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Experimental Prophylaxis of Antibiotics in Urological Patients

Rakhimov Farrukh Farkhodovich [1], Bakhromov Bekzod Shavkatovich [2]

[1] Assistant, Department of Urology, Nephrology and Hemodialysis, Bukhara state medical institute, Bukhara, Republic of Uzbekistan

[2] Master, Department of Urology, Nephrology and Hemodialysis, Bukhara State Medical Institute, Bukhara, Republic of Uzbekistan

Abstract: This article provides an analysis of the main provisions of the methods of antibacterial prevention before surgery and the basic requirements for antibacterial prevention drugs. Approaches to empirical antibiotic prophylaxis in operations on the kidneys, ureters, bladder, prostate, scrotum organs, as well as reconstructive interventions using a fragment of the intestine are described. A separate review of antibacterial prophylaxis in surgical interventions on the blood vessels of the genitourinary system, penile implantation, testicular prostheses and artificial bladder sphincter, as well as surgical treatment of injuries of the genitourinary tract. Possible infectious and inflammatory complications of the most frequently performed operations in urological practice and ways of their prevention are analyzed in detail. We examined the choice of antibacterial agents depending on the patient's diagnosis, previously used antimicrobial agents and the type of surgical intervention. All the proposed schemes are optimized in three directions: clinical efficacy, economic feasibility, epidemiological safety (prevention of multiplication of strains of microorganisms with multidrug resistance). Particular attention is paid to the choice of a drug for empirical antibiotic prophylaxis in patients with severe concomitant diseases affecting the pharmacokinetics of drugs and reducing the immunological reactivity of the body – renal insufficiency and HIV infection.

Keywords: antimicrobial prophylaxis, antimicrobial drugs, urological surgery.

The term "antimicrobial (antibacterial) prophylaxis" according to the authors of the management team "Rational antimicrobial pharmacotherapy" is "the prevention of infections resulting from surgical or other invasive interventions or having a connection with them, but not the treatment of background infection, the elimination of which is directed surgical intervention" [1]. It follows from this definition that antibacterial prophylaxis should be directed exclusively against complications that have developed as a result of infection directly at the time of surgery. Prevention of exacerbation of a "background" infectious and inflammatory disease, for example, chronic pyelonephritis, is not an antibacterial prevention. The question remains, how to treat a patient with urolithiasis in the preoperative period? On the one hand, pre-existing chronic calculous pyelonephritis, which is in remission, excludes antibacterial prophylaxis. On the other hand, the stage of remission is not an indication for antibacterial therapy.

In our opinion, this definition more clearly reflects the essence of antibacterial prevention, but the word "occurrence" requires correction. In urological practice, antibacterial prophylaxis is often prescribed not to prevent the occurrence, but to prevent the exacerbation of an already existing chronic process, as a rule, prostatitis or pyelonephritis [2, 4].

How to carry out antibacterial prevention in urology

Today, the overwhelming majority of researchers have agreed that antibacterial prophylaxis significantly reduces the frequency of infectious and inflammatory complications and is unequivocally justified in open, percutaneous and endoscopic surgical interventions on the kidneys, urinary tract, male genitalia, with the exception of transurethral resection and prostate biopsy [1, 3-10].

Antibacterial prophylaxis is not indicated during cystoscopy in patients without concomitant immunodeficiency [1].

A comprehensive urodynamic study requires antibacterial prophylaxis in patients with severe neurological defects accompanied by neurogenic dysfunction of the bladder, as well as with prolonged drainage of the urinary tract [8]. It is in these patients that the presence of chronic urinary infection is natural and the risk of its activation after the study is high.

Many antibacterial drugs can be used for preoperative prevention: among them are second-generation cephalosporins; fluoroquinolones; protected beta-lactams. The drugs of the reserve group include aminoglycosides, third- to fourth-generation cephalosporins, carbapenems and vancomycin, piperacillin/tazobactam, aztreones. These drugs should be used for prevention extremely rarely and cautiously, only if there is confidence in the contamination of the surgical site with polyresistant hospital strains.

