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Independent Study Paper:
Recurrent Urinary Tract Infections in Adult Women
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Abstract

Background

Urinary tract infections (UTI's) are commonly found in adult, otherwise healthy women. The majority of the time they are uncomplicated and require no medical management after the infection has resolved. There are however, circumstances in which individuals are prone to recurrent urinary tract infections. In this population the use of prophylactic therapy should be strongly considered. Often practitioners are unsure of whether the natural route of cranberry supplementation is as effective as antimicrobial therapy. The increasing resistance to antimicrobials warrants that health care providers look further into this issue in order to determine the most appropriate prophylaxis and treatment options in women with recurrent UTI's.

Case Description

The following paper will discuss a clinical case scenario involving a 59-year-old Caucasian female who presents to her primary care provider for follow-up after being hospitalized for a urinary tract infection. She reports feeling overall well however has new onset dizziness beginning after her hospital stay. A thorough history, physical exam and laboratory testing was conducted in order to identify the etiology of her new onset dizziness.

Literature Review

A literature review was conducted in order to analyze the current recommendations regarding urinary tract infection prophylaxis. The use of cranberry supplementation vs. antibiotic prophylaxis was compared in hopes of providing more guidance for the practitioner caring for patients suffering from recurrent UTI's. The

guidelines of UTI treatment in pregnancy is summarized due to practitioners often caring for women with UTI's during their childbearing years. One must be aware of the negative outcomes associated with untreated UTI's in pregnant women while also carefully prescribing antibiotic therapy that is not teratogenic. Lastly, recommendations are given regarding antibiotic treatment for acute complicated and uncomplicated UTI's. The growing rates of antimicrobial resistance highlight the need for practitioners to be educated in appropriate treatment options and targeted antibiotic therapy.

Clinical Relevance

Although Cranberry supplementation has been found to have some effect on UTI recurrence, it falls well behind its competitor for several reasons. Antibiotic prophylaxis using trimethoprim-sulfamethoxazole (TMP-SMX) was highly successful in preventing further UTI's while also being very cost effective. This paper serves as a guide for the treatment of acute complicated and uncomplicated UTI's as well as those suffering from three or more UTI's in a twelve-month period. This is significant for providers and healthcare workers as a whole striving towards providing quality patient care while also working to reducing the rates of antibiotic resistant microorganisms.

Background

The purpose of this report is to gain a better understanding of how Urinary Tract Infections (UTI's) present in women, how to adequately treat UTI's and the ways in which one can best prevent a recurrence. A 59-year-old Caucasian women presents to her primary care clinic for follow up after being hospitalized for three days for a urinary tract infection and fatigue. She was discharged with instructions to complete her seven-day antibiotic regimen and was prescribed Nitrofurantoin extended release 100mg by mouth to be taken two times per day. During her follow up appointment, she reports feeling significantly better however complains of dizziness.

The topic of this paper stems from the described patient history and diagnosis. Urinary tract infections can occur in any gender or age however the infections tend to occur most commonly in adult women. Acute cystitis is used to describe an infection of the bladder while pyelonephritis affects the upper urinary tract such as the kidneys (Hooton & Gupta, 2016)^b. The majority of cases of urinary tract infections are uncomplicated, given that the patient is not pregnant or suffering from recurrent urinary tract infections. Recurrent urinary tract infections can occur due to anatomical abnormalities or comorbidities.

Case Report

A 59-year-old Caucasian female presented to clinic for follow-up after being hospitalized for three days due to her urinary tract infection and fatigue. Today she is currently complaining of feeling fatigued, and dizzy. She reports the dizziness began approximately one week ago. She states the dizziness comes and goes throughout the day and worsens when she is ambulating. She feels as though the room is spinning and as if

she is falling. The patient denies fevers, chills or night sweats. She denies any nausea, vomiting, diarrhea or constipation. She denies any recent fall or injury. The patient denies alcohol, tobacco or illicit drug use. She currently resides in an assisted living facility due to her dementia. She has no other acute complaints at this time. The patient has a pertinent past medical history of dementia, type two diabetes mellitus, COPD, anemia, hypertension, depression and neuropathy.

During the patient's clinic visit her vital signs were measured and she was physically assessed to gather objective findings during her visit. Her vital signs were as follows; blood pressure 88/40, heart rate 50, respiratory rate of 24, temperature of 98.6F orally and a fasting blood glucose level of 107. She denies any allergies to medications or other allergens. She states she is generally in good health with no new weight loss or weight gain. She denies any skin, hair or nail changes. She reports no thyroid enlargement or sore throat. The patient denies any vision or hearing changes although she admits to wearing corrective lenses, which has been her baseline for several years. The patient also denies any shortness of breath or cough that accompanies her new onset dizziness. She reports that she is free of chest pain, pressure or palpitations. The patient is free of any bowel changes such as nausea, vomiting, diarrhea or constipation. She denies an increase in her thirst sensation, increased urination, and heat or cold intolerance. It appears all of her urinary tract infection symptoms have resolved as she denies burning on urination, frequency, urgency, hematuria or flank pain. She reports a normal musculoskeletal review free of joint pain or tenderness and decreased range of motion. There are no neurologic findings present in the patient such as new weakness, slurred

speech, numbness or tingling. Lastly, she reports good mood and organized thought process. She admits to a diagnosis of dementia and reports this is stable.

