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Research Article

Rational antimicrobial chemotherapy: assessment of the level of basic knowledge of general practitioners. Final results of the KANT project

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Abstract

Introduction: The irrational use of medicines leads to a decrease in the quality of care, an increase in treatment costs and side effects. In the case of antibacterial drugs, in addition to all the above-mentioned consequences, their improper use can lead to an aggravation of the existing and quite challenging problem of our time – the growth of antibiotic resistance among pathogenic microorganisms.

The aim of the study: to determine the level of basic knowledge of medical specialists in the field of a rational use of antimicrobial drugs (AMD).

Materials and methods: The study was based on an analysis of an anonymous multicenter survey in the framework of the KANT project (the full name of the project is "Physicians' (Students') Knowledge of Antimicrobials Usage"). It was conducted in 2018–2019 in 10 major centers of Russia.

Results and iscussion: According to the results of the study, the respondents showed a low level of knowledge of the rational use of antibacterial drugs. The best results are obtained for questions No.1 (time interval for evaluating the effectiveness of the initial antimicrobial therapy (AMT)), No.2 (rationality and period of AMD change with a positive clinical effect), and No.9 (determining the mode of using the proposed drugs), whereas the worst results were obtained

for questions No.3 (determining irrational combinations of AMD), No.4 (determining a situation requiring a long course of AMT), and No.7 (choosing auxiliary drugs for bacterial respiratory infections).

Conclusion: The results obtained in the study indicate the need for additional educational activities among health professionals.

Keywords

questionnaires, antimicrobials, general practitioner, rational antibiotic therapy, knowledge level, pharmacoepidemiology.

Introduction

In the first decade of the XXI century, the consumption of antibiotics in the world increased by 36%, 76% of which fell on Brazil, Russia, India, China and South Africa (Van Boeckel et al. 2014). In 2015, according to the WHO Report on Surveillance of Antibiotic Consumption: 2016–2018 Early Implementation (2018), the rates of antibiotic use in Russia were 14.82 daily doses per 1000 people; 915.65 tons of antimicrobial drugs were used per year. In the ranking of 65 countries studied, Russia was in the middle position, exceeding the indicators of a number of European countries, such as Germany and the Netherlands (World Health Organization 2018). An increase in the consumption of antibiotics will inevitably lead to the development of antibiotic resistance, which, according to experts, will cause 10 million deaths annually by 2050, exceeding the mortality rate from cancer (O'Neill 2016).

Massive irrational and unjustified prescription of drugs is due to the fact that not every medical specialist today has the necessary knowledge in the field of microbiology and clinical pharmacology of antibiotics.

The aim of study is to determine the level of physicians' basic knowledge in the field of the rational antimicrobials usage.

Material and methods

This article presents the results of an anonymous questionnaire within the framework of the multicenter KANT project (the full name of the project is "Physicians' (Students') Knowledge of Antimicrobials Usage"), assessing the physicians' basic knowledge of a rational antimicrobial chemotherapy (AMC) and empiric regimen of antibiotics. The study was conducted in 2018–2019, the results of the survey of 434 specialists from 10 centers of Russia were obtained and analyzed during this period.

The method of an anonymous survey was used in this study, for which an original questionnaire was developed. The questionnaire included multiple choice questions and open-end questions. The medical professionals were to indicate their specialties, work experience, and a professional category, if any. In order to determine the statistical significance of the differences, the respondents were divided into four groups: doctors with work experience from 1 to 5 years, from 6 to 10 years, from 11 to 20 years, and more than 20 years. The respondent was awarded 0 point for an incorrect answer; depending on the completeness of the answer, for an incomplete or partially correct answer – from 0.25 to 0.75 point; for a true answer – 1 point. Therefore, with all the correct answers, the maximum average score was 1.0. The average completeness rate for the correct, partially correct and wrong answers was defined as the average response completeness (ARC) rate, which is an equivalent for the average level of correct answers. The average scores of each respondent, the average scores for individual questions, and the average scores for the entire questionnaire were evaluated. The patterns of answers to individual questions were also analyzed; statistically non-systemic question skips were allowed.

In the eighth question of the questionnaire, which consisted in the choice of the first-line drug for therapy of the proposed infectious diseases, the options of answers were also taken into account, in which there were alternative groups and/or drugs of choice according to the regulatory documents of other countries. Thus, when the specialists chose the drug(s) belonging to the second or third lines of therapy, the answer was counted and scored 0.5 point, and when the respondents chose the main and additional groups at the same time, the score for the answer did not decrease and was calculated based on the completeness of the choice of the first-line drug(s).

Human Rights were not violated, the ethical principles of the Helsinki Declaration by the World Medical Association were observed during the study.

