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AHIL VƏ DAHA YAŞLI XƏSTƏLƏRDƏ RESİDİVVERƏN XRONİK PROSTATİT: DİAQNOSTİKA, ADEKVAT TERAPİYA METODUNUN SEÇİMİ

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Xülasə. *Məqalədə ahıl və daha yaşlı şəxslərdə residivləşən xronik prostatitin kompleks və standart müalicə metodlarını qiymətləndirmək məqsədilə aparılmış tədqiqat işi haqqında məlumat verilmişdir. Kompleks terapiya sxeminə yeni nəsil flüorxinolon preparatı – levofloksasin (tavanik), immunomodulyator – polioksidonium və ferment preparatı – vobenzim daxil edilmişdir. Prospektiv tədqiqat planını "xronik residivləşən bakterial prostatit" diaqnozu qoyulmuş 102 xəstənin müayisəli qiymətləndirilməsi təşkil etmişdir. 51 xəstə standart etiopatogenetik müalicə almış (müqayisə qrupu), əsas qrupa daxil edilən 51 xəstə isə əlavə olaraq immunomodulyator (polioksidonium) və poliferment preparatı (vobenzim) almışdır.*

Xəstələrin müalicədən 3 ay sonrakı növbəti həkimə gəlişində müayyən edilmişdir ki, kompleks terapiya üsulunun klinik-mikrobioloji effektivliyi müqayisə qrupundakına nisbətən artıq olmuşdur (müvafiq olaraq 72,4% və 35,7%).

Aparılmış müalicə üsulunun müqayisəli qiymətləndirilməsi göstərmişdir ki, müqayisə qrupuna aid olan xəstələrdə sidiyin 3-cü porsiyasında və prostat vəzi şirəsində leykositlərin sayı kompleks müalicə alan xəstələrdəkinə nisbətən xeyli artıqdır. Müalicə kompleksinə immunomodulyator – polioksidonium və poliferment preparatı – vobenzim daxil edilməsi xəstələrdə sidik ifrazının asanlaşmasına və ağrı sindromunun zəifləməsinə səbəb olmuş, həyat keyfiyyətini (QoL) isə orta hesabla 4,8 bal (müqayisə qrupunda 4,2 bal) artırmışdır. Əsas tədqiqat qrupuna aparılmış kompleks müalicə xəstəliyin residivlərinin də azalmasına səbəb olmuşdur.

Açar sözlər: *prostatit, levoflaksasin, polioksidonium, vobenzim*

Ключевые слова: *простатит, левофлоксацин, полиоксидоний, вобэнзим*

Key words: *prostatitis, levofloxacin, polyoxidonium, wobenzym*

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RECURRENT CHRONIC BACTERIAL PROSTATITIS IN ELDERLY PATIENTS AND OLDER: DIAGNOSTICS. SELECTION OF ADEQUATE THERAPY

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The study assesses the effectiveness of complex and standard treatment of elderly and older patients with recurrent chronic bacterial prostatitis. The complex therapy included a new generation fluoroquinolone levofloxacin (tavanic), an immunomodulator polyoxidonium and an enzyme wo-

benzym. A prospective comparative study was carried out, which included 102 patients with a diagnosis of recurrent chronic bacterial prostatitis. 51 patients (comparison group) received standard etiopathogenetic therapy, and patients of the main group (51 people) additionally received the immunomodulator polyoxidonium and the polyenzyme wobenzym.

At the third visit after 3 months, it was found that the clinical and microbiological effectiveness of complex therapy was almost 2 times higher than in patients in the comparison group (72.4% and 35.7%, respectively). the main group (51 people) - additionally took the immunomodulator polyoxidonium and the polyenzyme wobenzym.

Comparative evaluation of the therapy showed that in patients of the comparison group, the parameters of the number of leukocytes in the secretion of the prostate and the 3rd portion of urine were significantly higher than in patients who received complex therapy. The inclusion in the complex therapy of the immunomodulator polyoxidonium and the polyenzyme wobenzym contributed to the improvement of impaired urination, reduction of pain syndrome, and the quality of life (Qol) improved and averaged up to 3.8 points (and in the comparison group up to 7.2 points). As a result of the complex therapy, the relapses of the disease also decreased in the patients of the main group.