A physical exam focused primarily on assessing if her urinary tract infection was resolved as well as trying to locate the cause of her dizziness was conducted. She is dressed casually, with good hygiene. She is seated making good eye contact and relaxed body movements. Her head is normocephalic with no obvious injury and deformity. Her face and body are symmetrical, and she engages in organized speech and thought. Her physical exam reveals clear lungs on auscultation with equal air entry and bilateral lung expansion. During her cardiac evaluation S1 and S2 are heard with regular rate and rhythm. She was assessed for costovertebral angle tenderness which was negative. The patient was asked to stand and ambulate to the examination bed. Her gait was steady, and symmetrical and independent of an assistive device. Sensation was intact throughout.

The following is a list of the patients' medications:

1. Donepezil 5mg by mouth daily
2. Fluticasone proprionate and salmeterol 250/50 1 puff two times per day
3. Losartan 50 mg by mouth daily
4. Metoprolol 50 mg by mouth two times per day
5. Gabapentin 300 mg by mouth three times per day
6. Paroxetine 20 mg by mouth daily
7. Quetiapine 200 mg by mouth two times per day
8. Insulin glargine 30 units subcutaneous at night
9. Nitrofurantoin extended release 100 mg by mouth two times per day for total 7 days

10. Multivitamin by mouth daily
11. Iron sulfate 325 mg by mouth two times per day
12. Furosemide 20 mg by mouth daily

The provider diagnosed her condition of dizziness as multifactorial. After a thorough interview, physical exam and medication review it is difficult to pinpoint a single cause for her symptoms. The first noted is her hypotension of 88/50. This can be caused by a number of reasons including incorrect medications, incorrect dosing and dehydration. She is on metoprolol, which belongs to a class of drugs called Beta-agonist receptor blockers. These have an effect on blood pressure and heart rate, ultimately reducing them. She is not only hypotensive but also bradycardic with a heart rate of 50. The practitioner has therefore chosen to reduce her dose in half, equaling 25 mg by mouth daily. Furthermore, she can benefit from measuring orthostatic hypotension as she mentions it is worsened with ambulation. These symptoms may be a result of hypoperfusion causing the patient to feel dizzy and faint (Kaufmann & Kaplan, 2015).

In addition to lowering her metoprolol dose, the practitioner has requested that she discontinue taking her furosemide 20 mg tablet daily. The patient was unsure of why she was prescribed this medication or how long she is to be taking this. Dizziness is a potential central nervous system side effect of furosemide therefore supporting the discontinuation of this medication in this patient (Sterns, 2016).

In addition to the above recommendations, lab work was ordered to assess for any underlying anemia or thyroid condition. Her RBC's were 3.9 and her TSH was 3.41 both of which were within normal, thereby safely excluding an endocrine or hematologic origin. Studies show that most common contributing factor to dizziness in the older adult

is cardiac in nature (Kaufmann & Kaplan, 2015). For such reason it is a wise idea to conduct an EKG in the clinic to look for abnormalities, arrhythmias or evidence of a past myocardial infarction. Her EKG revealed a normal rhythm however a slowed rate; sinus bradycardia.

In conclusion, the patient was sent home with instructions to reduce her metoprolol by half, stop taking her furosemide, increase her fluid intake, check her blood pressures daily and have them recorded. She was also reminded to finish her course of antibiotic therapy. She is expected to return to the clinic in 3-4 days to reassess her symptoms. She has been instructed to seek immediate medical attention if her dizziness worsens, she experiences vision changes or begins to have slurred speech. These instructions were also sent to her assisted living facility as the patient has underlying dementia, which may affect her ability to apply all of the instructions she received today.

Literature Review

Recurrent urinary tract infections are defined as three or more occurrences over a 12-month period (Arnold, Hehn & Klein, 2016). Although not necessary, it is often found that the following occurrences of urinary tracts infections are caused by the same species (Arnold et al., 2016). This literature review will discuss the occurrence of UTIs in adult women. A review of the literature will be conducted in order to identify the most common species responsible, the signs and symptoms on presentation and the treatment/prophylactic therapies available for uncomplicated and complicated acute cystitis and pyelonephritis. Lastly, literature guidelines outlining the treatment options for urinary tract infections in pregnancy will be addressed.

