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Review Article

Kidney Stone Disease: A Brief Review

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Abstract

Kidney stone disease is the crystal formation within the kidneys. It's affecting about 12% of the population. It is associated with increased risk of the renal–failure. The most common type of stone formation is calcium oxalate formed at Randall's plaque on the renal papillary surfaces. The mechanism of stone formation involves nucleation, crystal growth, aggregation, and retention of urinary stone constituents within the kidney. An imbalance between factors that encourage or inhibit urinary crystallization modulates these steps.

Keywords: Kidney Stone; Calcium Oxalate

Introduction

Overview of kidney stones

Kidney stones are mostly found in the kidney. And it's the most serious urinary tract infection.Preventing the recurrence of renal stone remains a serious human health problem. Preventing stone recurrence requires a better understanding of the mechanisms involved in the formation of stone [1].

Kidney stones were associated with an increased risk of chronic renal diseases, renal failure at the end of a the stage, cardiac disease, diabetes and hypertension. Kidney stone signs are linked to the destination in the kidney, ureter, or urinary bladder. Initially, there's no sign of stone creation. Eventually, stone disorder clinical signs consist of renal colic (intense cramping pain), flank pain (back pain), hematuria (bloody urine), obstructive uropathy (urinary tract disease). Infections of the urinary tract, blockage of the flow of urine and hydronephrosis (kidney dilation). These conditions can contribute to nausea and vomiting induced by the stone event [2].

Epidemiology of kidney stones

Urolithiasis affects about 12% of the world population in their lifetime and at a certain stage. It affects all ages, sexes and races, but occur more often than in men than in women between certain ages of 20 and 49. If patients can not apply metaphylaxis, the remission rate of secondary stone formations is reported at 10–23% per year, 50% in 5–10 years and 75% in 20 decades of the patient [3].

Recent studies has shown that the incidence of urolithiasis has increased over the past decades in both developing countries. This trend is believed to be linked to shifts in lifestyle changes such as lack of exercise and nutritional habits.

Kidney stone affects 1 in 11 people in the United States, and it is estimated that every year 600,000 Americans are suffering from urinary stones. In the Indian population, approximately 12% of them will be projected to have urinary stones and 50% of them may end up with renal function failure [4].

The urinary system and stones

The urinary filtrate is produced in the glomerulus and flows through the tubules where the volume and material shift due to reabsorption or secretions. Most of the solute reabsorption occurs in the proximal tubules, whereas in the distal tubule, as well as in the collection of ducts, subtle variations in urine composition occur. loop of henle's helps to concentrate 95% water, 2.5% urea, 2.5% mineral, salt, hormone, and enzyme mixture urine. In the proximal tubules, fructose, sodium, chloride and water are reabsorbed and added to the bloodstream together with essential nutrients such as

amino acids, proteins, bicarbonate, calcium, phosphate and potassium. Salt and acid base balance in the distal tubule [5].

Types of kidney stones

Calcium stones: calcium oxalate

Calcium stones are predominant renal stones comprising about 80% of all urinary calculi, Calcium oxalates stone are crystalline component of calcium oxalate monohydrate, calcium oxalate dihydrate and calcium oxalate trihydrate.

Calcium phosphate

Calcium phosphate stone includes crystalline components such as hydroxyapatite, calcium hydrogen phosphate, dihydrate, rare calcium phosphate shape, tricalcium phosphate, ammonium magnesium, phosphate hexahydrate, ammonium magnesium, phosphate monohydrate, magnesium hydrogen, phosphate trihydrate, apatite carbonate and octacalcium phosphate. There are calcium oxalate stones and calcium phosphate rocks. In urinary system like hypercalciuria, hypomagnesuria, hyperuricosuria, hyperoxolourea and hypocitraturia [6].

Uric acid stones or urate

Uric acid stone is a crystalline component of uric acid anhydrous and uric acid dehydrate, with uric acid stone usually affecting 5-10% of the analyzed population of renal stone. Uric acid is a metabolic product and gout disorder also affects about 25 percent of patients with this block. Low urine volume, hyperuricosuria and acid urine pH (pH < 5.05) are the main reasons for this type of stone.

Cystine stone

Cystine stone is caused by cystine in the urine due to high levels of essential amino acid. Cystine stone usually occurs in childhood and is a rare hereditary metabolic disorder that affects 1-3% of the studied kidney stone population.

