (88%) and sensitivity (43%) were reached when the type of stone, age and body weight were considered together. As expected, the prevalence of HT increased with age, particularly in the calcium stone group (fig. 1) in which the prevalence of HT by age was very similar to that reported in the general population [9, 10]. As far as the different type of stone disease was concerned (table 2), in uric acid and struvite nephrolithiasis the prevalence of HT was greater than in calcium stone disease (χ^2 16.31, $p < 0.001$). Patients with uric acid stone disease were older, heavier and with higher plasma levels of uric acid and triglycerides than calcium or struvite stone patients (table 3). Also in the struvite group the age was higher than in the calcium stone group (table 3).

As expected, the prevalence of hypercalciuria was significantly higher in the patients forming calcium stones than uric acid or struvite stones (respectively 36.4 vs. 9.7 vs. 13.7%; χ^2 10.35, $p < 0.01$). Furthermore, in the calcium stone group, the hypercalciuria showed a trend higher in the untreated (47.0%) than in the treated (31.2%) hypertensives or in normotensives (35.1%).

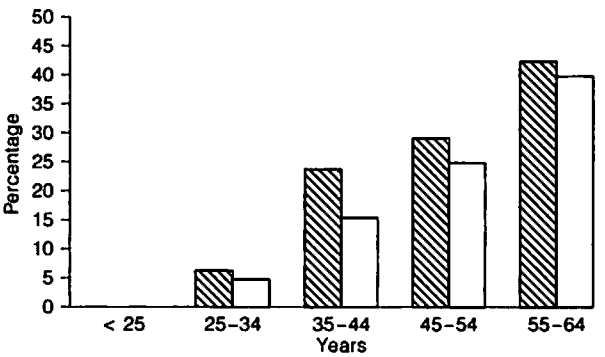

Fig. 1. Prevalence of HT by age in the overall population of stone patients (shaded bars) and in the subgroup of calcium stone formers (empty bars).

Discussion

The results of our study demonstrate that the prevalence of HT in stone formers is quite similar to that observed in the general population [9, 10]. The types of stone, other than the body weight and the age of the patients, are the main factors associated with HT. In fact, the prevalence of HT in uric acid and struvite patients was higher than in calcium stone patients (table 2), in the latter (fig. 1) being very similar to that reported in a general population [1, 9, 10].

Uric acid stone formers were heavier and older than calcium stone patients and showed elevated triglycerides and uric acid serum levels (table 3): these features are often associated with HT. In addition, chronic pyelonephritis is often present in struvite stone patients who are also older than calcium stone formers. These arguments can account for the higher prevalence of hypertension in uric acid and struvite stone patients.

The prevalence of hypercalciuria is much higher in calcium stone formers than in uric acid or struvite stone patients, accordingly to its role of risk factor for calcium urolithiasis. Notwithstanding, the risk of hypertension is higher in the uric acid (and struvite) stone disease than in

calcium stone formers (table 2) where the prevalence of HT is quite similar to that of a general population [9, 10]. Consequently, at least in stone patients, hypercalciuria does not seem the link for HT-urolithiasis association.

Increased urinary calcium excretion has been described in patients with essential HT. It is caused by a defective renal tubular handling of calcium, dependent [4] or not [3] on sodium urinary excretion. This study failed to clearly demonstrate a significantly greater prevalence of hypercalciuria in the untreated hypertensives in respect to the nonhypertensives. It could be due to the presence, in the stone patients, of changes in dietary intake, or in intestinal, renal and bone calcium metabolism that are additional factors able to affect urinary calcium excretion [11–13].

In this study the hypercalciuria showed a trend to be higher in the untreated hypertensive than in the treated hypertensives. There is evidence that the increased urinary calcium excretion in hypertensive patients is primary to, and not induced by, the elevated blood pressure per se [14]. Then, the trend to a lower prevalence of hypercalciuria in the treated patients could be due to the antihypertensive treatment. Thiazides are well-known agents capable of lowering urinary calcium, and also β-blockers decreased the fasting excretion of calcium [15]. On the contrary, ACE inhibitors or calcium channel blockers, in particular dihydropyridine derivatives [15, 16], do not induce major changes in urinary calcium excretion; instead, nifedipine reduces urinary calcium excretion in hypercalciuric patients [17]. In addition, it is possible that the patients already on antihypertensive treatment were also on a restricted sodium diet, contributing to the underestimation of the prevalence of hypercalciuria in the treated hypertensive stone formers.

