CLINICAL UPDATE

Diagnosis and Management of Urinary Tract Stone in Family Practice

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Background: Urinary tract stones or calculi are low-density crystals in any part of the urinary tract that result from either excessive excretion or precipitation of salts in the urine or lack of substances to inhibit its formation. Prevention and management of urinary tract stones is also now medically feasible and recommended.

Objectives: This clinical pathway was developed to guide family and community physicians on the diagnosis and initial management of urinary tract stone in terms of: 1) clinical history and physical examination; 2) laboratory and ancillary procedures to be requested; 3) pharmacologic interventions; 4) non-pharmacologic interventions; and 5) patient outcomes to expect.

Methods: The PAFP Clinical Pathways Group reviewed the previous guidelines for the treatment of urinary tract stones, published medical literature (PubMed and HERDIN) to identify, summarize, and operationalize the clinical content of diagnostics, interventions and clinical indicators or outcomes to develop an evidence-based clinical pathway in family medicine practice.

Recommendations: Family physicians should elicit patient history of flank pain, tenderness, dysuria and hematuria. They must be described in detail in terms of, characteristics, date of onset and severity. Other patient history to elicit should include stone passage, recurrent UTI, dietary history, fluid intake, recurrent UTI, medications and family history of being a stone former or some metabolic disorder. The laboratory should include ultrasound of kidney, ureter and bladder (plain CT is second line imaging study), urinalysis and blood chemistry (BUN, creatinine, calcium and uric acid). Symptomatic treatment with non-steroidal anti-inflammatory drugs or opioid analgesic in severe pain should be started even before the definitive diagnosis. Anti-spasmodic therapy may also be given. If stone is present, medical dissolution therapy for all stone sizes (alone or as complementary to medical expulsion, lithotripsy or surgery), medical expulsion therapy for stone size 5-10 mm and lithotripsy or surgery if greater than 10 mm. Non-pharmacologic treatment includes patient education, increased fluid intake to achieve at least 2-2.5 liters of urine per day and limit sodium intake (no evidence to limit calcium or protein intake). Family intervention to adjust family diet preference to low sodium is also recommended.

Implementation: To promote rational management of urinary tract stone in family practice, outreach visits to individual family physician's clinic have been identified as an intervention that may improve the practice of health care professionals. This type of 'face to face' visit has been referred to educational detailing or academic detailing. Organizational activities such as quality improvement activities will also be encouraged.

Introduction

Urinary tract stone or calculi are low-density crystals in any part of the urinary tract. Their chemical compositions often include calcium oxalate, magnesium ammonium phosphate (struvite), cysteine or uric acid.[1] They result from either excessive excretion or precipitation of salts in the urine or lack of substances to inhibit its formation. It is more common among men than women. Its incidence increases with age until 60 and in some, they tend to be recurrent.[2] Most stones are composed of calcium oxalate and some are composed of calcium phosphate. Crystal deposits result in local tissue damage and serve as a site of mineral overgrowth and with urine supersaturation lead to stone formation.[3]

Urinary stone formation involves a combination of metabolic, genetic, and environmental factors. It is also associated with systemic disorders, including chronic kidney insufficiency, hematologic malignancies, endocrine disorders, autoimmune diseases, inflammatory bowel diseases, bone loss and fractures, hypertension, type 2 diabetes mellitus, metabolic syndrome, and vascular diseases like coronary heart diseases and ischemic strokes.[4] In a large prevalence study in China, male gender, age, family history of urinary stones, concurrent diabetes mellitus, hyperuricemia, increased consumption of meat, dehydration and residence in rural areas were all statistically significantly associated with a greater risk of kidney stones.[5]

The current diagnosis and treatment of urinary tract stone in hospitals, include the use of non-contrast CT scans for the diagnosis, increased hydration for the improvement of stone elimination (39.3%) and multiple drug combination that includes non-steroidal anti-inflammatory drugs and opioids. Alpha blockers are prescribed by about only 20% of doctors.[6] For large urinary tract stones (>10 mm), 73% of urologists in the US perform percutaneous nephrolithotomy especially those who were trained during residency. Others recommended shock wave lithotripsy for moderate/large renal stones.[7]

Prevention of urinary tract stones is also now medically feasible and recommended. However, diagnosis and treatment of remediable causes requires testing and drugs that entail cost. This cost is balanced by the presumed reductions in stone related events and medical encounters i.e. hospitalizations, cystoscopies, and surgical procedures. In a financial analysis by Parks and Coe, medical stone prevention will result in an average saving of $2,158/patient/year. Medical prevention also reduces morbidity, complications from surgical procedures like obstruction and infection.[8]

Objectives

This clinical pathway was developed to guide family and community physicians on the diagnosis and initial management of urinary tract stone. It provides recommendations to the following clinical decisions: 1) clinical history and physical examination; 2) laboratory and ancillary procedures to be requested; 3) pharmacologic interventions; 4) non-pharmacologic interventions; and 5) patient outcomes to expect.