Struvite stone

Struvite stone is an infectious urinary stone of hexahydrate or struvite ammonium magnesium phosphate. It is a fascinating inorganic mineral of phosphate closely associated with chronic urinary tract infection due to certain microorganisms such as bacteria causing urease. The bacterium transforms urea into ammonium in combination with magnesium and phosphate. Phosphate is less soluble in alkaline than in acidic pH, so phosphate precipitates on to the insoluble ammonium products, yielding to a large stag horn stone formation.

Drug –induced stone

Renal stone drugs are produced by renal calculus due to excessive high intake of drugs such as ephedrine, ciprofloxacin, guaifenesin, indianvir, nelfinavir, xypurinol, topimarate, sulfa and triamterene. Individuals taking indinavir sulphate protease inhibitor, a drug used to treat HIV infection, are at risk of developing kidney stones. Such lithogenic drugs or their metabolites may be deposited to form a nidus or already present on renal calculus. On the other hand, these drugs can induce calculus formation by interfering with calcium oxalate or purine metabolisms through their metabolic action [7].

Mechanism of action

Stone forming processes include nucleation of stone constituent crystals, their growth or accumulation to a size that may interfere with some intra-renal structure, persistence within the collection system of the kidney or renal, and further aggregation and/or secondary nucleation to form the clinical stone.

Nucleation

Nucleation is the method of associating free ions into microscopic particles in the solution. Crystallization can occur in microenvironments of solution, as can occur at certain points in the nephron, as well as on surfaces such as cells and extracellular matrix.

There is considerable controversy over the value of free solution crystallization versus crystallization at other locations, in renal tubules or on bladder walls, in normal or broken cells, in areas denuded by certain types of injury, or in interstitial sites [8].

Crystal growth

Microscopic crystal growth is accomplished by transferring ions out of solution to the growing crystal. While some growth of nuclear crystals must occur through the movement of ions from solution, this is clearly a limited process, since giant single crystals of stone constituents are generally not observed. Stone growth is more likely to be accomplished by aggregating preformed crystals or secondary crystal nucleation on another's matrix-coated layer. It has been suggested that the development of these microscopic crystals cannot occur without aggregation or attachment to different intra renal structures to the degree that they can be maintained in the kidney on the basis of size alone. It has been proposed that the growth of these microscopic crystals to the extent that they can be retained in the kidney on the basis of size alone cannot occur without aggregation or attachment to specific intra renal structures [9].

Aggregation

Aggregation is a process through which crystals are agglomerated that form into larger multicomponent particles in a free solution. It may also include the secondary nucleation phenomenon of new crystals on the surface of those already formed. Stones are an accumulation of crystals and an organic matrix, which is the binding agent. The organic matrix includes proteins, lipids, polysaccharides and other substances derived from cells [10].

Crystal-Cell interaction

The attachment of grown crystals to the renal tubular lining of epithelial cells is referred to as crystal retention or contact between crystal cells. Renal tubular epithelial cells were injured in individuals with hyperoxaluria due to exposure to high concentrations of oxalates or sharp crystals of calcium oxalate monohydrate (COM).

Crystal cell contact results in the passage of crystals to the basement membrane from the basolateral side of the cells. COM crystal's contact with the renal epithelial cell surface could be a crucial initiating activity in nephrolithiasis.

The increased retaining pressure between the epithelium cells of the crystal and the weakened renal tubule facilitates CaOx crystallization. Some crystals attached to epithelial cells are believed to be digested in cells by macrophages and/or lysosomes and then discharged with urine [11].

After renal tubular cell injury, cell degradation produces numerous membrane vesicles that are calcium crystal nucleates as supported by in-vitro and in-vivo studies. Injured cells release substances such as renal prothrombin fragment-1 or other anionic proteins that cause agglomeration of COM crystals. One of the factors involved in renal cell injury is considered to be reactive oxygen species. Renal oxidative stress reduction could therefore be an effective treatment choice.

Injured cells potentiate to invert their anionic cell membrane to the urinary environment and act as a site of adherence to crystals. COM crystals have a greater attachment to the inverted anionic membrane than crystals with calcium oxalate dihydrate (COD) [12].

Endocytosis of CaOx crystals

Endocytosis or crystal swallowing by renal tubular cells is the earliest process in the formation of renal stones. Studies on crystal-cell tissue culture interactions showed that COM crystals quickly adhere to microvilli on the surface of the cell and then internalize it. Polyanion molecules present in tubular fluid/urine such as glycosaminoglycans, glycoproteins and citrate can coat crystals and inhibit the binding of COM crystals to the cell membrane [13].

Cell injury and apoptosis

Exposure to high oxalate or CaOx crystals contributes to epithelial cell damage, which is a predisposing factor for the subsequent formation of stone. CaOx crystal deposits in the kidneys up regulate the macromolecules expression and synthesis that can promote inflammation.

