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Original article

Resistance of microorganisms isolated from patients with COVID-19

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Abstract

The rational use of antibiotics plays a crucial role in slowing the spread of resistant strains of pathogens. Excessive use of antibiotics, combined with reduced surveillance capabilities for the formation of antibiotic-resistant microorganisms, may lead to an increase in antibiotic resistance as a long-term consequence of the COVID-19 pandemic. The study of antibiotic resistance of microbes will allow the rational use of antibacterial drugs.

The aim of the study was to study the antibiotic resistance of pathogens isolated from the respiratory tract in patients with confirmed COVID–19 in the period from 2020 to 2022.

Methods. A retrospective study was conducted on the medical records of patients undergoing inpatient treatment with a diagnosis of COVID-19 in 2020-2022. The antibioticogram was presented by the following groups of antibacterial drugs: Gentamicin, Ceftriaxone, Amoxiclav, Ofloxacin, Cefazolin, Cefuroxime, Cefoperazone.

*Results. Candida, S.Pneumoniae, S.Haemolyticus, S.Pyogenes, S.Aegeis, Ps.Aeruginosae were isolated in the structure of pathogens obtained from patients with coronavirus infection. The highest sensitivity to antibiotics was found in gentamicin 53 (70.7%), slightly less than 37 (49.3%) in ceftriaxone, sensitivity to amoxiclav was detected in 26 (34.7%) cases. The lowest sensitivity was found to cefoperazone 7 (9.3%). Statistically significant antibiotic sensitivity to Candida 10*6, S.Pneumoniae 10*6, S.Haemolyticus 10*7, S.Pyogenes 10*7 was revealed. There was no statistically significant sensitivity to S.Aegeis 10*5, Ps.Aeruginosae 10*6 of any of the antibiotics used.*

Conclusions. The results of a retrospective study confirmed the need for microbiological monitoring of pathogens affecting the respiratory tract and changes in the tactics of antibiotic therapy based on an assessment of the antibioticogram of the microorganisms prevalent in the region isolated during COVID-19.

Keywords: antibiotic resistance, coronavirus infection.

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Introduction

Antibiotic resistance of microbes is related to the frequency and quantity of used antibacterial drugs. The rational use of antibiotics plays a crucial role in slowing the spread of resistant strains of pathogens. 2020 year marked the beginning of a new coronavirus infection. The lack of etiotropic therapy, the rapid progression and unfavorable outcome of the infection forced doctors to look for various therapeutic approaches and drugs [1]. Antibiotics have become a group of drugs that have become widely used to treat COVID-19. The assumption about their possible effectiveness was based on the information that antibiotics can be effective in the treatment of bacterial complications [2-5]. According to literature data, up to 74.6% of hospitalized patients with COVID-19 received antimicrobial therapy [6]. At the same time, data on the prevalence of bacterial coinfection in such patients vary significantly. Documented bacterial coinfection has been reported in hospitalized patients with COVID-19 in the range from 8 to 81% [7]. Excessive use of antibacterial drugs combined with reduced surveillance capabilities over the formation of antibiotic-resistant microorganisms can lead to an increase in antibiotic resistance as long-term consequences of the COVID-19 pandemic [8,9]. The study of antibiotic resistance of microbes will allow rational use of antibacterial drugs.

The aim of the study was to study the antibiotic resistance of pathogens isolated from the respiratory tract in patients with confirmed COVID–19 in the period from 2020 to 2022.

Material and methods

In the infectious diseases hospital in Semey, a retrospective study was conducted on the medical records of patients undergoing inpatient treatment with a diagnosis of COVID-19 in 2020-2022 years. The study included cases with documented confirmation of the diagnosis of COVID-19. Sputum samples were collected from patients during the first 24 hours upon admission to the hospital. The results of bacteriological examination of sputum from patients by the disco-diffusion method of 74 patients were analyzed. The analysis of the results was carried out by measuring the diameter of the growth suppression zone, the interpretation of the data obtained was carried out based on the criteria of the European Committee for the Determination of Antimicrobial Sensitivity (EUCAST). The isolated strains were recorded using the microbiological monitoring programs WHONET and AMRcloud.