All the information of the questionnaire was processed and entered into an electronic database and analyzed using the application programs of Microsoft Excel and IBM SPSS Statistics 26. The nominal variables were processed based on the analysis of arbitrary contingency tables, using the Pearson's chi-square (x2) test. The significance of the differences was recorded at a bilateral level of $p<0.05$. To assess the link strength between the categorical features, the Cramer's V was used. To compare the averaged quantitative data from the centers, a nonparametric Kruskal-Wallis test was used (the significance of differences was recorded at a bilateral level of $p < 0.05$, taking into account the Bonferroni correction for the multiplicity of comparisons).

Observing the conditions and restrictions on the use of arbitrary contingency tables, small centers that did not have statistical significance of differences when compared with one another ($p < 0.05$) were combined.

This method of knowledge evaluation was specially developed for this study, and it is not an objective indicator of the general level of competence among doctors.

A similar study based on this questionnaire was carried out in 2018–2019 to assess senior medical students' knowledge; the final results were submitted to Clinical Microbiology and Antimicrobial Chemotherapy Journal. In addition, the results of studying the knowledge of doctors on AMT in the previous stages of the project were presented at the congresses of the European Respiratory Society and published in the European Respiratory Journal (Bontsevich 2007; Pertseva et al. 2012; Bontsevich et al. 2014).

Results and discussion

The survey involved 434 medical specialists from 10 centers of Russia: 29.5% – from the Republic of Tatarstan, 20.4% – from Primorsky Krai, 10.0% – from Belgorod, 8.7% – from Voronezh, 14.0% – from Krasnoyarsk and Krasnodar (joint center No.1) and 17.2% – from Chelyabinsk, Tambov, Novosibirsk, and Lipetsk (joint center No.2).

Depending on work experience, most doctors (28.4%) have work experience more than 20 years, 26.5% – from one to five years, 21.2% – from eleven to twenty years, and 11.7% of the participants have work experience from six to ten years. The remaining 12.2% of the doctors did not indicate their length of service. When assessing the relationship between the ARC and work experience of the specialists, no statistically significant correlation was found ($p = 0.502$).

According to the results of the study, ARC for all the questions of the questionnaire was 49.5% (from 38.8% to 56.4% for different centers), which indicates an insufficient level of knowledge among the respondents (Figs 1, 2). The best results were shown for questions No.1 (time interval for assessing the effectiveness of the initial antimicrobial therapy), No.2 (rationality and period of AMD change with a positive clinical effect), and No.9 (treatment regimen for the proposed drugs). The minimum level of correct answers was received to questions No.3 (irrational combinations of AMD), No.4 (indicate a situation requiring a long course of AMT), and No.7 (auxiliary drugs for bacterial respiratory tract infections).

In the first question of the questionnaire, the specialists were to determine after what period of time it was possible to judge the effectiveness of the initial AMT. The following options were presented as answers: after 2–3 days, after 4–5 days, after 7–10 days from the moment of starting the treatment and "Not sure". The majority of doctors (88.1%) know that the initial assessment of the results of therapy should be carried out in the first 48–72 hours after

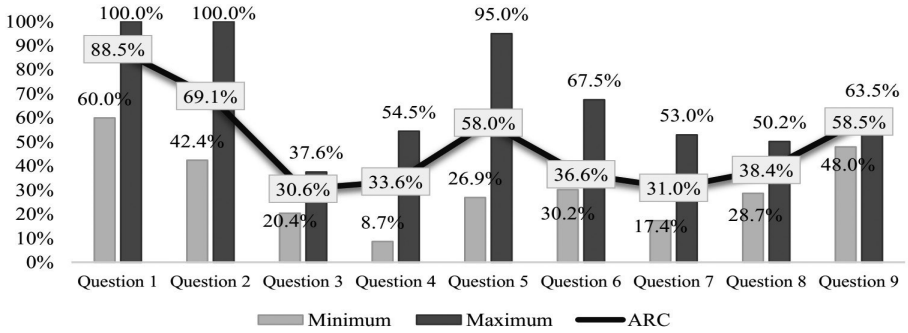

Figure 1. Minimum, maximum and ARC for all questions in the field of rational AMT. **Note**: ARC – average response completeness rate; AMT - antimicrobial therapy.

