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Etiological circumstances and pathogenic aspects of pulmonary infectious complications in recipients of kidney transplant

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ABSTRACT

Aim. This study aimed to determine the spectrum of pathogens and its resistance in the dynamics in patients with infectious complications after kidney transplantation.

Methods. The results of the study of biomaterials from patients with infectious complications on the background of acute and chronic kidney transplant rejection have been studied.

Results. During the analyzed period, there was a tendency to change the spectrum of pathogens, the growth of the value of gram-negative bacteria. The sensitivity analysis of the isolated microorganisms over the study period (2010-2017) showed an increase in the resistance of the dominant pathogens. Also, there was a significant increase in the frequency of occurrence of Candida fungi.

Conclusion. In most kidney transplant recipients with nosocomial infections is unavoidable. Therefore, a timely and adequate antibiotic therapy is required to constant control of modern pathogens with increased resistance.

Recommendations. The increase in antibiotic resistance of the leading pathogens makes it necessary to study the antibioticogram of all strains isolated from patients for an adequate choice of effective antibiotic therapy. The obtained data should be used to optimize empirical antibiotic therapy in patients with purulent-septic complications after kidney transplantation.

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INTRODUCTION

Rehabilitation of patients with a renal transplant is a complex clinical task and is often associated with a number of problems, one of which is the problem of infectious complications. Immunosuppressive therapy, suppressing transplant immunity, reduces the patient's resistance to infections. Therefore, the success of kidney transplantation largely depends on the ability to achieve a balance between obtaining effective immunosuppression in order to prevent the transplant-rejection and maintaining immune protection at a level sufficient to protect the recipient from developing infectious complications [1-3]. Improvement of methods of preventing, diagnosing and treating infections, optimization immunosuppressive therapy over the past 10 years has made decreasing the rate of infectious complications after organ transplantation. But this group of complications continues to occupy one of the main places among the causes of death of patients after kidney transplantation. The incidence of infectious complications leading to fatal outcomes during the first year after transplantation, according to various sources, is from 2.6 to 51.7%, and in recipients over 60 years of age – 18% to 42.8% [2].

Infection remains one of the main causes of death for patients receiving various types of renal replacement therapy – hemodialysis, peritoneal dialysis, and after kidney transplantation [3-5]. In this case, the most common causative agent of infection are bacteria, which often have multiple antibacterial resistance. Irreversible damage to the lungs, as a result of an excessive immunopathological reaction to cytomegalovirus

(CMV) antigens, the expression of specific cytotoxic lymphocytes on infected lung cells leads to damage to the alveoli.

Taking into account the constantly changing sensitivity of pathogens of bacterial infections to antibiotics, the growing resistance of pathogens requires a constant analysis of the composition and sensitivity of microflora. In this regard, the study of the etiological structure and antibiotic resistance of major pathogens is necessary for timely adequate antibiotic prophylaxis and empirical antibiotic therapy [6-8].

The aim of study was to identify the spectrum of pathogens and its resistance over time in patients with infectious complications after kidney transplantation.

MATERIAL AND METHODS

The foundation of the study was the results of the examination and treatment of 105 patients after heterotopic related TP for the period 2010-2017. Of these, 101 patients were operated on in our center. Pulmonary complications with the development of bilateral interstitial pneumonia were observed in 7 patients in the immediate postoperative period, in 4 patients in the late, during the observation period from 1 month to 4 years.

Four more patients operated in clinics in India and Pakistan were hospitalized to our center with a clinic for acute lung injury syndrome in one case against acute and in three chronic kidney transplant rejection, pyelonephritis and bacterial pneumonia with further development of sepsis were also diagnosed.