Currently, prostatitis is considered as a multifactorial, polyetiological disease of the prostate gland associated with pain in the genital area, urinary disorders and the quality of life of patients [1-3].

Chronic bacterial prostatitis is one of the most common and intractable diseases. The incidence of the disease before the age of 50 is 8%, and with age this figure reaches 30-70% [4]. A number of domestic and foreign researchers have found that chronic prostatitis (CP) is observed in 40-90% of men in the age group from 50 to 80 years old and older [4-6].

The etiological structure of the microbiota of the urogenital tract is well studied: the spectrum of etiological agents is the same for infections of both the lower and upper urinary tract and represents Escherichia coli in 70-95% of cases and Staphylococcus saprophyticus in 5-10% [5]. Other members of the Enterobacteriaceae family (Proteus mirabilis, Klebsiella spp., Serratia marcescens, etc.) can also be isolated. Conditionally pathogenic microorganisms (UPM) are representatives of the normal microbiota, but with a decrease in the reactivity of the organism, they cause an infectious and inflammatory pathology of the urogenital tract. Currently, in all countries of the world, there is an activation of the UPM [6]. UPM in association with pathogenic microorganisms in the focus of inflammation form biofilms that prevent the penetration of antibacterial drugs into the biotope "Prostate gland" [7-9].

Among infectious diseases of the urogenital tract (UGT), mixed infections account for 30-50%. Sexually transmitted uropathogens (chlamydia, mycoplasma, ureaplasma) can also be etiological factors of chronic prostatitis [10, 11]. Under conditions of mixed infection, the virulence of each of the pathogens of CP sharply increases.

One of the important aspects indicating the importance of preventing recurrence of CP is the etiological relationship between the inflammatory process in the tissues of the prostate and the occurrence of hyperplasia in it [12, 13].

CP treatment currently remains a serious problem for practical health care. Very often conducted antibiotic therapy is not always effective, and sometimes its unreasonableness serves as a factor leading to the chronicity of the infectious process, violations of local and general immunoregulatory mechanisms [14, 15]. That is why, in order to increase the effectiveness of treatment in recent years, alternative methods have become relevant: probiotics, phytopreparations, immunomodu-lators [16-18]. The most effective elimination of bacteria from the urogenital tract is achieved as a result of complex therapy of CP with antibiotics in combination with immunemodulators [19].

Until now, in our region there is no single integrated approach to the choice of tactics for managing elderly and older patients with infectious and inflammatory pathology of the prostate gland. For the period from 2012 to 2018 (Makhachkala, Republic of Dagestan), the incidence rate of this nosological form

increased from 32.5% to 62%, i.e. almost 2.0 times [Dzhalilov H.N., 2018].

It should be noted that empirical etiotropic antibiotic therapy of CKD both in Russia and abroad has been developed and carried out quite effectively, with regard to recurrent chronic bacterial prostatitis in elderly people and older, the spectrum of microbiota and its antibiotic resistance in infectious and inflammatory pathology of the prostate gland in our region remain unexplored.

The aim of the study was to evaluate modern approaches to the diagnosis and treatment of recurrent chronic bacterial prostatitis in elderly patients and older.

Given the high prevalence of recurrent CKD in elderly and senile patients complicated by prostatic hyperplasia, the choice of adequate therapy and the improvement in the quality of life of patients, the question of their adequate and effective treatment remains open. For the combination of fluoroquinolone levofloxacin (tavanic), the immunomodulator polyoxidonium and the polyenzyme wobenzym, we conducted a clinical, laboratory and instrumental study in 102 elderly and older patients with CKD.

