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PHARMACEUTICAL CARE IN THE TREATMENT OF PATIENTS WITH LOWER URINARY TRACT INFECTIONS

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Urinary tract infection (UTI) is a non-specific infectious processes, which include all kinds of infections affecting various parts of it's anatomy: kidneys, ureters, bladder and urethra. Traditionally, they are divided into the infection of lower portion of UTI (urethritis, cystitis), which are found in the vast majority of cases, and the upper (nephritis). According to statistics, the incidence of UTI in the world is about 150 million cases per year and costs the health care systems of different countries in more than \$ 6 billion. In the U.S., they are the cause of more than 8 million annual visits to physicians and more than 100 thousand hospitalizations. This pathology is about 50 times more common in women, and is generally about 5% of the population morbidity. The tasks of pharmaceutical care of patients with a UTI in the treatment process is directly related to this important medical and social problem [1, 2].

The annual forums of the American Urological Association (AUA) is traditionally considered to be "trend setters" in matters of treatment recommendations of UTI. Last Consensus on the recommended drugs and rational schemes of their use in UTI was adopted in

2002 [3] and since then a number of positions was improved and supplemented. It should be remembered that, as used in the treatment of antimicrobial agents are, in most countries, including Ukraine, prescription drugs, appointed solely by physician. The trend of mentioned changes, and review tasks of pharmaceutical care for these patients is the aim of this publication. In this case, we deliberately placed outside the brackets sufficiently specific discussion topic of drug treatment of nephritis.

Materials and methods

The analysis includes the AUA resolution for the last 7 years and the corresponding publication on the review of controlled clinical trials, completed in 2012, according to the database of the National Institute of Health, USA. Evaluated the use of various drugs and schemes of its applications for the various categories of patients (children, pregnant women, patients with the presence of comorbidity, chronicity factors of UTI, etc.) and the role of the pharmacist in the treatment process.

Results and discussion

The vast majority of UTI in practice is uncomplicated bacterial cystitis, that are most common in women. It refers to the presence of non-virulent strains of microorganisms in the absence of recurrence process and chronicity of the process factors (Table 1.). Most of these forms is *E. coli* (approximately 80%) and *S. saprophyticus* (5-15%). Among the complicated UTI of about 40% are infectious processes that accompany the use of urinary catheters, which in the U.S. is about one million cases per year [2, 4].

Table 1. Potentially infectious microorganisms of urinary tract

Common causative agents of UTI in adults	The normal flora of the perineum
<i>Escherichia coli</i>	<i>Lactobacillus</i>
<i>Klebsiella; Enterobacter</i>	<i>Corynebacteria</i>
<i>Proteus</i>	<i>Staphylococcus</i>
<i>Pseudomonas</i>	<i>Streptococcus</i>
<i>Staphylococcus saprophyticus</i>	<i>Anaerobes</i>
<i>Enterococcus</i>	
<i>Candida</i>	
<i>Adenovirus type 11</i>	

Provocative factors that are important for the pathogenesis of UTI in recent years have been greatly detailed. For women there are many more, as determined their anatomical features (shorter urethra and perineum that facilitate penetration of bacteria into the urinary tract). Sexually active women have a greater frequency of UTI, due to increased irritation of mucous membranes including the urethra. In climacteric period UTI is even more frequent because of a general decline in estrogen and increased vulnerability of the mucous membranes. Studies show that virtually every other woman has UTI at least one in their lifetime, and most of them suffer more often. With this many authors have

noted a significant role of a pharmacist in the prevention various forms of UTI [3, 5].

Treatment of UTI is a combination of antibiotics and removal, if possible, of provoking factors. That is the explanation of these features and is one of the tasks of the modern pharmacist in pharmaceutical care. For example, it is necessary to pay particular attention to adequate hydration of the patient. It becomes particularly important in the elderly, because of the age-impaired sense of thirst [6].

