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Review

The role of the 24-h urine collection in the management of nephrolithiasis

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HIGHLIGHTS

- Recurrent stone formers should have a full metabolic evaluation including serum chemistries and 24- hour urine collection(s).
- Maintaining urine flow rates above 2.5 l/day reduces risk of formation for all stone types.
- Hypercalciuria is very common in stone formers and is influenced by calcium, sodium, and protein intake.
- Uric acid stone risk is greatest at low urine pH and calcium phosphate stone risk at higher pH values.

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ABSTRACT

Recurrent nephrolithiasis is a common chronic condition that is often preventable with dietary modification and pharmacologic therapy. Patients with recurrent kidney stones should have a metabolic evaluation, consisting of radiologic studies to assess stone burden, crystallographic stone analysis, and laboratory studies including standard serum chemistries and 24 h urine collection(s). This article focuses on the interpretation of urine chemistries to identify lithogenic risk factors and assess the contribution of diet to the formation of kidney stones.

1. Introduction

The goals of metabolic evaluation are to provide a guide for treatment to reduce the risk of stone formation and to identify systemic disease presenting as kidney stone disease. The American Urological Association recommends that an evaluation consisting of a detailed medical and dietary history, serum chemistries, and urinalysis be performed upon initial presentation with a stone [1]. Urine culture should be obtained to rule out urinary tract infection (UTI) if urinalysis is abnormal or if there is a history of recurrent UTIs. If the stone is available, its composition should be determined. Radiologic evaluation should also be performed in all patients at the time of their initial stone event. Many patients have a non-contrast CT scan when they present with their first attack of renal colic. If the symptomatic stone event resolved without radiologic evaluation, a KUB X-ray or an ultrasound can be used to estimate stone burden. Ultrasound is often the preferred technique for children and pregnant women. If multiple stones are found on imaging at their first presentation, the patient should be considered a recurrent stone former and a full metabolic evaluation undertaken. The evaluation includes serum chemistries and 24 h urine collection(s) to identify the patient's specific risk factors for stone disease. In the case of children with stone disease, a full evaluation should be performed at initial presentation. Children are more likely to have inherited diseases such as cystinuria and primary hyperoxaluria as the cause of their stones [2]. The details of the laboratory evaluation of the stone patient are the focus of this article.

2. Serum chemistries and stone analysis

Measurement of serum chemistries is an important part of the

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metabolic evaluation of the stone former. Serum creatinine provides an estimate of kidney function. Electrolytes (sodium, potassium, chloride, bicarbonate) are used to screen for renal tubular acidosis. Serum calcium should be used to screen for primary hyperparathyroidism and other mineral disorders. Even minimal elevations of serum calcium should be repeated and accompanied by parathyroid hormone measurement. Serum chemistries need to be monitored during active drug therapy for stone prevention to diagnose hypokalemia and hyponatremia from thiazides and hyperkalemia from potassium citrate.

Stone analysis should be performed on whatever stones are passed or removed surgically at initial presentation. Optimally, stone analysis should be performed by infra-red (IR) analysis or X-ray diffraction. Optical microscopy is often employed as an adjunct to IR or X-ray [3]. Knowledge of kidney stone composition guides prophylactic therapy along with urine chemistries. Once prophylactic therapy has been initiated, any new stones that form should be analyzed. Patients can form different types of stones and may transform from one stone type to another during medical therapy [4].

3. 24-hr urine chemistries

Current guidelines call for 24-hr urine collection(s) to identify the risk factors leading to stones. The minimum tests recommended by the AUA for a stone evaluation are urine volume, calcium, oxalate, citrate, uric acid, pH, and creatinine [1]. Inclusion of additional tests such as phosphorus, magnesium, sodium, potassium, chloride, urea nitrogen, and sulfate allows better understanding of diet and physiology related to stone formation. Metabolic evaluation is an outpatient process; urine collections are done with the patient consuming their normal diet and pursuing normal activities in order to identify the factors that contributed to the formation of the stones. In-hospital collections should be considered only for young children who may need catheterization to get an adequate sample.

