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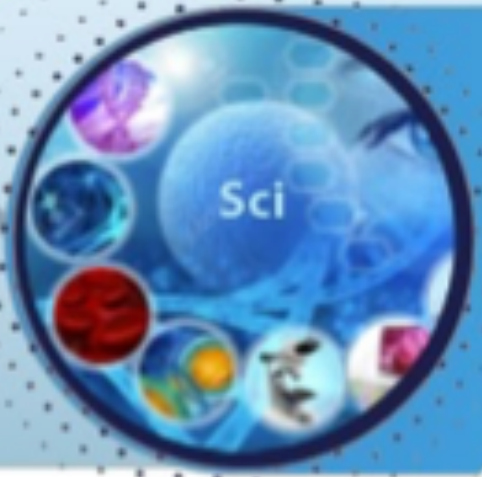

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Pharmacodynamic Substantiated Approaches to the Choice of Antimicrobial Therapy for Nosocomial and Non-Nosocomial Pneumonia

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ABSTRACT

Background. The strategy of choosing antimicrobials has recently been complicated by the expansion and modification of the list of pneumonia pathogens, as well as the growth of antibiotic resistance. This requires periodic review of existing approaches to the selection of antimicrobials since their irrational use is an independent risk factor for the development of death.

Material and methods. The article presents the materials of research that were carried out in two directions: the identification of the main causative agents of severe pneumonia with a fatal outcome and a retrospective analysis of antibiotic therapy of severe nosocomial and non-nosocomial pneumonia with a fatal outcome using pharmacological research.

Results. Considering the structure of pathogens and the profile of resistance to antimicrobial drugs, it is advisable to use 3-4 generation cephalosporins or amoxicillin/clavulanate, ertapenem or respiratory fluoroquinolones in empirical therapy regimens for severe non-nosocomial pneumonia. In empirical treatment regimens for severe nosocomial pneumonia, it is advisable to use Imipenem or Meropenem and Vancomycin or Linezolid.

Conclusion. The need to include drugs active against MRSA (Vancomycin, Linezolid, etc.) in the regimens of initial therapy for non-nosocomial pneumonia requires additional study. Cephalosporins of 3-4 generations, fluoroquinolones and Amikacin can be recommended for the treatment of severe nosocomial pneumonia only based on the results of determining the sensitivity of the isolated pathogens.

Keywords: Nosocomial pneumonia, non-nosocomial pneumonia, antimicrobial pharmacotherapy, antibiotic resistance, antibiotic sensitivity, pharmacodynamics of antimicrobial therapy

INTRODUCTION

Despite significant advances in etiological diagnosis and therapy, pneumonia remains a widespread and potentially life-threatening disease, occupying the 6th place among all causes of death and the 1st among infectious diseases in industrialized countries, and the current situation has not changed for many years [1,18,19].

The aetiology of pneumonia is largely determined by the conditions of its development, therefore, the division into nosocomial and non-nosocomial pneumonia is clinically significant [2,20,21].

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The basis for the treatment of pneumonia is timely starting adequate antibiotic therapy, in most cases empirical [3,22,23].

It is extremely important to isolate patients with severe pneumonia, given the high probability of developing serious complications [4,24,25], the high mortality rate [5,26,27], the peculiarities of the aetiology of the disease [628,29] and the special requirements for antibiotic therapy [7,30,31,32,33,34,35,36].

To predict the strategy of antibiotic therapy in severe pneumonia, a microbiological study of autopsy material may be of particular interest since intravital etiological diagnosis in this category of patients is often difficult due to the severity of the condition and the rapid progression of the pathological process. For an objective assessment and interpretation of isolated microorganisms, a combination of microbiological and histological examination of autopsy material (lung tissue, etc.) is of great importance. [8,37,38,39,40].

Our study aimed to study the structures and antibiotic resistance of bacterial pathogens isolated from adult hospitalized patients who died from various forms of pneumonia (nosocomial and non-nosocomial) using a bacteriological examination of autopsy material and pharmacological data.

MATERIAL AND METHODS

The material for microbiological and histological studies was the tissue of the lungs, liver, spleen, and blood from the right heart, obtained at the autopsy of 130 adult patients (21-96 years old) with clinical and/or pathoanatomical diagnoses of pneumonia. Autopsy material was taken no later than 24 hours from the moment of death.