Antibacterial prevention never compensates for poor surgical technique, it is only one of the components in infection management. It is necessary to strictly observe other important conditions that contribute to the prevention of hospital infection in general:

- ✓ short hospital stay;
- ✓ short preoperative period;
- ✓ careful care of catheters and drains do not flush! By

catheter obstruction change to a sterile catheter. With antegrade pyelography, a change to sterile nephrostomy drainage and the introduction of a radiopaque substance along it. It is necessary to develop a protocol for catheter care in each urological department and strictly observe it! When flushing any drainage, the urethral catheter, nephrostomy or cystostomy drainage, vascular catheters, biofilm (microorganisms of various genera and families adhered to drains) is washed into the urinary tract or vascular bed, thereby causing bacteremia, bacteriuria, hyperthermia and the possible development of focal purulent processes in the kidney, prostate, testicles, lungs, endocardium, etc.;

- ➢ using a "closed drainage system" do not disconnect the urethral catheter and the urine collector! The places of contamination are: the external opening of the urethra, the connection of the catheter with the urine collector, the drain tap of the urine collector;
- ➢ strict compliance with sanitary and hygienic requirements washing hands or using sterile gloves when in contact with the drainage system [5]

An antibacterial drug for the purpose of antibacterial prevention is always administered 0.5-1 hour before the start of surgery. Currently, it has been proven that the administration of an antibacterial drug after the intervention does not affect the frequency of infectious and inflammatory complications in the postoperative period. An intravenous route of administration is considered preferable, which, unlike intramuscular and, especially, oral, ensures the creation of a guaranteed and predictable bactericidal concentration of the drug.

If an antibiotic is prescribed to a patient more than 1 hour before surgery, there is an increase in postoperative infectious and inflammatory complications [6, 7]

Any antibiotic prescribed after the wound is sewn up does not change the level of wound infection. However, this does not apply to endoscopic operations.

It is not recommended to use the same antibiotic for treatment and prevention, it is necessary to use antibiotics that create a high concentration in urine, periodically change drugs for antibacterial prevention in the clinic to reduce the selection of resistant strains of microorganisms.

We consider the following approximate dates of antibacterial prophylaxis appropriate: one dose – for pancreatic biopsy, complex urodynamic examination, removal of an internal stent, retrograde ureteropyelography, as well as for small–volume interventions for varicocele, hydrocele, testicular appendage cyst, etc.; 3 days - for transurethral resection of the bladder, testicular prosthetics; 5 days – with transurethral resection, contact ureterolithotripsy, kidney resection for neoplasm, pelvic-ureteral segment plastic surgery and other clean surgical interventions on the kidneys and upper urinary tract, penile prosthetics, installation of artificial bladder sphincter; 7 days – with percutaneous nephrostomy. When performing large-volume surgical interventions in conditions of chronic urinary infection, antibacterial drugs should not be canceled until the drains are removed [5, 6].

Which antibiotics can be used for antibacterial prophylaxis.

An antibacterial drug is not able to directly prevent an infectious and inflammatory complication, it can only suppress or slow down the reproduction of a microorganism sensitive to it.

The choice of an antibacterial drug is determined by the patient's diagnosis, the type of surgical intervention, as well as pharmacokinetic features. In particular, it is undesirable to use antibiotics with an excessively wide spectrum of activity for antibacterial prevention – this may slightly increase the percentage of patients who have not received complications, but it will dramatically increase the frequency of dysbiosis. With the very idea of antibacterial prevention, drugs with an excessively short half-life are poorly combined (the drug will be excreted before the operation ends; for example, natural penicillins), as well as with a bacteriostatic mechanism of action. Unless absolutely necessary, toxic antibiotics (aminoglycosides and glycopeptides) should not be used, as well as those that increase the risk of bleeding (in urology, this is mainly cefoperazone) [1, 2].

Therefore, the main criteria for selecting a drug for antibacterial prophylaxis are:

- ✓ high activity against the suspected pathogen;
- ✓ stable serum and tissue concentration;
- ✓ bactericidal effect;
- ✓ low toxicity;
- ✓ economic accessibility.