Male are prevailed - 46 men (61.3%), women – 29 (38.7%). Representatives of the Kazakh population were 60 (80.0%) people, other nationalities made up 15 (20.0%). The average age of patients was 56.0 (95%CI:52.5-59.4) years, CO=15.06. The youngest patient was 19 years old, the oldest 92 years old. At the same time, the average age of men was 55.3 (95%CI:50.3-60.3) years, CO=16.83. The youngest man was 19 years old, the oldest 92 years old. The average age of women was 57.1 (95%CI:52.5-61.6) years, CO=11.92, the youngest woman was 32 years old, the oldest was 83 years old. The age group under 29 years was 4 (5.3%), 30-39 years - 6 (8.0%), 40-49 years – 14 (18.7%), 50-59 years - 17 (22.7%), over 60 years -34 (45.3%). Concomitant diseases were present in 22 (29.3%) patients. Arterial hypertension was present in 9 (12.0%) people. 4 (5.3%) people had diabetes mellitus. Bilateral pneumonia was diagnosed in 36 (48.0%) patients, COVID-19 pneumonia was diagnosed in 20 (26.7%) people, right-sided pneumonia in 8 (10.7%) patients, left-sided pneumonia in 2 (2.7%) people, acute bronchitis in 4 (5.3%) patients, in 5 (6.7%) patients with acute pharyngitis. Statistical data processing was carried out using Microsoft Office Excel software, Statistica 10.

The antibioticogram was presented by the following groups of antibacterial drugs: Gentamicin, Ceftriaxone, Amoxiclav, Ofloxacin, Cefazolin, Cefuroxime, Cefoperazone.

Results

Candida, S.Pneumoniae, S.Haemolyticus, S.Pyogenes, S.Aegeis, Ps.Aeruginosae were isolated in the structure of pathogens obtained from patients with coronavirus infection.

The results of bacteriological examination of sputum revealed the following sensitivity to antibiotics (Table 1).

Table 1 - Antibiotic sensitivity

№	Antibiotic	abs	%
1	Gentamicin	53	70,7
2	Ceftrioxone	37	49,3
3	Amoxiclav	26	34,7
4	Ofloxacin	17	22,7
5	Cefazolin	13	17,3
6	Cefuroxime	4	5,3
7	Cefoperazone	7	9,3

As can be seen from Table 1, the greatest sensitivity to antibiotics was found in gentamicin 53 (70.7%), slightly less than 37 (49.3%) in ceftriaxone, sensitivity to amoxiclav was detected in 26 (34.7%) cases. The lowest sensitivity to cefoperazone was detected in 7 (9.3%).

At the same time, sensitivity was not determined in 11 (14.7%) cases, sensitivity to one antibiotic was determined in 49 (65.3%) patients, to two antibiotics in 13 (17.3%) patients, to three antibiotics in 2 (2.7%) patients.

The sensitivity of the pathogen to antibiotics is shown in Table 2.