During a histological examination, the obtained material was fixed in an aqueous 10% neutral solution of formalin, Carnois liquid and subjected to standard wiring pouring into paraffin. From the blocks obtained, sections of lung, liver, and spleen tissues with a thickness of 5-7 microns were prepared, which were stained with hematoxylin and eosin, according to van Gieson, Gomori, according Weigert.

In the microbiological study, a semi-quantitative method of seeding clinical material was used. Isolation and identification of microorganisms were performed by standard laboratory procedures.

Determination of the sensitivity of isolated microorganisms to antimicrobials was carried out by the guidelines "Determination of the sensitivity of microorganisms to antibacterial drugs" and the recommendations of the US Committee on Clinical and Laboratory Research (CLSI, 2007). The minimum inhibitory concentrations of chemically pure substances of antimicrobials were determined: for gram-negative non-fermenting bacteria, representatives of the Enterobacteriaceae and S. aureus families - by double serial dilutions in Mueller-Hinton II agar (BBL, USA), for Streptococcus spp. and Haemophilus spp. - by serial dilutions in Mueller-Hinton broth (BBL, USA). To assess susceptibility to drugs not included in these guidelines, the CLSI 2007 and the Antibiotic Committee of the French Society of Microbiology (SFM, 2006) were used. Quality control of sensitivity determination was carried out using reference strains: for S. pneumoniae - S. pneumoniae ATCC 49619; for H. influenzae - H. influenzae ATCC 49247; E. coli ATCC 35218; for gram-negative non-fermenting bacteria and Enterobacteriaceae - E. coli ATCC 25922; E. Coli ATCC 35218; P. aeruginosa ATCC 27853; for S. aureus - S. aureus ATCC 29213.

Determination of production by Enterobacteriaceae strains was carried out by comparing the minimum inhibitory concentration of Ceftazidime, Ceftazidime / Clavulanate and Cefotaxime, Cefotaxime/Clavulanate and the double disc method using discs with Amoxicillin/Clavulanate (20/10 μg), Ceftazidime (30 μg) and Cefotaxime (30 μg) or Cefepime (30 μg).

Statistical processing of all data was carried out in the SAS statistical analysis system (SAS Institute software package, USA, version 8.02 for Windows XP).

RESULTS AND DISCUSSION

The study of the structure and sensitivity to antimicrobials of pathogens of fatal non-nosocomial pneumonia included 57 patients with histologically confirmed non-nosocomial pneumonia aged 26 to 85 years (mean age 51.1±14.5 years), including 37 (64.9%) men and 20 (35.1%) women. The patients were treated in the multidisciplinary clinic of the Tashkent Medical Academy in the departments of various profiles; 43 (75.4%) - therapy, 5 (8.8%) - intensive care units, 3 (5.3%) - cardiology and neurology, 2 (3.5%) - surgery, 1 (1.8%) - traumatology.

Clinical symptoms of non-nosocomial pneumonia occurred in 41 (71.9%) cases, laboratory signs in 30 (52.6%), and X-ray data in 37 (64.9%). The diagnosis of pneumonia during life was not made in 13 (22.8%) patients. Of the background and concomitant diseases, alcoholism was most often noted - in 34 (59.6%) cases and diseases of the cardiovascular system - in 17 (29.8%). Pneumonia as the main disease occurred in 47 (82.5%)

patients, as a complication of other diseases - in 10 (17.5%) patients and was the cause of death in 50 (87.7%) cases. The average length of hospitalization before death was 2±1.2 days.

For microbiological and histological studies, 170 samples were obtained from patients with histologically confirmed pneumonia. When analyzing the localization and volume of the lesion, it was revealed that bilateral lesions prevailed in 37 (64.9%) deceased, of which subtotal and total lesions occurred in 12 (30.8%) cases. Right-sided lesions were observed in 14 (24.6%) of the deceased and left-sided lesions in 4 (7.0%). By the nature of the inflammatory process, fibrinous-purulent pneumonia occurred more often - 53 (93.0%) cases. In 4 (7.0%) cases, serous-purulent pneumonia was noted.

Bacterial pathogens were isolated in 52 (91.2%) patients, most often they were isolated from the lower lobes of the right and left lungs - in 41 (36.0%) cases.