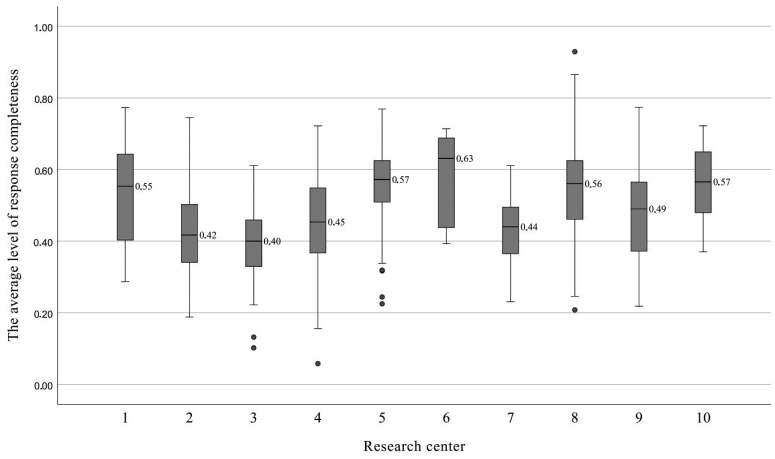

Figure 2. Distribution of correct answers in the field of rational AMT among centers. Note: AMT – antimicrobial therapy.

the start of antibiotic administration, focusing primarily on the dynamics of the clinical symptoms. About 1.0% of the respondents answered partially correctly, indicating both correct and incorrect periods, and 11.0% indicated an incorrect time interval. ARC was 88.5% (from 62.8 to 100.0% in different centers, $p < 0.001$, Cramer's $V = 0.31$).

The question about correcting the initial regimen of empiric therapy is considered only 2–3 days after the start of treatment in the absence of a positive clinical effect and/or isolation of a pathogen resistant to the used drug. In the second question of the questionnaire, the specialists chose which of their actions would be most rational with a positive clinical effect from AMT if a long course of therapy was required: to change AMD after 10 days, to change AMD after 14 days, to change AMD is not required until the end of the course. When facing difficulties, a respondent could choose the "not sure" option. Unfortunately, not all the respondents would have done the right thing in the described situation: only 69.0% decided that the presence of a positive effect made the intention to change the drug senseless and irrational; less than 1.0% were uncertain and answered partially correctly, and 30.8% of the respondents did not cope with the task. ARC was 69.1%, from 42.4 to 92.3% in different centers ($p < 0.05$, Cramer's $V = 0.21$).

In the third question of the questionnaire, the respondents were offered variants of drugs, from which they were to choose irrational combinations for prescription in clinical practice due to a similar spectrum of action on pathogenic microflora. The following answers were offered: "ceftriaxone + amoxicillin", "ampicillin + gentamicin", "ofloxacin + doxycycline", "levofloxacin + clarithromycin", "azithromycin + ampicillin + amikacin", and "not sure".

Despite practical experience, only 4.7% of the doctors were able to fully cope with the task, indicating all the three irrational combinations as an answer: "ceftriaxone + amoxicillin", "ofloxacin + doxycycline", and "levofloxacin + clarithromycin". The majority of the specialists (65.0%) answered partially correctly, defining only some combinations as irrational or choosing right and wrong options at the same time, another 27.8% did not cope with the task, and 2.5% of the respondents left the question unattended. ARC was 30.6%, from 20.4 to 37.6% in the centers ($p < 0.001$; Cramer's $V = 0.25$).

Erroneous answers were distributed as follows: 5.3% each accounted for the combinations "ampicillin + gentamicin" and "azithromycin + ampicillin + amikacin", 4.2% accounted for the answer "not sure", and the remaining 13.0% were the combinations of correct and incorrect answers, in the structure of which the erroneous judgments prevailed. The share of the proposed options in the general structure of specialists' answers is shown in Figure 3.

In the fourth question of the questionnaire, the respondents were to determine the situation in which they would decide to continue the AMT course for more than 5–7 days with positive clinical dynamics in a patient with community-acquired pneumonia (CAP). According to the current clinical guidelines, the presence of individual clinical, laboratory symptoms and signs of the disease is not an absolute indication for continuing the therapy. As a rule, their disappearance occurs independently or against the background of a symptomatic therapy (Chuchalin et al. 2010, 2019). Of the proposed answers – prevalence of subfebrile condition, prevalence of increased ESR (the erythrocyte sedimentation rate), prevalence of residual infiltration on radiography of the thoracic region 2 weeks after the start of a pneumonia treatment, in none of the indicated situations (correct answer) – 32.8% of the specialists made the right choice, and fewer than 1.0% answered partially correctly. The majority of the respondents (65.4%) gave an incorrect answer, and 1.1% of the doctors left the field blank. ARC was 33.6%, from 8.7% to 54.5% in the centers ($p < 0.001$; Cramer's $V = 0.34$).

