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Effects of secondary infections on the multidrug-resistant Tuberculosis: A cohort study

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Abstract

Background: Tuberculosis (TB) causes over a million deaths annually and is still one of the most important public health problems worldwide. According to the World Health Organization estimates, the highest rates of TB in the European Region are in Tajikistan, Kazakhstan, Moldova, Kyrgyzstan, Romania, and Uzbekistan. The purpose of this study was to investigate the spectrum of nonspecific microorganisms isolated in patients with multidrug-resistant TB in Central Kazakhstan and to assess their susceptibility to antimicrobial drugs.

Methods: The patients were divided into 2 groups: group 1 with multidrug-resistant forms of pulmonary TB (n = 107 patients); group 2 with sensitive forms of pulmonary TB (n = 122 patients). Gender, age, and social status of the patients were studied. Microorganisms were identified using the MALDI-TOF method. The statistical significance of different values for binary and nominal parameters was determined using the chi-square test. Changes in binary variables were analyzed using the McNeimer test.

Results: During the study, an expectedly high proportion of tetracycline-resistant pneumococcal strains (66.7% and 60%, respectively) was isolated, which was a consequence of a long-term and practically uncontrolled use of these drugs in Kazakhstan. Fluoroquinolones showed low activity. The results showed that beta-lactam antibacterial drugs maintained their high activity against the causative agents of pneumococcal infection.

Conclusion: It was concluded that secondary microorganisms isolated in patients with multidrug-resistant TB were represented by the strains that were resistant to modern antibacterial drugs. Therefore, for appropriate antibiotic prescription, it is necessary to study materials from the respiratory system in all patients admitted for TB treatment to study the spectrum of nonspecific microorganisms and assess their susceptibility to antimicrobial drugs.

Keywords: Health care, Treatment efficacy, Non-specific microorganisms, Antibacterial drugs

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Introduction

Tuberculosis (TB) causes over a million deaths annually and is still one of the most important public health prob-

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↑What is "already known" in this topic:
Although patients with pulmonary TB receive long courses of antibiotic therapy (streptomycin, rifampicin, etc), they often develop secondary infections commonly caused by opportunistic microorganisms (OMs) resistant to these drugs. OMs create favorable conditions for the spread of mycobacteria and new lesions.

→What this article adds:
Secondary microorganisms isolated in patients with multidrug-resistant TB are represented by the strains that are resistant to modern antibacterial drugs, and for appropriate antibiotic prescription, it is necessary to study materials from the respiratory organs in all patients admitted for TB treatment to obtain the spectrum of nonspecific microorganisms and assess their sensitivity to antimicrobial drugs.

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lems worldwide. According to the World Health Organization estimates, the highest rates of TB in the European Region are in Tajikistan, Kazakhstan, Moldova, Kyrgyzstan, Romania, and Uzbekistan (1-3). Kazakhstan is one of 18 countries in the European Region with high rates of multidrug-resistant TB (MDR-TB). Despite active measures for the diagnosi s and treatment of TB in Kazakhstan, the rates remain high (3). The problem of multidrug resistance poses a great problem for TB treatment and remains the subject of thorough monitoring by global health care (4-7). A steady increase in the spread of resistant Mycobacterium TB strains is of particular concern, including the most dangerous strains with extensive and multidrug resistance (XDR-TB and MDR-TB, respectively). Multidrug-resistant TB is one of the main factors resulting in an increased mortality and low efficacy of treatment (8-12).

The course of TB is often complicated with a nonspecific inflammation, which changes both clinical manifestations of TB and the course and outcome of the disease (13). Despite the fact that patients with pulmonary TB receive long courses of antibiotic therapy (streptomycin, rifampicin, etc.), they often develop secondary infections commonly caused by opportunistic microorganisms (OMs) resistant to these drugs (14). Antibacterial chemotherapy, which has prolonged the life of patients with TB, has increased the importance of OMs as etiological agents of pyoinflammatory diseases of the lower respiratory tract (LRT) in patients with pulmonary TB. The airways of patients with pulmonary TB are nonsterile. OMs often colonize them even during remission, as the level of colonization resistance in such patients is lower. Causing a pathological process in the lungs, OMs aggravate the course of the underlying disease. OMs create favorable conditions for the spread of mycobacteria and new lesions.