A total of 70 aerobic bacteria were identified, with monoculture isolated in 75.0% and microbial associations in 25.0% of cases. The predominant causative agents of community-acquired pneumonia were K. pneumoniae and S. aureus, which accounted for 31.4% and 28.6% of all isolated strains, respectively. Monoculture of these pathogens was isolated in 15 (28.8%) and 13 (25.0%) patients, respectively, in 5 (9.6%) patients, their association with each other was revealed. S. pneumoniae - 12.9%, H. influenzae - 11.4% and E. soli - 10.0% of all isolated strains were less common.

All strains of K. pneumoniae were susceptible to 3rd-4th generation cephalosporins, amoxicillin/clavulanate, carbapenems, fluoroquinolones, aminoglycosides, and cotrimoxazole [9].

E. coli was characterized by 100% sensitivity to cephalosporins of 3-4 generations, carbapenems and aminoglycosides. Fluoroquinolones, Co-trimoxazole and Amoxicillin/Clavulanate were active against 6 out of 7 strains of E. soli, and Ampicillin against four [10].

Of the 32 strains of enterobacteria studied, one strain of E. coli was simultaneously resistant to class 3 antimicrobials: Amoxicillin/Clavulanate, fluoroquinolones and Co-trimoxazole.

All strains of S. aureus were susceptible to vancomycin, linezolid, cotrimoxazole and fusidic acid. Lincosamides were also characterized by high activity: Clindamycin was active against 100% of the tested strains, and Lincomycin - 95%.

A low frequency of resistance was noted to fluoroquinolones, Gentamicin and Rifampicin - 10% of strains turned out to be resistant. A higher incidence of S. aureus resistance was observed for tetracycline (15%), chloramphenicol (20%) and erythromycin (20%). Two strains (10%) of S. aureus were resistant to oxacillin. They were also insensitive to several other antimicrobials - fluoroquinolones, gentamicin, rifampicin, tetracycline, chloramphenicol, erythromycin and lincomycin. Since patients with methicillin-resistant S. aureus were on mechanical ventilation from the moment of admission to the hospital until the time of death, nosocomial infection and/or postmortem contamination of lung tissue with MRSA strains colonizing the respiratory tract can be assumed in these cases [11].

All isolated 9 strains of S. pneumoniae were susceptible to all tested antimicrobials at minimum inhibitory concentrations: amoxicillin (0.03 mg/l), penicillin (0.016 mg/l), amoxicillin/clavulanate (0.03 mg/l), ceftriaxone (0.03 mg/l), cefotaxime (0.06 mg/l), cefepime (0.03 mg/l), Cefoperazone (0.06 mg/l), imipenem (0.008 mg/l), azithromycin (0.25 mg/l), erythromycin (0.06 mg/l), Clarithromycin (0.03 mg/l), clindamycin (0.06 mg/l), ciprofloxacin (1.0 mg/l), levofloxacin (1.0 mg/l), moxifloxacin (0.125 mg/l), chloramphenicol (2.0 mg/l), tetracycline (2.0 mg/l), co-trimoxazole (0.125 mg/l) and vancomycin (0.5 mg/l), Based on the results obtained, it can be concluded that both penicillin and 3rd generation cephalosporins retain clinical significance in the treatment of severe pneumococcal infections, Of the fluoroquinolones, Moxifloxacin proved to be the most active drug.

Among the 8 strains of H. influenzae isolated by us, one turned out to be insensitive to ampicillin (minimum inhibitory concentration of 2.0 mg/l), while all strains remained sensitive to amoxicillin/clavulanate (minimum inhibitory concentration 4.0 mg/l), Ceftriaxone (minimum inhibitory concentration 0.125 mg/l), cefepime (minimum inhibitory concentration 0.5 mg/l) and imipenem (minimum inhibitory concentration 2.0 mg/l). Azithromycin was active against all isolated strains of H. influenzae (minimum inhibitory concentration of 2.0 mg/l), while clarithromycin was active against only four (minimum inhibitory concentration of 16.0 mg/l). However, the resistance to clarithromycin detected in vitro cannot be the basis for predicting its clinical ineffectiveness, since in vivo clarithromycin forms the active metabolite 14-hydroxyclarithromycin, which is 2-4 times higher than the parent compound in terms of activity against H. influenzae [12]. Fluoroquinolones were characterized by equally high activity against this pathogen (minimum inhibitory concentration of 0.06 mg/l). All strains of H. influenzae were also susceptible to tetracy-

cline (minimum inhibitory concentration of 0.5 mg/l) and chloramphenicol (minimum inhibitory concentration of 0.5 mg/l), one strain was resistant to Co-trimoxazole (minimum inhibitory concentration of 16 mg/l).