Material and research methods. The study included 102 patients of the older age group diagnosed with recurrent chronic bacterial prostatitis, divided into two groups (main and comparison), 51 people each. Patients of the main group received the antibiotic levofloxacin 500 mg daily once a day for 4 weeks (after meals), probiotic bifiform, 2 caps. twice a day for 4 weeks, α-blockers, drugs that improve microcirculation and hemodynamics in the pancreas (escusan, trental - any of them), polyenzyme wobenzym (30 minutes before meals) - 3 tab. 3 times a day for 4 weeks, polyoxidonium immunomodulator (rectal suppositories, 12 mg) No. 10 (preferably after a cleansing enema or after bowel movement). Patients in the comparison group received standard therapy (without immunomodulator and polyenzyme). Doctor visits were made at the screening stage (1 visit). Subsequent 3 visits were carried out after 4 weeks, 3 months and 6 months.

All patients underwent a clinical examination, which included the study of anamnesis, an assessment of complaints expressed in points according to the International Assessment of Prostate Diseases (IPSS) with the definition of a standardized indicator of quality of life (Qol) in points, sexological testing, involving a questionnaire and the definition of an international index of erectile function (according to ICEF-6 questionnaire), frequency of urination (Q max), pain syndrome. During physical examination, blood pressure (blood pressure) and heart rate (heart rate) were taken into account. DRE (digital rectal examination), ultrasound (ultrasound) of the prostate gland, uroflowmetry, TRUS (transrectal ultrasound) were performed. Indicators DRE, ultrasound, TRUS in both groups did not differ.

Questioning of patients on the IPSS scale with an assessment of Qol (quality of life) revealed moderate and mild urination disorders in 91 patients, and severe urination in 11 patients. In the main group, the average rate of impaired urination was 4.2-0.53 points. According to the results of the ICEF-16 questionnaire, moderate erectile dysfunction was detected in 47%, and severe erectile dysfunction in 53% of patients. For all studied parameters, patients of both groups are comparable. A biochemical study showed that PSA (prostate-specific antigen) levels ranged from 1.6 ng/ml to 2.2 ng/ml.

In order to study the spectrum of the microbiota and its antibiotic resistance, the secretion of the prostate and the third portion of urine (according to Mearey-Stamey) were subjected to bacteriological research.

In the bacteriological study of clinical material, we used a modified scheme to isolate different taxonomic groups of microorganisms. The scheme uses a complex of nutrient media for the isolation of gram-negative and gram-positive microorganisms. For representatives of the families Enterobacteriaceae and Pseudomonadoceae, experimental series of domestic chromogenic nutrient media and MTS (microtest systems) were used for the simultaneous isolation and identification of enterobacteria. An antibiogram of the leading etiopathogens of CKD was performed. The study used discs with antibiotics manufactured by NICF (St. Petersburg) (disc-diffusion method).

For the detection of intracellular pathogens (chlamydia, mycoplasma, ureaplasma, cytomegalovirus, herpes viruses - types 1,2), the method of enzyme-linked immunosorbent assay (ELISA) and a valuable polymerase reaction - PCR (in Real time online) were used.

Study inclusion criteria: patients aged 60 years and older with symptoms of recurrent CKD for 3 months or more. Patients signed written informed consent, are able to adequately fill out the urination diary, International questionnaires IPSS, NIH - CPSI , Qol , ICEF-6.

Evaluation of the effectiveness of complex therapy was carried out according to the dynamics of erectile dysfunction using the MIEF-6 questionnaire, according to the change in the dynamics

of indicators of DRE, ultrasound, TRUS, uroflowmetry, the dynamics of quality of life scores (Qol) according to the International questionnaire IPSS, Qmax indicators, pain syndrome according to VAS (visual analogue scale).

Statistical processing of the research data was carried out using Microsoft Excel spreadsheets from the Microsoft Office 2007 software package statistical package STATISTICA 6.1 (Statsoft Inc., USA) was carried out on a personal computer IBM PC using Microsoft Statistica 6.0 software.

Research results and their discussion. In total, for the period from 2012 to 2018, 936 strains of etiologically significant microorganisms were isolated at the State Budgetary Institution "Geriatric Center" RD (Makhachkala). The secretions of the prostate and the third portion of urine were subjected to microbiological examination. 587 strains were isolated and identified to the species, which accounted for 62.7% of the total number of identified pathogens. In the general structure of the isolated microbiota, gram-negative bacteria of the families Enterobacteriaceae and Pseudomonadoceae (87.7%) predominated, the proportion of gram-positive bacteria was significantly lower (12.3%).