The basis of medical treatment are antibiotics, although for uncomplicated UTI it saved the recommendation to use the combination of trimethoprim-sulfamethoxazole (TMP-SMX) - Co-trimoxazole (Biseptol,

Bactrim, etc.). For the purpose of rational antibiotic use a combination of a typical clinical presentation and analysis of urine with the identification of the pathogen (if indicated), as well as taking into account the mentioned predisposing factors. Most antibiotics have high concentrations in the urine and therefore are effective for the eradication of bacteria from the urinary tract. At the same time, considering the possibility of complications UTI, is important to create a high concentration of drug in the tissues. The largest concentration in the urine create the following antimicrobial agents (in descending order): Carbenicillin - Cephalexin - Ampicillin - TMP-SMX - Ciprofloxacin - Nitrofurantoin [4, 7].

Uncomplicated UTI (mostly cystitis) treated with 3 or 7-day courses of TMP-SMX in the so-called "background regime" - without changing the normal rhythm of life (Table 2.). The efficiency of courses is approximately equal at around 95%. Currently followed in the Consensus 2002 it was excluded from the recommendations using of a single dose of TMP-SMX. At high resistance microorganisms to TMP-SMX in a particular geographic region (more than 10-20%) are used fluoroquinolones (Ciprofloxacin, Ofloxacin) generally designated at 3-4 days. If a patient has diabetes, pregnancy, age greater than 65 years, anamnesis of UTI in the past, as well as UTI symptoms more than 7 days, it is necessary to use the full course of antibiotics for 7-14 days. In case of ineffectiveness of TMP-SMX during pregnancy should be use fosfomycin (Monural, Urofesfabol) as the most safe for the fetus. Although it is less effective than other antibiotics, but the frequency of occurrence of resistant strains to it is very low. If the UTI symptoms do not disappear during the first two or three days of treatment, it is recommended to stop and perform a urine culture to determine the composition and the sensitivity of microflora.

At complicated UTI, after confirmation of the culture, its recommended the appointment of a combination of ampicillin with an aminoglycoside (Gentamicin, Amikacin, Netilmicin) + ampicillin or vancomycin (if

allergic to beta-lactam antibiotics), or a combination of ampicillin with III generation cephalosporin (in the absence of pathogenic enterococci). Combinations of antibiotics are adjusted according to the results of blood culture (they are positive in 20-40% of patients). Treatment lasted 14 days, which is different from the previously recommended 10-day period, and the transition to oral drugs are now allowed only 48 hours after the relief of symptoms of UTI. At epididymitis use TMP-SMX or a fluoroquinolone for at least 3 weeks, and acute bacterial prostatitis requires receiving TMP-SMX or fluoroquinolones for at least 4 weeks, and chronic forms – 6-12 weeks (Table 2.) [4, 5].

In some cases it prescribes the use of 6-12 months courses of prophylactic administration of antibiotics. This type of treatment is the key to some women who are ineffective other measures. They often use TMP-SMX, nitrofurantoin or cephalexin at relatively low dosage (1/3 to 1/2 daily dose usually once per day). Drug administration in bedtime is more effective. Research suggests that such prophylactic course of UTI reduces relapses by 95% and prevents infection of the kidneys. Side effects of treatment include indigestion and various fungal infections. It is therefore recommended the parallel use of probiotics or yogurt, which definitely reduces the infection of yeast fungi [4, 7].

Recurrent UTI imply the impossibility of bacterial eradication, despite an adequate course of treatment. They are found in about 10% of women and very rare in men. In these cases, additional studies are needed, including imaging (MRI, arteriography, etc.) to identify possible anatomic reasons. In the case of "avoidable factors" of this type, indicated the appropriate surgical treatment [1, 9].

Asymptomatic bacteriuria in most cases do not require treatment. An exception is pregnancy. Treatment, according to current guidelines, not indicated in the elderly (70 years and older) and in patients with a permanent catheter. At the same time in these patients categories bacteriuria noted respectively in 20-40% and 90% [7, 8].

Table 2. The most commonly used antibiotics and conventional modes of their application.