Methods of Development and Implementation

The PAFP Clinical Pathways Group reviewed the published medical literature to identify, summarize, and operationalize the clinical publication to develop an evidence-based clinical pathway for the management of patients with urinary tract stone in family medicine practice. The recommendations are time-bound tasks patient care processes, in terms of history and physical examination, laboratory tests, pharmacologic and non-pharmacologic interventions.

The group adopted several strategies and undergo regular review in developing the recommendations. The first strategy is emphasizing on evidence-based recommendations as recommended assessments and interventions. The second strategy is recognition of potential variations between-patients and between specific practice settings. The third strategy is the recognition of "stakeholder groups" in family and community practice with careful attention to getting their opinion and support but without

sacrificing the objectives of the project. The fourth strategy is emphasis on the commitment to establishment of the ultimate goal of improving the effectiveness, efficiency and quality of patient care in family and community practice.

For the first strategy, the group searched PubMed and HERDIN using the terms "urinary tract stone", "diagnosis" and "treatment". Retrieval of articles was focused on the following type of clinical publications, clinical practice guidelines, meta-analysis, randomized controlled trials and clinical trials. The more rigorous meta-analysis of clinical trials and observational studies were prioritized over low quality trials in the formulation of the recommendations. The evidences for the patient care processes were reviewed and summarized as notes to justify the recommendations. The second strategy was to present the recommendations to the QA Committee who acted as panel of experts and discussed potential variations in different settings of family practice. As part of the third strategy, the clinical pathway will then be disseminated to the selected PAFP chapters and members and other stakeholders for consensus development. Dissemination will be publication in the Filipino Family Physician Journal, conference presentations (PAFP Annual Convention) and focused group discussions.

As a fourth strategy, the implementation of clinical pathways to be adopted by the PAFP will be quality improvement activities in a form of patient record reviews, audit and feedback. Audit standards will be the assessment and intervention recommendations in the clinical pathway. Implementation of clinical pathways will be at the practice level and the organizational level. Practice level can be a simple count of family and community medicine practitioners using and applying the clinical pathways. Organizational outcomes can be activities of the PAFP devoted to the promotion, development, dissemination and implementation of clinical pathways.

Grading of the Recommendations

The PAFP QA Committee met as a panel and graded the recommendations as shown in Table 1. The grading system was a mix of the strength of the reviewed published evidence and the consensus of a panel of experts. In some cases, the published evidence may not be applicable in Philippine family practice setting, so a panel grade based on the consensus of clinical experts was also used. Thus, if the recommendation was based on a published evidence that is a well done randomized controlled trial and the panel of experts voted unanimously for the recommendation, it was given a grade of A-I. If the level of evidence is based on an observational study but the panel still unanimously considered the recommendation, the grade given was A-II and if the level of evidence is just an opinion and the panel still unanimously recommended it, the grade was A-III.

Table 1. Grading of the Recommendations

Panel Grade Level	Evidence Grade Level		
	1	2	3
A	A-I	A-II	A-III
B	B-I	B-II	B-III
C	C-I	C-II	C-III

Panel Grade Levels

A - All the panel members agree that the recommendation should be adopted because it is relevant, applicable and will benefit many patients.

B - Majority of the panel members agree that the recommendation should be adopted because it is relevant, applicable in many areas and will benefit many patients.

C - Panel members were divided that the recommendation should be adopted and is not sure if it will be applicable in many areas or will benefit many patients.

Evidence Grade Levels

I - The best evidence cited to support the recommendation is a well-conducted randomized controlled trial. The

CONSORT standard may be used to evaluate a well-conducted randomized controlled trial.

II - The best evidence cited to support the recommendation is a well-conducted observational study i.e. match control or before and after clinical trial, cohort studies, case control studies and cross-sectional studies. The STROBE statement may be used to evaluate a well-conducted observational study.

III - The best evidence cited to support the recommendation is based on expert opinion or observational study that did not meet the criteria for level II.

In the implementation of the clinical pathways, the PAFP QA committee recommends adherence to guideline recommendations that are graded as either A-I, A-II or B-I. However, the committee also recommend using sound clinical judgment and patient involvement in the decision making before applying the recommendations.