The materials for analysis were: urine (236 samples), blood (195 samples), discharge from drainages (220 samples), sputum (217 samples), material of broncho-alveolar lavage (56 samples), and tracheal wash (220 samples). Traditional methods for isolating and identifying microorganisms and determining their sensitivity to antimicrobial agents by the disk diffusion method were used. The species specificity of the isolated microorganisms was determined using standard methods using identification media (production "HiMedia", India). Investigated the effectiveness of cephalosporins, aminoglycosides, fluoroquinolones, tetracyclines, carbapenems, glycopeptides, inhibitor-protected antibiotics.

In event of bronchopulmonary infection in the complex of conventional therapy, the new antimicrobial biotechnological medication FarGALS was used, which is characterized by a pronounced antiseptic and local anti-inflammatory effect. The antimicrobial activity of the FarGALS with respect to the isolated strains was determined by diffusion into agar. Accounting for the results was to measure the diameters of the zones of inhibition of the growth of test cultures around the wells. With zones up to 10 mm, cultures were considered stable, with zones of 11-14 mm being moderately resistant, with zones of 15 mm and above being sensitive.

FarGALS has a broad spectrum of antimicrobial activity (active against gram-positive and gram-negative, aerobic and anaerobic, nesporoobrazuyushchy and spore-forming bacteria, etc., fungi of the genus Candida). In addition, the presence of antibodies against CMV in the serum was determined and the presence of CMV DNA was detected by a quantitative polymerase chain reaction method. Polymerase chain reaction (PCR), quantitative determination showed 3,5x106ME / ml in the blood. As well as dynamic control of C-reactive protein.

Ethical approval

The review board and ethics committee of RSSPMCS named after acad. V.Vakhidov approved the study protocol and informed consents were taken from all the participants.

RESULTS AND DISCUSSION

The number of microbiological positive samples is reduced from 85% to 47%. A total of 236 cultures were isolated, of which gram-positive - 20%, gram-negative - 46%, fungi of the Candida river - 34%. From gram-positive: Staphylococcus aureus and Enterococcus spp. met in 4.0-2.0% of cases, from gram-negative - Pseudomonas aerugenosa 20–13.6%, Klebsiella pneumonia 43.2–8.7%, E. coli 11–23.0%, Acinetobacter spp. - 8-39%. Strains Acinetobacter spp. excreted mainly from the trachea (patients on prolonged mechanical ventilation) - 77%. Among the samples of tracheobronchial aspirate in 25% of cases - were allocated, associated, most of the microbial associations included fungi. The results of the study of samples of biological media are represented in table 1. Most of all we studied the drain bag biological media (7.3-19%).

Table 1. The results of the study of samples of biological media (%)

Type of biomaterial	2010 г.	2011 г.	2012 г.	2013 г.	2014 г.	2015 г.	2016 г.	2017 г.
	0.6	2.6	-	-	-	-	-	-
Surgical wound	11	14	5.4	1.7	-	-	0.6	-
Blood	0.3	0.9	2	-	-	-	0.3	-
From the pleura	5.3	4.8	6.7	2.6	2.3	1.4	3.8	2.6
From drain bag	7.3	9.6	11	19	17	10	14	19
From the trachea	3.1	3.8	2.6	1.4	0.6	1.6	0.6	1
From the bronchi (Sputum)	3	1.4	2	-	-	-	-	0.6

Table 2. Acinetobacter spp. resistance in ICU (%)

