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ESTIMATION OF EFFICIENCY OF EMPIRICAL ANTIBIOTIC THERAPY OF CATHETER-ASSOCIATED INFECTION IN A UROLOGICAL HOSPITAL

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An analysis of case histories of 119 patients who underwent treatment in the urology department of the Voronezh City Clinical Emergency Hospital No. 10 was performed. All patients were drained with a urethral catheter, a bacteriological examination of the urine was performed, and empirical antibiotic therapy was prescribed. Microflora growth was detected in the urine of 30 (25.2%) patients, most often revealed *Klebsiella* spp. and *Enterococcus faecalis*. A high frequency of resistance of uropathogens to antibacterial drugs prescribed as empirical therapy was noted. 66% were resistant to ceftriaxone, and 70% of the isolated microorganism strains to ciprofloxacin. Significantly lower resistance was noted for amikacin and doxycycline. To increase the effectiveness of empirical antibiotic therapy in patients with catheter-associated urinary tract infections, it is necessary to select antibacterial drugs based on the results of monitoring the sensitivity of hospital strains, followed by treatment correction in accordance with the results of urine bacteriological studies.

Keywords: antibiotic resistance; catheter-associated infection; antibiotic therapy; lower urinary tract infections.

ОЦЕНКА ЭФФЕКТИВНОСТИ ЭМПИРИЧЕСКОЙ АНТИБИОТИКОТЕРАПИИ КАТЕТЕР-АССОЦИИРОВАННОЙ ИНФЕКЦИИ В УРОЛОГИЧЕСКОМ СТАЦИОНАРЕ

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Проведен анализ историй болезни 119 пациентов, проходивших лечение в урологическом отделении Воронежской городской клинической больницы скорой медицинской помощи № 10. Всем больным дренировали мочевой пузырь уретральным катетером, проводили бактериологическое исследование мочи и назначали эмпирическую антибактериальную терапию. Рост микрофлоры обнаружен в моче 30 (25,2 %) больных, чаще всего выявляли *Klebsiella* spp. и *Enterococcus faecalis*. Отмечена высокая частота резистентности уропатогенов к антибактериальным препаратам, назначаемым в качестве эмпирической терапии. Устойчивыми к цефтриаксону оказалось 66 %, а к ципрофлоксацину — 70 % выделенных штаммов микроорганизмов. Значительно меньшая резистентность отмечена для амикацина и доксициклина. Для повышения эффективности эмпирической антибиотикотерапии у больных катетер-ассоциированными инфекциями мочевыводящих путей необходимо подбирать антибактериальные препараты на основе результатов мониторинга чувствительности госпитальных штаммов с последующей коррекцией лечения в соответствии с результатами бактериологического исследования мочи.

Ключевые слова: антибиотикорезистентность; катетер-ассоциированная инфекция; антибиотикотерапия; инфекции нижних мочевыводящих путей.

INTRODUCTION

Recently, one of the priorities in modern medicine is to improve the effectiveness of prevention and treatment strategies for nosocomial infections. Urinary tract infections (UTI) account for at least 40% of all hospital-acquired infections [1, 2]. Their significance is due not only to the high prevalence but also to the insufficient effectiveness of treatment strategies and the frequent development of severe complications, leading to prolonged hospitalization, increased economic costs, and worse prognosis [3, 4]. Up to 80% of nosocomial UTI are associated with bladder catheterization and can be classified as catheter-associated [5, 6]. Catheter-associated UTI develop in patients with an installed catheter or in patients who were catheterized in the last 48 hours [2].

Most often, UTI are caused by *Escherichia coli*, which is detected in 64%–76% of cases of uncomplicated infections [6–10]. However, in complicated infections, which include catheter-associated UTI, the detection rate of *Escherichia coli* is reduced to 30%–40% [5, 6, 11–13]. The etiological structure of nosocomial UTI is different from that of community-acquired UTI and is characterized, as a rule, by a lower frequency of *Escherichia coli*, greater proportion of gram-negative nonfermenting bacteria, and antibacterial polyresistance of uropathogens [3, 6, 12, 14].