The combination of infectious pathogens (15-17) has negative effects on the prognosis and the possibility of clinical recovery (18, 19). Secondary infections, occurring in the form of exacerbation of nonspecific bronchitis and pneumonia and complicating the course of fibrous-cavernous TB, infiltrative TB, TB, et cetera, are diverse and are not caused by a specific pathogen (20, 21). The rates of combination of TB with nonspecific respiratory diseases and other non-TBinfections vary from 7% to 49% (16-19). In patients with recurrent pulmonary TB, chronic nonspecific respiratory diseases occur in 17.5-63.2% of cases (22, 23). The combination of TB with nonspecific pulmonary diseases significantly complicates the course of TB, causing multiple symptoms, predominance of alterative and exudative changes. Combined pathologies result in the worst treatment results in pulmonary TB, decreased rates of cavity closure and sputum abacillation, and longer treatment duration (24, 25).

Timely diagnosis of secondary LRT infections in patients with pulmonary TB and targeted treatment of complications is one of the urgent problems of modern phthisiology (14). Treatment of both TB and concomitant diseases caused by nonspecific microorganisms requires the use of broad-spectrum antibiotics together with anti-TB drugs. Treatment of nosocomial infections is a difficult process, as nosocomial microorganisms have a different spectrum of susceptibility to antibacterial drugs than community-acquired pathogens. The emergence and administration of new generations of antibiotics result primarily in qualitative changes in nosocomial flora (26). Accumulated data on antibiotic resistance of secondary microorganisms in pulmonary TB show the need to study the spectrum of isolated microorganisms and their sensitivity to antimicrobial drugs (27, 28).

The purpose of this study was to investigate the spectrum of nonspecific microorganisms isolated in patients with multidrug-resistant TB in Central Kazakhstan and to assess their susceptibility to antimicrobial drugs.

Methods

A cohort study was performed at the microbiological laboratory of the Medical University of Karaganda. The strains of nonspecific microorganisms were obtained from sputum samples from the patients with a confirmed diagnosis of TB. The results of microbiological examination of sputum obtained from 229 TB patients admitted for treatment to inpatient departments of the Regional TB Dispensary in Karaganda in 2014-2015 and 2018-2019 were analyzed. To achieve the purpose of the study and assess the studied (quantitative) parameters, depending on the isolation method, the patients were divided into 2 groups: group 1 with multidrug-resistant forms of pulmonary TB (n = 107 patients); group 2 with sensitive forms of pulmonary TB (n = 122 patients). To study the spectrum of nonspecific microorganisms isolated in the patients with MDR-TB and assess their susceptibility to antimicrobial drugs, we studied gender, age, and social status of the patients, analyzed cases by type, clinical structure of TB, extent of the process, and destructive changes in the lungs.

The studied materials were collected into sterile containers and delivered to the microbiological laboratory no later than 2 hours after sputum collection. Inoculation of nonspecific microorganisms was done in culture media with the isolation of pure cultures. Microorganisms were identified using the MALDI-TOF method with the Microflex mass spectrometer (Bruker Daltonics). During the MALDI-TOF, a double (duplicate) application of the culture with identification according to the standard protocol recommended by Bruker Daltonics was used. Mass spectra were calibrated using Escherichia coli ribosomal proteins (bacterial standard). Protein spectra were analyzed using the MALDI Biotyper (Version 3, Bruker Daltonics).

