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THE CHOICE OF ANTIMICROBIAL THERAPY AMONG PHYSICIANS IN THE TREATMENT OF GESTATIONAL PYELONEPHRITIS

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Annotation. From 1 to 10% of the physiological pregnancy complicated by acute pyelonephritis. **The purpose work-** analyze the choice of antimicrobial therapy among physicians in the treatment of gestational pyelonephritis. **Materials and methods-** analysis of the anonymous survey in the framework of the second stage of the All-Russian pharmacoepidemiological study, "Epidemiology of the use of drugs in pregnant women", which was conducted from February to April 2015. On the basis of this was carried out to compare the results with the results of the survey of doctors of the Belgorod region. **Results and discussion.** Approximately half of the doctors choose the treatment of pyelonephritis in pregnant cephalosporins of generations II and III, as well as amoxicillin / clavulanate. Up to 30% of physicians prescribe ineffective in this case macrolides. A third of doctors sent patients for treatment to other specialists. **Conclusion.** An analysis of the responses of doctors tactics purpose of antimicrobial therapy in gestational pyelonephritis showed that only half of practitioners prescribed therapy based on the rational use of antimicrobials.

Keywords: pregnancy, pyelonephritis, protected penicillins, cephalosporins II and III generation, rational pharmacotherapy.

Introduction:

Gestational pyelonephritis – an inflammatory process that occurs in the interstitial kidney tissue and renal pelvis system, which can occur during pregnancy, childbirth or the postpartum period. The prevalence of the disease is sufficiently large – noted that during gestation they suffer from 1 to 10% of women [1, 2]. Acute pyelonephritis is the most common inflammatory process (10-12%) [3, 4, 5] occurring in the kidney during pregnancy.

It is believed that a woman's body becomes more susceptible to the disease during pregnancy for many reasons – a violation of passage of urine by the ureters iz-za hormonal changes (relaxation of smooth muscles of the ureter, renal pelvis expansion of the system under the influence of progesterone, the occurrence of vesicoureteral reflux), compression of

the ureter enlarged uterus (particularly common in nulliparous due to the elasticity of muscles anterior abdominal wall) [6], the strong growth of pathogenic microflora under the influence of estrogens [2, 4, 7]. Under the influence of these causes may occur stagnation of urine with infection and the development of gestational pyelonephritis.

The causative agents of pyelonephritis well understood – most often found in the urine of pregnant microorganisms of the family Enterobacteriaceae (88%) [3, 4], the most typical representatives of which is Escherichia coli (E. coli) (65%) [3, 8], seldom – Klebsiella spp. (10%), Proteus spp, even rarer – Enterococcus faecalis (4,6%) [4, 7].

Gestational pyelonephritis and worsens the prognosis of pregnancy and can cause premature delivery, hypertensive disorders, pre-eclampsia and

eclampsia, placental insufficiency, hypoxia and infection of the fetus in utero, and even abortion [2].

Timely detection and appropriate treatment initiated pyelonephritis can significantly improve the quality of life of the pregnant, prevent most complications both during pregnancy and in the postpartum period.

According to clinical guidelines, the main treatment of pyelonephritis in pregnant women is antibiotic therapy, which would meet the basic requirements of safety and efficiency for both the mother and the fetus [9, 10]. Due to the large number of complications and the risk of pyelonephritis treatment should begin immediately after diagnosis, without waiting for the results of urine culture, that is, conduct empirical antibacterial drugs treatment of a wide spectrum of action, based on the most common causative agents of the disease [6, 8].

According to the Federal Clinical guidelines in 2014 the drugs of choice in the treatment of pyelonephritis in pregnant women are cephalosporins III generation – ceftibuten, cefixime, cefotaxime, ceftriaxone, which have a broad spectrum of antibacterial activity and can be used at any stage of pregnancy. According to the USA classification of drugs FDA (Food and Drug Administration – FDA) cephalosporins are classified in safety of use during pregnancy [11, 12]. In addition to the cephalosporins, as a rational pharmacotherapy is possible to use the drug group monobactams – aztreonam (Category B classification FDA) [8].