Groups	Subgroups/Preparations	Typical use	Notes
Beta-lactams	<u>Penicillin (Amoxicillin)</u> Amoxicillin or combination of amoxicillin/clavulanate (Augmentin, Amoxiclav) for resistant infections	Amoxicillin 10-14 days	
	<u>Cephalosporins</u> The first generation - cephalexin (Keflex, Lexin) cefadroxil (Duricef, Cefangin, Ultracef) and cefradin (Velocef, Tracilarin) The second generation - cefaclor (Ceclor, Keflor), cefuroxime (Ceftin, Cefurim) cefprozil (Cefzil) and loracarbef (Lorabid) Third Generation - cefpodoxime (Vantin), cefdinir (Omnicef), cefditoren (Sprectracef), cefixime (Suprax) and ceftibuten (Cedax), ceftriax-	0.25-0.5 g 1-2 times/day orally 0,25 g 2 times/day orally 1-2 g 1	Pervert the indexes of glucose of blood and urine

	one (Cefaxon, Cefogram, Rocephin)	times/day orally	
	Other beta-lactam – pivmecillinam (Selexid, Penomax, Coactabs), methicillin (Staphcillin, Celbenin, Metin)		
Trimethoprim/Sulfamethoxazole (TMP-SMX)	TMP-SMX Biseptol, Bactrim, Bactrimel, Septra, Co-trimoxazole, Groseptol, Sulfatrim Trimethoprim Proloprim, Trimpex	Three-day or 7-14 days reception	Diminish the effect of peroral contraceptives, oppress an erythropoiesis
Fluoroquinolones	ofloxacin (Floxacin, Zanocin, Ofloxsin), ciprofloxacin (Cipro, Cifran, Ciprobay), norfloxacin (Noroxin, Nolicin, Norbactin), levofloxacin (Levaquin, Tavanic, Lefloc), gatifloxacin (Tequin, Gatispan, Bigaflon) and sparfloxacin (Zaham, Sparflo)		
Antibiotics of other groups	Nitrofurantoin (Furadonin, Furadantin, Macrochantin)	from 7 to 14 days	Quite often cause diarrhea reaction. Do not use in pregnant or lactating women
	Fosfomycin (Monural, Urofesfabol)	receiving a single dose	
	Tetracyclines (Doxycycline, Unidox, Vibramycin, Tetracycline, Minocycline)	10-14 days or more (mycoplasmosis or/and chlamydiosis)	Increase of photosensitivity of skin, burning in a throat and teeth discoloration
	Aminoglycosides (Gentamicin, Kanamycin, Garamycin, Tobramycin, Amikacin)	Injection in combination with other antibiotics	There can be serious side effects (proof defeat of ear, kidney and other).

Treatment of pregnant women. According to statistics, even with asymptomatic bacteriuria in pregnancy has 30% increase in the risk of acute pyelonephritis in the second or third trimester. In this regard, these states should be promptly evaluated and treated. Used short-course of antibiotics (3-5 days). Use of amoxicillin, ampicillin, nitrofurantoin or oral cephalosporins. Fosfomycin (Monural) is less effective than others, but the most safe during pregnancy. Fluoroquinolones and TMP-SMX (category C on the effects on the fetus) in this case have contraindications. In carrying out pharmaceutical care pharmacist must ensure that no pregnancy in women of childbearing age [7, 10].

Treatment of patients with diabetes mellitus. The presence of diabetes causes more frequent and more severe forms of UTI manifestations. Most experts recommend in these patients, even in cases of uncomplicated infection, treatment with antibiotics for 7 to 14 days. People with diabetes mellitus have a higher incidence of asymptomatic bacteriuria, but among profes-

sionals there is still no consensus about their mandatory identification and treatment on this basis. A large-scale controlled study in 2003 showed that treatment under this condition is almost no influence on the UTI prognosis and did not prevent infection [9, 11].

Treatment of children. Children with UTI are usually treated using TMP-SMX scheme or cephalexin (Keflex). Drugs are taken orally, and the effect of therapy usually occurs within a few days. At the same time, as noted in the literature, resistance to cephalosporins (cephalexin) recently increased, which leads to use aminoglycoside antibiotics. Most effective among them is now considered gentamicin (Garamycin), which in this group of patients normally used intravenously. In the mechanism of UTI complications in children is important the presence of vesicoureteral reflux in which urine from the bladder enters the kidney, and renal pelvis can infect them with the development of pyelonephritis. About a third of children have reflux. Most experts now recommend to treat relapsing forms of UTI by surgery grounds are controlled by a 2006

study showed even long-term use of antibiotics does not prevent the complications of reflux. But it was also found that the average and reasonable degree of vesicoureteral reflux does not increase the frequency of UTI or pyelonephritis [8, 12].