The study of the structure and sensitivity to antimicrobials of pathogens of nosocomial pneumonia was carried out in 73 patients with histologically confirmed nosocomial pneumonia aged 21 to 96 years (58.0±16.2 years), including 51 (69.9%) men and 22 (30.1%) women.

Patients with nosocomial pneumonia were hospitalized in various departments: 29 (39.7%) - therapy, 11 (15.1%) - intensive care units, 10 (13.7%) - traumatology, 9 (12.3%) - neurology, 6 (8.2%) - surgery, 4 (5.5%) - cardiology and neurosurgery. Clinical symptoms of pneumonia occurred in 35 (47.9%) cases, laboratory signs in 38 (52.1%), and X-ray data in 39 (53.4%). The diagnosis of pneumonia was not made during the lifetime of 28 (38.4%) patients. The severity of the course and adverse outcome of the disease was influenced by the presence of background and concomitant diseases in patients. Most often there was alcoholism - in 21 (28.8%) cases and diseases of the cardiovascular system - in 20 (27.4%), less often chronic bronchitis - in 12 (16.4%) and pathology of the central nervous system - in 6 (8.2%) cases. Nosocomial pneumonia as the main disease occurred in 41 (56.2%) cases and as a complication of other diseases - in 32 (43.8%) cases. Nosocomial pneumonia was often a complication of diseases of the central nervous system (various types of acute disorders of cerebral circulation) - 16 (21.9%) cases, diseases of the cardiovascular system - 10 (13.7%), diseases of the traumatological and surgical profile - 11 (15.1%). In 63 (86.3%) cases, nosocomial pneumonia was the cause of death. The duration of hospitalization until death averaged 13.5±12.2 days (range 1 day to 59 days). The time interval from the time of death of patients to the moment of autopsy averaged 14 hours 23 minutes±7 hours 26 minutes (from 1 hour 40 minutes to 35 hours, median - 14 hours 35 minutes).

For microbiological and histological studies, 190 samples were obtained from patients with histologically confirmed pneumonia. Bacterial pathogens were isolated in 70 (95.9%) patients, most often they were isolated from the lower lobes of the right and left lungs - in 61 (36.7%) and 60 (34.9%) cases, respectively.

When analyzing the localization and volume of the lesion, it was revealed that bilateral lesions prevailed in 55 (75.3%) of the deceased, of which subtotal and total lesions occurred in 12 (23.6%) cases. Right-sided and left-sided lesions were observed in 9 (12.3%) cases. By the nature of the inflammatory response, fibrinous-purulent pneumonia was more common - 67 (91.8%) cases. In 6 (8.2%) cases, serous-purulent pneumonia occurred.

The predominant causative agents of nosocomial pneumonia were S. aureus and K. pneumoniae, which accounted for 35.0% and 26.5% of all isolated strains, respectively.

Monoculture of these microorganisms was identified in 31 (44.3%) and 25 (35.7%) patients, respectively. Association of S. aureus and K. pneumoniae with other pathogens occurred in 23 (32.9%) and 21 (30%) patients, and in 14 (20.0%) cases their association with each other was revealed. E. coli and P. aeruginosa were less common, accounting for 13.7% and 9.4% of all isolated strains.

Despite the absence of clear indications of the time of development of nosocomial pneumonia in the case histories of deceased patients, given the average duration of hospitalization and the identified spectrum of pathogens, it can be assumed that late nosocomial pneumonia predominates [13].

All tested strains of Enterobacteriaceae were highly sensitive to Imipenem, Meropenem and Ertapenem. Other classes of antimicrobials showed lower activity: 45.6%, 45.6%, 45.6%, 49.2% and 42.1% of resistant strains were detected against Ceftazidime, Ceftriaxone, Cefotaxime and Cefepime, 38.6%, 31.1% and 33.3% of strains, respectively, to Ciprofloxacin, Amikacin and Gentamicin.

All strains of K. pneumoniae, E. coli and Enterobacter spp., resistant to cephalosporins of the 3rd-4th generation were resistant to antimicrobials of the 3rd class: Amoxicillin/Clavulanate, cephalosporins of the 3rd-4th generation and fluoroquinolones. 11 of them additionally had resistance to gentamicin, and 7 to Co-trimoxazole.