The main uropathogens - causative agents of infectious and inflammatory pathology of the urogenital tract are presented in charts 1, 2.

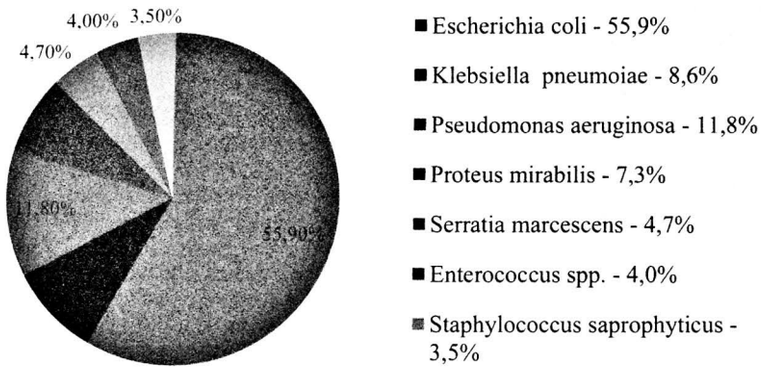

Chart 1. Microbiota structure of the 3rd urine portion in elderly and older patients with recurrent chronic bacterial prostatitis

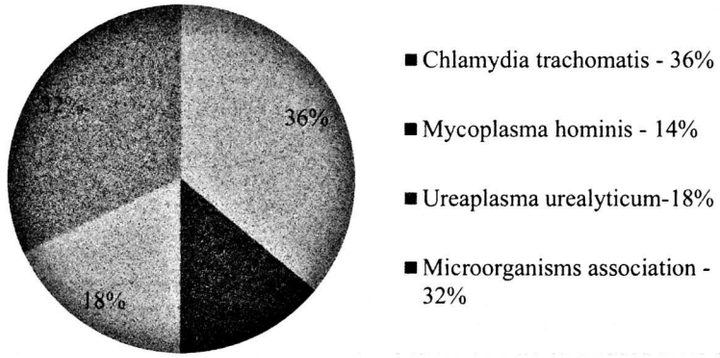

Chart 2. Structure of atypical microbiota of prostate secretion in elderly and older patients with recurrent chronic bacterial prostatitis

From the results presented in charts 1, 2, it can be seen that the most common causative agents of infectious and inflammatory pathology of the prostate gland are opportunistic microorganisms, in particular Escherichia coli (55.9%), and from intracellular – Chlamydia trachomatis (36%), and mycoplasma and ureaplasma, respectively, in 14% and 18% of cases.

The results of the study showed that the resistance of the main uropathogens to antibiotics used in the treatment of urological diseases is different (Chart 3).

The data presented in chart 3 indicate a high resistance of the microbiota to antibiotics recommended by the EAU (European Association of Urology). Against this background, there is a very low resistance of the microbiota isolated from the biomaterial of patients to the new generation of fluoroquinolones. This is probably due to the fact that urological patients of the Geriatric Center received fluoroquinolones relatively recently and the microbiota of the urogenital tract did not have time to develop resistance to them.

The results of this study indicate the clinical and microbiological efficacy of complex antibacterial therapy - the symptoms of the lower urinary tract (LUTS), dysuric phenomena (maximum urine flow rate (Qmax -14.5 ml / sec., Residual urine (Vres -20-25 ml per average), decreased prostate volume (V -32.5-34.0 on average). The average indicators of microcirculation and hemodynamics of the prostate improved, the pain syndrome decreased to 26% (initially 92%), while in the comparison group (who received standard therapy), the pain syndrome remained in 69% of patients 4 weeks after completion of treatment. The dynamics of the average pain scores according to the VAS (visual analogue scale) is shown in Chart 4.

The difference in the compared groups was 3.57 points 4 weeks after the end of treatment ($p<0.05$).

