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Review article

INFECTION OF URINARY TRACT IN MENOPAUSAL WOMEN

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Abstract: Urinary infections are, by frequency, in the second place, immediately behind respiratory infections. The prevalence of urinary tract infections is generally increasing. UTI (urinary tract infections) is more common in women and very young people. The rates of occurrence generally reflect predisposing factors such as congenital anomalies in childhood, the onset of sexual activity, especially in women, and, of course, postmenopausal changes in older women. It is assumed that 50-60% of women can expect an episode of urinary infection during their lifetime. In postmenopausal women, there is a deficit in estrogen. It is one of the important factors that indirectly protects the vaginal mucous membranes as well as the uroepitel from infection. Bacteria from the digestive tract colonize the skin of the perineum, then the vulva, the vagina and the outer opening of the urethra. Normal vaginal flora (lactobacilli) protects the vagina from colonization by fecal bacteria because it lowers pH and creates unfavorable conditions for survival of bacteria.

Key words: urinary tract, infections, menopausal, women.

INTRODUCTION

Urinary infections are, by frequency, in the second place, immediately behind respiratory infections. The prevalence of urinary tract infections is generally increasing. UTI (urinary tract infections) is more common in women and very young people. The rates of occurrence generally reflect predisposing factors such as congenital anomalies in childhood, the onset of sexual activity, especially in women, and, of course, postmenopausal changes in older women. It is assumed that 50-60% of women can expect an episode of urinary infection during their lifetime. Studies confirm that annually, consulting a general practitioner for urinary infection, requires 14 men and 60 women out of 1,000 examined. If E. coli is previously isolated, the risk of the infection recurring over the next 6 months is 23.7%, unlike other causes, when the infection returns to 7.7% of cases (1). It is estimated that around 150 million cases worldwide have an annual incidence of this type of infection, with more than 5.3 million euros being spent for direct care. The most common causes of urinary infections are bacteria, but other microorganisms such as fungi, parasites and protozoa can cause the development of urinary infections. Although Escherichia coli is the most common cause of urinary infections, only some of its strains have the ability to adhere to the mucous membrane and challenge the change. She is Gram-negative, optional anaerobic, movable bacilli. They are arranged individually, in pairs or in irregular groups. They have chains or fimbres that have an adhesive role. They have complex antigen material. The most important are O antigen that is thermostable and H antigen that is thermolabile. Fimbria antigens have appropriate adhesive properties. Additional surface virulence factors are flagels that allow mobility and easier access to the target tissue (1, 2, 3).

PATHOGENESIS

Urinary infection occurs when the bacteria enter the urine and overpower the defenses of uroepithel by their virulence. Urine is under normal circumstances sterile, i.e. It does not contain bacteria or other microorganisms. Most urinary infections are caused by bacteria that make up the normal flora of the gut (Escherichia coli, Enterobacter, Klebsiella, Proteus spp.) These bacteria are normal inhabitants of the bowel, but if they find themselves in the urinary tract they cause an infection. Because of the close proximity of the anus and urethral opening, the urethra is often contaminated through the perineum and urethritis is formed. Given that infection usually develops accidently, inflammation spreads to the urinary bladder, causing cystitis. If the etiological factor is very virulent or there are signif-

icant host risk factors, then the infection can easily spread to the kidneys in which pyelonephritis occurs. If the human defenses are very weak and the therapy is not introduced timely, microorganisms enter the blood with the resulting bacteremia and sepsis, which can end up fatal. Ascendant spread of the infection is particularly characteristic for strains with specific adhesins, i.e. P-fimbriums adhering to the urotel (4, 5, 6, 7).

In postmenopausal women, there is a deficit in estrogen. It is one of the important factors that indirectly protects the vaginal mucous membranes as well as the uroepitel from infection. Bacteria from the digestive tract colonize the skin of the perineum, then the vulva, the vagina and the outer opening of the urethra. Normal vaginal flora (lactobacilli) protects the vagina from colonization by fecal bacteria because it lowers pH and creates unfavorable conditions for survival of bacteria. However, the disruption of this flora (the use of some spermicides and broad spectrum antibiotics, post-menopausal estrogen deficiency, irregular hygiene) makes it easier to colonize the vagina with uropathogenic bacterial strains, their settlement in the urethra and the onset of IUT (8, 9, 10, 11). Incontinence of the urine and, consequently, constant moistening of the periphery region allows easier duplication of bacteria and facilitates penetration into the urethra and the occurrence of inflammation. In addition to menopause, which leads to decreased uropeal defenses, and diabetes can lead to microalbuminuria with later impaired glomerular filtration and more difficult to wash bacteria that are left in the urinary tract and easily lead to infection (12, 13). There is also the possibility of spreading infection from distant hematogenic or lymphatic pathways, although this is a much less common way of urinary infections (14, 15, 16).