Despite the fact that the prescription of a drug in the mode of antibacterial prophylaxis is essentially non-directional, for an adequate choice it is necessary to have a clear idea of what exactly we want to prevent. This should be the most frequent, clinically significant, and most importantly, preventable infectious and inflammatory complication [5, 7-8].

It is quite obvious that the best results are obtained by prescribing antibacterial agents according to the antibiotic gram, however, it also requires a critical attitude. It is necessary to pay special attention to the compliance of the results of the study with the natural sensitivity of the identified pathogen. This is especially true for aerobic gram-positive cocci and non-fermenting gram-negative rods. For example, do not prescribe against Enterococcus spp. or P. aeruginosa ceftriaxone, even if it shows high activity against these microorganisms in vitro.

And yet, the greatest difficulties arise when solving the question of empirical antibacterial prevention. Situations when an antibacterial drug with a preventive purpose is prescribed in an empirical mode are quite frequent even with the ideal work of the laboratory service. First of all, these are emergency surgical interventions in the absence of an active inflammatory process (otherwise, the appointment of an antibacterial agent will be considered antibacterial therapy).

Planned surgical intervention implies a comprehensive examination of the patient and, if necessary, preoperative preparation, including antimicrobial agents. The absence of microflora growth during urine culture does not cancel antibacterial prevention, however, the choice of the drug will be carried out in an experimental mode.

It should be remembered that experimental prevention is possible only with an antibacterial drug, the resistance to which the main pathogen does not exceed 20%. With a higher level of resistance, the drug should be used only according to the antibiotic chart [13, 14].

Classification of urological operations and interventions

Taking into account the requirements for preoperative antibacterial prevention, all urological interventions are divided into:

1. Open operations:

a) on the urinary tract using intestinal segments;

b) on the urinary tract without the use of intestinal segments;

c) operations outside the urinary tract, using implants and prostheses of the penis, testicles, artificial sphincters, synthetic filaments, etc.;

d) reconstructive genital operations: urgent and planned;

2. Endoscopic instrumental operations:

a) on the urethra;

b) on the prostate gland;

c) on the bladder;

d) on the ureter and kidney;

e) percutaneous nephrolitholapaxy;

f) extracorporeal lithotripsy;

g) laparoscopic operations;

3. Diagnostic procedures:

a) Prostate biopsy: transrectal, perineal;

b) urethrocystoscopy;

c) ureterocystoscopy;

d) percutaneous pyeloscopy;

e) laparoscopic procedures.

Experimental antibacterial prophylaxis during prostate and bladder surgeries

Transurethral surgery on the prostate and bladder is one of the most widespread in modern urological practice [15]. The main feature of all transurethral interventions is the absence of skin damage. For antibacterial prevention, this is fundamentally important – you can not be afraid of suppuration of a postoperative wound, and the preventable complication is acute or exacerbation of chronic prostatitis, which is most often caused by gram-negative rods, less often by reactivation of intracellular pathogens. The choice of a drug for empirical antibacterial prophylaxis is determined by anamnesis. If the patient does not have recurrent prostatitis, there are no other infectious and inflammatory diseases of the genitourinary system that have required long and repeated courses of antibiotic therapy, then the drugs of choice are cefotaxime or ceftriaxone. In the presence of concomitant chronic prostatitis, especially in patients who continue to live a sexual life, due to the real possibility of the presence of intracellular pathogens, fluoroquinolones of the second generation are preferable [10].

If the bladder has been drained by a cystostoma for a long time, then it should be assumed that there is a possibility of gram-negative flora with a moderate or high level of resistance. In this situation, P. aeruginosa is not uncommon. Therefore, the drugs of choice should have antisynegin activity. These are ciprofloxacin and ceftazidime. Ciprofloxacin has a high activity against gram-negative rods with a moderate level of resistance, its antisynegin activity has recently decreased significantly [14, 16]. Ceftazidime is currently a basic anti-pseudomonas drug, however, in order to prevent the selection of polyresistant strains in the hospital, in an empirical mode it should be prescribed only if fluoroquinolones are ineffective or the presence of non-fermenting flora is suspected.