Table 2 - Sensitivity of pathogens to antibiotics

№	Pathogens	Antibiotics	χ2, df, p
1	Candida 10*6	Gentamicin	χ2=1,497, df=1, p=0,221
2	Candida 10*6	Amoxiclav	χ2=0,343, df=1, p=0,591
3	Candida 10*6	Ofloxacin	χ2=4,675, df=1, p=0,031
4	Candida 10*6	Ceftriaxone	χ2=4,078, df=1, p=0,043
5	Candida 10*6	Cefazolin	χ2=0,104, df=1, p=0,748
6	Candida 10*6	Cefuroxime	χ2=1,536, df=1, p=0,215
7	Candida 10*6	Cefoperazone	χ2=2,807, df=1, p=0,094
8	S.Pneumoniae 10*6	Gentamicin	χ2=9,228, df=1, p=0,002
9	S.Pneumoniae 10*6	Amoxiclav	χ2=30,56, df=1, p=0,000
10	S.Pneumoniae 10*6	Ofloxacin	χ2=3,332, df=1, p=0,068
11	S.Pneumoniae 10*6	Ceftriaxone	χ2=9,723, df=1, p=0,002
12	S.Pneumoniae 10*6	Cefazolin	χ2=0,632, df=1, p=0,427
13	S.Pneumoniae 10*6	Cefuroxime	χ2=0,871, df=1, p=0,351
14	S.Pneumoniae 10*6	Cefoperazone	χ2=11,84, df=1, p=0,001
15	S.Haemolyticus 10*7	Gentamicin	χ2=7,783, df=1, p=0,005
16	S.Haemolyticus 10*7	Amoxiclav	χ2=0,530, df=1, p=0,467
17	S.Haemolyticus 10*7	Ofloxacin	χ2=6,161, df=1, p=0,013
18	S.Haemolyticus 10*7	Ceftriaxone	χ2=0,053, df=1, p=0,817
19	S.Haemolyticus 10*7	Cefazolin	χ2=1,140, df=1, p=0,286
20	S.Haemolyticus 10*7	Cefuroxime	χ2=0,066, df=1, p=0,797
21	S.Haemolyticus 10*7	Cefoperazone	χ2=1,930, df=1, p=0,165
22	S.Pyogenes 10*7	Gentamicin	χ2=3,039, df=1, p=0,081
23	S.Pyogenes 10*7	Amoxiclav	χ2=0,011, df=1, p=0,916
24	S.Pyogenes 10*7	Ofloxacin	χ2=1,674, df=1, p=0,196
25	S.Pyogenes 10*7	Ceftriaxone	χ2=6,607, df=1, p=0,010
26	S.Pyogenes 10*7	Cefazolin	χ2=0,586, df=1, p=0,444
27	S.Pyogenes 10*7	Cefuroxime	χ2=0,255, df=1, p=0,614
28	S.Pyogenes 10*7	Cefoperazone	χ2=0,017, df=1, p=0,897
29	S.Aureus 10*5	Gentamicin	χ2=0,081, df=1, p=0,776
30	S.Aureus 10*5	Amoxiclav	χ2=0,032, df=1, p=0,859
31	S.Aureus 10*5	Ofloxacin	χ2=0,028, df=1, p=0,868
32	S.Aureus 10*5	Ceftriaxone	χ2=0,502, df=1, p=0,479
33	S.Aureus 10*5	Cefazolin	χ2=0,367, df=1, p=0,544
34	S.Aureus 10*5	Cefuroxime	χ2=0,505, df=1, p=0,478
35	S.Aureus 10*5	Cefoperazone	χ2=0,922, df=1, p=0,337
36	Ps.Aeruginosae 10*6	Gentamicin	χ2=0,038, df=1, p=0,845
37	Ps.Aeruginosae 10*6	Amoxiclav	χ2=2,242, df=1, p=0,134
38	Ps.Aeruginosae 10*6	Ofloxacin	χ2=1,238, df=1, p=0,266
39	Ps.Aeruginosae 10*6	Ceftriaxone	χ2=0,001, df=1, p=0,978
40	Ps.Aeruginosae 10*6	Cefazolin	χ2=0,886, df=1, p=0,347
41	Ps.Aeruginosae 10*6	Cefuroxime	χ2=0,238, df=1, p=0,626
42	Ps.Aeruginosae 10*6	Cefoperazone	χ2=0,435, df=1, p=0,510