The results were expressed as a score from 0 to 3. A score >1.7 corresponded to a high degree of reliability of identification up to genus, and a score >2.0 corresponded to reliable identification up to species. At the same time, a score >1.7 was considered as the minimum value of the score coefficient required for species identification. At a score <1.7, the identification result was considered invalid and the test was repeated (28). To determine the susceptibility of microorganisms to antibiotics, a disc diffusion method was used, according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI 2012) (29). Resistance to methicillin (oxacillin) and other β-lactam antibiotics of S.aureus isolates was determined

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based on the resistance to oxacillin and cefoxitin (30). The extended β-lactamase spectrum in gram-negative bacteria was determined using phenotypic methods (31).

The 2 groups were compared on a quantitative scale using the nonparametric Mann-Whitney U test. The relative attribute rates in different independent populations were compared using a z test. The statistical significance of different values for binary and nominal parameters was determined using the chi-square test. Changes in binary variables were analyzed using the McNemar test. To describe quantitative parameters, the means and standard deviations were used in the "M ± S" format. The level of statistical significance was accepted as an error probability level of .05. Statistical data processing was performed using the Statistica 10 and SAS JMP 11 software packages.

Results

Gender characteristics of the patients showed the prevalence of men in both groups: 84 (78.5%) in group 1 and 85 (69.7%) in group 2; and also, 23 (21.5%) and 37 (30.3%) women in groups 1 and 2, respectively. There were no significant differences between the groups, p>0.005. The analysis of the age of the patients showed that the groups did not differ in age, p>0.005 (Table 1).

The analysis of patients by case type is shown in Table 2. The development of multidrug resistance is caused by ineffective treatment, noncompliance during previous treatment, and accordingly disease recurrence.

Table 3 shows patient distribution by diagnosis of tuberculous process. Infiltrative tuberculosis was most common in both groups.

A history of nonspecific pulmonary diseases was observed in 16 (15.0%) patients in group 1 and 22 (18.0%) patients in group 2 (p>0.005). Another TB comorbidity, HIV infection, was observed in 5 (4.7%) patients in group 1 and 7 (5.7%) patients from Group 2 (p>0.005). Before therapy, acid-fast mycobacteria in sputum was detected using bacterioscopy in 46 (43.0%) patients in group 1 and in 59 (48.4%) patients in group 2; there were no significant differences between the groups (p>0.005). Therefore, the characteristics of the compared groups showed that multidrug resistance affected the distribution of clinical forms, as evidenced by the prevalence of common destructive forms of TB with a severe progressive course and predominant and massive isolation of mycobacterium TB. The above-mentioned unfavorable factors could influence the structure and sensitivity of the secondary nonspecific flora. The comparison groups did not differ in gender, age, or bacteria isolation.

The study included 229 strains isolated in patients with respiratory infections of various localization who were admitted to the Regional TB Dispensary in Karaganda; 218 strains were isolated from sputum, 5 from pleural fluid, and 6 from throat swabs. The spectrum of isolated microorganisms is presented in Table 4 in descending

Table 1. Age Distribution of the Patients

	Group 1 (n = 107)		Group 2 (n = 122)	
	N	P %	N	P %
Under 20	3	2.8	6	4.92
21-30	14	13.08	16	13.11
31-40	30	28.04	23	18.85
41-50	30	28.04	31	25.41
51-60	18	16.82	23	18.85
Over 61	12	11.21	23	18.85

Table 2. Case Type Distribution

	Group 1(n = 107)		Group 2 (n = 122)	
	N	P %	N	P %
New case	48	44.86	97	79.51
Treatment failure	13	12.15	3	2.46
Relapse	33	30.84	17	13.93
Treatment after discontinuation	9	8.41	3	2.46
Switched	2	1.87	1	0.82
Other	1	0.93	1	0.82
Noncompliance	1	0.93		0.00

