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Review Article

RECURRENT URINARY TRACT INFECTIONS IN MEN

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Abstract:

Introduction: it is relatively uncommon to develop a urinary tract infection in a male who is younger than sixty years and does not have a urinary catheter. However, this incidence significantly elevates following the age of sixty years and continues to increase as the patient ages. the worldwide incidence of urinary tract infections among male elderly individuals who are older than eighty-five years can be as high as 7.7 per 1000 person-years.

Aim of work: In this review, we will discuss the most recent evidence regarding Recurrent Urinary Tract Infections in men

Methodology: We did a systematic search for Recurrent Urinary Tract Infections in men in the emergency department using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

Conclusions: E. coli infection that manifests as acute episodes of febrile urinary tract infection. Imaging of the upper urinary tract and referral to a urologist for cultures to localize the infection to the prostate are recommended. If imaging of the upper urinary tract identifies any abnormalities, correction should be considered. The patient should be aware of potential adverse effects of long-term antimicrobial therapy.

Key words: Recurrent urinary tract infection, men, management, diagnosis.

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INTRODUCTION:

Usually, it is relatively uncommon to develop a urinary tract infection in a male who is younger than sixty years and does not have a urinary catheter. However, this incidence significantly elevates following the age of sixty years and continues to increase as the patient ages.¹ Recent reports estimate the worldwide incidence of urinary tract infections among healthy male adults who are younger than fifty-five years to range between 0.9 and 2.4 per 1000 person-years. On the other hand, the worldwide incidence of urinary tract infections among male elderly individuals who are older than eighty-five years can be as high as 7.7 per 1000 person-years.² In addition to the significant increase in the incidence of urinary tract infections, older age is correlated with more severe clinical manifestations of the disease, and older patients have a higher risk of hospital admissions following a urinary tract infection.³ Moreover, within the elderly males population, most cause of bacteremia result from a urinary tract infection. However, mortality due to urinary tract infections remains to be low in male patients.⁴ Older age has also been found to be associated with higher risk of urinary tract infections recurrence. Recurrence could be associated with the development of long-term complications and the development of chronic kidney disease, if an obstruction of the urinary tract is present.

Despite the significant increase in the incidence of urinary tract infections among older males, the overall urinary tract infections incidence among old males remains to be significantly lower than older females. However, among individuals who are older than eighty years, incidence of urinary tract infections become almost the same among both sexes.

The development of asymptomatic bacteriuria is generally rare in the young adults male population. However, in the population of males older than eighty years, it can be present in up to 10% in normal individuals, and up to 40% of elderly who live in a care facility.⁵ The presence of this asymptomatic bacteriuria has been found to be associated with a significantly higher risk of acquiring a symptomatic urinary tract infection. Generally, it is not recommended to use antibiotics therapy to treat asymptomatic bacteria, as this could be associated with increased resistance against antibiotics.⁶

As males become older, both functional and structural abnormalities occur within their urinary tract leading to abnormal voiding process. The most

common urinary abnormality to occur in old males is benign prostatic hyperplasia, which is associated with higher risk of developing urinary tract infection due to causing obstruction and disturbing the normal flow of urine. Acute bacterial prostatitis is a less common condition that occurs following an infection of the prostate and leads to the development of a severe and possibly fatal systemic disease.⁷ Chronic bacterial prostatitis, on the other hand, is a less serious condition that presents with recurrent infections of the prostate, most likely with the isolation of the same causing organism each event.⁸ Infections of the prostate are usually difficult, or even impossible, to be eradicated due to the limited ability of most used antibiotics to diffuse into the prostate. Another factor that increase the rates of treatment failure in patients with prostatic infections despite antibiotics use is the bacterial colonization of a prostatic stone.⁹

The presence of other chronic comorbidities (like diabetes mellitus) among elderly patients is another factor that predisposes them for the development of a urinary tract infection by making them more vulnerable to infections. The presence of comorbid urinary conditions like urinary incontinence or retention does also increase the risk of urinary tract infections as most of these patients will have to use urinary catheters.¹⁰ On the other hand, postvoiding residual urine volume has not been found to be correlated with developing asymptomatic or symptomatic bacteriuria and urinary tract infection.¹¹ Several factors have been found to be associated with higher risk of developing asymptomatic bacteriuria, including the presence of functional disabilities, urinary incontinence, decreased physical activity and immobility, and the presence of altered mental status or dementia.¹²