As can be seen from Table 2, statistically significant sensitivity to Candida 10*6 of the following antibiotics was revealed: Ofloxacin (χ^2=4.675, df=1, p=0.031), Ceftriaxone (p=0.043). Statistically significant sensitivity to S.Pneumoniae 10*6 was revealed: Gentamicin (p=0.002), Amoxiclav (p=0.000), Ceftriaxone (p=0.002), Cefoperazone (p=0.001). Statistically significant sensitivity to S.Haemolyticus 10*7 of the following antibiotics was revealed: Gentamicin (p=0.005), Ofloxacin (p=0.013). Statistically significant sensitivity to S.Pyogenes 10*7 of the antibiotic Ceftrioxone was revealed (p=0.010). At the same time, there was no statistically significant sensitivity to S.Aegeis 10*5, Ps.Aeruginosae 10*6 of any of the antibiotics used.

Discussion

A study by Turkish scientists showed that 28.2% of patients diagnosed with COVID-19 had a clinical diagnosis of bacterial infection, while only in 7.1% of cases the diagnosis was confirmed bacteriologically [10]. In a systematic review in 2021y, it was reported that in patients with COVID-19, the average frequency of prescribing antibiotics was 74.0%, antiviral drugs - 56.9%, glucocorticoids - 36.9% of cases [11]. In a study by American scientists, it was found that more often patients with COVID-19 were prescribed ceftriaxone, vancomycin, doxycycline, cefepim, azithromycin. The authors noted that in 25.8% of cases, patients were prescribed antimicrobial drugs active against Methicillin-resistant Staphylococcus aureus (MRSA), and in 26.3% of cases – against P. aeruginosa [12]. In a study conducted in Nepal, the prevalence of antibiotic use in patients with COVID-19 reached 98.1%. About 71.15% of patients were treated with two or more antimicrobial drugs. The average duration of antibiotic use was 6.33 days. The most common class of antibiotics used were cephalosporins (81.73%) and macrolides (54.81%) [13].

The most common gram-negative microbes of coinfections in patients with COVID-19 were K. pneumoniae, P. aeruginosa, A. baumannii, E. coli, St. maltophilia and E. Cloacae, gram-positive ones were S. hominis, S. epidermidis, E. faecium, E. Faecalis and S. aureus [14]. The presence of coinfection increased the risk of an adverse outcome in patients with COVID-19 [15]. According to S.S. Adeiza et al. [16], the average incidence of S. aureus and COVID-19 coinfection in the world is 25.6%. In our study, S.Pneumoniae, S.Haemolyticus, S.Pyogenes, S.Aegeis, Ps.Aeruginosae prevailed. A study conducted by Russian scientists showed that the overall prevalence of coinfections caused by resistant bacterial and fungal microorganisms is 24% [17].

Conclusions

The results of a retrospective study confirmed the need for microbiological monitoring of pathogens affecting the respiratory tract and changes in the tactics of antibiotic therapy based on an assessment of the antibioticogram of the microorganisms prevalent in the region isolated during COVID-19.

Conflict of interest. No conflicts of interest have been declared.

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COVID-19 пациенттерінен оқшауланған микроорганизмдердің төзімділігі

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Түйіндеме

Антибиотиктерді ұтымды қолдану қоздырғыштардың төзімді штамдарының таралуын бәсеңдету үшін шешуші рөл атқарады. Антибиотиктерді шамадан тыс қолдану антибиотиктерге төзімді микроорганизмдердің пайда болуын қадағалау мүмкіндіктерінің төмендеуімен бірге COVID-19 пандемиясының ұзақ мерзімді салдары ретінде антибиотикке төзімділіктің өсуіне әкелуі мүмкін. Микробтардың антибиотикке төзімділігін зерттеу Бактерияға қарсы препараттарды ұтымды пайдалануға мүмкіндік береді.

Зерттеудің мақсаты. 2020 және 2022 жылдар аралығында COVID-19 расталған науқастарда тыныс алу жолдарынан оқшауланған патогендердің антибиотикке төзімділігін зерттеу.

Әдістері. Антибиотикограмма Бактерияға қарсы препараттардың келесі топтарымен ұсынылды: Гентамицин, Цефтриаксон, Амоксиклав, Офлоксацин, Цефазолин, Цефуроксим, Цефоперазон.

