The Role of the Pharmacist in the Management of Kidney Stone Disease

Self-Assessment Questions

1. Which of the following is the most common type of kidney stone seen in the general population:

   A. Calcium***
   B. Uric acid
   C. Struvite
   D. Cystine

   Answer: A
   The 4 stated options are different types of kidney stones. Calcium stones, whether they are oxalate- or phosphate-type stones, are the most common, accounting for approximately 80% of all stones. The majority of calcium type stones are oxalate stones.

2. When kidney stones start to develop there are many different changes that occur. Which of the following changes in the urine explains why kidney stones can develop in the kidney or ureter:

   A. Solubility and precipitation of salts become balanced
   B. Increased urine output caused by excessive fluid intake
   C. Increased urination because of the use of a thiazide diuretic
   D. Insoluble materials become supersaturated***

   Answer: D
   When solubility and precipitation in the urine is balanced, risk of kidney stones is small. Excessive fluid intake to the point that there is an increase in urine output will minimize formation of kidney stones. Similarly, increased urination because of a thiazide diuretic would, if anything, have a positive effect of decreasing the risk of stone development because it decreases release of calcium into the urine. The only changes that increase stone formation are related to the supersaturation of insoluble materials. When insoluble materials become supersaturated, they crystalize. This crystallization leads to the development of a kidney stone.

3. Which of the following chronic medical conditions can increase the risk of kidney stone disease:

   A. Hypertension
   B. Type 2 Diabetes***
   C. Osteoporosis
   D. Chronic Obstructive Pulmonary Disease (COPD)

   Answer: B
   Hypertension, osteoporosis, or COPD have not been identified as independent risk factors for the development of kidney stones. There is no underlying mechanism identified with any of these diseases that would explain an increased risk of kidney stones. However, diabetes has been identified as a risk factor for kidney stone development. The underlying insulin resistance seen in
patients with type 2 diabetes has been linked to a more acidic urine pH, which facilitates stone formation. It has been estimated that patients with diabetes have a 59% higher odds of developing kidney stones. Some of this may also be attributed to obesity, which also increases risk of kidney stones.

4. Of the following dietary eating patterns, which can increases risk of stone formation:
   A. High fluid intake
   B. High ingestion of citric acid based drinks
   C. Low intake of animal protein
   D. Low intake of calcium foods***

   **Answer: D**
   High fluid intake is actually a strategy to prevent the recurrence of kidney stones, so it is not a risk factor for the development of stones. Increased ingestion of citric acid-based drinks seems to have little effect on the recurrence of kidney stones (unlike cola-based drinks, which seems to increase recurrence), as does limiting the intake of animal protein. However, maintaining a low intake of calcium foods can promote calcium-type stone development by decreasing calcium binding in the gut, which can increase oxalate absorption and urinary excretion.

5. A man, 50 years of age, with a history of hypertension, dyslipidemia, and diabetes is vacationing in the Colorado Rocky Mountains. His current medications are metformin, atorvastatin, and hydrochlorothiazide. He starts taking acetazolamide to prevent altitude sickness the day prior to his vacation. After 5 days, he is diagnosed with a kidney stone. Which of the following medications was a risk factor for this patient developing acute kidney stone disease:
   A. Acetazolamide***
   B. Atorvastatin
   C. Hydrochlorothiazide
   D. Metformin

   **Answer: A**
   Acetazolamide is a carbonic anhydrase inhibitor. Use of this drug can result in metabolic acidosis that can cause alkaline urine and hypocitraturia. These effects can lead to stone formation, so acetazolamide is a drug that can cause kidney stones. Atorvastatin and metformin have no effect on kidney stone development, although they are often used to treat patients with insulin resistance, which in itself can increase risk of kidney stones. Moreover, hydrochlorothiazide is a treatment to prevent stone recurrence and is not a secondary cause.