It should be noted a higher resistance of gram-negative non-fermenting bacteria to the studied drugs, compared with enterobacteria. All isolated 5 strains of A. baumannii were resistant to piperacillin/tazobactam, ceftazidime, cefotaxime, cefoperazone, cefepime and gentamicin (the minimum inhibitory concentration of all antimicrobials was 256 mg/l). Cefoperazone/Sulbactam was active against 3 strains (minimum inhibitory concentration of 64 mg/L), and Amikacin against one (minimum inhibitory concentration of 512 mg/L). 100% of strains were insensitive to ciprofloxacin (minimum inhibitory concentration of 128 mg/l). Polymyxin B, Imipenem and Meropenem were characterized by high activity against all isolated strains of A. baumannii (min-

imum inhibitory concentration of 1 mg/l, 2 mg/l and 4 mg/l, respectively). Of the 5 isolated strains of A. baumannii, 4 were simultaneously resistant to antimicrobials of 3 classes: 3 - to aminoglycosides, cephalosporins of 3-4 generations and fluoroquinolones, 1 - to cephalosporins of 3-4 generations, fluoroquinolones and Co-trimoxazole.

All isolated strains of P. aeruginosa were sensitive to Piperacillin/Tazobactam and Polymyxin B. A low frequency of resistance was observed to Imipenem - 9.1%. Other antimicrobials were characterized by low activity against this pathogen - 72.7% of insensitive strains were detected for Ceftazidime, Cefepime, Cefoperazone, Cefoperazone/Sulbactam, Amikacin, Gentamicin and Ciprofloxacin. Of the 11 strains studied, P. aeruginosa 6 were simultaneously resistant to class 4 antimicrobials: aminoglycosides, 3-4 generation cephalosporins, fluoroquinolones and Co-trimoxazole, while one of them still had resistance to carbapenems.

All strains of S. aureus were susceptible to vancomycin, linezolid and fusidic acid, a low incidence of resistance (2.4%) was noted to Co-trimoxazole. Ciprofloxacin, Gentamicin, Erythromycin and Clindamycin were resistant to 39.0%, 39.0%, 29.3% and 9.8% of strains, respectively. The frequency of isolation of methicillin-resistant strains of S. aureus was 41.5%.

As evidenced by the data obtained, the choice of antimicrobials for the treatment of severe non-nosocomial pneumonia in most cases was carried out without taking into account the most likely pathogens and data on antibiotic resistance.

The leading drugs in the treatment of severe non-nosocomial pneumonia were 3rd generation cephalosporins, but only in 4 patients they were prescribed in combination with macrolides (Azithromycin), while the presence of a drug active against "atypical" microorganisms in the initial mode of therapy improves the prognosis [14,41,42]. The second most common antimicrobial drug was Cefazolin, characterized by low activity against S. pneumoniae, lack of clinically significant activity against H. influenzae and a weak effect on other gram-negative bacteria. The high frequency of use of aminoglycosides is not justified, since the drugs of this group do not act on the main pathogens of non-nosocomial pneumonia, poorly penetrate the bronchial secretion and cause potentially dangerous undesirable reactions. Of the fluoroquinolones group, ciprofloxacin was used for the treatment of severe non-nosocomial pneumonia, while "respiratory" quinolones have unconditional advantages in the treatment of respiratory tract infections [15,43,44].

29 (59.2%) patients received monotherapy, 20 (40.8%) received combination therapy (2-3 drugs), and there were no significant differences in the frequency of combination therapy between medical institutions (p=0.07273). The median duration of antimicrobial use was 2.2±1.6 days. In 59/75 (78.7%) cases, antimicrobials were administered intravenously, in 11/75 (14.7%) - intramuscularly, and in 5/75 (6.7%) - orally. Cefazolin was most often used intramuscularly; azithromycin was administered orally. In 71/75 (94.7%) cases of antimicrobial use, the dosage regimen was correct. The main mistake in the case of inadequate dosing was the use of an underestimated single and daily dose of an antibiotic.

Of particular interest was the choice of antibiotics for "starting" therapy. Initial monotherapy was used in 29 (59.2%) patients. At the same time, Ceftriaxone was most often used - 14 (48.3%) and Cefazolin - 12 (41.4%) cases. For combined initial antibiotic therapy, combinations of 3rd generation cephalosporins with aminoglycosides were most often used - 6/16 of cases (37.5%), 3rd generation cephalosporins with Azithromycin - 4/16 (25.0%), 1st generation cephalosporins with aminoglycosides - 3/16 (18.8%). In 7/16 cases (43.8%), metronidazole was included in the combination antibiotic therapy regimens.