A previous study has found that among elderly males who live in the community, up to 80% can have a gram-negative organism isolated from their urine samples.¹³ *E. coli* has been found to be the most commonly isolated organisms followed by *Klebsiella pneumoniae* and *Proteus mirabilis*. In rare cases, gram-positive bacterial organisms can also be isolated like *Enterococcus* species. Some strains of *E. coli* have been found to be more virulent leading to more severe manifestations. Strains associated with highest virulence are those that are usually isolated from males who develop a severe febrile urinary tract infection complicated by pyelonephritis. Less virulent strains are usually isolated from males who have cystitis.

When studying elderly males who live in a care

institution and do not use a urinary catheter, *E. coli* is also the commonest isolated bacterial organism in cases of symptomatic bacteriuria. However, the prevalence of other bacterial organisms like *P. mirabilis*, and *Pseudomonas aeruginosa* has been increasing recently. 1 A recent Spanish study has concluded that males have a higher risk than females to have bacteriuria with bacterial organisms that are resistant to beta-lactams. Higher prevalence of these organisms was seen with increased age. ¹⁴

In this review, we will discuss the most recent evidence regarding Recurrent Urinary Tract Infections in men

METHODOLOGY:

We did a systematic search for Recurrent Urinary Tract Infections in men in the emergency department using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Recurrent urinary tract infection, men, management, diagnosis.

Diagnosis and Evaluation:

Community-acquired urinary tract infections, like cystitis, usually manifest as the present of irritation in the lower tract, dysuria, frequency, urgency, nocturia, discomfort in the suprapubic area, and gross hematuria in severe cases. Fever is generally absent in uncomplicated cystitis. Pyelonephritis, on the other hand, usually manifests as high fever, pain and tenderness in the costovertebral angle, along with the previous symptoms of lower tract infections like dysuria, frequency, urgency, nocturia, and discomfort in the suprapubic area.

A previous prospective cohort found that older males who had a urinary tract infection and fever had elevated concentrations of the serum prostate-specific antigen level, along with an increase in the volume of the prostate, despite the inability to localize the infection to the prostate. Generally, acute bacterial prostatitis presents with lower tract infection symptoms that are associated with fever and, in some cases, obstruction. On the other hand, clinical manifestations of chronic bacterial prostatitis are usually similar to those of cystitis but are recurrent.

Usually, urinary tract infections in older males have similar clinical manifestations in patients who live in care institutions when compared to the general population. however, these patients are more challenging to be evaluated and assessed for multiple

reasons including the decreased functionality, the absence of clear communication, the possible altered mental status, and/or the high prevalence of coexisting urological conditions which could be attributed to the presence of underlying chronic neurological dysfunctions. ¹⁵

Obtaining a urine sample for culture and sensitivity is a crucial step during the assessment of suspected infection and will help plan further management. However, it is only recommended in males who are symptomatic and with high suspicion to have a urinary tract infection. Asymptomatic patients, who might have bacteriuria are not recommended to do a urine culture and sensitivity test to prevent unnecessary treatment and antibiotics use. It is important to be aware that urine sample must be obtained for culture before any empiric antibiotics therapy is started. Otherwise, false negative results may come back. To avoid sample contamination, it is recommended to wipe the glans penis with a moist gauze and retract the foreskin before taking the sample, then the sample is obtained from the midstream void. When dealing with a patient who has an external urinary catheter, it is also important to clean the foreskin and apply a clean catheter before collecting the specimen. ¹⁶ However, in patients who have intermittent catheterization the sample can be directly acquired from the urinary bladder.