In conclusion, the prevalence of HT in calcium stone formers seems to be quite similar to that of the general population, and the role of hypercalciuria in the HT-urolithiasis association is quite uncertain. Instead, the uric acid and struvite stone formers present an increased risk of HT and this can be influenced, at least in part, by other associated factors such as overweight and old age.

In our opinion, the next studies concerning the relations between kidney stones and HT must not leave aside the chemical composition of stones, that is associated with different etiopathogenetic factors and clinical features.

References

1 Cappuccio FP, Strazzullo P, Mancini M: Kidney stones and hypertension: Population-based study of an independent clinical association. Br J Med 1990;300:1234–1236.

2 Cirillo M, Laurenzi M: Elevated blood pressure and positive history of kidney stones: Results from a population-based study. J Hypertens 1988;6(suppl 4):S485–S486.

3 Strazzullo P, Nunziata V, Cirillo M, Giannattasio R, Ferrara LA, Mattioli PL, Mancini P: Abnormalities of calcium metabolism in essential hypertension. Clin Sci 1983;65:137–141.

4 Tillman DM, Semple PF: Calcium and magnesium in essential hypertension. Clin Sci 1988; 75:395–402.

5 Zoccali C, Mallamaci F, Curatola G, Cuzzola F, Postorino M, Parlongo S, Salnitro F, Curatola A: Mechanism of hypercalciuria in essential hypertension and primary nephrolithiasis. Contrib Nephrol. Basel, Karger, 1991, vol 90, pp 49–53.

6 Nordin BEC, Peacock M, Wilkinson R: Hypercalciuria and renal stone disease. Clin Endocrinol Metab 1972;1:169–183.

7 Robertson WG, Peacock M, Heyburn PJ, Marshall DH, Clark PB: Risk factors in calcium stone disease of the urinary tract. Br J Urol 1978;50:449–454.

8 Pak CYC, Britton FB, Peterson R, et al: Ambulatory evaluation of nephrolithiasis. Am J Med 1980;69:19–30.

9 Cirillo M, Laurenzi M, Trevisan M, Stamler J: Hematocrit, blood pressure, and hypertension. The Gubbio population study. Hypertension 1992;20:319–326.

10 Lew EA: Hypertension and longevity; in Laragh JH, Brenner BM (eds): Hypertension: Pathophysiology, Diagnosis, and Management. New York, Raven Press, 1990, pp 175–192.

11 Harlan WR, Harlan LC: Blood pressure and calcium and magnesium intake; in Laragh JH, Brenner BM (eds): Hypertension: Pathophysiology, Diagnosis, and Management. New York, Raven Press, 1990, pp 229–241.

12 Pak CYC, Kaplan R, Bone H, Townsend J, Waters O: A simple test for the diagnosis of absorptive, resorptive and renal hypercalciuria. N Engl J Med 1975;190:175–179.

13 Broadus AE, Burtis WJ, Oren DA, Sartori L, Gay L, Ellison AF, Insogna KL: Concerning the pathogenesis of idiopathic hypercalciuria. Contrib Nephrol. Basel, Karger, 1987, vol 58, pp 127–136.

14 Hvarfner A, Bergstrom R, Lithell H, Morlin C, Wide L, Ljunghall S: Changes in calcium metabolic indices during long-term treatment of patients with essential hypertension. Clin Sci 1988;75:543–549.

15 Soro S, Cocca A, Pasanisi F, Tommaselli A, De Simone G, Costantino G, Ferrara LA: The effects of nicardipine on sodium and calcium metabolism in hypertensive patients: A chronic study. J Clin Pharmacol 1990;20:133–137.

16 Lind L, Hanni A, Hvarfner A, Pollare T, Ljunghall S, Lithell H: Influences of different antihypertensive treatments on indices of systemic mineral metabolism. Am J Hypertens 1994;7:302–307.

17 Calò L, Cantaro S, Piccoli A, D'Angelo A, Giannini S, Williams HE, Borsatti A: Effect of nifedipine on urinary excretion of calcium and calcium-controlling hormones in essential hypercalciuria. Cardiovasc Drug Ther 1990; 4(suppl 5):983–986.