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Review

Epidemiology, pathophysiology, and management of uric acid urolithiasis: A narrative review

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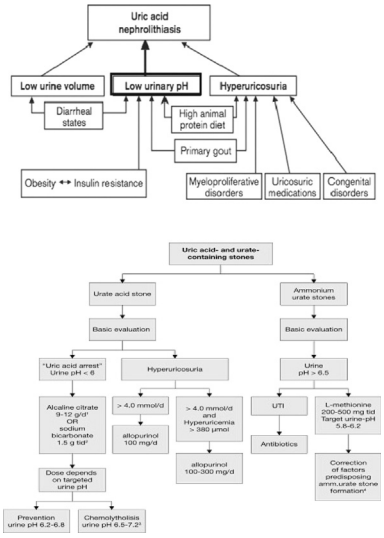
GRAPHICAL ABSTRACT



Quoted from Urolithiasis – EAU Guidelines 2016 with adaptation.

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ABSTRACT

An in-depth comprehension of the epidemiology as well as pathophysiology of uric acid urolithiasis is important for the identification, treatment, and prophylaxis of calculi in these patients. Persistently low urinary pH, hyperuricosuria, and low urinary volume are the most important factors in pathogenesis of uric acid urolithiasis. Other various causes of calculus formation comprises of chronic diarrhea, renal hyperuricosuria, insulin resistance, primary gout, extra purine in the diet, neoplastic syndromes, and congenital hyperuricemia. Non-contrast-enhanced computed tomography is the radiologic modality of choice for early assessment of patients with renal colic. Excluding situations where there is acute obstruction, rising blood chemistry, severe infection, or unresolved pain, the initial management ought to be medical dissolution by oral chemolysis since this method has proved to be effective in most of the cases.

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Background

Uric acid calculi constitutes around 10% of calculi. These calculi are radiolucent and can be efficiently treated with chemolysis as well as endoscopic and surgical procedures. In developed countries the occurrence rates of urolithiasis has constantly increased over years. Calcareous calculi is responsible for the majority of urinary calculi cases followed by uric acid calculi [1]. The pathogenesis of uric acid urolithiasis is somewhat is still unclear. The risk factors include persistently low urinary pH, hyperuricosuria, and low urinary volume [2]. Diseases that causes hyperuricosuria and predispose to uric acid urolithiasis include uncontrolled diarrhea, myeloproliferative conditions, resistance to insulin encompassing diabetes mellitus, and monogenic metabolic conditions for instance Lesch-Nyhan condition. Researchers detected a gene linked to uric acid calculus formation; however, its purpose is yet to be well defined [3]. The clinical presentation of patients with calculi are usually the same irrelevant to the composition of the calculus. Among others, some of these signs and symptoms consists of; loin dull aching or colicky pain, nausea and vomiting, fatigue, lower urinary tract symptoms, and hematuria. Non-contrast computerized tomography of the urinary tract is the modality of choice in the diagnosis of uric acid calculi, and has the ability to detect calculi with a low attenuation coefficient value. Medical dissolution treatment approach is effective in most of the cases except in certain situations where there is rising blood chemistry, advanced uremia, sepsis, or constant pain. From that perspective, it can therefore be explained that uric acid calculi are without a doubt exceptional as they liquefy readily in an ideal urinary pH milieu, attainable with oral medical intervention.

Purine and uric acid metabolism

Uric acid (2,6,8-trioxypurine) is the final product of purine metabolism and has no known physiological function in humans. Uricase enzyme is lacking in humans and found in most mammals convert uric acid to allantoin (10–100 times more soluble). Urinary concentration of uric acid depends on urine pH, urine volume and excretion of uric acid. Urinary pH is the most important factor of uric acid solubility. Loss of a single proton from uric acid and hence dissociation of uric acid is controlled by two dissociation constants (p*K*a). The first p*K*a of pH 5.5, govern the conversion of uric acid to the more soluble anionic urate. The second p*K*a of pH 10.3 is not clinically significant sine the mean human urine pH is 5.9 and normally ranges from 4.8 to 7.4. At a urinary pH < 5.5 almost 100% of uric acid is undissociated and urine will be supersaturated with uric acid. Inversely, at a pH of >6.5 the majority of the uric acid in the form as anionic urate [4].

