Scandinavian Journal of Primary Health Care

ISSN: 0281-3432 (Print) 1502-7724 (Online) Journal homepage: https://www.tandfonline.com/loi/ipri20

Aetiological Examination of Recurrent Urinary Stone Formers in General Practice

Even Leærum

To cite this article: Even Leærum (1983) Aetiological Examination of Recurrent Urinary Stone Formers in General Practice, Scandinavian Journal of Primary Health Care, 1:2, 56-62, DOI: 10.3109/02813438309034935

To link to this article: https://doi.org/10.3109/02813438309034935

Scand J Prim Health Care 1983:1; 56–62

Aetiological Examination of Recurrent Urinary Stone Formers in General Practice

by
EVEN LÆRUM

Even Lærum: Former general practitioner, Nedre Eiker Legesenter, Mjøndalen, Norway. Now: Research fellow, Institute of General Practice, Oslo, Norway.

ABSTRACT. As a part of a project performed in general practice 93 recurrent urinary stone formers were examined by means of a programme comprising a thorough medical history, clinical examination, serum determinations, a chemical stone analysis, two consecutive 24 h urine collections and i.v.-pyelography. The diagnostic information obtained from the different examinations is presented.

In 64 (69%) of the patients the probable aetiology of the stone formation was revealed. Twenty seven (29%) of all patients had combined aetiology. Hyperuricosuria and hypercalciuria were groups of equal size, comprising alltogether 45 patients, and emphasizing the necessity of 24 h urine collections. Hyperparathyreoidism (surgically verified) was diagnosed in four patients, based on serum calcium. Seven patients had infectious stone. It is stated that an aetiological examination of the recurrent stone former may be adequately carried out in general practice and lead to important therapeutical consequences.

KEY WORDS: Urolithiasis. Aetiological examination. General practice.

INTRODUCTION

Stone formation in the urinary tract involves many aetiological and pathogenetic factors (1, 2), for instance the urinary content of calcium, oxalate, uric acid, acid mucopoly-saccharides and pH (3). In addition urinary infection with urea splitting bacteria, urinary obstruction, drugs, climate and dietary and drinking habits may be of importance (2, 3).

Urinary stone disease can be classified in the following main groups:

1. Idiopathic stone disease.
2. Different states with hypercalciuria.
3. Lithiasis connected with uric acid disorders.
4. Tubular defects.
   Renal tubular acidosis (RTA)
   Cystinuria
5. Hyperparathyreoidism (HPT).
6. Stones caused by urinary tract infection (UTI).
7. Congenital, anatomical defects, i.e. medullary sponge kidney.

Several examination programmes have been devised for urolithiasis patients (1,4,5) of which the majority have been developed for hospital patients.

The purpose of the present study was to investigate the underlying causes in patients with recurrent urolithiasis seen in general practice, and thereby develop an examination programme with sufficient diagnostic precision and simple enough to be useful for the general practitioner.

MATERIAL AND METHODS

The study was carried out between 1.XII.1976 and 1.VI.80 at a group practice in a predominantly rural district in central Norway. The material comprised 67 males, mean age 48 (±12.3SD), and 26 females, mean age 41 (±13.2SD) years. Two local hospitals referred 17 patients, the remainder contacted the author directly or were referred by other practitioners (6).

Indications for inclusion were: Stone recurrence during the last two years, and/or growth of preformed stones and/or bilateral stones in patients above 15 years of age. The diagnosis was verified by stone passage, X-ray or surgery.

Blood examinations

A regular medical history and clinical examination were supplemented by the following blood tests: Haemoglobin, sedimentation rate and leucocyte count (at the group practice). Albumin, uric acid, calcium, creatinine, phosphate, alkaline phosphatase, and fasting glucose were analyzed (serum sent from the group practice) at the Department of Clinical Chemistry, Buskerud Central Hospital, using Technicon SMA 12/60 autoanalyzer (7,8,9,10). The analysis of magnesium was performed by atomic absorption spectrophotometry (Perkin Elmer 300), sodium and potassium by flame photometry (IL 743) and chloride by a titration method. Albumin, calcium, uric acid, creatinine and phosphate were determined on three occasions with an interval of minimum one week. Calcium was albumin corrected ad

modum Payne (11) when pathological values were found for albumin or calcium, using the following formula:

Corrected calcium = total calcium $-$ ($\frac{1}{4}$albumin $-$ 1).