	Pathway Tasks				
Visit	**History and Physical Examination**	**Laboratory**	**Pharmacologic Intervention**	**Non-pharmacologic Interventions**	**Patient Outcomes**
First Visit	___Elicit patient history of flank pain, tenderness, dysuria and hematuria. They must be described in detail in terms of, characteristics, date of onset and severity. **(A-II)** ___Other patient history to elicit should include stone passage, recurrent UTI, dietary history, fluid intake and medications (minerals, vitamins, antibiotics etc. **(A-II)** ___Family history should include stone former, metabolic and endocrine disorders etc. **(A-II)** ___A complete and thorough physical examination of the abdomen, flank and back must be done. **(A-II)** **Decision Point** ___If the patient consulted with an imaging of urinary tract stone, discuss treatment options i.e. medical expulsion therapy for 5-10mm, lithotripsy or surgery for more than 10 mm. Proceed to shared decision. **(A-I)**	___Request for ultrasound of kidney, ureter and bladder (plain CT is second line imaging study) **(A-I)** ___Request for urinalysis and blood chemistry (BUN, creatinine, calcium and uric acid) **(A-II)** **If stone is already present, recurrent or high-risk patient** ___Request for stone analysis, parathyroid hormones and 24-hour urine collection **(A-II)**	___Symptomatic treatment with nonsteroidal anti-inflammatory drugs or opioid analgesic in severe pain should be started **(A-I)** ___Anti-spasmodic therapy may also be given **(A-I)** **For patients with available stone imaging, start** ___Medical dissolution therapy (alone or as complementary to medical expulsion, lithotripsy or surgery) **(A-I)** ___Medical expulsion therapy for stone size 5-10mm **(A-I)**	**Patient Intervention** ___Patient education on the prognosis of the stone disease and details of treatment that includes dietary intervention, medical dissolution and expulsion therapy, shockwave lithotripsy and surgery **(A-II)** ___Increase fluid intake fluid intake to achieve at least 2-2.5 liters of urine per day **(A-I)** ___Limit sodium intake (no evidence to limit calcium or protein intake) **(A-I)** **Family Intervention** ___Adjust family diet preference to low sodium **(A-III)** **Follow-up Visit** ___Follow-up after one week **(A-III)**	___Awareness of the stone disease and details of treatment **(A-II)** ___Awareness of the drugs prescribed, dose and potential side effects **(A-II)** ___Intention to follow treatment plan **(A-II)** **For patients with available stone imaging** ___Obtain written patient consent prior initiation of treatment options **(A-I)**
Variations					

	Pathway Tasks				
Visit	**History and Physical Examination**	**Laboratory**	**Pharmacologic Intervention**	**Non-pharmacologic Interventions**	**Patient Outcomes**
Second Visit	___Repeat history and physical examination and note any change in the severity of symptoms and physical examination findings **(A-II)** ___Review results of ultrasound and laboratory examinations **(A-II)** ___Obtain health-related quality of life measure **(A-I)**	___Complete other requested laboratory tests if stone is demonstrated on imaging studies **(A-II)**	___Continue symptomatic treatment **(A-I)** ___Medical dissolution therapy (alone or as complementary to medical expulsion, lithotripsy or surgery) **(A-I)** ___Medical expulsion therapy for stone size 5-10mm **(A-I)**	___Enhance patient education on the prognosis of the stone disease and potential for recurrence **(A-II)** ___Enhance advice to increase fluid intake and limit sodium intake **(A-I)** Family Intervention ___Enhance family diet preference to low sodium **(A-III)** Follow-up Visit ___Follow-up monthly for the next three months **(A-III)**	___Resolution of symptoms (adjust pharmacologic treatment or refer to specialist if severity of symptoms worsen) **(A-I)** ___Patient satisfaction **(A-II)** ___Obtain written patient consent prior initiation of treatment options **(A-I)**
Variations					

	Pathway Tasks				
Visit	**History and Physical Examination**	**Laboratory**	**Pharmacologic Intervention**	**Non-pharmacologic Interventions**	**Patient Outcomes**
Continuing Visit (until 3 months)	___Repeat history and physical examination and note any change in the severity of symptoms and physical examination findings **(A-II)** ___Review results of ultrasound and laboratory examinations **(A-II)** ___Obtain health-related quality of life measure **(A-I)**	___After 3 months of medical treatment, repeat ultrasound and other baseline laboratory tests **(A-II)**	___Continue medical dissolution and/or expulsion therapy **(A-I)**	___Enhanced patient education on the prognosis of the stone disease and potential for recurrence **(A-II)** ___Enhance advice to increase fluid intake fluid intake and limit sodium intake **(A-I)** Family Intervention ___Enhance family diet preference to low sodium **(A-III)**	___Resolution of symptoms **(A-I)** ___Decrease stone size or expulsion of stone (refer to Urology if stone size is unchanged) **(A-I)** ___Patient satisfaction and improved quality of life **(A-I)**
Variations					

Clinical Evidence of the Recommendations

First Visit

Clinical History and Physical Examination

Patients with urinary tract stone usually present with flank pain, tenderness, dysuria and hematuria. These signs and symptoms should be described in detail in terms of, characteristics, date of onset and severity in the patient's clinical history. Dietary history should also be inquired including daily average volume of water intake, juice and salts. Intake of medications like mineral (calcium) and vitamin supplements (vitamin C and D) should also be noted.[9] Other medications like protease inhibitors (HIV drugs), antibiotics, and some diuretics also increase the risk of some types of urinary tract stones and should also be asked.[10]