Table 3. Distribution by Diagnosis of Tuberculous Process

	Group 1 (n = 107)		Group 2 (n = 122)	
	n	P %	N	P %
Disseminated tuberculosis	4	3.74	12	9.84
Focal tuberculosis	1	0.93	2	1.64
Infiltrative tuberculosis	68	63.55	76	62.3
Caseous pneumonia	4	3.74		0
Tuberculoma	8	7.48	11	9.02
Cavernous tuberculosis	1	0.93	1	0.82
Fibrous-cavernous tuberculosis	17	15.89	4	3.28
Tuberculous pleuritis	1	0.93	6	4.92
Miliary tuberculosis	-		1	0.82
Extrapulmonary forms of tuberculosis combined with nonspecific respiratory diseases	2	1.87	9	7.38

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order of detection rates. The analysis of species showed a predominance of Escherichia coli in group 1 (n = 27; 25.2%) and in group 2 (n = 39; 32.0%), Staphylococcus aureus in group 1 (n = 15; 14%) and in group 2 (n = 10; 8.2%), Klebsiella pneumoniae in group 1 (n= 14; 13.1%) and in group 2 (31; 25.4%), and Pseudomonas aeruginosa in group 1 (n = 13; 12.1%) and in group 2 (1.8; 6.6%).

Following the isolation of nonspecific flora, the susceptibility of the isolated pathogens to antibacterial drugs was determined during further microbiological tests. The results of this analysis are shown in Table 5, where antibiotics are categorized.

Glycopeptides (Vancomycin, Teicoplanin) and oxazolidinones (Linezolid) appeared to be the most effective in vitro against pathogens isolated from pathological materials. In our study, resistance to these drugs was not observed, which is consistent with the re-results of similar Russian and Kazakh studies (32, 33). Microorganisms in both groups were equally more susceptible to carbapenems (Imipenem, Meropenem, Doripenem), 87% and 94.5%, respectively; chloramphenicol, 86.2% and 88.8%, respectively;

Table 4. Results of microbiological studies of secondary microorganisms in patients with Tuberculosis

	Group 1 (n = 107)		Group 2 (n = 122)	
	N	p%	N	P%
Escherichia coli	27	25.23	39	31.97
Staphylococcus aureus	15	14.02	10	8.20
Klepsiella pneumonia	14	13.08	31	25.41
Pseudomonas aeruginosa	13	12.15	8	6.56
Klepsiella oxytoca	6	5.61	7	5.74
Streptococcus pneumonia	6	5.61	5	4.10
Acinetobacter baumann2	5	4.67	5	4.10
Enterobacter cloacae	5	4.67	2	1.64
Serratia marcescens	3	2.80	4	3.28
Enterobacter aerogenes	3	2.80	1	0.82
Enterococcus faecalis	2	1.87	3	2.46
Stenotrophomanas maltrophilia	2	1.87	0	0.00
Streptococcus mitis	1	0.93	0	0.00
Proteus mirabilis	1	0.93	1	0.82
Enterobacter sp.	0	0.00	2	1.64
Staphylococcus saprophyticus	1	0.93	0	0.00
Streptococcus sanguis	1	0.93	0	0.00
Acinetobacter jun2	1	0.93	0	0.00
Citrobacter freund2	0	0.00	2	1.64
Streptococcus anginosus	1	0.93	0	0.00
Enterococcus faecium	0	0.00	1	0.82
Klebsiella sp.	0	0.00	1	0.82
Pseudomonas alcaligenes	0	0.00	1	0.82

Table 5. Comparison of susceptibility of secondary microorganisms to antibacterial drugs in patients with Tuberculosis