Background

As discussed in our case above, a 59-year-old woman was hospitalized for a urinary tract infection: a well too common finding. Urinary tract infections are the most common bacterial infection affecting women across the lifespan (Bosmans, Beerepoot, Prins, Ter Riet & Geerlings, 2014). *Escherichia coli* is the most common species to cause a UTI making up 75% of the cases, followed by *enterococcus faecalis*, *proteus mirabilis*, *klebsiella*, or *staphylococcus saprophyticus* (Arnold et al., 2016). The rate of recurrence is often not discussed in great detail amongst patients by their providers. Approximately 40% of women who have had a UTI will have a recurrence within six months (Arnold et al., 2016). The significance of this statistic is the high rate of recurrence and how this impacts our health care system.

Signs and Symptoms

Urinary tract infections may go unnoticed however in a significant portion of the population there are key signs and symptoms that accompany the disease. Burning on urination, urgency, hematuria, frequency and pelvic pain are amongst the most common symptoms in women (Mayo Clinic, 2017). Furthermore, symptoms may be able to give an indication of the location of infection. For example, flank pain, fever and chills are often indicative of acute pyelonephritis while burning on urination and vaginal discharge coincides with urethritis (Mayo Clinic, 2017). Women often find the symptoms to be a nuisance and an overall negative impact on their quality of life (Bosmans et al., 2014).

Cranberries as Prophylaxis

There are currently numerous medicinal and non-medicinal options to both treat and prevent the recurrence of urinary tract infections. As the rate of antimicrobial resistance continues to rise, the need for non-antibiotic prophylaxis for UTI's is crucial.

One commonly used non-medicinal method for UTI prophylaxis is cranberries (Beerepoot & Geerlings, 2016). The active ingredient in cranberry known as proanthocyanidins (PACs) has been found to inhibit adherence of P-fimbriated *E. coli* to the users uroepithelial cell receptors thereby reducing ones risk of being infected resulting in a UTI (Beerepoot & Geerlings, 2016). The reduction of risk is tied directly to the dose of cranberry received per day. It has been estimated that 36 mg of cranberry PACs is required to be effective as prophylactic therapy for recurrent UTI's (Ledda et al., 2017). A similar study suggested that a 500 mg dose of cranberry taken twice daily was the suggested dose for UTI prevention (Bosmans et al., 2014). *Proteus mirabilis* and the swarmer-cell differentiation process is inhibited by cranberries hence acting as a mechanisms of UTI reduction (Kong-Sang, Chih-Kuang, Wen-Kai, Ming-Chung & Che-Sheng, 2016). Furthermore, the adhesion of *E coli* to the bladder epithelium is another mechanism in which cranberries inhibit colonization and infection.

Antibiotics as Prophylaxis

Antibiotics are often a preferred method of UTI prophylaxis as they are very effective in those susceptible to recurrent urinary tract infections. A randomized clinical trial conducted by Bosmans et al., (2014) was able to highlight benefits of antibiotic prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) over cranberries. The study measured the rate of UTI recurrence over a 12-month period in premenopausal women (Bosmans et al., 2014). It was able to conclude that the major advantage of TMX-SMX was its effectiveness as well as its cheaper cost compared to cranberry prophylaxis (Bosmans et al., 2014). In addition to this, the overall cost of treatment was also higher in the cranberry group because of a higher rate of UTI's requiring further management

(Bosmans et al., 2014). Exposure to antibiotic therapy was amongst the negatives of this treatment option. Studies show that the single most important risk factor for antimicrobial resistance was previous use and exposure to such agents (Kong-Sang et al., 2016). Rates of resistance for E coli to antimicrobial agents such as TMX-SMX are as high as 20-31% (Kong-Sang et al., 2016). This is a significant health care concern as antimicrobial resistance not only puts a limitation on our available treatment options but also increases health care costs.

Antibiotic Treatment

Urinary tract infections are treated dependent on the location of the infection and whether the infection is complicated or not. Acute uncomplicated cystitis is adequately treated with Nitrofurantoin monohydrate/macrocrystals 100 mg orally, twice daily for a total of five days (Hooton, 2016). Acute complicated cystitis is often treated with an oral fluoroquinolone, often ciprofloxacin 500 mg two times per day (Hooton, 2016). This regimen can also be substituted for a 1000 mg extended release tablet taken once per day. Another appropriate antibiotic regimen includes levofloxacin 750 mg daily tablet (Hooton, 2016). Both should be continued for five to seven days to ensure the infection is cleared. Although commonly used as UTI prophylaxis, TMX-SMX is a poor choice of antimicrobial therapy for those with complicated recurrent UTI's (Hooton, 2016). Acute pyelonephritis is much more involved and therefore best treated in a hospital setting. It is suggested that those with moderate illness severity be treated with third generation cephalosporins or fluoroquinolones. This however would not be appropriate if there is suspicion that a resistant organism is to blame (Hooton, 2016). Combining a beta lactam/beta lactamase inhibitor or carbapenem is often recommended to treat severe

pyelonephritis requiring a broader spectrum antibiotic (Hooton, 2016). Treatment is administered for seven to fourteen days for the majority of patients.