An important indicator of the effectiveness of complex antibiotic therapy is a long relapse-free period. In our study, the indicators of the state of urination, pain syndrome and quality of life of patients were assessed after 3, 6 months and a year. After 3 months. after the completion of complex antibiotic therapy, recurrence of chronic bacterial prostatitis was noted in 7.9% of patients, and in patients of the comparison group 49.7%, after 6 months - 8.7% and 52.3%, respectively, i.e. in patients who received only standard therapy, relapse of the disease occurred 4.3 times more often. Against the background of the ongoing complex antibacterial therapy, the indicators of the International Index of Erectile Function (IIEF-6) also improved.

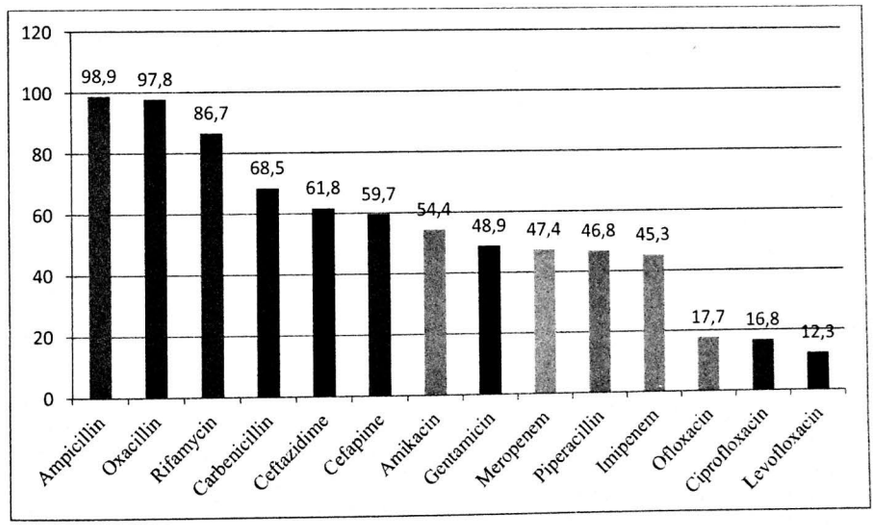

Chart 3. Antibiotic Resistance (%) of strains of E. coli isolated from urine of elderly and senile outpatients with chronic bacterial prostatitis

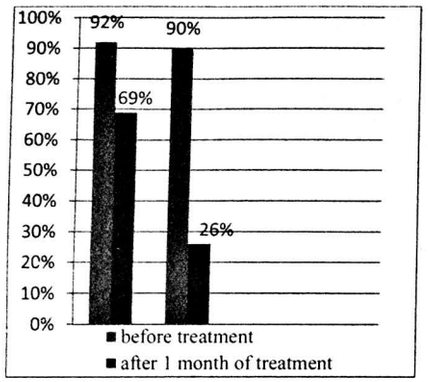

Chart 4. Dynamics of pain syndrome according to the VAS scale in elderly and older patients with recurrent chronic bacterial prostatitis against the background of standard antibiotic therapy and standard, supplemented with polyoxidonium and wobenzym preparations

Based on the results of the study, we formed the clinical course and immune status of patients of the older age group with recurrent chronic bacterial prostatitis complicated by prostatic hyperplasia and showed that the complex antibacterial approach we used to treat these patients is clinically and laboratory-effective. And most importantly, the therapy has significantly improved the quality of life (Qol) of patients - complex in age, various somatic pathologies, impaired psycho-emotional status and somewhat maladjusted in society.

Based on the data of the study, the following conclusions were made:

1. Risk factors for the disease are the age of patients, various somatic pathologies, immunodeficiency, hemodynamic disturbances, microcirculation in the prostate gland caused by edema, venous congestion and obstruction of the acini.

2. The species composition of the microbiota isolated from clinical samples (3rd portion of morning urine and prostate secretion) of the urogenital tract was gram-negative uropathogens (82.7%) from the families Enterobacteriaceae and Pseudomonadoceae, and gram-positive bacteria were within 17.3%.