In the course of the study, a retrospective analysis of 66 case histories of patients with severe nosocomial pneumonia was conducted. As the results show, the choice of drugs for the treatment of nosocomial pneumonia in 48.3% of cases did not meet domestic and foreign recommendations [16]. The most commonly prescribed were Ceftriaxone, Cefazolin, Amikacin and Ampicillin.

The number of antimicrobials given to 1 patient ranged from 1 to 7. 23 (39.6%) patients received monotherapy, and 35 (60.4%) patients received combined therapy. Most often, combinations of 3rd generation cephalosporin + aminoglycoside were prescribed - 6/35 (17.1%) of cases, 1st generation cephalosporin + aminoglycoside - 3/35 (8.6%), Ampicillin + aminoglycoside - 2/35 (5.7%). In 11/58 (19.0%) cases, Metronidazole was included in the treatment regimen. Cefazolin and Ampicillin were most often used for the initial therapy of nosocomial pneumonia in 23 (39.7%) and 12 (20.7%) patients, respectively. Changing the starting regimen and conducting several courses of antibacterial drugs (from 2 to 5) were carried out in 23 (39.7%) patients. As second-line drugs, 3rd generation cephalosporins were more often used in 78.3% (18/23) of patients, aminoglycosides in 39.1% (9/23), fluoroquinolones and

Metronidazole in 26.1% (6/23). The average duration of antibiotic therapy was 8.6±6.3 days.

Of the 120 prescriptions of antimicrobial drugs, along with intravenous administration – in 93 (77.5%) cases, in 24 (20.0%) cases the drugs were administered intramuscularly, in 3 (2.5%) - orally. Intramuscularly, Cefazolin and Ampicillin were most often prescribed, orally - Clarithromycin. In 116/120 (92.5%) cases, the dosage regimen of antimicrobials was adequate. The main mistakes were a decrease in the frequency of administration and dose of the antibiotic [17].

CONCLUSION

The main bacterial pathogens of fatal non-nosocomial pneumonia in adults according to the results of bacteriological examination of autopsy material are K. pneumoniae (31.4%), S. aureus (28.6%), S. pneumoniae (12.9%) and H. influenzae (11.4%).

The highest activity in vitro against Enterobacteriaceae strains isolated in fatal non-nosocomial pneumonia was shown by cephalosporins of 3-4 generations and carbapenems, to which all tested strains were sensitive. Among the 20 strains of S. aureus that caused non-fatal nosocomial pneumonia, 2 were resistant to methicillin; the highest (100%) activity against staphylococci was demonstrated by Co-trimoxazole, Vancomycin, Linezolid, Fusidic acid and Clindamycin. S. pneumoniae was sensitive to all antimicrobials tested. The highest activity against H. influenzae was possessed by cephalosporins of 3-4 generations and fluoroquinolones, which were active against all tested strains.

The main bacterial pathogens of fatal nosocomial pneumonia in adults according to the results of bacteriological examination of autopsy material are S. aureus (35.0%), K. pneumoniae (26.5%), E. coli (13.7%) and P. aeruginosa (9.4%). Carbapenems, to which all tested strains were sensitive, had high pharmacodynamic activity against Enterobacteriaceae isolated in nosocomial pneumonia. Concerning gram-negative non-fermenting bacteria, Polymyxin B and Imipenem showed the highest activity (100% and 93.7% of sensitive strains, respectively). Among the 41 strains of S. aureus that caused nosocomial pneumonia, 17 were resistant to methicillin; the highest activity against staphylococci was demonstrated by Vancomycin (100%), Linezolid (100%), Fusidic acid (100%) and Co-trimoxazole (97.6%).

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Conflict of interest - The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Ethics approval and consent to participate - All patients gave written informed consent to participate in the study.

Consent for publication - The study is valid, and recognition by the organization is not required. The authors agree to open the publication.