6. Which of the following drugs is most effective when used in medical expulsive therapy (MET) for the treatment of kidney stones:
   A. Carvediolol
   B. Doxazosin
   C. Tamsulosin***
   D. Terazosin

   **Answer: C**
All the drugs listed have alpha blocking effects. However, options A, B, and D are primarily antihypertensive medications that have nonselective alpha blocking effects. Tamsulosin is the only uroselective alpha blocker listed and is most studied in MET. This is because it acts on the $\alpha-1D$ receptor that is predominant in the ureter and more heavily found in the distal ureter. Antagonism of this receptor can result in a reduced frequency and force of ureteral contraction, and can aid stone passage.

7. Which of the following is the most appropriate first-line treatment for a patient with an 8 mm calcium oxalate stone who has well-controlled symptoms?

   A. MET***
   B. Shock-wave lithotripsy (SWL)
   C. Ureteroscopy
   D. No therapy because the stone should pass on its own

Answer: A
MET is considered the first-line treatment for the acute management of kidney stones that are small (< 10 mm) and associated with well-controlled symptoms, according to the American Urologic Association. Though kidney stones may pass on their own, MET is recommended for initial therapy to expedite resolution. The 2 listed procedures, SWL and ureteroscopy, are recommended when stones do not pass spontaneously, typically after MET has been attempted. They may also be an initial treatment option for larger (> 10 mm) stones or other, more severe, presentations (i.e., struvite stones).

8. A woman has a history of recurrent calcium stones. Which of the following diuretics is most effective for preventing the recurrence of stone formation in this patient:

   A. Chlorthalidone 25 mg daily
   B. Furosemide 20 mg twice daily
   C. Hydrochlorothiazide 12.5 mg daily
   D. Spironolactone 25 mg daily

Answer: A
Spironolactone, as an aldosterone antagonist that has some diuretic effect, does not alter urinary calcium and is not effective in reducing the recurrence of calcium stones. Furosemide, being a loop diuretic, will not lessen the risk of stone recurrence. It can increase calcium excretion in the urine and this would not have a positive effect on calcium stone recurrence. Thiazide and thiazide-like diuretics decrease calcium in the urine and are used to lessen calcium kidney stone recurrence. Both hydrochlorothiazide and chlorthalidone may be used, but an effective dose is needed for the most efficacious response. A 12.5 mg daily dose of hydrochlorothiazide is too low (25 to 50 mg daily is recommended), but chlorthalidone 25 mg daily is considered a therapeutic dose.

9. Allopurinol is effective for minimizing stone recurrence in patients with which of the following characteristics:

   A. Obesity
   B. Type 2 diabetes
   C. Hyperuricosuria***
D. Struvite-type stones

Answer: C

Although patients with obesity and/or type 2 diabetes are at risk for developing kidney stones, patients with these comorbidities are not necessarily candidates for allopurinol therapy. Allopurinol is a xanthine oxidase inhibitor, which decreases the production of serum uric acid. High serum uric acid can lead to hyperuricosuria, which is the patient population that would respond best to allopurinol. Struvite-type stones are infectious stones and do not respond to allopurinol therapy.

10. Which of the following treatments is effective for decreasing stone recurrence:

   A. Potassium citrate for calcium oxalate stones
   B. Tiopronin for cysteine stones
   C. Acetohydroxamic acid for struvite stones
   D. All of the above are effective treatment for the stated stone type***

Answer: D

All of the answer options represent effective treatments for the listed stone type. Potassium citrate helps patients with hypocitraturia by increasing citrate in the urine. This can decrease crystallization and also prevent the urine from becoming too acidic, both of which will decrease stone recurrence. Tiopronin works by making cystine more dissolvable in the urine and can reduce cystine stone recurrence. Acetohydroxamic acid is a bacterial urease inhibitor that can have positive effects on struvite stones, which are infectious stones, by decreasing urinary ammonia and alkalinity. While this treatment is typically an alternative to surgery to remove struvite stones, acetohydroxamic acid can enhance the effectiveness of antimicrobial agents and allow an increased cure rate of these infections.