The fifth question of the questionnaire also related to the practical side of doctors' activities. The respondents were to determine the most rational algorithm for the diagnosis of acute tonsillitis/pharyngitis at the appointment, scoring 2 points by McIsaac's scale. The answer options were as follows: the appointment of local antiseptics; prescribing the systemic AMD, prescribing local antiseptics + systemic AMD, performing express diagnostics for group A β-hemolytic streptococcus (GABHS), for example, 'Streptatest', with the subsequent decision to prescribe systemic AMD; as well as the option "other", providing with an opportunity to give one's own opinion to the question, and the "not sure" option. Since the patient's clinical symptoms scored 2 points by McIsaac's scale,

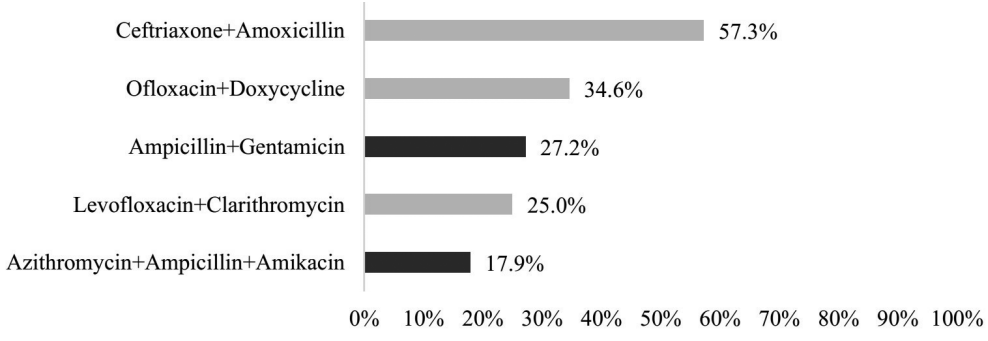

Figure 3. Share of the proposed options in the structure of specialists' answers to the question of choosing irrational AMD combinations. **Note**: Gray corresponds to correct answers, black – to incorrect answers, AMD – antimicrobial drugs.

which corresponds to only 11–17% of the probability of streptococcal genesis of the disease, before prescribing a systemic antimicrobial therapy, it is rational to clarify the etiology of the inflammatory process by performing express diagnostics using second generation tests or by bacteriological studies of the material from the palatine tonsils and the posterior pharyngeal wall (Polykov et al. 2016). Fewer than half of the surveyed specialists turned out to be competent in this issue – 46.0%; and 24.2% answered partially correctly. Wrong approaches were chosen by 29.7% of the respondents, whereas fewer than 1.0% ignored this task. ARC was 58.0%, from 26.9% to 72.0% in the centers ($p < 0.05$; Cramer's $V = 0.22$).

Currently, CAP is one of the most common infectious diseases, the prognosis of which in some cases is rather poor. Considering not only the medical, but also the social significance of the pathology, a modern doctor needs to develop the correct approach to treating a patient, taking into account both the parameters of the underlying disease, and also the concomitant background.

In the sixth question of the questionnaire, the respondents were to indicate the typical mistakes in the initial AMT for mild CAP in adult patients under 60–65 without risk factors and comorbidities. The drug of choice for the treatment of this category of patients is amoxicillin, which remains highly active against the main causative agent of CAP – *S. pneumoniae*, whereas macrolides are alternative drugs. Each of the proposed options – the use of doxycycline, the use of ciprofloxacin, the use of cefazolin, the use of ampicillin per os, or the use of respiratory fluoroquinolones – was erroneous, that is, for the completeness and correctness of the answer it was necessary to choose all the above options.

To varying degrees, 95.1% of the specialists successfully coped with this task, 89.8% of the respondents answered partially correctly, and only 5.3% of the doctors indicated all the correct answers. Among the partially correct answers, doxycycline has the highest specific weight among the proposed options – 60.3% but its use in our country is irrational due to the high resistance of *S. pneumoniae* to tetracyclines; the second most frequent choice is ciprofloxacin – 46.8%, it is ineffective against *S. pneumoniae*; next came the group of respiratory fluoroquinolones – 40.9%, the appointment of which to patients with non-severe CAP without risk factors is inappropriate; then came ampicillin for oral administration – 24.1%, which has low bioavailability with this route of drug administration (40.0%) compared with amoxicillin (75–93.0%), and, finally, cefazolin – 23.2%, characterized by a low activity against pneumococci and the lack of clinically significant activity against *H. influenzae* (Russian Respiratory Society 2018, Chuchalin et al. 2010) (Fig. 4). Wrong answers to this question are equivalent to the "not sure" option, amounting to 4.0%, and fewer than 1.0% of the respondents left the field blank. ARC was 37.1%, from 30.5 to 63.1% in the cities ($p < 0.001$; Cramer's $V = 0.32$).