Urine

The following were examined in a freshly voided midstream urine sample: Albumin, glucose, blood and pH using Ames Labstix, bacteria culture by a dip slide method (Uricult) and specific gravity. The urine was examined microscopically (magnification × 400) for haematuria (>3–5 erythrocytes), pyuria (>10–15) leukocytes, crystalluria (in acid urine) and other formed components. Two consecutive 24h urine collections were performed. Ten ml. conc. HCl was used as a preservative and to prevent electrolyte precipitation. Cheese and milk were to be avoided three days before and during the collection. Uric acid, calcium, magnesium and creatinine were determined with the same methods as used for the serum. If the difference in creatinine value on the two determinations exceeded 25% a new collection was performed (eight patients). Reference values for these urinary excretions were based on 95% interfractile range calculated from 24 healthy volunteers (employees at the group practice and their relatives).

The renal tubular calcium rearbsorption was calculated ad modum Peacock, Robertson & Nordin (12) and related to serum calcium in a nomogram for diagnosis of hyperparathyroidism.

Stone analysis

Stones were examined by a conventional qualitative chemical method in the same laboratory as did the other determinations, including calcium, oxalate, phosphate, magnesium, ammonium, carbonate, cystine and uric acid. A visible nucleus was examined separately.

X-ray

I.v.-pyelography was taken in all patients if not performed during the last year. Otherwise a plane film was made of the urinary tract.

Diagnostic criteria

Urinary tract infection (UTI) was supposed as the cause of the stone formation when chronic (< one year) or recurrent infection was present before and/or during the stone formation period. UTI was diagnosed by the presence of one or more of the following criteria: pyuria and bacterial growth, triple phosphate stone or X-ray findings including chronic pyelonephritis or staghorn calculi. Hyperparathyreoidism (HPT) was suspected when the albumin corrected serum calcium exceeded 2.65 mmol/l, or the Nordin-Peacock index indicated the diagnosis. Medullary sponge kidney and other anatomical aetiology were based on i.v.-pyelography or cystoscopic findings.

The main aetiological diagnosis in patients with more than one diagnosis, was based on the degree of the abnormalities.

RESULTS

Diagnostic procedure

History and clinical examination

The case history revealed information on the aetiological diagnosis in two patients with probable acetazolamide (treated for glaucoma) induced stones, in one patient with known sarcoidosis and in the seven patients with infectious stones (Table I). The dietary history did not give information of apparent significance.

In 26 patients profuse perspiration through heavy work and/or sport was reported, in four of them combined with a stay in a very hot climate. This profuse perspiration occurred one year before or during the stone formation period, and is considered as a provoking factor for the stone formation.

The clinical examination confirmed or revealed the diagnosis hypertension in eight patients (four of them on treatment). In one 64 year old patient a considerably enlarged prostatic gland was found.

Alltogether history and clinical examination indicated an underlying cause or a provoking factor for the stone formation in 37 patients.

Serum and blood

Table II shows that seven patients had hypercalcaemia, which was present in two of the three determinations, with or without albumin correction. Four of them had later surgically verified HPT. One patient with probable normocalcaemic HPT was not operated on. These five patients also had reduced phosphate on two or three occasions and three of

Table I. Main aetiological or pathogenetic diagnoses in 93 recurrent stone formers. Total number of diagnoses (shown in brackets): 114.

	Males		Females	
Idiopathic stone formers	19(19)		10(10)	
Hypercalciuria	9(10)		2(3)	
Uric acid disorders:	21(24)		4(5)	
Uric acid stone		3(3)		1(1)
Hyperuricosuria		9(10)		1(2)
Hyperuricaemia		1(3)		–
Hypercalciuria and Hyperuricosuria		8(8)		2(2)
Infectious stone	2(2)		5(5)	
Hyperparathyreoidism (HPT)	3(3)		2(2)	
Drug induced (acetazolamide)	1(1)		1(1)	
Magnesium deficit (urine/blood)	2(4)		–(1)	
Medullary sponge kidney	1(1)		–	
Anatomical aetiology	2(9)		1(7)	
Sarcoidosis	1(1)		–	
Other*	6(7)		1(1)	
Total	67(80)		26(34)	
Number of main diagnoses previously not known (Idiopathic not included)	35		14	

*Patients without 24h urine collections, but with one or another cause for the stone formation.

Table II. Number of recurrent stone formers with abnormal serum constituents.