In 40% of cases, the cause of catheter-associated UTI is a gram-negative microorganism; less often, the cause is enterococci, staphylococci, and fungi [6]. If the leading role in the etiology of catheter-associated UTI is naturally assigned to its intestinal microflora, the duration of catheterization is considered the most significant risk factor for the development of UTI [15]. Studies have reported that infection develops in 100% of patients within the first 5 days in the case of prolonged catheterization of the bladder using open systems and in 50% of patients by the tenth day and 100% of patients within 1 month after catheterization using closed systems [16, 17]. Other significant risk factors for developing catheter-associated UTI include the presence of bacteria in the urethra, failure to follow the rules for installing and caring for the catheter [18], and a long preoperative period [19]. Thus, UTI develop five times less frequently in patients with a preoperative period of less than 2 days compared with that in patients with a longer postoperative period [19].

In the case of short-term and intermittent catheterization, routine antibiotic prophylaxis is not required. However, in the case of a clinically significant infection, patients should be prescribed systemic antibacterial therapy, the correction of which is possible only after a bacteriological urine analysis [18]. Ideally, a narrow-spectrum antimicrobial drug with specific activity against the microorganism isolated during microbiological examination should be prescribed. However, in practice, a nosocomial infection, especially in the initial days, is almost always treated empirically. The choice of the optimal antimicrobial therapy scheme depends on the prevailing microflora in the hospital department and the spectrum of its antibiotic resistance. One of the reasons for the increase in the proportion of resistant strains of microorganisms is the irrational use of antibacterial agents, which significantly reduces the effectiveness of an antibiotic therapy [3, 6, 20]. Formation of microbial biofilms on the inner surface of catheters plays an important role in causing antimicrobial resistance in catheter-associated UTI. Compared with plankton cells, microorganisms that are part of these biofilms are much less sensitive to most antibiotics and other biocidal substances [6]. This poses an acute problem, especially for doctors of urological and surgical departments.

With the increased resistance of microorganisms against antimicrobial drugs, it is even more difficult to select the optimal antibiotic, leading to significant difficulties in deciding the treatment for UTI. One of the strategy to improve the effectiveness of the prevention and treatment of nosocomial UTI, including catheter-associated UTI, is constant microbiological monitoring aimed at identifying the hospital strains of pathogens and assessing their sensitivity to antibacterial drugs [21].

The aim of the study was to assess the sensitivity of microorganisms against the most common antibacterial agents used for the empirical treatment of nosocomial catheter-associated UTI and to study the factors involved in improving the effectiveness of an empirical antibiotic therapy.

MATERIALS AND METHODS

The medical histories of 119 patients (all men) who were treated at the Urology Department of the Voronezh City Clinical Emergency Hospital No. 10 were included in the analysis. The most common diagnosis was benign prostatic hyperplasia in 110 patients (92.4%), followed by a bladder tumor in 6 (5%) and prostate cancer in 3 (2.6%). Overall, 94 (79%)

patients underwent surgical treatment: 70 (58.8%) underwent transurethral resection of the prostate, 20 (16.8%) underwent transpusic adenomectomy, and 6 (5%) underwent transurethral resection of the bladder wall. Conservative treatment was prescribed to 25 (21%) patients. All patients had their bladders drained with a urethral catheter. Indications for bladder catheterization were acute urinary retention when the patient was admitted to the hospital or ensuring the outflow of urine in the postoperative period. After installing a urethral catheter, patients were prescribed an antibacterial therapy.

For all patients, urine samples were collected simultaneously with the drainage of the bladder. The urine was collected in sterile disposable containers and delivered to the bacteriological laboratory within 2 hours of collection. Seeding on nutrient media, isolation, and identification of pure crops were performed according to the set standard methods. The sensitivity of microorganisms to antibacterial drugs was determined using the disco

Statistical analysis of the results was performed using the Statistica 10.0 software package. Differences were assumed to be reliable at $p < 0.05$.