With the ineffectiveness of these drugs, chronic and long-term course of the disease, in pregnant women for indications of alternative treatment may be applied -gentamicin + ampicillin (appointed after the II trimester) [9], category C by the FDA, [8, 13]. If you have restrictions on the use of aminoglycosides can be assigned to the group preparations of carbapenems, including meropenem, ertapenem, imipenem / cilastatin (Category B classification FDA) [9]. Also as can be seen alternativnoy therapy drugs penicillins in combination with β -lactamase inhibitors – piperacillin / tazobactam, ticarcillin / clavulanate (B according to FDA) [9] and generation cephalosporin IV – cefepime.

The most prominent common and useful drug for gestational pyelonephritis – amoxicillin / clavulanate, currently can not be recommended as empirical therapy, because of the large kolichesvo isolated strains of E. coli, resistant to the drug (up 43.0%) [3]. Amoxicillin / clavulanic acid, as well as cephalosporin II generation (cefuroxime) appointed

in pregnant women only after the culture results of urine on chuvsvitelnost to antibiotics.

Contraindicated for use at any stage of pregnancy, fluoroquinolones, trimethoprim-sulfamethoxazole (contraindicated in I and III trimester) and antibiotics group sulfonamides, tetracyclines, chloramphenicol, aminoglycosides individual (only for health reasons) [14, 15, 16, 17].

In view of the prevalence and social significance of the disease, a large number of complications, the empirical selection of antibacterial therapy at the beginning of treatment due to the timing of gestation and the severity of the patient's condition [18], it is expedient to hold a pharmacoepidemiological study in order to identify the preferences of physicians in the selection of Antimicrobial Chemotherapy (ACT) pyelonephritis pregnant.

Objective: To analyze the choice of Belgorod region ACT doctors in the treatment of pyelonephritis in pregnancy. Compare the data with the results obtained as a result of the survey, which was conducted from February to April 2015, four federal districts of the Russian Federation – the Central, Volga, Urals and Far East.

Materials and Methods: In this study based on the method of anonymous questionnaire in the framework of the second stage of the All-Russian pharmacoepidemiological study, "Epidemiology of the use of drugs in pregnant women", which was conducted from February to April 2015. All-Russian Pharmacoepidemiological 1066 questionnaires were analyzed in the study, of which 734 obstetricians and gynecologists, and 332 physician [19].

In a survey in the Belgorod region (BR) 94 doctors took part (28.7% and 69.1% inpatient outpatient Profile, $p < 0, 01$), of which 77 (81.9%) of Obstetricians and Gynecologists, 17 (18, 1%), physicians ($p < 0,0001$), with a total work experience of less than 5 years – 21.3% of physicians, 5-10 years – 26.6%, 10-20 years – 20.2% of doctors more than 20 years and 26.6%. The survey was conducted on the basis of women's clinics, city polyclinics and municipal race. Home Belgorod, as well as in the central district hospital.

Information obtained from the survey were entered and processed using MicrosoftExcel program.

Main part:

To determine the preferences of physicians in the treatment of acute pyelonephritis in the questionnaire presented a list of the most commonly used drugs:

- Penicillin – benzyl penicillin, ampicillin, amoxicillin, amoxicillin / clavulanate;

- Cephalosporins – cefazolin, cefuroxime, cefotaxime, ceftriaxone, cefixime ("Supraks"), cefepime;

- Macrolides – erythromycin, spiramycin, josamycin, clarithromycin, azithromycin;

- Fluoroquinolones – norfloxacin, ofloxacin, pefloxacin, ciprofloxacin, "Avelox", "tavanic";

- Aminoglycosides – streptomycin, gentamicin, amikacin;

- Nitroxoline;

- Fosfomycin (Monural);

- Nitrofurans (furadonin, Furamat, Furagin);

- lincomycin, clindamycin, vancomycin, meropenem;

As it was provided for your answer and the option "not to appoint, send to another specialist."

Based on clinical guidelines for the treatment of pyelonephritis in pregnant women as a starting cephalosporin III generation empirical therapy (cefotaxime, ceftriaxone and cefixime), 56.4% of physicians chose BR (63.6% of obstetricians and gynecologists and 23,5% of the therapist, $p = 0,002$) and 46.1% of physicians All-Russia study ($p = 0,054$).

Amoxicillin / clavulanate (without preliminary urine culture sensitivity to the drug) 50.0% of physicians chose the Belgorod region (57.1% of obstetricians and gynecologists and 17.7% of physicians, $p = 0,003$) and 49.1% of the doctors at the All-Russia study ($p = 0,861$).