	Reference values	Males	Females
Albumin	36–52 g/l	1	0
Magnesium	0.75–1.10 mmol/l	1	1
Calcium	2.2–2.7 mmol/l	5	2
Phosphate	0.8–1.5 mmol/l	3	3
Sodium	137–148 mmol/l	0	0
Potassium	3.5–5.0 mmol/l	0	0
Chloride	89–106 mmol/l	0	0
Uric acid			
Males	150–430 μmol/l	3	–
Females	120–400 μmol/l	–	0
Creatinine	60–120 μmol/l	0	0
Alkaline phosphatase	<270 U/l	4	0
Total		17	6

them had a raised alkaline phosphatase. In five other patients serum calcium was on one occasion higher than 2.7 mmol, though normal when albumin corrected.

Haemoglobin, sedimentation rate and leucocyte count gave no information of clinical significance.

One of three patients with hyperuricaemia had pathological values in all three samples, while the two others had one normal and two pathological values. Two patients had significantly lowered serum magnesium. One of them was on thiazide medication.

In all patients serum creatinine, sodium potassium and chloride were within the normal limits. Thus, serum analysis gave the diagnosis hyperparathyroidism, hyperuricaemia and hypomagnesaemia in alltogether nine out of 93 patients.

False negative values might have been the result from only one determination in eight of the patients as compared with the result from two determinations, while three samples appeared to be superfluous. In eight patients no 24h urine collection was performed because of other diseases or for social reasons.

Table III. Mean urinary excretion of calcium, uric acid, magnesium and creatinine from two consecutive 24h collections in 85 of 93 recurrent stone formers.

	Reference values	No of patients with pathological values	
		Males	Females
Calcium	1.3–6.0 mmol/24 h	23	7
Uric acid	1.3–3.5 mmol/24h	23	4
Magnesium	2.4–5.4 mmol/24h	2	3
Creatinine	8.5–18 mmol/24h	–	–

Urine

Table III shows the mean values of the two 24h urine collections. Hyperuricosuria or hypercalciuria were found in 45 patients. Five patients had an abnormal urinary magnesium excretion. Due to sampling error and variation in the day to day excretion, 27 of the 85 patients would have had another diagnostic classification if the collection had been from only one 24h interval.

Expected false positive values would be 5% from sampling on two occasions (95% interfractile range and one-tailed test). The microscopic examination showed haematuria in 24%, and oxalate or urate crystals in acid urine in 22% of the patients.

The examination with stix did not give additional diagnostic information (except pH), neither did the specific gravity test. Significant bacterial growth of E. coli or Proteus combined with pyuria was found in six patients. All these patients had the criteria used for infectious stone. (see Methods).

The renal tubular reabsorption index related to serum calcium revealed one probable, though not surgically verified, normocalcaemic hyperparathyreoidism. This rather laborious diagnostic procedure was therefore of little significance in the present material.

Stone analysis

Table IV shows that in 48 patients with a stone available for chemical analysis, 73% had a pure calcium oxalate stone or combined with phosphate.

In four patients with uric acid stone one had phosphate on the outside of a uric acid nucleus. In none had an uric acid disorder been diagnosed previously and all had a very high stone forming rate. The finding of triple phosphate in six patients supported the diagnoses of infectious stone. Thus, aetiologically significant information was obtained from 21% of the stones analyzed.

X-ray examination

In 16 patients an anatomical abnormality was found, such as hydronephrosis, double kidney/ureter, diverticulae and stenosis/stricture. In three of them this was considered through urinary stasis as the main aetiology, and they were referred for further treatment. In addition chronic pyelonephritis and staghorn calculus were found in three patients, and medullary sponge kidney in one case. Altogether X-ray examination gave diagnostic information of clinical significance in 23 of the patients.

Table IV. Types of stones in 48 of 93 recurrent stone formers.

		Males	Females
1	Calcium oxalate and phosphate	17	1
2	Calcium oxalate	13	4
3	Calcium phosphate	–	1
4	Carbonate combined with 1, 2 or 3	–	2
5	Uric acid	3	1
6	Triple phosphate	4	2
Total		37	11

Combined aetiology

Twentyseven (29%) of the patients had a mean of 2.2 aetiological diagnoses. In ten of the 16 patients with anatomical abnormalities this was combined with other diagnoses, mainly hyperuricosuria and infectious stones. In ten of the patients with hyperuricosuria this was combined with hypercalciuria (Table I). Two patients with hyperuricaemia had this condition in combination with other aetiological diagnoses.

Six patients with a very high stone formation rate (in total 17–59 stones) had hyperuricosuria and/or uric acid stones.

Seventyfive per cent (49 of 64 patients, idiopatic stone formers excluded) of the main aetiological diagnoses were previously unidentified.

DISCUSSION

Two basic problems arise from this study: Firstly, which methods are adequate for aetiological examination of recurrent stone formers, and secondly, what is the clinical significance of a positive finding?