Treatment of menopausal women. The disappearance of vaginal lactobacilli in postmenopausal women increases the risk of UTI. Studies have shown that dietary supplementation with the inclusion of cranberry products reduced the relapse rate of UTI by 35% and are effective only in one third of patients. It was confirmed the importance of the topical use of hormonal vaginal suppositories (Ovestin, Premarin, Prempro) [13, 14].

Treatment of patients using a catheter. The main problem of the treatment of UTI in this group of patients is a constant change of microflora. It is therefore recommended the use antibiotics with broad-spectrum antimicrobial action. First of all that are fluoroquinolones and combinations such as ampicillin plus gentamicin or imipenem + cilastatin (Sinerpen, Tienam). The prophylactic use of antibiotics is not currently recommended. They need to be removed as quickly as possible and, if possible, use only intermittent administration. It is now considered mandatory for permanent catheterization using a special coating catheters (hydrophilic with the inclusion of metals), which provides a reduction in the frequency of UTI [9, 10].

It is important in carrying out pharmaceutical care of patient with a UTI as highlighted in the literature:

– Clarify that the symptoms of UTI disappear within a few days of starting treatment. However, patient should continue taking the drugs prescribed by the doctor all the time. This alone can be a guarantee of cure.

– The patient should drink plenty of fluids. Drinking large amounts of water dilutes the urine and helps remove bacteria from the urinary tract.

– Patient should avoid drinking coffee, alcoholic and soft drinks, which contain caffeine and citrus components. They irritate the bladder and can cause frequent urination.

– In the case of pain associated with UTI (in the region of the bladder, urethra), after consulting with the doctor, the patient may use a heating pad. Sometimes a hot water bottle placed on the bottom of the stomach, eliminates the debilitating feeling of pressure and pain.

– In some cases of pain associated with UTI can help non-prescription medications (OTC-drugs) – non-salicylate NSAIDs containing paracetamol (Efferalgan, Daleron, Tylenol, etc.).

– To increase the effectiveness of treatment (especially important for recurrent infections) may be useful adoption of 250-500 ml of cranberry juice daily. This gives the prevention of overflow bladder and has an additional effect on the microflora. But it is worth remembering that the juice is contraindicated in combination with warfarin.

– The patient should be reminded of some of the features of hygiene procedures at UTI. So, it is advisable to use the shower instead of a bath and after its adoption must be carefully wiped. Additional humidity promotes recurrence of UTI. Patient must carefully preserve the purity of the perineum, including after using the toilet. It is important to use a bidet.

– In the presence of UTI should be avoided intimate cosmetics in the crotch. Deodorants and gels can irritate the mucous membranes, contributing to the development of relapse [7, 10, 15, 16].

Thus, the modern arsenal of antimicrobial agents can successfully treat various forms of UTI. But certain categories of patients with this type of infection may account for significant complications of medical and non-medical. In this context, pharmaceutical care of patient with UTI of particular role and, of course, will increase the effectiveness of treatment.

Conclusions

1. Bacterial urinary tract infections (UTI) are the result of the interaction of several medical and biological factors that must be considered for the rational choice of treatment and antimicrobial drug.

2. Effective treatment of UTI depends on the pathogen infection, the severity and complications of the disease, as well as other complicating factors for recurrent infections often require additional methods of diagnosis and treatment.

3. Conducting the pharmaceutical care of patients with UTI is an important component of the success of treatment and prevention of recurrence of the disease.