	Group 1		Group 2								
	Sensitive	Total	Sensitive	Total	p1%	"-" 95CI	"+" 95CI	p2%	"-" 95CI	"+" 95CI	z	p-value
First generation aminoglycosides (Kanamycin, Neomycin, Streptomycin)	47	69	33	43	68.12	57.12	79.11	76.74	64.12	89.37	-1.01	0.315
Second generation aminoglycosides (Netilmicin, Gentamicin, Tobramycin, Sisomicin)	226	293	289	332	77.13	72.32	81.94	87.05	83.44	90.66	-3.23	0.001
Third generation aminoglycosides (Amikacin, Isepamicin)	72	85	93	99	84.71	77.05	92.36	93.94	89.24	98.64	-2.02	0.045
First generation fluoroquinolones Nalidixid acid	44	60	77	90	73.33	62.14	84.52	85.56	78.29	92.82	-1.80	0.075
Second generation fluoroquinolones (Ciprofloxacin, Ofloxacin, Norfloxacin)	112	170	129	159	65.88	58.76	73.01	81.13	75.05	87.21	-3.19	0.002
Third generation fluoroquinolones (Levofloxacin)	45	70	47	60	64.29	53.06	75.51	78.33	67.91	88.76	-1.80	0.075

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Table 5. Ctd

	Group 1				Group 2							
	Sensitive	Total	Sensitive	Total	p1%	"-" 95CI	"+" 95CI	p2%	"-" 95CI	"+" 95CI	z	p-value
First generation cephalosporins (Cefazolin)	2	3	3	3	66.67	13.32	120.01	100	100	100	-1.22	0.288
Second generation cephalosporins (Cefuroxime, Cefamandole, Cefoxitin)	43	59	68	78	72.88	61.54	84.23	87.18	79.76	94.60	-2.07	0.041
Third generation cephalosporins (Cefotaxime, Ceftriaxone, Ceftazidime, Cefixime, Cefoperazone, Cefpodoxime)	73	114	103	136	64.04	55.23	72.84	75.74	68.53	82.94	-2.02	0.045
Fourth generation cephalosporins (Cefepime)	50	67	82	94	74.63	64.21	85.05	87.23	80.49	93.98	-1.99	0.048
Penicillins (Ampicillin, Piperacilin, Oxacilin, Carbenicilin, Penicillin G)	53	95	59	121	55.79	45.80	65.78	48.76	39.85	57.67	1.03	0.304
Inhibitor-protected penicillins (Piperacillin/Tazobactam, Amoxicillin Clavulanic acid, Ampicillin Sulbactam, Ticarcillin/ Clavulanic acid)	76	100	88	120	76.00	67.63	84.37	73.33	65.42	81.25	0.45	0.650
Carbapenems (Imipenem, Meropenem, Doripenem)	133	153	191	202	86.93	81.59	92.27	94.55	91.43	97.68	-2.41	0.016
Tetracyclines (Tetracycline)	49	66	77	95	74.24	63.69	84.79	81.05	73.17	88.93	-1.01	0.312
Glycopeptides (Vancomycin, Teicoplanin)	42	42	23	23	100	100	100	100	100	100	100	100
Oxazolidinones (Linezolid)	24	24	9	9	100	100	100	100	100	100	100	100
Lincosamides (Lincomycin, Clindamycin)	26	35	16	21	74.29	59.81	88.77	76.19	57.97	94.41	-0.16	0.873
Macrolides (Azithromycin)	18	28	16	20	64.29	46.54	82.03	80.00	62.47	97.53	-1.23	0.223
Amphenicols (Chloramphenicol)	25	29	24	27	86.21	73.66	98.76	88.89	77.03	100.74	-0.30	0.762
Ansamycins (Rifampicin)	13	15	6	6	86.67	69.46	103.87	100	100	100	-1.52	0.145
Monobactams (Aztreonam)	14	21	7	10	66.67	46.50	86.83	70.00	41.60	98.40	-0.19	0.853
Other antibiotics (Polymixin B, Fusidic acid, Fosfomycin)	86	98	98	107	87.76	81.26	94.25	91.59	86.33	96.85	-0.90	0.369
Other synthetic antibacterial agents (Nitrofurantion, Trimethoprim)	12	16	4	7	75.00	53.78	96.22	57.14	20.48	93.80	0.83	0.418