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Periodically, there are patients suffering from benign prostatic hyperplasia who have previously undergone numerous courses of antibacterial therapy for infectious and inflammatory diseases of other organs, for example, chronic obstructive bronchitis. Regardless of the pre-existing infection of the urinary tract, in the event of an infectious and inflammatory complication, the alleged pathogen will be resistant to at least those drugs with which it has already been treated. Therefore, if such a patient has already been treated with anti-gram-negative drugs, for example, fluoroquinolones, it is advisable to carry out prevention with ceftazidime.

If you are intolerant to betalactam antibiotics or fluoroquinolones, fosfomycin (parenteral form) can be used as an antibacterial prophylaxis during operations on the prostate gland, bladder. The drug is relatively new, as a result of which E. coli resistance to it is still rare [14]. However, non-fermenting flora has a natural resistance to this antibacterial agent. Therefore , if the patient has previously detected P. aeruginosa or previous exacerbations of the infectious and inflammatory process required the appointment of anti-pseudomonas preparations, fosfomycin should not be prescribed.

Oral administration of fosfomycin (Phosphorol) can be recommended only for small-volume and short-time therapeutic and diagnostic manipulations. For example, in a complex urodynamic study in complicated patients [10]. In this situation, it is advisable to prescribe one dose (3 g) of fosfomycin before the study, and the next day the drug can be repeated [12].

Antibacterial prophylaxis during cystic resection is carried out according to the same principles.

As for antibacterial prophylaxis during prostate biopsy, this issue remains controversial. Given the advanced age and the somatic burden of the overwhelming number of men suffering from pancreatic neoplasms, we recommend that all patients undergo antibacterial prophylaxis during this

manipulation. The basic drugs are cefotaxime and ceftriaxone. In patients suffering from chronic prostatitis for a long time, as well as during drainage of the bladder with cystostomy, fluoroquinolones of the second generation, especially ciprofloxacin. When performing a transrectal biopsy of the pancreas, due to the interest of the rectum, it is advisable to supplement antibacterial prophylaxis with a drug with high anti–anaerobic activity - metronidazole.

Experimental antibacterial prophylaxis during surgical interventions on the kidneys and upper urinary tract

The main infectious and inflammatory complication in these patients is acute or exacerbation of chronic pyelonephritis. It is necessary to make a reservation right away that a very significant part of the postoperative attacks of pyelonephritis is associated with inadequate drainage of the urinary tract. It is well known that the drug treatment of obstructive pyelonephritis is effective only after kidney drainage, so we can safely say that the above situation has nothing to do with antibacterial prevention [14].

From the point of view of antibacterial prevention, surgical interventions on the kidneys and upper urinary tract can be divided into two groups. One group consists of interventions on initially uninfected urinary tract. These are all kinds of plastic surgery for uninfected hydronephrosis, nephrectomy and kidney resection for oncological indications, emergency contact ureterolithotripsy and remote lithotripsy, especially with the first episode of urolithiasis, etc. Another group includes surgical interventions in conditions of chronic urinary infection [15,17].

In patients who do not have infectious and inflammatory diseases and have not received massive antibacterial therapy, during operations on the kidneys and upper urinary tract, antibacterial prophylaxis is carried out with non-anthelmintic cephalosporins of the third generation – cefotaxime and ceftriaxone. They are highly active against non-hospital E. coli, which is the main causative agent of pyelonephritis in uncomplicated patients [17].