In the seventh question of the questionnaire, the specialists were asked to choose ancillary drugs that they would consider rational to prescribe in addition to the reasonable prescription of AMD in the treatment of bacterial infections of the respiratory tract, such as CAP, COPD, and acute sinusitis. There were the following answers: immunocorrectors (modulators); interferon; N-acetylcysteine/carbocysteine (correct answer); fenspiride; vitamin C / multivitamins; antihistamine drugs; bacterial lysates; pre- and/or probiotics, and the "other" for offering other drugs. Anyway, 52.6% of the respondents coped with the task, 17.8% of them indicated only one correct answer, and 34.8% in addition to the correct one chose the wrong drugs. As many as 45.6% of the doctors made a mistake in their prescription, and 1.7% of the respondents ignored the task. ARC was 31.0%, from 17.4% to 53.0% in the different centers (the level of significance adjusted for the multiplicity of Bonferroni comparisons was $p = 0.045$).

The absolute percentage of each of the proposed options was analyzed from the total number all the respondents' answers. The most responses in the total structure included N-acetylcysteine/carbocysteine – 65.4%, the next in frequency were immunocorrectors (modulators) – 31.3%, then pre- and/or probiotics – 30.7%, vitamin C/multivitamins – 24.2%, antihistamine drugs – 22.0%, bacterial lysates – 19.4%, fenspiride – 15.7%, interferon – 4.9%, and the "other" option – 1.7%. The share of each of the proposed options in the structure of partially correct and incorrect answers is shown in Figure 5.

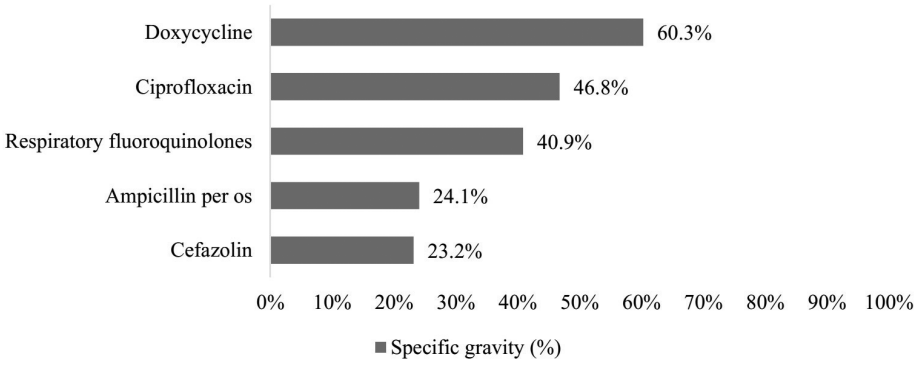

Figure 4. Proportion of the proposed options in the structure of respondents' answers to the question about typical mistakes in the initial AMT for mild CAP in adult patients under 60–65 without risk factors and concomitant pathologies. **Note**: AMT – antimicrobial therapy, CAP – community-acquired pneumonia.

In the eighth question, the specialists were asked among the listed AMD to determine the drug of the first line of therapy for the following infectious diseases: acute uncomplicated tracheobronchitis, mild community-acquired pneumonia, acute cystitis, and uncomplicated pyelonephritis. The patient's category was conditional and the same for all nosologies: without comorbidity, not having taken AMD in the last 3 months.

In general, the doctors show a rather low level of knowledge of this issue – ARC is 38.4%, from 28.7 to 50.2% in the different centers. Completely correct answers, which meant choosing the main and/or the main and alternative AMD for all four nosologies, were not registered. The majority of respondents (88.8%) gave a partially correct answer, 7.8% solved the task incorrectly, and 3.4% ignored the question.

The specialists coped best with the treatment of mild CAP and acute cystitis, worse – with the choice of AMD for the treatment of acute uncomplicated forms of tracheobronchitis and pyelonephritis. The structure of the respondents' answers is presented below (Fig. 6).

The choice of therapy for acute uncomplicated tracheobronchitis in this question was a kind of provocation for the specialists, because in most cases this disease has a viral etiology, so the routine administration of AMD is completely unreasonable (Smith 2017). The obtained results were unexpectedly low: only 33.9% of the doctors thought about the irrationality of AMT, 62.0% of the respondents made a mistake, choosing one or another antibiotic(s) for therapy, and 4.1% ignored this question.