The classic presentation of urinary tract stone is the sudden onset of very severe pain in the flank and back primarily caused by the acute ureteral obstruction. Detailed physical examination of the abdomen, flank and back must be done. The diagnosis can be made on clinical symptoms and physical examination especially in the presence of gross hematuria, but confirmatory exams are needed to rule out life-threatening emergency such as abdominal aortic aneurysm.[11]

The character of the clinical signs and symptoms may be due to the size and location of urinary stone. A stone that passes into the ureter may cause blockage of urine flow with distension of the upper urinary tract. Ureteral hyper-peristalsis occurs, resulting in acute onset of sharp, spasmodic or colicky flank pain. Irritation of and trauma to the ureter may also result in hematuria. The ureter contains several areas where stones commonly become lodged (e.g., at the uretero-pelvic junction, the iliac vessels, and the uretero-vesical junction). The location of the stone can characterize the site of the pain.[2]

Urinary stone is more prevalent in population at risk for frequent dehydration. In a study among steel workers, a significant number had concentrated post-shift and 24-h urines and elevated levels of urinary analytes. The incidence of urinary tract stone is higher in this population compared to the published incidence in the general population.[12]

There is a debate on the association between the intake of calcium and vitamin D supplements and the increased risk of formation of urinary tract stone. In a study among healthy volunteers taking calcium supplements, there was no significant increase in calcium oxalate. The increased urinary citrate, reduced oxalates counterbalanced the increased calcium absorption.[13] In another study among post-menopausal women where long-term calcium supplement intake was present, there was also no significant difference found in the 24-hour urine and blood calcium levels before and after the one year of calcium and vitamin D supplementation.[14] Thus there is no basis for the fear of increased stone formation among those taking calcium supplement in short-term or long-term supplementation. While both studies cited earlier led to increased absorption and urinary excretion of calcium, variation in the timing of calcium supplement may affect gastrointestinal absorption. It is therefore recommended that calcium supplement is taken with meals as this can decrease urinary excretion of oxalate.[15]

Vitamin C supplementation was also considered to be important to be elicited in the medical history. In a study of 47 adult calcium stone-forming patients, there was a significant increase in mean Tiselius index after 1 or 2g of vitamin C. Similar findings were observed in healthy subjects.[16] This finding was confirmed in a randomized, crossover, controlled design in which subjects consumed a controlled diet, the Tiselius Risk Index was also higher in those getting high dose (2g per day) of ascorbic acid supplementation compared to the low dose. Urinary oxalate was found to be increased thereby raising the risk of calcium oxalate stone formation.[17]

After the clinical history and physical examination, the family physician may have to make some decisions. If during the first visit the patient consulted with an available imaging result that confirmed the presence of urinary tract stone, the family physician may adopt the pharmacologic

treatment strategy discussed under the second follow-up section.

Laboratory and Ancillary Procedures

In family practice, ultrasound imaging should be done to identify and quantify stone burden. In the presence of urinary tract stone, a stone analysis when available may be done at least once.[9] The type of stone can guide the subsequent management. Although recurrent stone rate is important, extensive metabolic explorations are not recommended after an uncomplicated first episode.[18] Among high-risk or recurrent stone formers, parathyroid hormones, 24-hour urine collections for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium and creatinine may be done.[9] Referral to an endocrinologist and urologist may be necessary in high risk patients and those with recurrence.

Urinalysis and blood chemistry should also be done on a patient newly diagnosed with kidney or ureteral stones.[9] Urinalysis should include sediment and pH determination. Hematuria is frequently present on urine analysis. Blood chemistry should include at least serum creatinine, calcium and uric acid.[19]

The probability of spontaneous passage of a stone is size dependent, and the probability is inversely proportional to stone size. Therefore, family physicians should know the size of the stone as well as its location using direct imaging techniques.[2] Ultrasound is the main imaging test to evaluate the size of urinary tract stone. It is also recommended for pregnant patients. Plain computed tomography is more accurate than ultrasound but can only be recommended as second line because of its limited accessibility and high cost. Magnetic resonance imaging and traditional radiography are less accurate for direct visualization of urinary tract stone.

Ultrasound can visualize stone as well as show evidence of urinary tract obstruction secondary to stone. It is 61% to 90% sensitive for the detection of stones. It is up to 100% sensitive and 90% specific for the detection of ureteral obstruction as evidenced by hydronephrosis, ureterectasis, and perinephric fluid. However, for the diagnosis of minor defects and small stones this technique still needs to be improved.[20] Ultrasound is also less sensitive and specific than plain computerized tomography. But in a large randomized study of 2759 individuals, there were no statistically significant difference in return emergency department visits, hospitalizations, or high-risk diagnoses with complications for individuals whose initial imaging workup was ultrasound or computerized tomography. The advantages of ultrasound are its lack of ionizing radiation while the disadvantage is the need for skilled personnel and limitation to accurately measure the size of the stone.[2]

Non-contrast or plain computed tomography can also be performed in the evaluation of patients with suspected urinary tract stone. It is more accurate than ultrasound for identifying and measuring the size of stones, detecting evidence of ureteral obstruction and identifying other causes of flank pain or renal colic. The major disadvantage is radiation exposure to the patient. However, low-dose computed tomography has been shown to yield equivalent stone measurements as compared to standard-dose.[2] Another disadvantage is its cost and limited accessibility compared to ultrasound.