As a provider, it is not standard practice to follow-up with urine cultures to ensure a UTI has resolved. Patients reporting their symptoms to be resolved and completing the recommended length of antibiotic therapy is sufficient as treatment and management regimens. However, it is recommended that patients who continue to have recurrent UTI's be further evaluated for other underlying etiologies.

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Parenteral regimens for empiric treatment of complicated pyelonephritis

Antimicrobial agent	Dose, interval
Mild to moderate pyelonephritis*	
Ceftriaxone	1 g every 24 hours
Ciprofloxacin	400 mg every 12 hours
Levofloxacin	750 mg every 24 hours
Aztreonam [†]	1 g every 8 to 12 hours
Severe pyelonephritis	
Cefepime	2 g every 12 hours
Piperacillin-tazobactam ^Δ	3.375 g every 6 hours
Ceftolozane-tazobactam	1.5 g every 8 hours
Ceftazidime-avibactam	2.5 g every 8 hours
Meropenem ^Δ	500 mg every 8 hours
Imipenem	500 mg every 6 hours
Doripenem	500 mg every 8 hours

Image; (Hooton, 2016)

Urinary Tract Infections in Pregnancy

Recurrent urinary tract infections in pregnant women is a topic of great importance as it occurs in up to 2% of all pregnant women. When caring for a woman who is or has the potential to be pregnant, it is important to note the relationship between maternal urinary tract infection and adverse pregnancy outcomes (Hooton & Gupta,

2016)^a. Recurrent UTI's are more common in pregnancy compared to the non-pregnant adult woman likely attributed to the physiologic changes undergone during ones pregnancy. Complications of pyelonephritis include increased risk of preterm birth, perinatal mortality and low birth weight (Hooton & Gupta, 2016)^a. The literature suggests treatment of asymptomatic UTI's in order to prevent progression to pyelonephritis. The table below summarizes antibiotic therapy recommendations for the pregnant adult. Unlike the general adult, it is highly suggested that follow-up cultures one week after completing the prescribed antibiotic course are done on pregnant women in order to ensure resolution of the infection (Hooton & Gupta, 2016)^a.

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Antibiotics for asymptomatic bacteriuria and cystitis in pregnancy

Antibiotic	Dose	Duration	Notes
Nitrofurantoin	100 mg orally every 12 hours	Five to seven days	Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected. Avoid use during the first trimester and at term if other options are available.
Amoxicillin	500 mg orally every 8 hours or 875 mg orally every 12 hours	Three to seven days	Resistance may limit its utility among gram-negative pathogens.
Amoxicillin-clavulanate	500 mg orally every 8 hours or 875 mg orally every 12 hours	Three to seven days	
Cephalexin	500 mg orally every 6 hours	Three to seven days	
Cefpodoxime	100 mg orally every 12 hours	Three to seven days	
Fosfomycin	3 g orally as single dose		Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected.
Trimethoprim-sulfamethoxazole	800/160 mg (one double strength tablet) every 12 hours	Three days	Avoid during the first trimester and at term.

The durations listed in the table are based on data from studies conducted in both nonpregnant and pregnant women.

Image; (Hooton & Gupta, 2016)^a

Learning Points

1. Often urinary tract infections are harmless with minimal long-term consequences however they can have a significant impact on a women's quality of life.
2. The rate of UTI recurrence within six months is high (40%) and therefore needs to be a topic that practitioners are familiar with. Patients often ask about prophylactic therapy and if they should be taking them.
3. Cranberries have been found to some effect in urinary tract infection prophylaxis however it shows significantly less success in comparison to antibiotic therapy. This would not be a good recommendation for those highly susceptible to recurrent UTI's. The literature has not found any negative consequences of cranberry supplementation outside of its high cost.
4. It is appropriate for practitioners to prescribe trimethoprim-sulfamethoxazole for those susceptible to recurrent UTI prophylaxis. It is a more effective but also cheaper option. This treatment option should be used sparingly as rates of *Escherichia coli* resistance to antimicrobial therapy has been and continues to be on the rise.
5. Pregnant women must be treated for UTI's whether symptomatic or asymptomatic due to the negative consequences of preterm infants, small birth weight and increased fetal mortality. Nitrofurantoin is a safe antibiotic option for pregnancy.

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