increasing exposure has highlighted the potential for such a methodology in future studies of this kind. We hope this exercise will encourage future and larger low-cost epidemiological studies in Bhopal to provide scientifically valid information on long term morbidity of the survivors of the disaster.

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Upper urinary tract stone analysis using X-ray diffraction: Results from a tertiary referral centre in northern India

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ABSTRACT

Background. The spectrum of urinary stone disease has changed considerably in India from the common childhood bladder stone to the more frequent upper tract calculi. We analysed the gravel retrieved from the upper urinary tract using X-ray diffraction analysis in an attempt to evaluate the composition of the stones.

Methods. We analysed 434 upper urinary tract calculi from May 1993 to June 1994 obtained endourologically, as well as by extracorporeal shock wave lithotripsy and open surgery. The stones were analysed using a Phillips compact X-ray diffractometer (PW1840). The PC-APD software was used for data collection and peak search. The phase matching was done by the software using the JCPDS reference database.

Results. Oxalate stones comprised 97% of the total stones with calcium oxalate monohydrate forming 90% and calcium oxalate dihydrate and mixed stones forming the remainder. Struvite stones were found in 1.4%, while uric acid and apatite stones were less than 1%. There were no cystine calculi. Seventy per cent of calcium oxalate monohydrate and 40% of calcium oxalate dihydrate stones were pure. All the struvite and apatite calculi were almost pure. Only 15% of staghorns did not consist of oxalate. Nine of the ten stones in children were of the calcium oxalate monohydrate variety. The stone composition in females was similar to that in males.

Conclusions. X-ray diffraction data indicate that urinary stone disease in north India is different from that in the western world. Calcium oxalate monohydrate stones predominate. These stones are hard to break and have a different metabolic origin from those consisting of calcium oxalate dihydrate. These findings might help in selecting the most appropriate method of treatment in north India and they indicate directions in which further metabolic studies might be planned.

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INTRODUCTION

With the dramatic upsurge of minimal invasive techniques to treat urolithiasis by endourological means and extracorporeal shock wave lithotripsy (ESWL), physicians seem to have lost interest in studying stone disease. This starts with the analysis of passed gravel because not only does stone composition affect the likelihood of success of medical dissolution therapy and the choice of a particular stone retrieval procedure by the percutaneous technique (PNL) or ESWL, it also forms the basis for any therapy to prevent recurrence.

The epidemiology of stone disease has changed worldwide. Till recently, vesical stone disease in children was important in Southeast Asia, a problem which existed in eighteenth century Europe. In India, over the last two decades, paediatric vesical stone disease has become less common and the majority of patients now present with upper tract urolithiasis at a later age. Using X-ray diffraction (XRD), we analysed the gravel recovered from the upper urinary tract in our patients to document the composition of urinary tract stones in Indian patients.

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MATERIAL AND METHODS

Between May 1993 and June 1994, we analysed 434 upper urinary tract calculi. The calculi were recovered from 363 males and 71 females whose ages ranged from 6 to 95 years. The average age in females was 39 years (range 14-67 years) and in males it was 37 years (range 6-95 years).

The distribution of stones according to site is shown in Fig. 1. The site classification was: pelvic, calyceal or ureteric. Calculi occupying both the pelvis and the calyces were classified as being pelvicalyceal if only one calyx was involved in addition to the pelvis; or staghorn if the pelvic mass extended into two or more calyces. Pelvic and ureteric calculi formed 30% each of the total.

While all stones recovered in the hospital by open surgery, percutaneous nephrolithotomy (PNL) or ureteroscopic (URS) retrieval methods (Fig. 2) were analysed, patients undergoing ESWL were asked to submit the gravel recovered from their urine for analysis. Except for 21 samples recovered intact by open operation, all other samples were in the form of fragments, due to intra- or extracorporeal disintegration during the endoscopic or lithotripsy procedures. The samples were ground to a fine powder, mounted on a sample holder using the backfilling method. Smaller amounts, insufficient to fill the sample holder, were mounted on glass slides with a drop of alcohol.