In surgical interventions for recurrent nephrolithiasis, repeated strictures of the ureter or pelvic ureteral segment, infected abnormalities of the genitourinary system, infectious and inflammatory complications are usually determined by gram-negative microorganisms with moderate or high levels of antibiotic resistance [18]. Strictly speaking, all such surgical interventions should be preceded by a bacteriological examination of urine, but this is not always technically possible. In the empirical mode, for antibacterial prophylaxis, you can use ciprofloxacin or ceftazidime, that is, drugs that have the greatest antisynegin activity in their pharmacological group. If the patient had previously been diagnosed with polyresistant flora or previous exacerbations of chronic pyelonephritis were stopped with antisynegnoid drugs, then in the absence of signs of renal insufficiency, simultaneous administration of ceftazidime and amikacin is possible. Although the appointment of amikacin somewhat contradicts the basic requirements for the drug for antibacterial prevention – low toxicity and maximum safety, specifically in this situation, this combination often helps to avoid the preventive use of carbapenems, preserving them as a reserve in case of postoperative complications.

If you are intolerant to betalactam antibiotics or fluoroquinolones, the parenteral form of fosfomycin is an alternative option. However, due to the lack of antisinegenic activity, this drug cannot be considered as a replacement for ceftazidime, cefepime, carbapenems. For the same reason, it is not a substitute for ceftazidime and ciprofloxacin [16]. According to the results of domestic microbiological studies, the antisinegenic activity of fluoroquinolones is so low that it does not allow them to be recommended for empirical use if a gram-negative infection with a high level of resistance is suspected. Practically no alternative option in a situation where a patient with an allergy to betalactam is assumed to have a polyresistant gram-negative infection and there is a need for empirical prescribing of antibacterial prophylaxis is amikacin, which should be prescribed 1 time / day. and necessarily taking into account kidney function [18].

Experimental antibacterial prophylaxis in reconstructive surgical interventions using a fragment of the intestine

In the surgical treatment of locally advanced bladder cancer, shrunken bladder, extended ureter strictures, for the formation of a urinary reservoir, replacement of a fragment of the bladder or ureter, intestinal sections are sometimes used [15]. Antibacterial prophylaxis is carried out by the same drugs – non-anthelmintic cephalosporins of the third generation and fluoroquinolones of the second generation. Nonantisinegnose cephalosporins are equally effective in this situation, in the group of fluoroquinolones ciprofloxacin is most appropriate. However, there is one fundamental feature. The opening of the intestine entails the possibility of contamination of the surgical wound with intestinal flora, primarily anaerobic. Therefore, when performing such surgical interventions, it is advisable to prescribe metronidazole prophylactically, one of the most active anti-anaerobic drugs.

It would seem that in the described situation it is preferable to use inhibitor-protected aminopenicillins, which are highly active both against E. coli and other non-hospital gram-negative rods, and against anaerobes, including bacteroids, in addition, most gram-positive cocci are sensitive to them. However, in practice, such a wide range of actions results in frequent dysbiosis. And antienterococcal activity encourages the preservation of inhibitor-protected aminopenicillins for a reserve in case of enterococcal superinfection, which is characteristic of this severe category of patients.

From the point of view of microbiology, fluoroquinolones of the IV generation are the option of choice. These drugs differ from the previous generations of fluoroquinolones by their high activity against anaerobic microorganisms, which is very important during operations on the intestine [1, 14]. However, the significant cost sharply limits their use in real urological practice. From the standpoint of pharmacoeconomics, combined prophylaxis, including cephalosporin or inexpensive fluorochonolone and metronidazole, is more profitable.

Experimental antibacterial prophylaxis during urethral surgery

A feature of surgical interventions on the urethra is the need for prolonged standing of the urethral catheter, which is accompanied by the risk of purulent urethritis and acute prostatitis, which in most cases devalue all the results of surgical treatment. Therefore, in real clinical practice, the patient receives antibacterial prophylaxis before removal of the urethral catheter [10].

The main causative agents of postoperative urethritis are gram-negative rods, however, in young men with urethral strictures, the possibility of an inadequately treated N. gonorrhoeae infection should not be overlooked. It should also be noted that in a significant proportion of patients, the bladder has been drained by cystostomy drainage for a long time, which creates prerequisites for chronic urinary infection, often with a high level of resistance. All this forces us to pay special attention to the preoperative bacteriological examination of urine.