CLINICAL PICTURE

Urinary infections in the general population, as well as in women in postmenopausal, can affect only certain parts of the urinary system or extend to the entire urinary tract and beyond.

Asymptomatic bacteriuria

It implies colonization of the urinary tract with bacteria, not a classic infection. There is significant bacteriuria, but it does not cause any problems. The frequency of asymptomatic bacteriuria increases with age, and especially in men and women after 65 years. The significance of asymptomatic bacteriuria and the indication for treatment varies depending on whether it is detected in patients with normal urinary system or in those who have any complicated disease or condition. In non-risk categories, therapy is not required because of the potential for antibiotic resistance to bacteria. Many studies have indicated that most women with asymptomatic bacteriuria who are not pregnant and who do not have complicated urinary tract disorders after a while spontaneously eliminate bacteria (17, 18, 19).

Cystitis

Acute uncomplicated cystitis is the most common form of urinary infection. It is characteristic for women in the sexually active period and for women in menopause. Symptoms generally develop rapidly, within hours or during the day. Begin with more frequent urination, baking in urination, pain in the bladder at the end and immediately after wetting. The patient very often wets a few drops of urine, has the impression that her bladder has not been emptied, false urine calls (tinges), accompanied by strong pain and feeling of pressure in the bladder area, occur. Terminal or total haematuria may occur. The general condition at the beginning is not disturbed, but if timely treatment is not started, anger, fever, and elevated temperatures can occur, which is already in favor of pyelonephritis.

Women in menopause are characterized by recurrent cystitis, 10-15% of women suffer from this type of disease. These women appear because of the weakened urotract defense defenses, and this is a re-entry of bacteria into the urinary tract, and not about the ill-treated previous acute cystitis (20, 21, 22).

Pyelonephritis

Pyelonephritis is a bacterial infection of the renal pelvis and kidney parenchyma. The most common inflammation extends ascendant from the urinary bladder, although possible haematogenous and lymphopenia pathways of expansion with the consequent renal inflammation. The clinical picture develops rapidly and is characterized by high temperature (up to 40 °C), anger, fever, lumbar pain and digestive symptoms (nausea and vomiting). Concurrent cystitis is present in one third of patients.

There is painful sensitivity of the lumbar lodge to succulent. Very often both kidneys are affected. The progression of uncomplicated bacterial cystitis into acute uncomplicated pyelonephritis is expected in only 2% of patients, regardless of whether they are treated or not (23).

COMPLICATIONS

Urosepsa

Urosepsa is a septic condition caused by the penetration of bacteria and bacterial toxins from the urinary tract into the bloodstream. It is reported in people with

urological manipulations, where bacteria are of extreme virulence, as well as in people with impaired immunity and associated illness. Menopausal women are especially affected due to extremely common urinary infections, some of which may lead to septic conditions. Especially dangerous is sepsis caused by pseudomonas due to the high mortality rate. Clinically, the temperature (over 38 °C) with fever or hypothermia (below 36 °C), leukocytosis (over 12,000), tachycardia and tachypnoea and disturbances of consciousness (24).

Abscess of the kidney

It represents a localized pulmonary collection that can be formed in the cortex (cortical abscess) or kidney medulla (medullary abscesses). Medullary abscesses mainly develop on the basis of the already existing urinary tract infection (acute pyelonephritis), while cortical abscesses are more often metastasized from a distant inflammatory site. The kidney abscess is expressed by signs of acute infection (high temperature, fever, fever) with pain in the affected area of the kidneys. Symptoms of lower urinary tract infection may not be present.

Perinefritic abscess

Perinefritic abscess is the acute inflammation of the tissue around the kidneys. It is most often the result of the penetration of bacteria from the inflammatory site of the kidney. The inflammatory process takes place in the loose connective tissue and fat tissue around the kidneys (25). Clinically manifests itself with febrile, painful sensation and redness of the skin in the lumbar region.

