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"TARGETING KIDNEY STONES" -LOOKING FOR THE FUTURE

Medicine

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ABSTRACT

Urine is filtered blood.It is normally slightly acidic. High levels of calcium in the urine may produce kidney stones. Some rare hereditary diseases also predispose some people to form kidney stones. People with renal tubular acidosis and people with problems metabolizing a variety of chemicals including cysteine, oxalate, and uric acid.Urolithiasis is a global problem. Dietary plants and their phytonutrients could be useful in the prevention and intervention of urolithiasis. Since natural dietary recommendation for patients with the risk of kidney stones are poorly provided and patients often request instructions for a beneficial dietary regimen,it is essential for physicians to have evidence-based knowledge regarding the efficacy Pharmacological mechanisms and side effects of the administration of a protective dietary regimen more investigations using clinical trials are needed to confirm the efficacy and safety of these dietary agents in patients with kidney stones. Systemic diseases such as hypertension,diabetes mellitus and hypercholesterolemia;infection; antibiotics,chemotherapeutics and radiocontrast agents and environmental toxins,occupational chemicals,radiation,smoking,as well as alcohol consumption induce renal oxidative stress.Kidney is highly vulnerable organ to damage caused by ROS(Reactive oxygen species) ,due to abundance of long-chain-polyunsaturated fatty acids Cystinuria is an incompletely dominant disorder characterized by defective urinary cystine reabsorption that results in the formation of cystine-based urinary stones.

KEYWORDS

Nephrolithiasis,calcium oxalate ,reactive oxygen species (ROS),Oxidative stress(OS),Uric acid, Calcium oxalate monohydrate(COM)

INTRODUCTION

This review explores possible reactive oxygen species involvement in plaque formation and calcium oxalate nephrolithiasis.(1) Antibiotics, chemotherapeutics, and radiocontrast agents; and environmental toxins, occupational chemicals, radiation, smoking, as well as alcohol consumption induce oxidative stress in kidney.(2) Oxidative stress has been the centre of focus in most of the research, and in the field of medicine it takes a special place especially in diseases associated with kidneys.(3)Kidney stones are comprised of mineral and organic components. Approximately 80% of the kidney stones contain calcium oxalate (CaOx) as the major mineral phase mixed mostly with calcium phosphate (CaP) and sometime uric acid.(4)They can also produce chemical modifications of, and damage to proteins, lipids, carbohydrates and nucleotides (5,6).When the stones increase in size, they progress with serious damage to the kidney, even with no clinical evidence, and can present complications, such as urinary tract obstruction and infection.(7)The literature has shown a greater incidence of nephrolithiasis in males; however, recent investigations have pointed to an increased incidence in females.(8)After a first stone episode, up to 50 percent of patients have at least a second stone within 10 years. (9)Uric acid stones are usually formed in people with gout or gouty arthritis. They can also form in patients with chronic diarrhea caused by Crohn's Disease and ulcerative colitis. The drug Allopurinol is also used to reduce uric acid excretion via the kidneys.(10)Using the nephrolithic animal model, Lin et al. reported that *Flos carthami*, an herbal plant, prevents stone formation in ethylene glycol (EG)-treated rats.(11) Traditionally, Ganoderma had been used from times immoral and is claimed to reduce the ill effect of various diseases and virtually cure all types' diseases. (12,!3)Calcium-containing stones are the most common kidney stones (75–90%). (14)The mechanisms related to the development of kidney stones are not completely understood. Generally, (15)Among all the pain, abdominal pain always dragsnot only patient's attention but also the curiosity of the surgeon. Theinformation regarding *Ashmari (16,17)* is available in almost all *samhita*(Ancient treatise) of Ayurveda.Urolithiasis is characterized by the creation of solid deposits inside of the urinary tract. It continues to be an important factor in chronic renal disease leading to chronic tubular interstitial nephritis, which is involved in 15%–20% of end-stage chronic kidney insufficiency.(18). It is expected that 11% of men and 5.6% of women in United States will develop solid deposits in their urinary tract by the age of seventy (19)

Nephrolithiasis is a chronic disease involving imbalance between crystallization of largely calcium salts & inhibition of crystal formation or their dissolution.(20).

HISTORY

The existence of kidney stones was first recorded thousands of years ago, and lithotomy for the removal of stones is one of the earliest known surgical procedures. (21) In 1901, a stone discovered in the pelvis of an ancient Egyptian mummy was dated to 4,800 BC. Medical texts from ancient Mesopotamia, India, China, Persia, Greece, and Rome all mentioned calculous disease. Part of the Hippocratic Oathsuggests there were practicing surgeons in ancient Greece to whom physicians were to defer for lithotomies. The Roman medical treatise *De Medicina* by Aulus Cornelius Celsus contained a description of lithotomy. (22)and this work served as the basis for this procedure until the 18th century. (23)