One issue that clinicians need to consider is how many 24-hr urine collections should be performed. In outpatients, serum values are fairly stable day to day, but urine chemistries can vary significantly based on changes in diet and environment [5]. Table 1 shows data on the variability of the key stone risk factors in urine samples done on consecutive days by stone forming patients [6]. Nearly one quarter of urine samples showed at a least a 50% variation in excretion of at least one of the major lithogenic factors. Finding such variations provides the clinician with an opportunity to identify lifestyle or dietary factors that have influenced stone risk. In an optimal situation, the patient has done one collection on a work-day and the other collection when at home as one environment may be particularly conducive to stone formation. Untimed urine specimens are not recommended for evaluation as there are no studies which show sufficiently good correlations between spot urines and 24-hr excretion rates for the main stone risk factors. In some situations, as in children who are not toilet trained, spot urines are used out of necessity.

Reference ranges and stone risk levels for excretion rates in children are usually defined in relation to body size or urine creatinine, which is beyond the scope of this article. When values are presented, they are for an adult population. When interpreting urine chemistries, one should know that definitions of abnormal in the literature are for research. Urine chemistries are continuous variables and strict cut-points of normal and abnormal are somewhat arbitrary. The risk of stone formation increases as values approach the limit of the normal range for lithogenic factors such as calcium, oxalate, citrate and uric acid [7].

4. Volume and creatinine

The volume of urine excreted daily is a critical measurement to guide prevention of nephrolithiasis. Low urine flow is a major risk factor for stones, raising the supersaturation of all stone forming salts. Borghi's prospective trial of high fluid intake provides a reasonable goal for stone forming patients, as the intervention group reduced stone formation by increasing their urine volume to approximately 2.5 L per day [8]. Urine volumes above 2.5 L per day provide even greater benefit, but many patients have trouble maintaining such a high urine flow. Urine flow is determined by the amount of fluid consumed and the amount lost from perspiration and the gut. It is best to provide the patient a goal of urine flow rather than a set fluid intake, since non-renal fluid losses can be difficult to quantify.

Creatinine excretion, not urine volume, should be used to determine the adequacy of a urine collection. Creatinine is a waste product of muscle metabolism; production of creatinine remains stable over time as long as muscle mass does not change. The expected creatinine excretion can be estimated from the subject's weight, with men having a higher creatinine/kg than women on average (male 18–24 mg/kg, female 15–20 mg/kg). Of course, expectations for creatinine/kg values should be adjusted for the patient's body habitus; a muscular young man would be expected to have a higher level than an obese older man. If multiple urines are collected during the initial evaluation, then comparison of creatinine from day to day provides an even better guide of collection quality as the creatinine excretion should be consistent. The same is true of urine collections done in follow up; creatinine excretion should be within 20% of the baseline samples.

5. Calcium

Hypercalciuria (>300 mg/d in men and >250 mg/d in women) is found in approximately 40% of calcium stone formers, making it the most common metabolic abnormality in stone patients. When interpreting urine calcium excretion it is important to take into account dietary intake of calcium, most of which comes from dairy products and calcium supplements. Dietary intake of sodium and protein can also influence calcium excretion [9,10]. Urine sodium and urea excretion can be used to estimate the dietary intake of

Table 1
Variability of 24-h urine chemistries between two consecutive collections.

	At least 30% variability	At least 50% variability
Volume	29.7%	9.6%
Calcium	30.3%	10.1%
Oxalate	15.0%	3.1%
Citrate	16.2%	4.7%
Uric acid	8.3%	2.0%
Any of the above	60.7%	23.4%

Calculated from 70,192 paired urine collections. Only sample pairs with creatinine excretion within 10% were included in the analysis [6].