DIAGNOSIS

The diagnosis of urinary infections is based on the anamnesis and clinical picture and is confirmed by additional analyzes. In addition to the clinical picture, biochemical analysis of urine and urinary culture is often used to prove the existence of an infection. The interpretation of the findings should be careful, because there is always a possibility of contamination of the sample, regardless of the method it was obtained. The most common method of taking a sample is to collect the medium jet of the first morning urine into the sterile container after allowing the first jet to drain in order to reduce the possibility of contamination.

The presence of bacteria in urine (bacteriuria) can, but does not necessarily mean, an infection. In order to delineate whether their presence signifies an infection or is a consequence of contamination, a concept of significant bacteriuria has been introduced, which indicates the presence of more than 100,000 bacteria in 1ml of urine, which most often represents infection rather than contamination.

Nitrites in the urine are highly specific for the presence of bacteria, but their absence does not necessarily mean the absence of infection, but can be the result of dilution of urine due to the introduction of a large amount of fluid or the use of diuretics. In addition, some bacteria that cause IUTs do not lead to the reduction of nitrates to nitrites (Staphylococcus, Enterococcus, and Pseudomonas). Nitrites can also be positive for green-eating nutrition. Diagnosis of acute uncomplicated cystitis with a high probability (> 90%) can be set only on the basis of a clinical picture (provided three or more typical symptoms are present at the same time). Urinoculture is a gold standard to prove infection, not only for determining the presence of a pathogen, but also for the ability to know what type of microorganism is and what its sensitivity to antimicrobial therapy is. However, there are limits to the diagnosis of infections in which the number of bacteria is less than 100 000 in ml of urine (in case of infections of the lower part of the UT). As many laboratories as the reference value for the detection of infection take a number of 100,000 or 10,000 bacteria per ml, negative urinary effects of the urinary crops should be interpreted with caution. In most cases, urine examination shows massive leukocytosis and bacteriuria. Proteinuria may also be present, as is the finding of leukocytic cylinders that, with massive leukocytes, provide reliable evidence of pyelonephritis. Of the other laboratory analyzes, complete blood count (CKS), C-reactive protein (CRP), serum creatinine and serum creatinine should be made. Radiological methods should be considered if it is necessary to exclude the existence of obstruction or calculus UTI.

THERAPY

The main therapy for urinary infections are antibiotics.

The treatment of acute uncomplicated cystitis and uncomplicated pyelonephritis in women in menopause is empirically. When selecting an adequate antimicrobial drug, care should be taken of the type of causative agent and its susceptibility to the drug, price and availability, as well as the possibility of allergic and other adverse reactions.

Trimethoprim-sulfamethoxazole (TMP-SMK) showed a high rate of eradication of uropathogens and many put it into the first-line treatment for the treatment of acute uncomplicated cystitis in menopausal women. Three-day TMP-SMK therapy leads to eradication of the causative factor in 93% of women. The

same studies showed the same three-day efficacy compared to seven-day therapy and significantly less frequent adverse reactions. In pyelonephritis, it is not enough that the medicine reaches a high concentration in the urine, but it must be sufficient in the blood to renal tissue. This drug is not the first choice in pyelonephritis, but is applied only after antibiography and proven sensitivity of the causative agent to it. What complicates the use of TMP-SMK is the emergence of an increasing number of resistant strains of E. coli on this drug. Alternatively, a single dose can be used with nitrofurantoin or phosphomycin-trometamol therapy. Both of these the drug has a low resistance rate, and only 5-10% have lower efficacy compared to the three-day TMP-SMK therapy in eradicating the cause and improving clinical symptoms. Nitrofurantoin should be used with caution in elderly women in menopause with comorbidities due to the potential for toxic effects that are most pronounced on the lungs and liver after long-term use.

Fluoroquinolones (ofloxacin, ciprofloxacin, levofloxacin) in many studies have shown the same efficacy as TMP-SMK. It is recommended that quinolones be used as drugs of the second choice in the treatment of uncomplicated cystitis, although in practice this is not observed. In the case of pyelonephritis, ciprofloxacin is a first-line medication. Initially, 1 g of ceftriaxone or aminoglycoside (24h-dose) may be administered parenterally in pyelonephritis and then continued with ciprofloxacin per so. Currently, in Europe and North America, resistance is less than 10%, but there is a trend of increasing resistance that is becoming worrying. In over 90% of cases, cystitis causes complete withdrawal of symptoms. If the symptoms are delayed even after the use of antibiotics, it is necessary to do urinology. If the symptoms are very pronounced then another antibiotic should be introduced immediately obtaining the antibiogram results (25).