Endogenous sources

Under normal conditions, nearly 300–400 mg/dL is produced from de novo synthesis and tissue catabolism. Abnormally high synthesis of uric acid occur with gout, myeloproliferative disorders, certain congenital metabolic defects and patients receiving chemotherapy due to rapid cell turnover.

Exogenous sources

High purines diet e.g. meat, animal organs, fish, sweetbreads, and yeast.

In the intestinal tract, purine → free nucleic acids → inosinic acid → hypoxanthine → xanthine (by xanthine oxidase) → uric acid [5].

Kidney handling and elimination

The kidney excretes two-thirds of uric acid. Skin, nails, hair, saliva, and the gastrointestinal tract (GIT) eliminates the remaining third. In the GIT, bacteria convert part of the uric acid to ammonia and carbon dioxide, which is expelled as gas. Ammonia is either absorbed and excreted in the urine or utilized by bacteria as an energy source [6].

The majority of serum uric acid (95%) is in the form of monosodium urate and is freely filtered at in the glomeruli, while the remaining is protein bound. Ninety-nine percent of the filtered urate is reabsorbed in the proximal convoluted tubule (PCT) through complex successive reabsorption, secretion, and again reabsorption and 50% is then secreted back into the PCT. Post secretory absorption of 80% of this urate occurs in the distal PCT. Therefore, about 10% of the filtered urate is excreted in the urine. The fractional excretion of urate ranges from 60% in a premature neonate to 12% in a 3 children and 7% in the adults [7,8].

Medications and factors affecting the renal handling of uric acid

The most important factors that affect the renal handling of uric acid include patient's hydration status and urine output, serum urate concentration, medications and extra-cellular volume expansion that is inversely proportionate to serum urate concentration. Salicylates, sulfinpyrazone, and probenecid are uricosuric through blocking urate absorption in the PCT. The hyperuricosuria caused by of thiazides is by producing extra-cellular volume depletion and hence increases urate secretion in the PCT. Hyperuricosuria during pregnancy is due to fetal urate production and increased intravascular volume [9,10].

Epidemiology

The incidence of uric acid calculi varies geographically, the worldwide incidence ranges from 5 to 40%. The frequency of nephrolithiasis in the US is approximated to be about 0.5% a year a prevalence rate that can be explained as been on the increase [10]. Indeed, when the data from US National Health and Nutrition Examination Survey II and III is summarized, it was reported that the calculus diseases occurrence rate has up surged from 3.8% in the year 1976 to 5.2% in the year 1980 to 1994 in most developed countries [11]. Similarly, the yearly economic expenses linked to the condition have also increased from a reported $1.3 billion in the year 1994 to a reported $2 billion in the year 2000 irrespective of the fact that various measures such as minimally invasive processes, decrease in periods of hospitalization, and changes in the care offered in outpatient clinics have been adopted [12].

Uric acid nephrolithiasis has been found to account for about 7–10 percent of all calculi. Calculi isolated from patients that were in the Administration System of the Veterans found that about 9.7% were made up only of uric acid. In another large series, it was reported that uric acid calculi was detected in the 7 percent of the calculi that were studied. Most authors consider this incidence is a miscalculation of the true frequency; however, it indicate the importance of this condition [13,14].

The occurrence of uric acid calculi differs with; age, sex, demographics, and even the local environmental aspects. For instance, patients who are more than sixty-five years were reported to develop uric acid calculi twice the prevalence in youth patients in a retrospective research that has six thousand patients Males were found to be more to females approximately by three times [15,16].

The variance in the ratio of uric acid calculi might also vary between various ethnic groups. Half of the Hmong patients that