Cephalosporin II generation (cefuroxime) (also without preliminary urine culture sensitivity to the drug) chose only obstetricians Belgorod region (7.8%) and physicians All-Russia study (8,3%), $p = 0.886$.

A large number of responses were given ineffective as a therapy of pyelonephritis is not protected against beta-lactamase penicillins – CP doctors pointed them in 55.3% of the questionnaires

(51.9% and 70.6% of obstetricians Physicians, $p = 0,161$), the All-Russian doctors in the study 32.9% of the questionnaires ($p < 0,0001$). Cefazolin (cephalosporin II generation) 27.7% of physicians chose the Belgorod region (32.5% of obstetrician-gynecologist and 5.9% of the therapist, $p = 0.02$) and 15.6% of physicians All-Russia study, $p = 0.002$.

Macrolides having low activity against gram-negative microflora was given to 31.9% of the responses in the BR (37.7% of obstetricians and gynecologists and internists 5.9%, $p = 0.01$) and 18.4% of responses at All-Russia study, $p = 0.0015$.

Fosfomycin, a drug that is used only for the treatment of cystitis and bacteriuria, indicated in their questionnaires, 30.9% of physicians BR (32.5% and 23.5% of obstetricians Physicians, $p = 0.470$) and 19.6% of doctors of All-Russian Research, $p = 0.009$.

Alternative drugs in the treatment of gestational pyelonephritis – aminoglycosides, vancomycin – not chosen any one of the doctors surveyed BR and in rare cases, doctors noticed All-Russia study (0.4% and 0.5%, respectively), $p > 0.5$. The cephalosporin IV generation, notes BR 4,2% of doctors (3.9% and 5.9%, obstetricians physicians) and 5.2% of physicians All-Russia study, $p = 0,702$.

Absolutely contraindicated in the treatment of gestational pyelonephritis fluoroquinolones are listed in the individual questionnaires BR physicians (2.1%) and the All-Russia survey (2.2%).

Send their patients for treatment to another specialist doctors decide 26.6% BR (28.7% of obstetricians and gynecologists and 17.6% of physicians, $p = 0.356$) and 32.3% of All-Russian research physicians ($p = 0.257$). Compare tactics ACT doctors BR and All-Russia study are shown in Table 1 and Figure 1.

Table 1

Comparison of tactics AMT doctors Belgorod Region and All-Russia Research

The drug	Doctors of Belgorod Region		Doctors of All-Russia Research		p
	N=94	Abs. %	N=1066	Abs. %	
Amoxicillin / clavulanate	47	50,0	523	49,1	0,861
Cephalosporin I generation	26	27,7	166	15,6	0,002
Cephalosporin II generation	6	6,4	88	8,3	0,523
Cephalosporin III generation	53	56,3	491	46,1	0,054
Cephalosporin IV generation	4	4,2	55	5,2	0,702
Not protected penicillins	52	55,3	350	32,9	<0,0001
Macrolides	30	31,9	196	18,4	0,0015
Fosfomycin	29	30,9	209	19,6	0,009
Fluoroquinolones	2	2,1	23	2,2	0,938
Aminoglycosides	0	0	4	0,4	>0,5
Vancomycin	0	0	5	0,5	>0,5
Do not prescribe pharmacotherapy	25	26,6	344	32,3	0,257

(Note: p -Hi-square Pearson)