rifampicin, 86.7% and 100%, respectively; and other anti-antibiotics (Polymixin B, Fusidic acid, Fosfomycin), 88% and 91.6%, respectively. Klepsiella oxytoca, Enterobacter aerogenes, Serratia marcescens, and Proteus mirabilis showed 100% susceptibility to carbapenems in both groups; Escherichia coli, Klebsiella pneumoniae, and Enterobacter cloacae were highly susceptible (more than 90%), moderate susceptibility was detected in Pseudomonas aeruginosa, 70% in group 1 and 84.6% in group 2; Acinetobacter baumanni were more resistant, 46.2% and 40%, respectively. Klebsiella pneumoniae and Klepsiella oxytoca were 100% susceptible to Chlorampenicol in both groups. Staphylococcus aureus and Acinetobacter baumanni were 100% susceptible to Rifampicin, and Streptococcus pneumonia was resistant. Staphylococcus aureus, Klepsiella oxytoca, and Enterobacter aerogenes showed 100% susceptibility to the group of other antibiotics; Acinetobacter baumanni was highly susceptible (more than 90%).

The following drugs are recommended by the Ministry of Health of the Republic of Kazakhstan for empiric treatment of pneumonia (community-acquired pneumonia) in adults, according to the clinical protocol (34): macrolides (64.3% and 80%, respectively), second (65.8% and 81.1%, respectively) and third generation fluoroquinolone (64.3% and 78.3%, respectively), and second generation cephalosporins (64% and 75.7%, respectively) showed moderate activity against infectious pathogens. The pathogens showed moderate susceptibility to the first generation aminoglycosides (68.1% and 76.7%, respectively), inhibitor-protected penicillins (76% and 73.3%, respectively), tetracyclines (74.2% and 81%, respectively), lincosamides (74.3% and 76.2%, respectively), monobactams (66.7% and 70%, respectively), and other synthetic antibacterial agents (75% and 57.1%, respectively). The pathogens were less

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susceptible to penicillins (55.8% and 49%) in both groups.

Discussion

Our results should be considered as an unfavorable trend towards an increase in the prevalence of resistant isolates. The key reasons for this phenomenon may include high popularity and availability of these drugs in Kazakh medical practice (35, 36) and a fairly wide range of mutant selection windows for antimicrobial drugs from this group (37). Due to a high risk of parallel environmental damage (ie, high probability of rapid growth of resistance of other epidemically important groups of microorganisms, eg, M. TB), fluoroquinolones are considered as reserve drugs and may be used to treat pneumococcal infections in cases of resistance to other antibacterial drugs (38).

The study showed that broad-spectrum antibiotics with antituberculosis activity as well as those recommended for the treatment of nosocomial infections, showed low in vitro activity against nonspecific microorganisms in the patients with multidrug-resistant tuberculosis compared to the control group. Susceptibility to aminoglycosides (amikacin and kanamycin) was 92 (77.3%) out of 119 in group 2 ($n = 106$; 90.6%; $p<0.05$) and to fluoroquinolones (levofloxacin, ofloxacin) ($n = 74$; 68.5%) out of 108 in group 2 ($n = 69$; 81.2% out of 85; $p<0.005$). Low activity of these drugs may be due to their long-term use by the patients from group I. Therefore, microorganisms gradually developed resistance to them. 2-IV generation cephalosporins also showed low in vitro activity against nonspecific microorganisms in multidrug-resistant TB patients compared to the control group ($p<0.05$).