When determining the drug for empirical treatment of mild CAP, first of all, it was necessary to assess the available parameters of the patient, basing on which he could be to referred to the group of outpatients without risk factors and concomitant diseases. The drugs of choice for this category of patients are amoxicillin, which is highly active against the main causative agent of infection - *S. pneumoniae*, and/or a group of macrolides with improved pharmacokinetic properties (azithromycin, clarithromycin, spiramycin) (Chuchalin et al. 2010, 2018; Gavrilova 2020). Despite a wide spectrum of action of doxycycline in relation to these pathogens, its use for empirical therapy in Russia is not contemplated due to the high occurrence of tetracycline-resistant strains of the pathogen, while in the USA, according to the updated recommendations of the American Thoracic Society and the International Society for Infectious Diseases, doxycycline may be used as a first-line drug for CAP treatment (Metlay et al. 2019). In the countries of the European Union, in patients who do not require intensive care, according to the recommendations of the European Society of Clinical Microbiology and Infectious Diseases, in addition to aminopenicillins and macrolides, the following groups of drugs can be used:

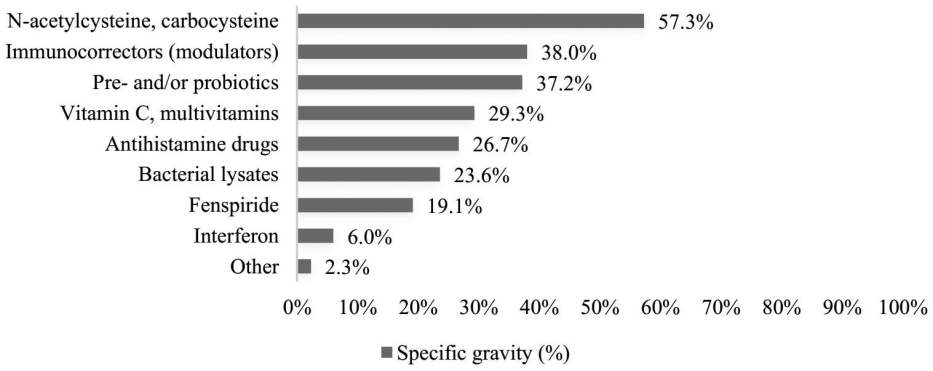

Figure 5. Proportion of the proposed options in the structure of specialists' answers to the question of choosing additional drugs for justified AMD treatment of bacterial respiratory tract infections. **Note**: AMD – antimicrobial drugs.

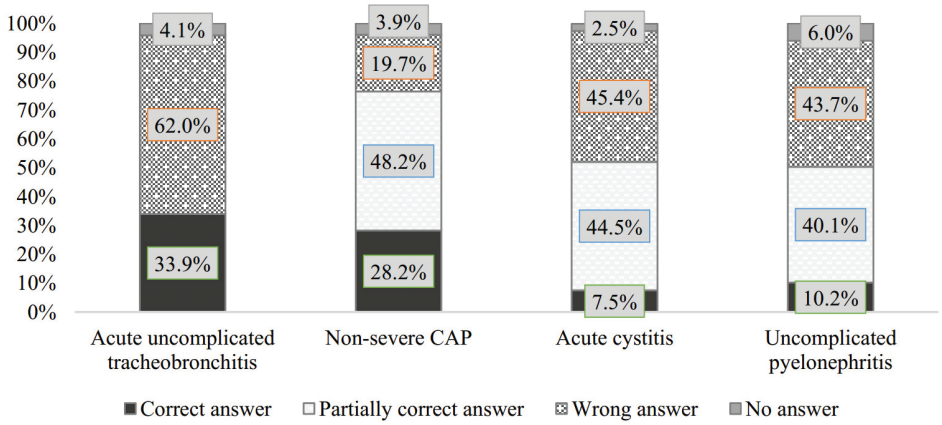

Figure 6. Structure of specialists' answers to the question of determining AMD for the first line treatment of presented infectious diseases. **Note**: AMD – antimicrobial drugs.

inhibitor-protected aminopenicillins, cefotaxime or ceftriaxone (cephalosporins without antipseudomonal activity), benzylpenicillin in combination with macrolides or without them; levo- or moxifloxacin, among which moxifloxacin is more preferable to use, because it has a higher antipneumococcal activity (Woodhead et al. 2011). The correct answers were given by 28.2% of the specialists, 14.2% of them chose only amoxicillin and 14.0% – the combination of amoxicillin with drugs of the second and/or third line of therapy. Partially correct answers account for 42.8%, 40.0% of them involved choosing alternative groups (the proportion of choosing amoxicillin + clavulanic acid was 58.6%, macrolides – 44.5%, cephalosporins – 36.1%, fluoroquinolones – 29.5%, and doxycycline – 3.9%). Incorrect answers were given by 19.7% of the specialists, and 3.9% of the respondents ignored the task.