Famous people who were kidney stone formers include Napoleon I, Epicurus, Napoleon III, Peter the Great, Louis XIV, George IV, Oliver Cromwell, Lyndon B. Johnson, Benjamin Franklin, Michel de Montaigne, Francis Bacon, Isaac Newton, Samuel Pepys, William Harvey, Herman Boerhaave, and Antonio Scarpa. (24) After Henry Jacob Bigelow popularized the technique of litholapaxy in 1878,(25) the mortality rate dropped from about 24% to 2.4%. However, other treatment techniques continued to produce a high level of mortality, especially among inexperienced urologists. (23,24) In 1980, Dornier MedTech introduced extracorporeal shock wave lithotripsy for breaking up stones via acoustical pulses, and this technique has since come into widespread use. (26)

MAJOR ADVANCES AND DISCOVERIES

-- High doses of Vitamin B6 reduce the risk of kidney stone formation i women. In addition, these prospective data do not support the belief that the risk of stone formation rises with the increased intake of Vitamin C.(27). Patients on renal replacement therapy, Lipoic acid (LA) supplementation did not influence creatine concentration or GRF values which indicates that LA administration in this group of patients is not reasonable. However,LA administration in non dialyzed patients seems promising since the obtained results indicate that 30-day LA supplementation in these patients led to to the mean reduction of creatinine concentration.(28)Various studies showed that oxidative stress occurs in patients with kidney stones CAO exposure causes oxidative damage by reactive oxygen species such as super oxide and H2O2. The produced ROS activates several signaling pathways. Inflammation can be induced by ethylene glycol. Renal damage is associated with oxidative stress. Antioxidants in royal jelly is considered to show anti inflammatory effects by affecting the signaling pathways. Further cell culture studies will help to clarify the mechanism.(29) Mineralization of collagen leds to the growth of the plaque,which eventually reaches the papillary epithelium, ulcerated to to the surface and develops in to a stone nidus. Once exposed to the pelvic urine, the plaque is overgrown by CaOx crystal, and promotes the formation of an idiopathic CaOx crystal and promotes the formation of an idiopathic CaOx kidney stone attached to the subepithelial RP (30)

WHERE THE RESEARCH GO NEXT?

Dietary plants and their phytonutrients could be useful in the prevention and intervention of urolithiasis. Since natural dietary recommendation for patients with the risk of kidney stones are poorly provided and patients often request instructions for a beneficial dietary regimen,it is essential for physicians to have evidence-based knowledge regarding the efficacy Pharmacological mechanisms and side effects of the administration of a protective dietary regimen more investigations using clinical trials are needed to confirm the efficacy and safety of these dietary agents in patients with kidney stones.(31)There is a growing evidence that cholesterol administration or 25-hydroxy vitamin D serum levels,in the higher ranges, may increase urinary calcium excretion and kidney stone formation in predisposed individuals or specific groups of patients.Over the past few decades,the observation of an association between loe levels of circulating 25 hydroxyvitamin D serum levels and a broad spectrum of diseases has been the origin of a dramatic increase in the prescription of vitamin D.However most of the studies evaluating the effect of Vitamin D administration, including studies dedicated to bone fractures, did not demonstrate a significant benefit of vitamin D..(32,33)

SIGNIFICANT GAP IN RESEARCH

Many inborn errors of metabolism,such as cystinuria and primary hyperoxaluria,provide examples of hereditary disease characterized by excessive production and excretion of stone forming substances.In about 5% of patients with hypercalcemia and hypercalciuria, occurs with hyperparathyroidism,diffuse bone disease,sarcoidosis and other hypercalcemic states About 55% have hypercalciuria with out hypercalcemia.As many 20% calcium oxalate stones are associated with increased uric acid secretion with or without hypercalciuria.Stones are unilateral in about 80% of patients.The favoured sites for their formation are with in the renal calyces and pelvis and the bladder.These may have smooth contours or may take the form of an irregular,jagged mass of spicules.Often many stones are found with in one kidney.On occasion,progressive accretion of salts leads to the development of branching structures known as staghorn calculi,which creates a cast of the pelvic and calyceal system(34).

CURRENT DEBATE

Kidney stones are solid concentrations formed in the kidneys from dissolved urinary minerals.Bladder stones can form or pass in to urinary bladder.Usually,kidney stones form when the urine becomes concentrated to a great extent.The most common varieties of calculi examined are Calcium oxalate monohydrate(COM) and hydroxyapatite (HAP) have the potential to take on prickly,tentacle-like forms,generating a painful experience for the patient..Other common components of calculi include calcium oxalate dihydrate(COD) (35)Systemic diseases such as hypertension,diabetes mellitus and hypercholesterolemia;infection; antibiotics, chemotherapeutics and radiocontrast agents and environmental toxins,occupational chemicals,radiation,smoking,as well as alcohol consumption induce renal oxidative stress.Kidney is highly vulnerable organ to damage caused by ROS(Reactive oxygen species) ,due to abundance of long-chain-polyunsaturated fatty acids.(36) Cystinuria is an incompletely dominant disorder characterized by defective urinary cystine reabsorption that results in the formation of cystine-based urinary stones (37)

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