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ФАРМАЦЕВТИЧЕСКАЯ ОПЕКА В ПРОЦЕССЕ ЛЕЧЕНИЯ ПАЦИЕНТОВ С ИНФЕКЦИЯМИ НИЖНИХ ОТДЕЛОВ МОЧЕВЫВОДЯЩЕГО ТРАКТА

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С целью мониторинга изменений в рекомендациях по лекарственному лечению инфекций нижних отделов мочевыводящего тракта (ИМТ) и фармацевтической опеки пациентов проанализированы резолюции и связанные с ними публикации Американской ассоциации урологов по состоянию на конец 2012 года. Отмечено усовершенствование детализации факторов хронизации ИМТ и выделение роли провизора для профилактики их рецидивирования.

В арсенале средств лечения неосложненных форм заболевания (около 80% случаев) оставлен Ко-тримоксазол, но исключен вариант его однократного приема. При осложненных ИМТ прием рекомендуемых комбинаций антибиотиков продлен до 14 дней, введены схемы длительного использования Ко-тримоксазола или фторхинолонов при эпидидимите и бактериальном простатите. Сформулированы принципы фармацевтической опеки пациентов с ИМТ и констатировано, что данная патология является результатом взаимодействия нескольких медико-биологических факторов, которые необходимо учитывать для рационального выбора тактики лечения. Проведение фармацевтической опеки пациентов с ИМТ является важной составляющей успеха лечения и профилактики рецидивирования данной патологии. **Ключевые слова:** инфекции мочевых путей, фармацевтическая опека, антибактериальная терапия, бактериурия.

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ФАРМАЦЕВТИЧНА ОПІКА В ПРОЦЕСІ ЛІКУВАННЯ ПАЦІЄНТІВ З ІНФЕКЦІЯМИ НИЖНІХ ВІДДІЛІВ СЕЧОВИВІДНОГО ТРАКТУ

Мороз В.А.

З метою моніторингу змін у рекомендаціях щодо медикаментозного лікування інфекцій нижніх відділів сечовивідного тракту (ІСТ) і фармацевтичної опіки пацієнтів проаналізовано резолюції та пов'язані з ними публікації Американської асоціації урологів станом на кінець 2012 року. Відзначено удосконалення деталізації факторів хронізації ІСТ та виділення ролі провизора для профілактики її рецидивування. В арсеналі засобів лікування неускладнених форм захворювання (близько 80% випадків) залишено Ко-тримоксазол, але виключено варіант його одноразового прийому. При ускладнених ІСТ прийом рекомендованих комбінацій антибіотиків подовжено до 14 днів, введено схеми тривалого використання Ко-тримоксазолу або фторхінолонів при епідидиміті і бактеріальному простатиті. Сформульовано принципи фармацевтичної опіки пацієнтів з ІСТ і констатовано, що дана патологія є результатом взаємодії декількох медико-біологічних факторів, які необхідно враховувати для раціонального вибору тактики лікування. Проведення фармацевтичної опіки пацієнтів з ІСТ є важливою складовою успіху лікування та профілактики рецидивування даної патології. **Ключові слова:** інфекції сечових шляхів, фармацевтична опіка, антибактеріальна терапія, бактеріурія.

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PHARMACEUTICAL CARE IN THE TREATMENT OF PATIENTS WITH INFECTIONS OF THE LOWER URINARY TRACT

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In order to monitor changes in the recommendations for drug treatment of lower urinary tract infections (UTI) and pharmaceutical care of patients analyzed resolution and related publications of American Urological Association at the end of 2012. Marked improvement of detail factors of chronicity UTI and allocation of roles pharmacist to prevent its recurrence. In the arsenal of treatments for uncomplicated disease (about 80%) left Co-trimoxazole, but exclude the scheme of its single administration. In complicated UTI the use of recommended combinations of antibiotics extended to 14

days, introduced the scheme extended use of Co-trimoxazole or fluoroquinolones in bacterial prostatitis and epididymitis. Formulated the principles of pharmaceutical care of patients with UTI and stated that this pathology are results from the interaction of several biomedical factors that must be considered for the rational choice of treatment strategy. Implementation of pharmaceutical care of patients with UTI is an important component of the treatment success and prevention of disease recurrence.

Key words: urinary tract infections, pharmaceutical care, antibiotic therapy, bacteriuria.