The leading pathogen of community-acquired urinary tract infections (UTI) is *E. coli*, which accounts for 70–90% of cases of acute cystitis and pyelonephritis; therefore, therapy for this group of diseases is prescribed taking into account the resistance of this pathogen to different groups of antibacterial drugs (Sidorenko et al. 2016).

In the case of acute uncomplicated cystitis, the drugs of choice are fosfomycins (fosfomycin trometamol), furazidine, and nitrofurantoin (Gupta et al. 2011; Grabe et al. 2015; Sidorenko et al. 2016; Lee 2018; Díez-Aguilar and Cantón 2019; Perepanova et al. 2019; Bonkat et al. 2019). In addition, according to the Eurasian guidelines, cefixime and ceftibuten can be used as the initial therapy (Sidorenko et al. 2016); therefore, in the countries of the European Union these AMD are used in exceptional cases due to the risk of microbiological collateral damage (Grabe et al. 2015; Bonkat et al. 2019). Currently, there is no consensus among experts regarding fluoroquinolones: in the countries of the European Union, since March 11, 2019, this group of AMD has been prohibited for treating this pathology due to a high risk of disablement and the development of long-term side effects, with the exception of cases when all the recommended basic drugs are ineffective (Bonkat et al. 2019). In Russia, fluoroquinolones are also limited in use, because as these drugs play an important role in the treatment of complicated UTIs; they should not be routinely used to treat uncomplicated forms, except situations when there is no alternative (Perepanova et al. 2019). In the USA, the situation is less definite: according to the current clinical guidelines, fluoroquinolones are also considered potentially dangerous in terms of the development of collateral damage, but they are allowed to be used in second or third line therapies in the form of 3-day courses (Gupta et al. 2011). Apprehensive attitude to fluoroquinolones and cephalosporins may also be associated with a high risk of developing *C. difficile* – associated colitis (Knecht et al. 2014).

According to the guidelines, oral fluoroquinolones (levofloxacin, ciprofloxacin) should be used as the first-line therapy for acute uncomplicated pyelonephritis (Gupta et al. 2011; Grabe et al. 2015; Chuhareva et al. 2016; Sidorenko et al. 2016; Zaycev et al. 2019; Bonkat et al. 2019). In addition, according to the recommendations of the European Association of Urology, for empiric therapy, oral and parenteral cephalosporins can be used, the latter of which are more effective, because they reach higher concentrations in blood and urine (Bonkat et al. 2019). The use of cephalosporins is also indicated with the development of a number of conditions, for example, with the development of an allergic reaction or the presence of other contraindications to the use of fluoroquinolones (in this case, cefixime is preferred), as well as with the development of over 10% resistance to this group of drugs, when the use of long-term intravenous cephalosporins (ceftriaxone) or aminoglycosides in a stable 24-hour dose (gentamicin, amikacin + ampicillin) is allowed (Gupta et al. 2011; Zaycev et al. 2019).

The group of aminopenicillins and inhibitor-protected penicillins cannot be used for empirical therapy of UT infections, with the exception of certain cases (for example, the proven gram-positive nature of the disease), due to the high resistance of *E. coli* throughout the world (on the territory of the Russian Federation it is more than 20%). In addition, the use of these drugs increases the risk of developing microbiological collateral damage (Gupta et al. 2011; Grabe et al. 2015; Sidorenko et al. 2016; Zaycev et al. 2019; Bonkat et al. 2019; Pitout and Finn 2020).

The correct choice of a therapy for the treatment of acute cystitis was made only by 7.5% of the specialists, 6.3% of whom indicated the main drugs, and the remaining 1.2% chose their combinations with the alternative groups. Partially correct answers made up 44.5%, including 27.5%, which involved the indication of second/third line therapies (the proportion of fluoroquinolones – 16.2%, cephalosporins – 8.4%, amoxicillin + clavulanic acid – 4.2 %).

The empiric therapy for acute uncomplicated pyelonephritis was correctly indicated by 10.2% of the doctors, 1.3% of them indicated both the main and alternative line of drugs. About 40.1% of the doctors answered partially correctly, 17.4% of them chose AMD of the second/third line of therapy (the proportion of cephalosporins – 30.2%, amoxicillin + clavulanic acid – 17.5%, gentamicin – 3.2%). As many as 43.7% of the respondents could not cope with the task, another 6.0% left the question unanswered.

The ninth question of the questionnaire was an open-end question. The specialists needed to determine the main parameters of the AMD regimen, namely, the daily dosage of the drug, the route(s) of administration and the frequency of administration. The most "popular" antibiotics were suggested in this question: ampicillin, amoxicillin, ceftriaxone, cefixime, azithromycin, and levofloxacin. According to the results, the level of doctors' knowledge of this task is average. ARC is 58.5%, from 48.0 to 63.5% in the centers (the level of significance adjusted for the multiplicity of Bonferroni comparisons was $p < 0.001$).