Antibiotics	2010 г.	2011г.	2012 г.	2013 г.	2014 г.	2015 г.	2016 г.	2017 г.
Ampicillin / Sulbactam	100	100	100	100	100	100	100	100
Amoxicillin / Clavulanate	100	100	100	100	100	100	100	100
Piperacillin / Tazobactam	-	-	82	66.6	76	87	100	100
Imipenem	11.7	21	11.7	13	21	43	85	100
Meropenem	41	41	60	66.6	76	87	100	100
Ertapenem	-	-	-	-	100	100	100	100
Cefazolin	100	100	100	100	100	100	100	100
Cefuroxime	100	100	100	100	100	100	100	100
Cefotaxime	100	100	100	100	100	100	100	100
Ceftazidime	100	100	100	100	100	100	100	100
Ceftriaxone	100	100	100	100	100	100	100	100
Cefoperazone	100	100	100	100	100	100	100	100
Cefoperazone / Sulbactam	66.6	84	82	66.6	73	85	100	100
Cefepime	100	100	100	100	100	100	100	100
Gentamicin	86	78	86	88	90	100	100	100
Amikacin	78	90	90	90	90	100	100	100
Tetracycline	46	17.6	17.6	26	68	66	57	20
Doxycycline	41	16	11.7	16	52	50	19	15
Ofloxacin	78	90	76	90	100	100	100	100
Ciprofloxacin	100	100	100	100	100	100	100	100
Levofloxacin	-	78	100	-	100	100	100	100
Gatifloxacin	-	-	-	-	100	100	100	100
Polymyxin	0	0	0	0	0	0	4	5

According to the data obtained, one of the most prevalent thing were respiratory diseases in the structure of severe infections. The sensitivity analysis of the isolated microorganisms over the study period (2010-2017) shows that there is a tendency to increase the resistance of the dominant pathogens. Gram-positive cocci in patients with a renal transplant currently retain sensitivity to vancomycin, rifampicin, IV generation cephalosporins, amikacin. Recently (2014-2017) among the most "topical" pathogens are Ps.aeruginosa, Klebsiella pneumonia, E.coli, Acinetobacter spp. There is a high increase in resistance (for example, Acinetobacter spp., Table 2), so the range of medications active in their regard was extremely limited: the latest generation cephalosporins (75-100% R), fluoroquinolones (75-100% R), imipenem (80, 0-70.0% R), polymyxin B (7.0-19.0% R), amikacin (69.0-55.0% R).

Analysis of the antimicrobial activity of the medication "FarGALS" in relation to the isolated strains showed high sensitivity - 22 mm. In detection of IgG antibodies, IgM against CMV, antiviral therapy with Ganciclovir and Valganciclovir was performed, after which the control determination of IgM against CMV, as well as the determination of CMV DNA by PCR showed a negative result, which gives us the opportunity to proceed to reduce the infection activity to latent forms.

The dynamics of the observation of the C-reactive protein level showed a generalization of the infection with C-reactive protein rates above 70 mg/l; in connection with which de-escalation antibacterial therapy was

carried out. The inclusion of the medication "FarGALS" in the complex for the prevention and treatment of purulent-inflammatory lung diseases in the form of nebulizer therapy and fibrobronchoscopic bronchial lavage can reduce the incidence of early and late specific bronchopulmonary complications and achieve a clinical improvement in patients already by 2-3 days and reduce their recovery time.

In the early postoperative period, one case death was observed in a 47-year-old man. The cause of death was the crisis of rejection, bilateral lower lobe pneumonia, severe acute respiratory distress syndrome, acute cardiovascular failure. These data demonstrate the leading position of respiratory diseases in the structure of severe infections. In the structure of nosocomial infection in ICU - Acinetobacter spp. is a leading pathogen that can cause infections of any location and is highly resistant to all groups of antibacterial medications. For example, over the past 10 years, the rate of seeding of this pathogen was 5.4-39%, i.e. increasing it by 7 times.

CONCLUSION

For most kidney transplant recipients, infection with nosocomial infections is unavoidable. Increasing resistance of modern pathogens requires its constant control for timely and adequate antibiotic therapy. Detection the risk factors for the development of bacterial and fungal infectious complications after kidney transplantation allowed the targeted implementation of preventive measures both before and after kidney transplantation, which led to a decrease in the frequency of these complications.

The increase in antibiotic resistance of the leading pathogens makes it necessary to study the antibioticogram of all strains isolated from patients for an adequate choice of effective antibiotic therapy. The obtained data should be used to optimize empirical antibiotic therapy in patients with purulent-septic complications after kidney transplantation.

DECLARATIONS

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Authors' Contributions

All authors contributed equally to this work.

Competing interests

The authors declare that they have no competing interests.

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