The samples were analysed using a Phillips Compact X-ray diffractometer system (PW1840) which consists of an X-ray tube, a goniometer driven by a stepper motor with an automatic divergent slit and a solid-state detector. The diffractometer had a copper anode with a long fine focus. The diffractometer was set at 40 kV and 55 mA and connected to a computer. The Phillips Automated Powder Diffractometry (PC-APD) software was used for data collection, peak search and phase matching. Scanning was done using a step width of 0.02, with start and end angles of 5° and 55°; the receiving slit was 0.05 mm. The scan time was 41.7 minutes, peak search was done without alpha-2 stripping and after conversion of data to the fixed slit type. The APD-matching using PC-APD software was done using the Joint Committee on Powder Diffractometry Society (JCPDS) reference database on CD-ROM. The software identified the compounds using the CIF method (compound identification with inverted search and fuzzy sets). The identified compounds were later checked manually.

If more than one phase was identified, semiquantitation was done on the basis of a percentage (1%) that indicated the scale factor applied to the reference pattern in order to fit the reference to the measured intensities. The subsequent phases were called major constituents if their 1% was more than 50% of the first phase 1%. A lower 1% indicated the subsequent phase to be a low-weight fraction, a minor constituent.

RESULTS

Oxalate stones—calcium oxalate monohydrate (COM), calcium oxalate dihydrate (COD), or a combination of the two comprised 97% of the 434 upper urinary tract calculi; 6 (1.4%) were struvite while uric acid and apatite contributed to less than 1% each (4 and 3 respectively). Oxalate stones were predominantly COM (377; 90%) and 20 (5%) were COD; the rest (24) contained both COM and COD as major constituents. There were no cystine calculi.

Three-fourths of the COM (292 of 377) were pure; COD and uric acid were present as minor constituents in 39 (10%) and 29 (8%) COM stones respectively. Other phases (apatite in 9, struvite in 6 or vaterite in 2) as minor constituents were detected in 5% of the COMs. Only 8 (40%) of the COD stones were pure, while 11 (55%) of them contained COM as the minor component. Uric acid and apatite were detected as minor constituents with COD in 1 stone each. COM also constituted a minor fraction in 2 of 4 uric acid calculi, the other 2 consisting of pure uric acid. All 6 struvite and 3 apatite calculi were also almost pure.

All 33 calyceal and 127 of 129 pelvic calculi were oxalates, 84% of them being predominantly COM. All 86 pelvicalyceal calculi were also of the oxalate variety, COM constituting 95% of the latter. Similarly, 98% of 131 ureteric calculi were oxalates, 89% of them being COM.

Contrary to the understanding that staghorns are usually struvite calculi, 8 (15%) of the 55 staghorns were non-oxalate stones; 3 each (5.5%) were struvite and uric acid, and 2 (4%) were apatite stones. Of 47 oxalate staghorn calculi, 37 (79%) were monohydrates. The review of plain abdominal X-rays revealed that the appearance and distribution pattern of the staghorns was related to their composition. While all 3 struvites were pelvicalyceal casts filling a part or the whole of the pelvicalyceal system, the oxalate staghorns were more dense with a main pelvic mass protruding into the infundibula, the calyceal component was usually made up of several secondary calculi. Radiolucency of uric acid stones was characteristic.

There were ten stones from children. The pelvic (6) and ureteric (1) calculi were composed of COM and 3 children had staghorns—1 was pure struvite, 1 consisted of COM with struvite as a minor constituent and in 1 child the bilateral staghorn calculi were composed of COM, with COD as a minor constituent. The distribution in females was similar. Of 14 staghorns, only 2 were struvite and 1 apatite; the rest were COM. All 6 calyceal and 9 pelvicalyceal calculi were composed of COM, as were 17 of 20 pelvic calculi. The other 3 pelvic calculi were composed of COD (1), a mixture of COD and COM (1) and apatite (1). Only 1 of 22 ureteric calculi was found to be of the non-oxalate variety (uric acid).
Our finding of predominant calcium oxalate urolithiasis in more than 95% of patients with upper urinary tract lithiasis is different from the experience in western countries. Even more striking is the predominance of COM in more than 85% of the oxalate stones; fewer uric acid and struvite calculi; and almost no cystine calculi. The X-ray diffraction method we used identifies the crystal lattice specific for each compound. Of the other techniques, wet chemical analysis (the most commonly used method) is ion-specific and the infrared spectroscopy (IRS) is atom-specific. Polarizing microscopy, thermo-analysis and solid-state chemistry are rarely used. International quality controls have shown that true-positive results for pure substances have been 65%, 94% and 95% by wet analysis, infrared spectroscopy and X-ray diffraction respectively.3 True-positive results for rare compounds have been 20% by wet analysis v. 90% by infrared spectroscopy and X-ray diffraction.4 The most disturbing aspect of wet chemical analysis has been the large number of false-positive results.