3. Antibiotic resistance of the isolated strains of uropathogens had multi-resistance to antibacterial drugs recommended by EAU. Resistance to the new generation fluoroquinolone levofloxacin was 12.6% -18%. Despite the widespread use of levofloxacin since 2012 to 2018 there was no significant increase in drug resistance.

4. In patients of the older age group with infectious and inflammatory pathology (IVP) of the prostate gland, in parallel with opportunistic microbiota (UPM), mixed infection (atypical bacteria) was revealed: Chlamydia trachomatis -36%, Mycoplasma spp . - 18%, Ureaplasma urealyticum - 14 %, which contributes to the formation of biofilms in the focus of inflammation and complicates the treatment of the disease.

5. The complex antibacterial therapy used by us, including the antibiotic levofloxacin, the immunomodulator polyoxidonium (azoxymer bromide), the polyenzyme of animal and plant origin wobenzym, contributed to the clinical improvement of the indicators of the International NIH questionnaires - CPSI, IPSS, Qol in 76% of cases, and the microbiological efficacy was 71,2% of cases. In the comparison group, these indicators were almost 2.0-2.5 times less (39.5% and 42.7%, respectively).

It has been established that the use of the immunomodulator polyoxidonium and the polyenzyme wobenzym in complex antibacterial treatment is clinically justified.

Conclusions

1) Adequate antibiotic therapy is the cornerstone of successful CKD therapy. It should be noted that taking an antibacterial drug is inappropriate in case of resistance to it in a population of 15-20 strains of microorganisms.

2) Local data on antibiotic resistance of pathogens of infectious and inflammatory pathology of the urogenital tract are a decisive factor in choosing an adequate therapy.

3) Treatment of CKD should be comprehensive with the inclusion of antibacterial, anti-inflammatory drugs, α-blockers, as well as drugs with a polymodal effect (immunomodulators, enzymes, etc.).

4) When choosing an antibiotic, one cannot rely only on literature data; it is necessary to know the spectrum of the microbiota and its antibiotic resistance in your region.

5) The results obtained have social and general medical significance for the Republic of Dagestan both in terms of improving the diagnosis of this nosology, and in terms of choosing effective methods of treatment and prevention of recurrence of the disease.

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РЕЦИДИВИРУЮЩИЙ ХРОНИЧЕСКИЙ БАКТЕРИАЛЬНЫЙ ПРОСТАТИТ У ПАЦИЕНТОВ ПОЖИЛОГО ВОЗРАСТА И СТАРШЕ: ДИАГНОСТИКА И ВЫБОР АДЕКВАТНОЙ ТЕРАПИИ

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Резюме. В исследовании дана оценка эффективности комплексного и стандартного лечения пациентов пожилого возраста и старше с рецидивирующим хроническим бактериальным простатитом. Комплексная терапия включала фторхинолон нового поколения левофлоксацин (таваник), иммуномодулятор полиоксидоний и фермент вобэнзим. Проведено проспективное сравнительное исследование, в которое включено 102 пациента с диагнозом «Рецидивирующий хронический бактериальный простатит». Стандартную этиопатогенетическую терапию получал 51 пациент (группа сравнения), а больные основной группы (51 чел.) – дополнительно принимали иммуномодулятор полиоксидоний и полифермент вобэнзим.

На третьем визите через 3 месяца было установлено, что клинико-микробиологическая эффективность комплексной терапии почти в 2 раза выше, чем у пациентов группы сравнения (72,4% и 35,7% соответственно).

Сравнительная оценка проводимой терапии показала, что у пациентов группы сравнения параметры количества лейкоцитов в секрете простаты и 3-й порции мочи были значительно выше, чем у больных, получивших комплексную терапию. Включение в комплексную терапию иммуномодулятора полиоксидоний и полифермента вобэнзим способствовало улучшению нарушенного мочеиспускания, снижению болевого синдрома, а качество жизни (Qol) улучшилось и составило в среднем до 3,8 балла (а в группе сравнения до 7,2 балла). В результате комплексной терапии у пациентов основной группы снизились и рецидивы заболевания.

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