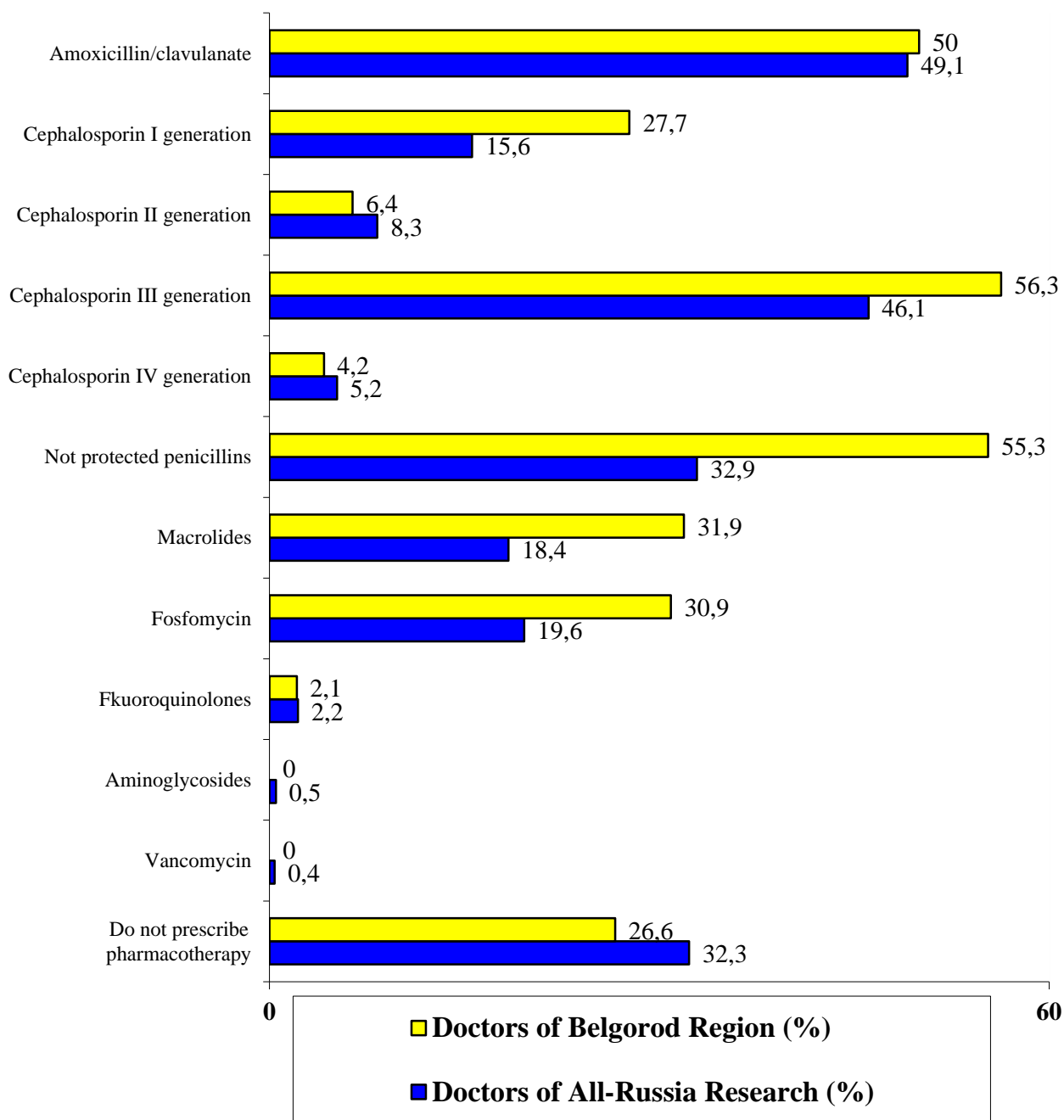


Figure 1. The purpose frequency pyelonefrite drugs in pregnant women among obstetrician-gynecologists and internists Belgorod region of the Russian Federation

Conclusion:

According to the data of the survey, about half of the doctors of the Belgorod region and the All-Russian Research prescribe rational pharmacotherapy in the treatment of gestational pyelonephritis (in particular, Cephalosporin III generation), $p = 0.054$.

From about the same, but without specifying what perparaty data can be allocated only after urine culture sensitivity operedeleniya rate doctors opt to amoxicillin / clavulanate ($p = 0.861$) and cephalosporin II generation ($p = 0.523$).

Regardless of the national recommendations, the canons of rational antibiotic therapy, doctors BR and

All-Russian Research continue to prescribe their patients previously ineffective drugs in the treatment of pyelonephritis – macrolides ($p = 0.0015$) and fosfomycin ($p = 0.009$).

Reserve antimicrobials – amnoglikozidy, vancomycin, meropenem – chose only doctors All-Russian Research; cephalosporin IV generation was given roughly equal number of votes ($p = 0.702$), however, none of the doctors did not indicate that they prescribe them for health reasons, in the case where the appointment of benefit to the mother outweighs the potential risk for the development of the fetus.

Conclusions:

According to the survey, more than 68% of obstetricians and gynecologists and internists Belgorod Region and All-Russia research independently carried out the treatment of pyelonephritis in pregnancy. An analysis of the responses of physicians BR and All-Russia research tactics destination ACT found that only half of practitioners prescribed therapy based on the rational use of antimicrobials. survey results once again demonstrate the relevance of women's adequate therapy problems during pregnancy with concomitant pathology.

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