When deciding on empirical antibacterial prevention, the choice is made between cephalosporins of the third generation and fluoroquinolones of the second generation. Often these drugs are prescribed sequentially, according to the principle of step therapy – first parenteral forms, then oral. Nonantisinegnous cephalosporins have been studied in uncomplicated patients, and ceftriaxone currently demonstrates high antigonococcal activity and is a basic drug for the treatment of gonorrhea [1, 14]. Fluoroquinolones have activity against gram-negative rods and intracellular flora, penetrate well into the pancreatic tissue, however, the increase in the number of resistant strains, as well as pronounced cross-resistance in this pharmacological group, forces us to approach antibacterial prophylaxis with fluoroquinolones cautiously, and at least not to prescribe them to all patients. In patients with recurrent structures, especially against the background of prolonged cystostomy, there is a high probability of having a polyresistant gram-negative infection, therefore, in such patients, the initial administration of the basic antisynegnoid drug ceftazidime with subsequent transition to oral ciprofloxacin is fully justified.

Urological operations outside the urinary tract

Preoperative antibacterial prophylaxis is generally not recommended, except for long-term reconstructive operations in the pelvic region or during implantation surgery. Usually 1-2 generation cephalosporins are recommended, because staphylococcal infection dominates [15].

Antibacterial prophylaxis during prosthetics operations in urology

In modern urological practice, prosthetics of the penis, testicle, implantation of the bladder sphincter are performed. Implantation of any foreign body into the body is accompanied by the risk of a purulent-inflammatory reaction. The main causative agent of this kind of complications is Staphylococcus spp. Therefore, during prosthetics operations, antibacterial prophylaxis should be carried out with drugs with high antistaphylococcal activity. These are cephalosporins of the I-II generation, inhibitor-protected aminopenicillins and glycopeptides. Taking into account the high cost of penile prostheses and artificial sphincters of the bladder, quite severe injury to tissues during their implantation, as well as due to the risk of infection with hospital strains of Staphylococcus Staphylococcus spp. (MRSA, MRSE), manufacturers of prostheses and sphincters specifically regulate antibacterial prevention, otherwise threatening non-fulfillment of warranty obligations. Therefore, when prosthetics of the penis and implantation of an artificial sphincter of the bladder, antibacterial prophylaxis is carried out with vancomycin [16].

With testicular prosthetics, tissue traumatization is significantly less and the intervention itself is less prolonged, therefore, in our opinion, it is possible to carry out antibacterial prophylaxis with cephalosporins of the I-II generation or inhibitor-protected aminopenicillins, which are inactive against hospital strains of Staphylococcus spp., but are significantly less toxic and have better tolerability.

It is worth noting that prosthetics operations do not involve opening the lumen of the urinary tract, therefore, gram-negative infection characteristic of the urological clinic can not be particularly feared. If a urinary tract infection is detected in a patient at the stage of preoperative examination, the prosthetics operation should be postponed and a preparatory course of antibacterial therapy should be carried out according to the sensitivity of the detected microorganism [19].

Situations when vancomycin cannot be prescribed are infrequent. Despite its rather high toxicity and poor tolerability, it rarely causes allergic reactions and does not cause cross-allergy with other groups of antibacterial drugs [1, 14]. The main limiting factor is concomitant renal failure. An alternative is currently linezolid, a relatively new antibacterial drug with a pronounced antigram–positive orientation, including against hospital strains resistant to glycopeptides (VRSA, VRSE, VRE). It is less toxic compared to vancomycin. However, due to the high cost, linezolid is used only to a limited extent, remaining a deep reserve drug [18, 19].

Antibacterial prophylaxis in emergency operations for injuries of the genitourinary system

Almost all urological hospitals receive patients with injuries of the genitourinary system with different frequency. Antibacterial prophylaxis in emergency surgical treatment of injuries has some features. Firstly, in these cases, antibacterial prophylaxis is always prescribed empirically. Secondly, you can not be afraid of polyresistant pathogens, except in a situation where the victim has some pre-existing infectious and inflammatory disease. Thirdly, the extent of the lesion and the mechanism of injury are of fundamental importance.