Availability of data and material - Available

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NOSOKOMIAL VA NOSOKOMIAL BO'LMAGAN PNEVMONIYA UCHUN ANTIMIKROBIYAL TERAPIYANI TANLASHNING FARMAKODINAMIK ASOSLI YO'NALISHLARI

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Abstrakt

Dolzarbligi. Yaqinda antimikrobiyallarni tanlash strategiyasi pnevmoniya patogenlari ro'yxatini kengaytirish va o'zgartirish, shuningdek antibiotiklarga chidamlilikning o'sishi bilan murakkablashdi. Buning uchun antimikrobiyallarni tanlashning mavjud yo'nalishlarini vaqti-vaqti bilan ko'rib chiqish kerak, chunki ularning irratsional qo'llanilishi o'lim rivojlanishi uchun mustaqil xavf omilidir.

Material va usullar. Maqolada ikki yo'nalishda olib borilgan tadqiqotlar materiallari keltirilgan: og'ir pnevmoniyaning asosiy sababchi agentlarini halokatli natija bilan aniqlash va farmakologik tadqiqotlar yordamida og'ir nosokomial va nosokomial bo'lmagan pnevmoniyaning antibiotik terapiyasini retrospektiv tahlil qilish.

Natijalar. Patogenlarning tuzilishini va antimikrobiyal dorilarga chidamlilik profilini hisobga olib, og'ir nosokomial bo'lmagan pnevmoniya uchun empirik terapiya rejimlarida 3-4 avlod sefalosporinlari yoki amoksitsilin / klavvulanat, ertapenem yoki nafas olish fluoroquinolonlarini qo'llash tavsiya etiladi. Og'ir nozokomial pnevmoniya uchun empirik davolash rejimlarida Imipenem yoki Meropenem va Vancomycin yoki Linezolid dan foydalanish tavsiya etiladi.

Xulosa. Nosokomial bo'lmagan pnevmoniya uchun boshlang'ich terapiya rejimiga MRSA (Vancomycin, Linezolid va boshqalar) ga qarshi faol dori-darmonlarni kiritish zarurati qo'shimcha o'rganishni talab qiladi. 3-4 avlod sefalosporinlari, fluoroquinolones va Amikacin faqat izolyatsiya qilingan patogenlarning sezgirligini aniqlash natijalariga asoslanib og'ir nozokomial pnevmoniyani davolash uchun tavsiya etilishi mumkin.

Tayanch iboralar: nosokomial pnevmoniya, non-nosokomial pnevmoniya, antimikrobiyal farmakoterapiya, antibiotiklarga chidamlilik, antibiotik sezuvchanlik, antimikrobiyal terapiyaning harmakodinamikasi

ФАРМАКОДИНАМИЧЕСКИ ОБОСНОВАННЫЕ ПОДХОДЫ К ВЫБОРУ АНТИМИКРОБНОЙ ТЕРАПИИ ПРИ ВНУТРИБОЛЬНИЧНОЙ И ВНЕБОЛЬНИЧНОЙ ПНЕВМОНИИ

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Абстракт

Актуальность. Стратегия выбора противомикробных препаратов в последнее время осложняется расширением и модификацией перечня возбудителей пневмонии, а также ростом антибиотикорезистентности. Это требует периодического пересмотра существующих подходов к подбору противомикробных препаратов, поскольку их нерациональное применение является самостоятельным фактором риска развития летального исхода.

Материал и методы. В статье представлены материалы исследований, которые проводились по двум направлениям: выявление основных возбудителей тяжелой пневмонии с летальным исходом и ретроспективный анализ антибиотикотерапии тяжелой внутрибольничной и внутрибольничной пневмонии с летальным исходом с использованием фармакологических исследований.

Результаты. Учитывая структуру возбудителей и профиль резистентности к антимикробным препаратам, целесообразно использовать цефалоспорины 3-4 поколения или амоксициллин/клавуланат, эртапенем или респираторные фторхинолоны в эмпирических схемах терапии тяжелой внутрибольничной пневмонии. В эмпирических схемах лечения тяжелой внутрибольничной пневмонии целесообразно использовать Имипенем или Меропенем и Ванкомицин или Линезолид.

Заключение. Необходимость включения препаратов, активных в отношении MRSA (Ванкомицин, Линезолид и др.) в схемы начальной терапии при внутрибольничной пневмонии, требует дополнительного изучения. Цефалоспорины 3-4 поколений, фторхинолоны и амикацин могут быть рекомендованы для лечения тяжелой внутрибольничной пневмонии только по результатам определения чувствительности выделенных возбудителей.

Ключевые слова: нозокомиальная пневмония, не нозокомиальная пневмония, антимикробная фармакотерапия, антибиотикорезистентность, чувствительность к антибиотикам, фармакодинамика антимикробной терапии