Traditional radiography of the kidney, ureter and bladder without contrast may be considered as it provides less ionizing radiation than computed tomography. But high dose contrast urography is still the standard.[21] Non-contrast radiography may only detect stone if it is significantly large and calcified.[2]

Magnetic resonance imaging can be an alternative to low-dose non-contrast computed tomography in pregnant women, young individuals and individuals who have undergone multiple prior computed tomography examinations. It is accurate for the diagnosis of hydronephrosis and perinephric edema but is less accurate in visualizing stones compared to non-contrast computed tomography.[2]

In a randomized trial in the emergency room, ultrasound, radiology plus ultrasound and computed tomography were compared for the diagnosis of urinary tract stones. A total of 2,759 patients at 15 emergency

departments were included in the study. The cost of testing was lower in the ultrasound group but the total cost of care did not significantly differ between groups. The cost of hospital admission significantly increased the cost.[22]

Pharmacologic Treatment

For patients with acute renal colic, the usual symptomatic treatment with analgesic (opioid analgesic in severe pain) and non-steroidal anti-inflammatory drugs should be started as soon as possible. Antispasmodic may also be given to patients with acute symptoms of urinary tract stones.[23] The size and location of the stone are the most important predictor of the severity of symptoms. A stone size greater than 10 mm in the ureter usually produce severe pain. Uncontrolled severe pain, fever, oliguria/anuria suggest complicated stone disease. Such conditions require emergency treatment or stone extraction.[18] Immediate referral to a urologist should be done for these patients.

Non-pharmacologic Intervention

Urinary tract stone may be a chronic disease with acute systemic manifestation. Diet and environment play an important role and may be an important factor in the success of treatment or recurrence. Dietary and lifestyle modification as a complementary and preventive treatment has gained interest because it is safer and affordable.[24] However, adherence to such intervention requires patient cooperation and adherence. Thus, regardless of the treatment choices for urinary stone disease, a standardized patient education and shared decision-making are recommended. Patient education that presents the prognosis of the stone disease and details of treatment that includes medical expulsion therapy, dietary intervention to prevent progression or recurrence, shockwave lithotripsy and surgery. The cost-effectiveness of each diagnostics and interventions should also be discussed. This can also be a very useful decision aid for both the physician and the patient. Such decision aids will have a very good impact on the patients' knowledge and decision-making process.[25]

Shared decision-making and follow-up have been compared with standard care for patients with urinary tract stone. The result of interventions showed significant reduction in uric acid, calcium, and sodium compared to standard care. The shared decision-making strategy lead to better follow-up compliance and more standardized education for patients.[26] Patients who participated in shared decision-making had a very good satisfaction rating and would recommend such approach to other patients. Because of the standardized education, the patients showed superior knowledge about prevention.[27]

Managing diet and nutrient intake can also help prevent the formation of urinary tract stones. Obesity is a risk factor for stone formation but weight loss intervention with high animal protein intake, laxative abuse, rapid loss of lean tissue, or poor hydration might increase the risk as well. To prevent calcium oxalate, cystine, and uric acid stones, urine should be alkalinized by eating a diet high in fruits and vegetables or drinking alkaline mineral waters. For prevention of calcium phosphate and struvite stones, urine should be acidified. Cranberry juice may achieve this purpose.[23] Even urologists are giving dietary intervention for stone prevention. Unfortunately, some of them don't have the time and skills to provide it in a more detailed and consistent manner.[28]

The basic dietary intervention in patient with urinary tract stone is increased fluid intake. It is recommended to have increased fluid intake to achieve at least 2-2.5 liters of urine per day. In a randomized trial of patients treated for urinary stones, increasing fluid intake with no dietary modification was compared with usual fluid intake. Within 5 years of follow up, recurrences were noted in 12 of 99 in high fluid intake and in 27 of 100 usual fluid intake group. The average interval for recurrences was 38.7 ± 13.2 months in high fluid intake and 25.1 ± 16.4 months in usual fluid intake group. The baseline values of calcium oxalate, brushite and uric acid were much greater decreased sharply in high fluid intake group. The results suggest that a large intake of water is the initial therapy for prevention of stone recurrences.[29]

Several studies have also been done in high fluid intake after this initial trial. In a more recent meta-analysis of these studies (2 randomized controlled trials with 269 patients; 7 observational studies with 273,685 individuals), the pooled risk ratio for stone formation 0.40 (95 % CI 0.20-0.79) in randomized controlled trials and 0.49 (0.34-0.71) in observational studies. There was also reduced risk ratio of recurrent kidney 0.40 (95 % CI 0.20-0.79) in randomized controlled trials and 0.20 (0.09-0.44) in observational studies.[30] Some evidence also show that decrease in the consumption of soft drinks like colas that are rich in phosphoric acid is associated with a reduced risk for stone recurrence.[31]