Klebsiella pneumoniae, isolated from pathological materials of the respiratory organs, was most often susceptible to carbapenems (imipenem, meropenem, and doripenem), 96.3% and 98.4%; polymyxin B, 94.1% and 96.8%; second generation aminoglycosides, 88.4% and 91.1%; and third generation aminoglycosides, 84.6% and 96.4%, respectively. Antibacterial drugs showed moderate activity against Pseudomonas aeruginosa and Serratia marcescens in both groups, 69.5% and 72.2%, in the patients with multidrug resistance and 71.2% and 81.1% in patients with preserved drug susceptibility. No resistance was found in Staphylococcus aureus to inhibitor-protected penicillins, glycopeptides, linezolid, rifampicin, tetracycline, and a group of other antibiotics in both groups, to second and third generation aminoglycosides and cephalosporins in group 2; high activity was shown for lincosamides, 84.6% and 89%, respectively; moderate activity was shown for second generation fluoroquinolones, 72% and 78.6%, third generation fluoroquinolones, 83.3% and 80%, and penicillins, 64.7% and 83.3%, respectively.

The strains of Acinetobacter baumanni had a high resistance to aminoglycosides (48% in group 1 and 28.6% in group 2), cephalosporins (30% and 12.5%), fluoroquinolones (41.7% and 20%), penicillins (38.9% and 31.3%), and carbapenems (46.2% and 40%), respectively; and tetracycline, glycopeptides, linezolid, lincosamides, azithromycin, rifampicin, and a group of other antibiotics showed high activity. Macrolides showed moderate activity against Streptococcus pneumonia in both groups, 50% in group 1 and 60% in group 2. Our results for the susceptibility of pneumococci to macrolides comply with the results of similar Russian studies: in 2014–2015, in Russia, 24.9% of clinical isolates were resistant to azithromycin (39).

Our study showed an expectedly high proportion of tetracycline-resistant pneumococcal strains (66.7% and 60%, respectively), which is a consequence of a prolonged and practically uncontrolled use of these drugs in Kazakhstan. Low activity was shown by fluoroquinolones, 20% to 25% in group 1 and 50% in group 2. The results obtained indicate that beta-lactam antibacterial drugs maintain their high activity against pneumococcal pathogens (100% sensitivity). Taking into account that pneumococci lack enzymatic mechanisms of resistance to antibiotics of this class, the optimal drug of choice for oral therapy of respiratory infections is amoxicillin. Therefore, this drug was included in the clinical protocols of the MoHRK for the treatment of community-acquired pneumonia as a first-line therapy (29); also, the maximum sensitivity was shown by glycopeptides and linezolid.

Antibacterial drugs showed high activity against Klepsiella oxytoca, Enterobacter aerogenes, and Proteus mirabilis in both groups, 88.1%, 98.2%, and 95.2% in patients with multidrug resistance and 92.2%, 94.1%, and 85.7% in patients with preserved drug susceptibility. Antibacterial drugs showed moderate activity against Enterobacter cloacae in the patients with multidrug resistance (67.5%) and high activity in the patients with preserved drug susceptibility (91.5%). Antibacterial drugs showed low activity against Enterococcus faecalis, 21.1% in the patients with multidrug resistance and 52.4% in patients with preserved drug susceptibility.

Conclusion

The Regional Tuberculosis Dispensary of Karaganda together with the shared-use laboratory developed, tested and implemented microbiological monitoring of the materials from the respiratory system of all patients admitted for tuberculosis treatment. The most promising groups of antibacterial drugs for the treatment of nonspecific respiratory infections in a phthisiatric clinic are vancomycin, teicoplanin, linezolid, rifampicin, carbapenems, amphenicols, second and third generation aminoglycosides, first generation fluoroquinolones, second and fourth generation cephalosporins, and a group of other antibiotics. Secondary microorganisms isolated in patients with multidrug-resistant tuberculosis are represented by the strains that are resistant to modern antibacterial drugs, and for appropriate antibiotic prescription, it is necessary to study materials from the respiratory organs in all patients admitted for tuberculosis treatment to obtain the spectrum of nonspecific microorganisms and assess their sensitivity to antimicrobial drugs.

Conflict of Interests

The authors declare that they have no competing interests.

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