If the injury is blunt, without violating the integrity of the skin, but the lumen of the urinary tract is opened, the basic drugs for antibacterial prophylaxis are non-anthelmintic cephalosporins of the third generation, since the main causative agent of inflammatory complications is E. coli with a low level of resistance [13]. The same statement is true for kidney injury, regardless of the lesion of the calyx-pelvic system and closed injury of the scrotum organs.

In a situation where a patient has an open wound that is more or less contaminated, inhibitor-protected aminopenicillin is preferable, which can prevent the reproduction of gram-positive flora characteristic of this situation, including anaerobic. With a significant amount of damage or severe contamination of the wound, a combination of inhibitor-protected aminopenicillin and aminoglycoside of the second generation is possible (amikacin is better left in reserve in case of nosocomial infection). The combined scheme implies a synergistic effect between betalactams and aminoglycosides, however, due to the nephrotoxicity of aminoglycosides, it is undesirable if a decrease in kidney function is suspected [11].

In case of combined damage to the organs of the genitourinary system and intestines, it is necessary to take into account the contamination of the wound with anaerobic microorganisms, therefore, the use of inhibitor-protected aminopenicillins or non-anthelmintic cephalosporins of the third generation in combination with metronidazole is indicated. The anti-gram-negative activity of the second scheme is higher, therefore, in real clinical practice it is used significantly more often. In addition, it is very desirable to prescribe anti–anaerobic drugs even with closed injuries, if there are prerequisites for the development of anaerobic flora - tissue crushing, large hematomas, a significant amount of tissue blood imbibition [11,12].

If it is impossible to prescribe betalactams, parenteral fluoroquinolone of the second generation acts as an anti–gram-negative drug (here we use the basic spectrum of activity of fluoroquinolones, therefore all drugs of this group are equally effective), and lincosamide is used as an anti-gram-positive drug for open injuries, clindamycin is better, as more active. Streptococci, staphylococci and non-spore-forming anaerobes are sensitive to lincosamides. However, this group of drugs has a bacteriostatic effect, which does not go well with the idea of antibacterial prevention, as well as a complete lack of activity against gram-negative rods. Therefore, it makes sense to combine clindamycin with an anti–gram-negative drug - fluoroquinolone or even aminoglycoside.

The use of fourth-generation fluoroquinolones capable of suppressing gram-positive and anaerobic flora is also justified [13].

Experimental antibacterial prophylaxis in conditions of renal insufficiency

Concomitant renal insufficiency significantly complicates the solution of the issue of antibacterial prevention, since along with the spectrum of antimicrobial activity of the drug, its pharmacokinetic features must also be taken into account. A specific complicating factor in this situation is the instability of renal function – in the early postoperative period, an increase in filtration deficiency is possible [20, 21]. This phenomenon is most noticeable during operations on the kidneys (especially on the only or only functioning one) in conditions of chronic renal failure, when acute renal failure often develops against the background of pre-existing chronic ("acute renal failure on CRF"). Moreover, this is not an "exacerbation of chronic renal failure", as it is often interpreted, but two completely different pathological processes. Chronic renal failure, if there is no violation of urine outflow, is a consequence of nephrosclerosis, a decrease in the mass of active nephrons, which is irreversible. And postoperative acute renal failure may be associated with traumatic edema of the organ, circulatory disorders in it, ischemic and, finally, toxic damage to the nephrons, which is potentially reversible [20, 21].

Considering the above, not only with any manifestations of renal insufficiency, but also in a situation where compensated renal insufficiency is highly probable, it is necessary to refrain from using nephrotoxic antibiotics – aminoglycosides, glycopeptides, if possible. Even when recalculating the dosage, taking into account the glomerular filtration rate, they can give severe overdoses in the postoperative period, leading to the death of the tubular epithelium and the development of acute renal failure (toxic acute tubular necrosis). Moreover, the disease often manifests as anuria, when conservative measures are already ineffective and the patient needs to be transferred to the hemodialysis department [20, 21].