While there is general agreement on the need to increase urinary volume in stone formers, there is controversy about the hardness of water i.e. mineral content and stone incidence. Consumption of mineral water containing relatively high concentrations of minerals have been studied in terms of their effect on risk for urinary stone formation but the results are mixed. In one study, hard water was shown to increase urinary calcium concentration with no change in oxalate excretion. The calcium-citrate index was also increased by hard water. The investigators suggested consumption of soft water to lower the risk for recurrence of calcium stones.[32] However, in another study, three types of mineral water were investigated. Mineral water with a higher calcium content induced increased calcium excretion but significantly decreased oxalate excretion. Thus, there is no definite evidence that hard water is more lithogenic than soft water. Water components other than calcium can modify the tendency toward stone formation.[33]

On the other hand, water specifically with high calcium and magnesium has been investigated to determine its effect on stone formation. In one study, twenty calcium oxalate stone-forming patients and 20 healthy volunteers were given a protocol of mineral water and tap water. The result showed that mineral water containing calcium and magnesium may be therapeutic or prophylactic agent against calcium oxalate stone formation.[34] In another study, a cross-over trial, calcium- and magnesium-rich water was shown to reduce the risk of calcium oxalate stone formation.[35] With these mixed results and soft non-clinical outcomes, total daily water volume is more important than the mineral content.

The urinary levels of calcium, oxalate and citrate are the main risk factors for urinary calcium stone formation. Patients are advised to limit sodium intake and maintain normal or increased dietary calcium. Increasing dietary calcium may decrease the absorption of dietary oxalate decreasing urinary oxalate excretion and eventually calcium oxalate stones. They should be encouraged to increase intake of fruits and vegetables, a good source of citrate.[9]

There is mixed results on the role of animal protein. In a randomized controlled trial, after adjustment for possible confounding, the risk of a recurrent stone in the intervention group was 5.6 (95% confidence interval 1.2 and 26.1) compared to the control group. The results showed that low animal protein, high fiber, high fluid diet has no advantage over increase fluid intake alone.[36] However, in another study on 23 patients with a history of calcium kidney stones, shifting protein source to consumption of plant proteins from legumes, nuts and grains resulted to increase in urinary sodium and potassium with no significant change in calcium. These findings suggest that plant protein may be effective in reducing calcium oxalate kidney stone risk.[37]

Orange juice containing potassium citrate delivered an equivalent alkali load and caused a similar increase in urinary pH compared to potassium citrate tablet. Thus, it may be beneficial in the control of calcareous and uric acid nephrolithiasis.[38] This finding however was not true for lemonade.[39] The effect of cranberry juice on urinary biochemical and physicochemical risk factors associated with the formation of calcium oxalate kidney stones has also been investigated. It was shown in a randomized cross-over trial that it significantly decreased oxalate and phosphate excretion and increased excretion of citrate. There was also decrease in supersaturation of calcium oxalate compared to increased fluid intake.[40] In another study, replacement of milk with apple juice in a diet containing moderate amounts of oxalate from whole grains, legumes, fruits, and vegetables did not increase the risk of calcium oxalate stone formation.[41]

Patient Outcome

During the first visit, the patient must be aware of the following: 1) the diagnosis or possibility of urinary tract stone and its consequences prescribed medications, its dose and side effects; 2) proposed diagnostic tests, its accuracy and cost; and 3) therapeutic options like medical, lithotripsy and surgical management, its effectiveness, recurrence rate, and its side effects and estimated cost.

The patients' knowledge, behaviors, and preferences to non-pharmacologic intervention may affect adherence to the planned intervention. In a survey among patients with urinary tract stone, those who were less aware of their future stone risk were less likely to adhere to increase fluid intake. It is also true among those patients who were not advised by their doctor about the risk and the value of increasing fluid intake.[42] It is therefore necessary to make sure the patients are aware about this during the first visit.

Follow-up of patients with urinary tract stone should after 1 week, 4 weeks and 12 weeks. This is based on the follow-up procedures used by the different clinical trials on the proposed medical interventions. After one week of treatment, symptomatic relief must have been achieved. After 4 weeks of treatment, the initial response to medical expulsion therapy will already be evident. After 12 weeks, the complete response to medical expulsion therapy may be evident and for those with incomplete response, lithotripsy or surgery may be offered as the next option.

Second Visit

Clinical History and Physical Examination

After one week, the family physician should repeat the history and physical examination and note any change in the severity of symptoms and physical examination findings. Review the results of the requested ultrasound and laboratory examinations and confirm or rule out the presence or absence of urinary tract stone to the patient. Correlate this with the change in symptoms and physical examination.