The mean age of occurrence in men and women was 39 and 37 years respectively, close to the distribution described by Robertson.6 There is a marked predominance of males, unlike the situation in western societies where differences due to sex are fast disappearing.7 Children and the elderly (>60 years) formed a small proportion, 2.5% and 3.5% of patients.

The higher number of shock waves and sessions required by these patients treated with ESWL is explained by the predominance of COM stones. The retreatment rate with ESWL for COM, struvite-apatite and COD stones has been 10.3%, 6.4% and 2.8% respectively.8 Even while using an in-contact ultrasonic lithotrite during percutaneous surgery, COM proves to be the hardest to crack.2 These findings should alert clinicians to be selective and to base their choice of the treatment modality on the background analysis of gravel passed. A calculus in our environment should be taken to consist of COM, unless it has other distinguishing features such as radiolucency for uric acid calculi.

Uric acid lithiasis seems to be uncommon in Indians. The exogenous hyperuricaemia of obese men in the western world does not occur in our population. Uric acid stones, therefore, may develop in response to a metabolic abnormality, myeloproliferative disease or the use of uricosuric drugs; hence, a thorough evaluation for these conditions in patients with uric acid stones is important. The high success rate of medical dissolution in pure uric acid stones is reassuring, though a Hounsfield density of less than 600 on CT evaluation may be essential in slightly radio-opaque stones, beyond which medical dissolution may fail. The coexistence of oxalates as found in 2 of 4 uric acid calculi may retard chemodissolution.

Using X-ray diffraction, the preponderance of COM in various layers has been found to be as high as 98% in stones seen in Delhi, although the sample size was small.9 Unfortunately, we could not do a layer-wise analysis as most of the stones were in the form of fragments. The clinical relevance of identifying COM and COD separately has not been useful till recently.1 Calcium oxalate can crystallize in three forms: as mono-, di- or tri-hydrates. The trihydrate form is unstable and is not seen in urinary calculi. It has been shown experimentally that the presence of a high calcium/oxalate ratio, citrate and colloidal phosphate favours the formation of dihydrate crystals.10 In clinical studies it has been found that COM stones are seen more commonly in normocalcaemic patients with lack of inhibitor activity, while a combination of COD and phosphates, or COD alone, is more common in patients who have hypercalcemia11 and in young patients with a high urinary pH.12 COM is more stable than COD, the latter changing spontaneously into COM with time. While patients with COD stones are likely to be metabolically active with higher recurrence rates and growth, COM stones grow slowly and have low recurrence rates. Thus most of our patients with COM stones are unlikely to have a derangement in calcium metabolism and should, instead, be investigated for lack of inhibitor activity. Another inference may be that minor stone residues in COM disease following ESWL or PNL management may be acceptable, as there is a low frequency of growth or recurrence; but the same may be unacceptable for COD stones.

Calcium phosphate stones without evidence of infection are an indication of a predisposing disease such as hyperparathyroidism, renal tubular acidosis or medullary sponge kidney. Comparison of patients with idiopathic oxalate and phosphate lithiasis has shown that one-third of patients with idiopathic phosphate stones may have renal tubular acidosis.13 The spectrum of urolithiasis in our population therefore requires a different treatment approach from that in western countries. There is a preponderance of slow-growing COM disease. The data from our hospital, which is a tertiary referral centre, may not be a true indicator of the prevalence and distribution of urolithiasis in the population at large but our findings indicate the need for a larger epidemiological study on urolithiasis in India.

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