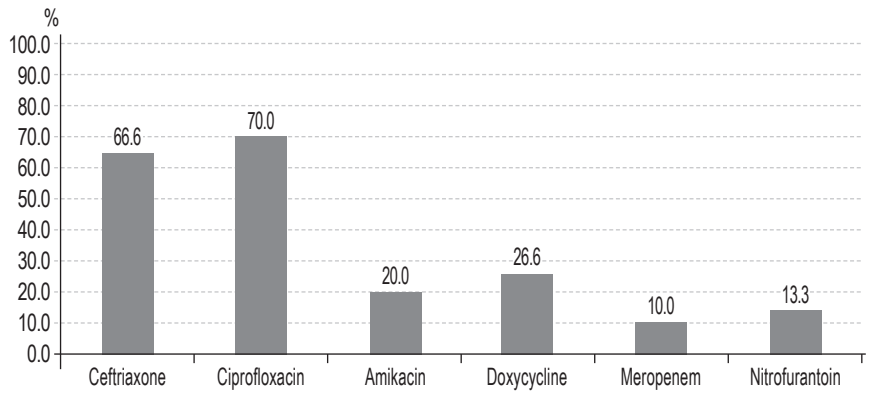
RESULTS AND DISCUSSION

The growth of microflora in a diagnostically significant titer was detected in the urine of 30 (25.2%) patients. Simultaneously, gram-negative microflora was detected in 18 cases, gram-positive microflora in 11, and mixed microflora in 1. These accounted for 60%, 36.7%, and 3.3% of all cases of the detection of microorganisms during a bacteriological urine examination, respectively. Among the selected strains of gram-negative microorganisms, *Klebsiella* spp. was most frequently detected in 36.7% of cases, followed by *Escherichia coli* in 16.6%, *Pseudomonas aeruginosa* in 6.6%, and *Proteus vulgaris* in 3.3% (one case). Among the gram-positive flora, *Enterococcus faecalis* prevailed in 33.3% of cases and *Enterococcus* spp. was detected in one patient (3.5%). Thus, the most common microorganisms in this study were found to be *Klebsiella* spp. and *Enterococcus faecalis*.

After the pathogens were isolated and identified, their sensitivity to antibacterial drugs was determined and the effectiveness of an empirical antibacterial therapy prescribed upon admission was studied. The results of the study of antibiotic resistance of the identified microorganisms are shown in Fig. 1.

Most often, the empirical antibiotic therapy initiated was ceftriaxone in 85.7% of cases. Among patients with a positive growth of pathogenic flora in the bacteriological urine culture, ceftriaxone was initiated in 100% of cases. At the same time, the resistance of microflora to the third-generation cephalosporins was 66.6%. In other cases, ciprofloxacin was used as a drug for an empirical antibiotic therapy, and the resistance of urine microflora to ciprofloxacin was 70%. The greatest resistance to drugs for empirical antibacterial therapy was observed in *Klebsiella* spp. and *Enterococcus faecalis*, consistent with the research data from other regions [5, 21, 22].

After receiving the results of urine seeding in accordance with the antibiogram, the antimicrobial drug was replaced in 43.3% of cases. The drug of choice was amikacin and ciprofloxacin in 38.4% and 23.4% of cases, respectively. A combination of amikacin and ciprofloxacin was prescribed in 15.3% of cases, cefotaxime was prescribed in 15.3%, and doxycycline was prescribed in 7.6%.



The frequency of resistance of microorganisms isolated from urine of urological patients to antibacterial drugs
Частота резистентности микроорганизмов, выделенных из мочи урологических больных, к антибактериальным препаратам

Thus, the results of the study showed a high resistance of uropathogens to ceftriaxone and ciprofloxacin (66% and 70%, respectively), which were used for empirical antibiotic therapy in patients with a urethral catheter. Significantly less resistance was observed for amikacin and doxycycline, which were prescribed after receiving the results of bacteriological urine examination. Considering the spectrum and antibiotic sensitivity of bacterial pathogens, it is advisable to initiate an antimicrobial treatment in patients with the appointment of drugs to which the microflora of the hospital has the least resistance. In this study, this drug was amikacin.

According to the literature, most UTI are caused by facultative anaerobic microorganisms, the source of which is the intestinal flora. *Escherichia coli* causes up to 40%–50% of hospital UTI [3, 5, 11, 21]. However, in recent years, there has been a tendency of a decrease in the involvement of *Escherichia coli* in the occurrence of a catheter-associated UTI and an increase in the involvement of *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Enterococcus faecalis* [5, 22]. The results of this study conducted at the Urological Department of the Voronezh Municipal Clinical Hospital of the emergency medical services No. 10 also confirmed this trend.

CONCLUSION

It can be concluded that the factors involved in improving the effectiveness of an empirical antibiotic therapy for patients with catheter-associated UTI at a urological hospital include the selection of antibacterial drugs based on the results of monitoring the sensitivity of hospital strains, followed by a treatment correction in accordance with the results of bacteriological urine examination.

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