Laboratory and Ancillary Procedures

Upon diagnosis of urinary stone, family physicians should request for a 24-hour urine specimen if available for evaluation of stone risk factors within six months of the initiation of treatment to assess response or further recurrence. If possible, a stone analysis may be requested if there is documented passage of stone. If urinary tract stone was already identified, the patient should be advised for follow-up imaging studies to assess for stone clearance, growth or new stone formation should also be done by repeat ultrasonography or low dose computed tomography after 8-12 weeks.[9] Periodic blood testing to assess adverse effects in patients undergoing therapy may also be done.

Pharmacologic Treatment

If the presence of urinary tract stone is confirmed by the imaging procedure, the size and location of the stone are the most important information to guide the succeeding management. On top of symptomatic treatment, the patient must be informed of the alternative strategies for removal i.e. medical dissolution, medical expulsion, lithotripsy or surgery. The advantages, disadvantages and costs must also be discussed. A urinary tract stone $\leq$5 mm has a 68% probability of spontaneous passage while a $\geq$10 mm stone, however, is very unlikely to pass spontaneously.[2] If the stone size is $<$10 mm, a collaborative decision on the planning of intervention preferably with written consent from the patient is necessary.

For stone size less than 5 mm and located in the kidneys or ureter, drugs with the ability to decrease stone size and promote expulsion are recommended (medical dissolution therapy). Citrate salts like potassium citrate have been shown to be effective in decreasing stone size and preventing new stone formation. In a meta-analysis of seven studies that included a total of 477 patients, citrate significantly reduced the stone size (RR 2.35, 95% CI 1.36 to 4.05) and prevented new stone formation (RR 0.26, 95% CI 0.10 to 0.68). The beneficial effect on stone size stability was also evident (4 studies, 160 participants: RR 1.97, 95%

CI 1.19 to 3.26). The main side effects noted in citrate was upper gastrointestinal disturbance.[43] The meta-analysis did not report citrate effect on stone expulsion rate. To enhance stone expulsion, thiazide diuretics may be combined with citrate therapy.[9]

Herbal or phytotherapy has also been studied for the treatment of stone in the urinary tract with reported effect on stone size and expulsion rate. In a meta-analysis, Didymocarpus pedicellate plant derivative preparation was better compared to placebo in terms of total stone clearance (risk ratio: 6.19, 95% CI: 2.60 to 14.74; $Z = 4.12$, $p < 0.0001$; $I2 = 0\%$) and stone size reduction (mean difference: Didymocarpus pedicellata preparation, 4.93 mm lower; 95% CI: -9.18 to -0.67; $Z = 2.27$, $p = 0.02$; $I2 = 99\%$) after 3 months of treatment. However, in the same meta-analysis, citrate was shown to be better than phytotherapy but citrate has more side effects.[44] Another meta-analysis was done on terpene compound drug (Rowatinex) in facilitating spontaneous passage of ureteral stone. Five randomized controlled trials (total of 344 subjects) of adequate methodological quality were included. The drug was shown to have a higher stone expulsion rate (pooled RR: 1.34; 95 % CI 1.12, 1.61) compared to placebo. In studies that compare terpene compound drug with alpha-blockers, the expulsion rate was similar (pooled RR: 0.79; 95 % CI 0.59, 1.06). Minor gastrointestinal side effects were noted among patients taking terpene compound drug.[45] Locally, sambong (Blumea balsamifera) is being promoted for urinary tract stone. There are locally published studies with limited number of participants that showed it to decrease the size of stone or is equally effective with terpenes or potassium citrate for urinary tract stones.[46-48]

Pharmacologic treatment or medical expulsion of stone is one option as the intervention after diagnosis if the stone size is 5-10 mm. It should be offered as an option to patients amenable to conservative management or while waiting for the optimal time for lithotripsy or surgery.[49] Alpha-blockers are the main choice for stones located in the ureter. In an updated Cochrane group meta-analysis, treatment with an alpha-blocker may result in a large increase in stone clearance (risk ratio 1.45; 95% confidence interval 1.36 to 1.55) and has little effect on major adverse events (risk ratio 1.25; 95% CI 0.80 to 1.96). Patients given alpha-blockers had shorter stone expulsion times, used lower pain medication and less hospitalizations. In the predefined subgroup analysis, the beneficial effects of alpha-blockers is highest when the stone size is more than 5 mm.[50]