The presence of bacteriuria indicates an infection of the urinary tract, which can be either symptomatic or asymptomatic. On the other hand, pyuria is nonspecific, does not indicate the presence of infection of the urinary tract, and does not require treatment with antibiotics. This is because pyuria can sometimes be found in normal older individuals regardless of having bacteriuria. However, pyuria is still associated with very high sensitivity and negative predictive value (more than 95%), so it is useful to exclude the presence of a urinary tract infection. ¹⁷ An infection of the urinary tract is confirmed when urine culture shows more than one hundred colony-forming units of a certain bacterial organism per milliliter. The presence of less colony-forming units per milliliters can also indicate infection but must be interpreted cautiously and based on clinical manifestations. These diagnostic criteria is similar in patients with urinary catheterization, and the presence of one hundred or more colony-forming units is generally diagnostic. When the same organism is isolated from both urine samples and blood samples, this will further confirm the diagnosis.

In patients who have developed a urinary tract infection for the first time, it is highly recommended to assess both the upper urinary tract and the lower urinary tract. The reason behind this is that many males who present with a urinary infection may in fact have abnormalities somewhere along their urinary tract.¹⁸

Ultrasound techniques provide an invasive modality to measure the volume of residual urine. In general, when the residual urine volume is higher than 100 milliliters, this is considered an abnormal finding that needs further assessment and interpretation according to the clinical picture, the severity of the infection, and the frequency of infections recurrence.

Any patient with a urinary tract infection who develops a fever must immediately have their upper tract examined using CT imaging with injection of contrast. When CT imaging is not available, ultrasound to the kidney could be used to exclude the presence of obstruction or other functional or mechanical abnormalities that might need immediate intervention. CT imaging with injection of contrast remains to be the test that the highest sensitivity in these settings. However, it is relatively expensive and not always available. Therefore, the use of ultrasound is considered more reliable in detecting clinically significant abnormalities.

A previous study was done in Sweden on eighty-five male patients with urinary tract infection complicated by fever. Investigators found that of included patients, fifteen were found to have a previous undetected lesion within the urinary tract that needed surgical operation to be corrected. These that predisposed for the development of the infection and fever included benign prostatic hypertrophy complicated with obstruction, strictures of the urethra, urinary bladder stones, kidney stones, and cancer of urinary bladder.¹⁹

It is important to know that sometimes the detected abnormalities may not be the direct underlying causes that led to the development of the infection. Therefore, following the detection of the abnormality, a thorough urological assessment is necessary to evaluate the relevance of this abnormality to the current infection. For example, a patient who presented with pyelonephritis may have an underlying ureteral obstruction that increased the risk of pyelonephritis.

Recurrent urinary tract infections that are found to result from infection from same strain may indicate

failure of eradication of the bacteria from the urinary tract, which may be caused by failure of treatment, or the presence of a mechanical abnormality in the upper tract. For example, the presence of a kidney stone may lead to bacterial persistence and the development of recurrent infections with the same bacterial strain. Bladder stones and prostate abnormalities can also lead to bacterial persistence and recurrent infections.

In patients with chronic prostatitis, the diagnosis may be confirmed by culturing the fluid of the prostate using the Meares–Stamey test. The ability to identify a pathogenic organism in the secretions and fluids of the prostate confirms the diagnosis of chronic prostatitis. Some cases negative results may be found despite the presence of high clinical suspicion. In these cases, the test should be repeated as this test is associated with relatively high false negative rates.

Treatment:

When treating a male with urinary tract infection, it is preferred to use pharmacological agents that are excreted in the urine to be able to address the infection. In uncomplicated cystitis, the first empirical choices for treatment are trimethoprim–sulfamethoxazole, nitrofurantoin, and levofloxacin or ciprofloxacin. These drugs generally used for a week, unless culture and sensitivity are performed, where it is preferred to change the drug accordingly.