If it is a severe clinical picture of acute uncomplicated pyelonephritis where systemic signs of infection (nausea, vomiting) are present, haemodynamic instability or signs of sepsis as well as in the suspected complication of the infection, it is necessary to hospitalize the patient. Complicated IUT is much more difficult to cure. The spectrum of possible causes is much higher. In addition, they are often resistant and sometimes multiresistant to antibiotics that are used. Therapy begins with empirical broad spectrum antibiotics (cephalosporin's III generation, fluorinated quinolones) and continues with targeted antibiogram therapy. Treatment of complicated IUT implies the simultaneous removal of factors that make them complicated. In recurrent IUT, if the infection recurs within one month of completion of the primary inflammation treatment, an antibiotic of the first therapeutic line should be included in the short-term regimen. In the event that the infection occurs within 6 months, it is necessary to choose another antibacterial drug, especially if the first choice was TMP-SMK. In other cases, recurrent infection should be treated by the same therapeutic protocol as sporadic cases of uncomplicated urinary infections. Treatment is always started empirically and, if necessary, corrected after getting antibiotics.

PREVENTION

Prevention of IUT in menopausal women is of utmost importance in the sound of high incidence of infection. Prior to the initiation of antimicrobial prophylaxis, non-medicaments prevention measures should be carried out. This implies a lifestyle change in order to reduce risk factors, but also other measures that have shown efficacy in the prevention of recurrent IUTs (cranberry consumption and vaginal use of estrogen). Changing the lifestyle of women in menopause involves, first and foremost:

Reduction of foods and beverages that irritate the bladder, especially caffeine preparations

• More often than not a little exercise to bubble bacteria (at 2-3 hours)

• Kegel exercises for muscle strengthening give pelvis and incontinence prevention

• Cessation of smoking - chronic cough stimulates urinary bladder urinary tract and easier penetration of bacteria

• Maintenance of normal body weight-elevated BMI stimulates incontinence

• After urinating, sweeping the perineum from front to back

• Consuming as much fluid as possible due to easier washing of bacteria from UT

• Avoiding hard and synthetic underwear.

CONCLUSION

Urinary infections are one of the most common infections in humans. According to the frequency they are located immediately behind the respiratory. Women at menopause are at particular risk due to decreased estrogen concentrations, which is a very important factor in the defense against urogenital infections. In women who have severe recurrent infection with vaginal disorders (dyspareunia, dryness), mandatory substitution therapy is required for local estrogens using topical tablets, creams or rats with gradual release of estrogens placed in the vagina. Per orally estrogen-containing estrogen does not have a sufficiently pronounced local effect that will reduce the incidence

of IUT and have more pronounced adverse effects. In addition to estrogen, personal hygiene, changes in lifestyle habits, use of cranberry preparations and, if necessary, long-term use of small doses of antibiotics, which in more than 95% of cases manage to completely prevent the development of IUT, is very important.

DECLARATION OF INTEREST

The authors declare that there are no conflicts of interest.

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Sažetak

INFEKCIJE URINARNOG TRAKTA KOD ŽENA U MENOPAUZI

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Urinarne infekcije su, prema učestalosti, na drugom mestu, odmah iza respiratornih. Prevalenca infekcije urinarnog sistema je generalno u porastu. UTI (infekcije urinarnog trakta) je češća kod žena i veoma mladih osoba. Stope pojave generalno reflektuju predisponirajuće faktore kao što su kongenitalne anomalije u detinjstvu, započinjanje seksualne aktivnosti, naročito kod žena, i naravno, postmenopauzalne promene kod starijih žena. Pretpostavlja se da 50-60% žena može očekivati epizodu urinarne infekcije u toku svog života. Kod žena u postmenopauzi dolazi do deficita u količini estrogena. On je jedan od važnih faktora koji indirektno štite vaginalnu sluznicu kao i uroepitel od infekcije. Bakterije iz digestivnog trakta kolonizuju kožu perineuma, zatim vulvu, vaginu i spoljni otvor uretre. Normalna vaginalna flora (laktobacili) štiti vaginu od kolonizacije fekalnim bakterijama jer snižava pH vrednost i stvara nepovoljne uslove za preživljavanje bakterija.

Ključne reči: urinarni trakt, infekcije, menopauza, žene.

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