*Нәтижелері. Коронавирустық инфекциясы бар науқастардан алынған патогендердің құрылымында Candida, S. Pneumoniae, S. Haemolyticus, S. Pyogenes, S. Aigeis, Ps оқшауланған.Aeruginosae. Н. антибиотиктерге ең жоғары сезімталдық гентамицинде 53 (70,7%), цефтриаксонда 37-ден (49,3%) сәл төмен, амоксиклавқа сезімталдық 26 (34,7%) жағдайда анықталды. Цефоперазонға ең төменгі сезімталдық 7 (9,3%) анықталды. Антибиотиктердің candida 10*6, S. Pneumoniae 10*6, S. Haemolyticus 10*7, S. Pyogenes 10*7-ге статистикалық маңызды сезімталдығы анықталды. Статистикалық маңызды сезімталдық анықталған жоқ S. Aigeis 10*5, Ps.Aeruginosae 10*6 қолданылған антибиотиктердің ешқайсысы жоқ.*

Қорытынды. Ретроспективті зерттеудің нәтижелері тыныс алу жолына әсер ететін қоздырғыштарға микробиологиялық мониторинг жүргізу және covid-19 кезінде бөлінген аймақта басым микроорганизмдердің антибиотикограммасын бағалауға негізделген антибиотикалық терапия жүргізу тактикасына өзгерістер енгізу қажеттілігін растады.

Түйін сөздер: антибиотикке төзімділік, коронавирустық инфекция.

Резистентность микроорганизмов, выделенных от пациентов с COVID-19

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Резюме

Рациональное использование антибиотиков играет решающую роль для замедления распространения устойчивых штаммов патогенов. Чрезмерное применение антибиотиков в сочетании со снижением возможностей эпиднадзора над формированием устойчивых к антибиотикам микроорганизмов могут привести к росту антибиотикорезистентности как долговременным последствиям пандемии COVID-19. Исследование антибиотикорезистентности микробов позволит рационально использовать антибактериальные препараты.

Цель исследования – изучить антибиотикорезистентность возбудителей, выделенных из дыхательных путей у больных с подтвержденным COVID-19 в период с 2020 по 2022 год.

Методы. Проведено ретроспективное исследование по историям болезни пациентов, проходящих стационарное лечение с диагнозом COVID-19 в 2020-2022гг. Антибиотикограмма была представлена следующими группами антибактериальных препаратов: Гентамицин, Цефтриаксон, Амоксиклав, Офлоксацин, Цефазолин, Цефуроксим, Цефоперазон

*Результаты. В структуре патогенов, полученных от пациентов с коронавирусной инфекцией было выделены Candida, S.Pneumoniae, S.Haemolyticus, S.Pyogenes, S.Aureus, Ps.Aeruginosae. Наибольшая чувствительность к антибиотикам была обнаружена у гентамицина 53 (70,7%), чуть меньше 37 (49,3%) у цефтриаксона, чувствительность к амоксиклаву было выявлено в 26 (34,7%) случаях. К цефоперазону была выявлена самая низкая чувствительность 7 (9,3%). Была выявлена статистически значимая чувствительность антибиотиков к Candida 10*6, S.Pneumoniae 10*6, S.Haemolyticus 10*7, S.Pyogenes 10*7. Не выявлена статистическая значимая чувствительность к S.Aureus 10*5, Ps.Aeruginosae 10*6 ни одного из использованных антибиотиков.*

Выводы. Результаты ретроспективного исследования подтвердили необходимость проведения микробиологического мониторинга возбудителей, поражающих респираторный тракт и внесения изменений в тактику проведения антибиотикотерапии, основанной на оценке антибиотикограммы, преобладающих в регионе микроорганизмов, выделенных при COVID-19.

Ключевые слова: антибиотикорезистенстность, коронавирусная инфекция.