The use of Nitrofurantoin has been found to be associated with high efficacy in patients with uncomplicated cystitis. However, it has limited effects in cases of prostatitis and pyelonephritis due to the poor penetration of tissues. Therefore, in patients with pyelonephritis, the preferred empiric therapy is ceftriaxone, ciprofloxacin or levofloxacin, or gentamicin. Treatment of patients with pyelonephritis should last longer than cystitis and up to two weeks. Antibiotic therapy may be changed later according to the results of culture and sensitivity. Performing another urine culture and sensitivity for follow up is usually not indicated unless therapy fails, symptoms persists, or complications develop. Several trials have been conducted on both sexes to determine the efficacy of each antibiotics in the treatment of complicated cystitis and pyelonephritis.²⁰ When the duration of antibiotics treatment was investigated, studies have found that the use of antibiotics for four weeks was associated with similar outcomes when compared to the use of antibiotics for two weeks in males with complicated cystitis.²¹

The treatment of acute prostatitis must start with empiric use of intravenous broad-spectrum agents like penicillins and ceftriaxone. Other antibiotics that can be used in these cases include aminoglycosides and fluoroquinolones. Proper therapy must be immediately started as any delay could be associated with severe rapid deterioration of the clinical picture and high mortality rates. Studies estimate that about 25 percent of patients with acute prostatitis already have bacteremia at presentation, and up to 10% can have prostatic abscesses.

The use of prostatic ultrasound for the detection of prostatic abscesses is not routinely recommended unless patients do not improve on antibiotics therapy. Most patients with acute prostatitis have difficult urination, which can be improved using alpha-blockers. In severe cases, the use of urinary catheters may be required to relieve retention.

Empiric treatment should continue until results of prostatic secretions culture are available. Treatment then will be modified according to the results and is recommended to continue for at least one month. Studies are still debating the ideal duration of treatment that will achieve the best results with the least rates of complications and development of bacterial resistance. Up to five percent of males with acute prostatitis will later develop a chronic prostatitis.

Chronic prostatitis is often treated with a fluoroquinolone or trimethoprim-sulfamethoxazole for at least a month.²² A fluoroquinolone is usually first-choice treatment; levofloxacin and ciprofloxacin are equally effective in eradicating the infection.^{45,46} In a trial comparing different regimens of levofloxacin (at a dose of 750 mg every day for two weeks, 750 mg every day for three weeks, or 500 mg every day for one month) in men with chronic prostatitis (median duration, approximately eight years), the clinical efficacy was similar among the regimens immediately after therapy but at six months the response rate was significantly higher in patients on the four-week regimen.²³

When antimicrobial resistance develops against the use of fluoroquinolones or trimethoprim-sulfamethoxazole, nitrofurantoin, minocycline, or other tetracyclines may be effective in controlling the symptoms of uncomplicated cystitis that are attributable to bacterial relapse, even though nitrofurantoin does not achieve penetration of the prostate. Possible adverse events associated with

long-term use, such as pulmonary or liver toxic effects with nitrofurantoin, should be monitored. For self-initiated therapy, the patient is provided with an oral antimicrobial agent that is appropriate for the prior infecting organism. When symptoms occur, a urine culture is obtained and the duration of treatment is usually seven days.

When the infection is not localized to the prostate and no other explanation for recurrent infection is apparent, a similar strategy of suppressive or self-initiated therapy can be considered for bacterial relapse. If recurring infection occurs with different strains isolated, treatment should address factors that increase susceptibility to reinfection. Such treatment may include alpha-blocker therapy or other interventions, such as transurethral resection of the prostate, to reduce residual urine volume.

CONCLUSIONS:

E. coli infection that manifests as acute episodes of febrile urinary tract infection. Imaging of the upper urinary tract and referral to a urologist for cultures to localize the infection to the prostate are recommended. If imaging of the upper urinary tract identifies any abnormalities, correction should be considered. If the testing to localize the infection to the prostate is positive and the organism is sensitive to a fluoroquinolone or trimethoprim-sulfamethoxazole, a 30-day course of treatment is indicated. If the bacteria are not susceptible to these preferred antimicrobial agents, alternative agents that penetrate the prostate, as discussed in the Strategies and Evidence section, may be considered for a trial of therapy. If the initial therapy fails or relapse occurs, watchful waiting, intermittent self-initiated therapy, or suppressive therapy should be considered. Given the severity of recurrent infection and the lack of potentially curative antimicrobial agents, if the patient is prescribed long-term suppressive therapy, we would adjust the dose and frequency to a level that would be sufficient to prevent recurrent symptoms of urinary tract infection. Therefore, because of two febrile infections, we favor suppressive therapy. The patient should be aware of potential adverse effects of long-term antimicrobial therapy.

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