Concerning the methods the results show that it is necessary to include serum calcium determinations and probably serum phosphate as a supplement on two occasions in order to diagnose HPT. Albumin correction is recommended to increase the diagnostic reliability of serum calcium (11). This was confirmed by the present study. Due to intra-individual variations serum uric acid should also be determined twice. Haemoglobin, sedimentation rate, leucocyte count, fasting glucose and alkaline phosphatase did not give any additional information contributing to the aetiological diagnosis of the stone, and may therefore be considered unnecessary in this connection.

Although serum creatinine was within normal limits in all the patients, it should be analysed to obtain a rough estimate of the kidney function. The determination of potassium and chloride, though normal in the present study, should probably be included as the simplest screening tests for the important, but rare RTA.

The question of whether it is possible to perform an adequate 24h urine collection is controversial. With a careful patient instruction and some enthusiasm this did not appear to be a major problem in the present study. A history of recurring painful attacks of renal colic seems to stimulate a positive patient attitude.

Most studies including a urine collection have been performed on a free diet, which may give a better picture of the patient's usual conditions, but is also more influenced by casual environmental factors. A free diet is probably preferable, not least because it is simpler.

One 24h collection only may give a misleading result in ⅓ of the patients. This is a high percentage and emphasizes the necessity for collecting urine from two consecutive 24h intervals.

The other examinations of the urine, all easily performed, gave information about conditions such as infection, crystalluria and haematuria. pH does not seem to discriminate between the different groups, but is recommended as one of the screening tests for a RTA (5). A nitroprusside sodium test to reveal cystinuria was not performed, because it is a very rare disorder (1) and because microscopic examination of acid urine serves as a screening test. Additionally, all available stones were analyzed for cystine. It is, however, recommended that recurrent stone formers under 25–30 years should be referred to a suitable laboratory for a nitroprusside test, because of the clinical and therapeutical consequences of the diagnosis (13).

The calcium excretion index contributed no additional information as compared to repeated serum calcium determinations, except for diagnosing one case with probable normocalcaemic hyperparathyreodism. The test is therefore considered superfluous in general practice.

A conventional chemical stone analysis is considered inferior to other examinations such as X-ray diffraction, spectrophotometry etc. as regards precision and accuracy (14). However, it is applicable and gives information of diagnostic and therapeutical importance when demonstrating uric acid, triple phosphate and cystine.

Pyelography is mandatory, at least on one occasion as it yields information about number, type (radiopaque), site and aetiology of the stones, parenchymatous changes and kidney function.

As a general conclusion all the above mentioned methods appear simple, reliable and adequate for outpatient use.

The multifactorial aspect of the disease is emphasized by the fact that ⅓ of the patients had more than one probable cause for the stone formation.

Hyperparathyreoidism is important to diagnose because it is potentially curable (15). A frequency of 5,5% of the patients with this diagnosis in recurrent stone formers is similar to the findings in other materials (1). Magnesium deficit (urine and/or serum) is

found in only a small group of patients and the exact aetiological importance of these findings is not clarified (16). It may, however, be of therapeutic significance and justify stone prophylaxis with magnesium (16).

The group with hypercalciuria, found in 11–61% of the patients in other reports (4), is possibly too small as a result in the present study because of the calcium restriction prior to the 24h urine collection. It can be asked, however, how important it is to diagnose hypercalciuria, since the stone prophylactic effect of thiazide seems to be independent of calcium excretion (4,17).

The group with a uric acid disorder is important because it is large and can be offered stone prophylactic treatment with allopurinol (18) as patients with normocalciuria and hypercalciuria can be treated with thiazide (1,17). It should be emphasized that patients with uric acid disorders may have a particularly severe form of the recurrent stone disease (19,20).

Stones due to urinary infection represent a small aetiological group, in most materials found in 7—10% of the patients, and with a female dominance (1). In many patients it might be a matter of judgement to decide whether the infection is the cause of stone formation or vice versa, and, an anatomical abnormality may be the underlying cause for both the UTI and the stone formation. It is also difficult to judge the aetiological significance of findings such as a double kidney/ureter or a ureterocele (21,22) and especially since these conditions were frequently combined with other aetiology.

In accordance with the results from the present study, an aetiological examination programme as outlined in table V is suggested for use in general practice. Based on the present material it should then be possible to detect the aetiology of recurrent stone formation in about 70% of the patients, of which 75% may be undiagnosed previously.

In consequence, all recurrent urolithiasis patients should be considered candidates for thorough aetiological examination and for specific stone prophylaxis either directed at the underlying cause or by using perhaps thiazide in idiopathic stone formers. This management of the recurrent stone patient is a challenge to the general practitioner.