Crystals can be transported to the interstitium or endocytized by cells. Injured cells have been suggested to develop a nidus that promotes particle retention on the renal papillary surface [14].

Randall's plaques

While urine is not generally supersaturated with respect to calcium phosphate, such conditions may exist in Henle's loop. This may result in calcium phosphate precipitation in the inner medulla at interstitial sites. These deposits often become large enough in the form of Randall's Plaques to be visible macroscopically. Such deposits have been suggested to serve as a nidus for the production of the most common variety of calcium oxalate stones. Several studies have shown that stones tend to have been directly attached to the plaque of the Randall's which has eroded on the surface of a renal papilla through the overlying uroepithelium [15].

Although Randall's plaques appear to be a risk factor for stone formation, it is still uncertain whether they are required in any forming stone, as both intra tubular crystals and prominent crystalluria are characteristics of stone disease.

Kidney stone inhibitors and promoters

Inhibitors are substances that reduce the initiation of supersaturation, nucleation, crystal growth, aggregation rate, or any other processes required for the formation of stones. Typically, it contains chemicals that prevent the formation of crystals.

Urine blockers include small organic anions like citrate, small inorganic anions like pyrophosphates, multivalent metal cations like magnesium, or macromolecules like osteopontin, glycosaminoglycans, glycoproteins, urinary tract. prothrombin fragment-1, and proteins of Tamm – Horsfall.

These inhibitors do not appear to work for everyone on an equal footing; therefore, some people develop stones. However, if formed crystals remain tiny, they usually travel through the urinary tract and splash out of the body without being noticed.

Inhibitors can act either directly or indirectly by influencing the urinary environment. By interacting with the crystal [16]. When inhibitory compounds adsorb on the crystal surface, nucleation, crystal growth, aggregation or adherence to crystal cells is inhibited.

In addition, promoters are substances that stimulate the creation of stones through different mechanisms. Other promoters include cell membrane lipids (phospholipids, cholesterol, and glycolipids), enhancement of calcitriol hormone by activating parathyroid hormone, oxalate, calcium, sodium, cystine, and low urine. The excretion of urinary oxalate was found to be higher among recurrent stone formers, whereas the excretion of citrate was lower. Studies have shown that oxalate in the proximal tubule can increase the reabsorption of chloride, sodium, and water and activate multiple signalling pathways in renal epithelial cells. In general, an imbalance has been suggested between urinary stone inhibitors and promoters [17].

Preventive options for urolithiasis

Kidney stone can be avoided by addressing the cause of stone formation. The first episode of kidney stone formation or secondary episodes, proper diet control and the use of suitable medicines. The underlying etiology and drug treatment for stone disorders, patients can take more water/liquid at least 2 litres per day. High sodium intake increases the risk of stone by reducing the reabsorption of renal tubular calcium and increasing urinary calcium. You may need to eat less meat, fish and poultry if you have very acidic urine and avoid vitamin D food. It is recommended to increase the intake of potassium-rich fruits and vegetables.

Those who get calcium stones used to be advised to avoid dairy products and other calcium-rich foods because of invivo conversion of ascorbic acid to oxalate, vitamin C was involved in stone formation. Therefore, it is recommended to reduce the intake of vitamin C [18].

Urine should be alkalinized to avoid calcium oxalate, cystine, and uric acid stones by eating a diet rich in fruits and vegetables, taking additional or prescription citrate, or drinking alkaline mineral waters. Gout needs to be controlled for uric acid stone formers, and sodium and protein intakes need to be limited for cystine stone formers. Urine should be acidified to remove calcium phosphate and struvite particles. For struvite rocks the most important step is to acidify the urine [19].

Conclusion

Despite significant advances in the development of new treatments for urinary stone treatment, the incidence of urolithiasis is growing throughout the world. Many aspects of the formation of the renal stone remain unclear. It is certain, however, that renal cell damage, crystal retention, cell apoptosis, randal's plaque and associated stone inhibitors or promoters play important roles in the formation of kidney stone. These seem to be important targets contributing to the development of a new approach to avoid kidney stone disorder and kidney stone medications. In addition, discovering new therapeutic targets in relation to stone formation based on molecular and cellular changes can help develop better drugs.

In addition, discovering novel therapeutic targets in relation to stone formation based on molecular and cellular modifications can help develop better drugs. In turn, better understanding of urolithiasis pathways associated with stone inhibitors or promoters will be critical for stone-removing medications.

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