Alfuzosin and tamsulosin are two alpha-blockers extensively studied for medical expulsion therapy. Tamsulosin was extensively studied for patients with ureteral stone less than 10 mm who do not require immediate urologic intervention. In a meta-analysis, patients with size of stone subgroup 5 to 10 mm, it had a larger effect on stone passage than those with stone size less than 5 mm. Expected side effects like dizziness or hypotension had no significant increase.[51] Alfuzosin also provided a significantly higher stone-free rate and shorter expulsion time compared to control. It was comparable to tamsulosin in terms of expulsion rate, time and side effects.[52] Silodosin is another alpha-blocker that has been shown to have a significant improvement in stone clearance versus placebo and even better than tamsulosin especially when the stone is in the distal ureteral stone and when the size was 5-10 mm. Retrograde ejaculation was a common side effect.[53] Naftopidil is also another alternative to tamsulosin, with similar expulsion rate (RR 1.05, 95% CI 0.74, 1.48; $p = 0.80$) and expulsion time (MD 0.18 days, 95% CI -0.49, 0.85; $p = 0.59$), and similar number of pain episodes. However, it has lower adverse event compared with tamsulosin (RR 0.47, 95% CI 0.23, 0.94; $p = 0.03$).[54]

These pharmacologic therapies may also be given concomitantly or following shock wave lithotripsy for kidney and ureteral stones. Pooled results of a meta-analysis demonstrated the efficacy of α-blockers and terpene compound in increasing stone clearance.[55]

Non-pharmacologic Intervention

The non-pharmacologic treatment started during the first visit must be continued. Educating the patient regarding the diagnosis, its potential complication, possibility of chronic or long-term symptoms if the stone is

Table 1. Pharmacologic options for management of urinary tract stones.

Drug	Dose	Expected Effect	Precaution and Side Effects
Potassium citrate	30-60 mEq per day	Reduced stone size or expulsion, prevention of stone recurrence or formation	Hyperkalemia, GI complaints
Pinene (Terpene) combination	1-2 capsule TID	Reduced stone size or expulsion, prevention of stone recurrence or formation	Contraindicated in 1st trimester of pregnancy
Sambong	1 gram TID (2-4 tablets TID)	Reduced stone size or expulsion, increase diuresis	Precaution in pregnancy and lactation
Alfuzosin	5-10 mg per day	Stone expulsion	Hypotension, tachycardia, angina, GI complaints
Tamsulosin	400 mcg per day	Stone expulsion	Hypotension, syncope, headache, priapism

not removed must be reinforced. The planned intervention must be explained in terms of its effectiveness, side effect and cost. Most clinical trials on medical expulsion and stone dissolution therapy lasted for 4-12 weeks. To monitor its effect and patient adherence to treatment, follow-up is recommended to be done every month up to maximum of 3 months to monitor and evaluate response to treatment. The patient may also be advised to follow-up when there is exacerbation or recurrence of symptoms.

Patient Outcome

During the second visit, the initial symptoms should have been relieved or diminished in severity. A baseline quality of life measurement should have been obtained. A review of literature from inception to May 2016 for all prospective English language articles on QOL in patients with urinary tract stone was done. Most used the SF-36 Quality of Life tool and demonstrated a lower QOL in patients with stone. Bodily pain and general health were significantly lower in scores compared to other QOL parameters.[56]

During the second visit, the patient should now have a more definite diagnosis of urinary tract stone, or the diagnosis is ruled out. The patient's awareness of the diagnosis of urinary tract stone and its consequences, prescribed medications, its dose and side effects must be enhanced. There must already be a collaborative written decision on the therapeutic option, method of monitoring and evaluation.

Third and Subsequent Visit

Clinical History and Physical Examination

After one month and during the continuing visits, family physician should repeat the history and physical examination and note any change in the severity of symptoms and physical examination findings. Review of the other requested laboratory examinations should be done.

Laboratory and Ancillary Procedures

Follow-up imaging studies to assess for stone clearance, growth or new tone formation should also be done by repeat ultrasonography or low dose computed tomography after 8-12 weeks of pharmacologic and non-pharmacologic treatment.[9] Periodic blood testing to assess adverse effects in patients undergoing therapy may also be done.

Pharmacologic Treatment and Non-pharmacologic Intervention

The family physician should re-emphasize pharmacologic and non-pharmacologic intervention and monitor the patient's adherence to it.

Patient Outcome

During the third visit (at least more than a month after the first consult), the initial symptoms should have disappeared or stable and bearable. Decrease in size or expulsion of the urinary tract stone should be expected after 3 months of medical intervention. Re-planning for subsequent intervention maybe done after 3 months.

Recommendations for Implementation

Clinic Level

The recommendations for implementation of this clinical pathway is similar to the recommended implementation of the other clinical pathways developed by the PAFP QA Committee. The Committee will disseminate the clinical pathways in a form of lectures and publications. Lectures and publications will also be supplemented by generating evidence of actual practice by family physicians. At the clinic level, self-audit using the recommendations of this clinical pathway as the standard may be done. Passively delivered, complex interventions targeted at identified barriers to change had little effect in changing practice.[57]

Organizational Level

Similarly, at the organizational level, the PAFP should establish a new model of quality improvement initiative where self-practice audits are included as part of the program. Within PAFP chapters, peer group discussions, individual feedback and quality improvement reports are the main components. This model has been shown to improve the care process for urinary problems in one randomized clinical trial. This trial showed that prescribing of first choice appropriate management increased in the intervention group from but remained the same in the control group.[58]

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