When choosing a drug for antibacterial prophylaxis in conditions of renal insufficiency, preference should be given to drugs that have a hepatic or double elimination pathway. In the group of cephalosporins, it is ceftriaxone, to a lesser extent cefoperazone; in the group of fluoroquinolones, it is pefloxacin. It is believed that the appointment of cefoperazone for antibacterial prophylaxis is undesirable, since it increases the risk of bleeding. However, of all cephalosporins, cefoperazone has the highest percentage of excretion through the liver, which allows it to be safely used in full dosage at any stage of chronic renal failure. The anticoagulant effect of this drug is weakly expressed, but the drug tends to potentiate the action of antiplatelet agents and anticoagulants, which really has significant clinical significance. In our opinion, in conditions of renal insufficiency, empirical antibacterial prophylaxis with cefoperazone is possible if the patient does not take antiplatelet agents and anticoagulants and has no violations of the hemostasis system.

Drugs of the antisinegenic series have a renal route of elimination, however, low toxicity allows them to be safely prescribed in full dosage at creatinine levels up to 200 mmol / l, with more pronounced renal insufficiency, the dose should be reduced by 2 times. Amoxicillin / clavulanate and metronidazole at a creatinine level of more than 200 mmol / l are prescribed 2/3 of the full dosage [20]

Empirical antibacterial prevention in conditions of immunodeficiency

The admission of emergency urological patients with clinically pronounced immunodeficiency has not been particularly rare lately. The most common situation is when a patient develops purulent-destructive damage to the organs of the genitourinary system against the background of decompensation of diabetes mellitus. However, the appointment of antibacterial drugs here belongs to the category of "antibacterial therapy". Surgical interventions for other, less urgent conditions in the conditions of decompensation of diabetes mellitus should be postponed, and the patient should receive insulin therapy according to an intensive program.

Antibacterial prophylaxis in patients receiving immunosuppressive therapy is usually not carried out in an empirical mode. If necessary, empirical antibacterial prophylaxis is carried out according to the previously described principles, since the spectrum of pathogens of infectious and inflammatory complications in this category of patients is the same as in the general population (the differences are greater in the nature of the course of complications) [22].

The only fairly frequent situation when antibacterial prophylaxis in conditions of immunodeficiency is prescribed empirically is the surgical treatment of HIV-infected patients.

When choosing a drug for empirical antibacterial prophylaxis, the following features should be taken into account:

- intravenous administration of narcotic substances creates prerequisites for staphylococcal lesions of internal organs. In this case, staphylococcus can be both sensitive to oxacillin and resistant to it;
- often such patients lead a promiscuous sexual life, as a result of which sexually transmitted infections are natural for them;
- with severe immunodeficiency, rare and uncharacteristic pathogens become relevant. We should not forget about the possibility of inflammatory processes caused by fungi, mycobacteria, viruses;
- if the patient has not previously taken antibacterial drugs and has not been in the hospital for a long time, polyresistant gram-negative rods are unlikely, especially non-fermenting ones [22].

CONCLUSION. It follows from this that the most fundamental requirement for an antibacterial drug is a wide spectrum of action. The basic means of empirical prophylaxis during operations on the kidneys and urinary tract is fluoroquinolone of the second generation, while ofloxacin has some advantage due to its renal excretion pathway (this is relevant with the simultaneous use of antiretroviral drugs metabolized in the liver) and good activity against Chlamydia spp., gram-positive cocci and mycobacteria. In complicated patients, it is possible to combine fluoroquinolone with metronidazole, one of the most effective antimicrobials against anaerobic flora and T. vaginalis.

When performing surgical interventions without opening the lumen of the urinary tract, inhibitor-protected aminopenicillin is preferable. It more effectively suppresses gram-positive flora, including non-hospital Staphylococcus spp., compared with fluoroquinolones of the second generation.

In addition, with severe immunodeficiency (CD4 < 200) due to the high probability of fungal complications, it is more advisable to supplement the scheme of antibacterial prophylaxis with fluconazole [22].

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