Table V. Aetiological examination programme suggested for recurrent stone formers in general practice.

Serum		Urine	2 consecutive 24h urine collections	Other
Albumin*			Calcium	Chemical stone analysis
Calcium	×2	Stix including pH	Uric acid	
Phosphate			Magnesium	
Uric Acid			Creatinine	I.v.-pyelography
Magnesium		Microscopic examination		
Potassium**		Cultivating of bacteria		
Chloride**		Sodium nitroprusside test for cystinuria***		

*For albumin correction of calcium
**Screening for renal tubular acidosis
***In patients without stones available for chemical analysis and <25–30 years of age

REFERENCES

1. Transbøl I. Nyrestenssygdomme: ætiologisk udredning, behandling og prævention. Specielt med henblik på urologisk ambulatorievirksomhed og almen praksis. Månedsskr prakt Lægergern 1975;X, 578.
2. Melick R A, Henneman P H Clinical and laboratory studies of 207 consecutive patients in a kidney-stone clinic. N Engl J Med 1958;259:307—14.
3. Robertson W G, Peacock M, Heyburn P J, Hanes F A. Epidemiological risk factors in calcium stone disease. In Proceedings of the Symposium on urolithiasis, 15—30. A Wellcome Foundation Symposium, Crete 1979. Uppsala, 1980.
4. Nielsen K H, Iversen T O. Ætiologisk udredning af 138 konsekutive nyrestenspatienter. Ugeskr Læger 1979; 141:575—9.

5. Danielson B G, Transbøl I. eds. Skandinavisk symposium om nyresten. Kristianstad, 1978:105—29.
6. Lærum E. Urolithiasis in general practice: An epidemiological study from a Norwegian district. Scand J Urol Nephrol (in press).
7. Doumas B T, Watson W, Biggs H G. Albumin standards and the measurement of serum albumin with bromcresol green. Clin Chim Acta 1971;31:87—96.
8. Musser A W, Ortigoza C. Automated determination of uric acid byt he hydroxylamine method. Tech Bull Reg Med Techs 1966;36:21—5.
9. Gitelman H J. An improved automated procedure for the determination of calcium in biochemical specimen. Anal Biochem 1967;18:521—31.
10. Chasson A L, Grady H J, Stanley M A. Determination of creatinine by means of automatic chemical analysis. Tech Bull Regist Med Techs 1960;30:207—12.
11. Payne R B, Little A J, Williams R B, Milner J R. Interpretation of serum calcium in patients with abnormal serum proteins. Br Med J 1973;4:643.
12. Peacock M, Robertson W G, Nordin B E C. Relation between serum and urinary calcium with particular reference to parathyroid activity. Lancet 1969;i:384—7
13. Burchardt P, Reinecke F. Grundlagen einer gezielten Harnsteinprophylaxe. Dtsch Med Wochenschr 1976;101:1326—33.
14. Uldall A. Analysis of urinary calculi; quality control programme. Scand J Clin Lab Invest 1981;41:339—45.
15. Mc. Geown M. Effect of parathyroidectomy on the incidence of renal calculi. Lancet 1961;i:586—7.
16. Johansson G, Backman U, Danielson B G. et al. Magnesium metabolism in renal stone formers. Effect of therapy with magnesium hydroxide. In Proceedings of the Symposium on urolithiasis. A Wellcome Foundation Symposium, Crete 1979. Uppsala, 1980.
17. Lærum E, Larsen S. Thiazide prophylaxis of urolithiasis: a double blind study in general practice. Acta Med Scand (Submitted for publication).
18. Smith M J V. Placebo versus allopurinol for renal calculi. J. Urol 1977;117:690.
19. Coe F L, Keck J, Norton E R. The natural history of calcium urolithiasis. JAMA 1977;238:1519—23.
20. Lærum E. Recurrent urolithiasis: Riskfactors and clinical consequences studied in patients in general practice. Scand J Urol Nephrol. (Accepted for publication.)
21. Pyrah L N. Intrarenal, pararenal and ureteric disorders complicated by renal calculi and calcification. In Renal Calculus. Berlin: Springer-Verlag. 1979:32—64.
22. Schulz E, Schneider H J. Der Einfluss der Strömungsverhältnisse im hydrodynamischen System der harnableitenden Wege auf die Harnsteingenese. Z Urol Nephrol 1979; 12:915—27.

Requests for reprints to:
Even Lærum
Institute of General Practice
Frederik Stangsgate 11–13
Oslo 2
Norway