After analyzing the most frequent errors in specifying the parameters of the AMD regimen among the proposed drugs, the following conclusion were made: the largest number of incorrect judgments concerned the determination of frequency of administration of AMD (70.5%), the wrong choice of the route(s) of administration of AMD (54.3%) and fewest number of errors (33.5%) were made when indicating wrong daily dosages of the drug (Fig. 7).

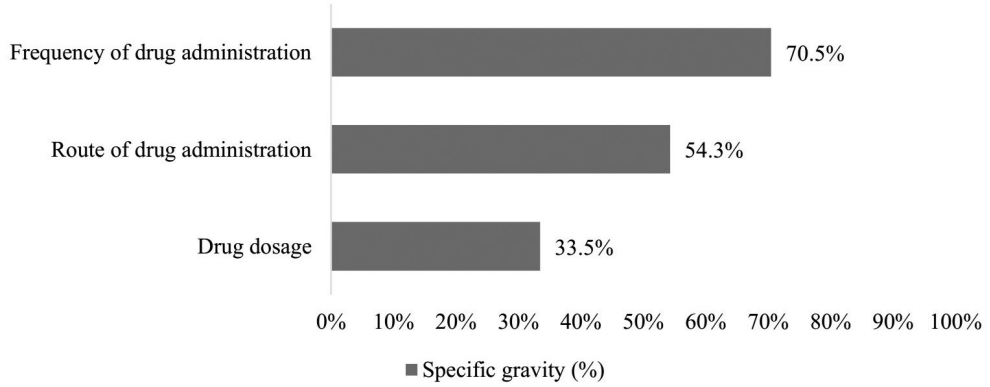

Figure 7. Proportion of errors of specialists when selecting parameters of AMD regimen in the structure of partially correct and incorrect answers. **Note**: AMD – antimicrobial drugs.

The best results were achieved when determining the regimen for cefixime, ceftriaxone, and azithromycin, while the worst – when indicating the regimen for amoxicillin, ampicillin, and levofloxacin.

With regard to amoxicillin, levofloxacin, and ceftriaxone, the most popular wrong option is an incorrect and/or incomplete indication of the frequency of administration of the drug; in the general structure of the responses, this error accounted for 30.0%, 21.0% and 28.6%, respectively (for the correct answer means the frequency of administration of amoxicillin being 2–3 times a day, ceftriaxone – once a day, levofloxacin – 1–2 times a day). Quite often the doctors incorrectly or incompletely indicated the route(s) of administration of ampicillin and azithromycin. Since ampicillin has a low oral bioavailability (35–40%), this route of administration was an incorrect answer (23.6% of the total answers). The existing dosage forms of azithromycin currently allow it to be used both enterally and parenterally (for example, if the drug cannot be administered orally or in severe forms of bacterial infections). In the structure of the responses, the choice of only one of two possible routes of macrolide administration was 23.2%. In the case of cefixime, the most difficult parameter is the daily dosage of the drug; the respondents either ignored the answer, or recommended taking 500, 1000 or 2000 mg of the antibiotic (whereas the prescribed dose for adults is 400 mg per day). This erroneous opinion accounts for 17.0% of the responses in the general structure.

A health care professional, regardless of work experience and the existing category, must be able to objectively assess the level of his knowledge and strive to improve the achieved results. At the end of the questionnaire, the respondents were asked to answer whether they feel the need to take some educational courses on the rational antibiotic therapy. Fortunately, only 1.0% of the specialists answered negatively, the majority of the doctors, namely 86.2%, would like to become more informed and answered affirmatively, with 12.8% of the specialists not wishing to share their opinions.

Conclusions

The results of the study, obtained after statistical processing and analysis of the respondents' answers, indicate the need to optimize the physicians' knowledge, because the degree of their awareness of all the issues of the rational antibiotic therapy is rather low. In a number of situations the level of doctors' knowledge is insufficient for the correct management of patients with diseases requiring AMT. The questions of determining irrational drug combinations, indicating a situation requiring a long course of antibiotic therapy for CAP, as well as the choice of auxiliary drugs for bacterial respiratory tract infections against the background of rationally prescribed antibiotic therapy turned out to be difficult for the respondents. There are also significant gaps in knowledge of rational antibiotic regimens.

The comparative analysis of the specialists' answers, ranked according to doctors' work experience – from 1 to 5 years, from 6 to 10 years, from 11 to 20 years, and over 20 years, showed that all groups of the respondents equally need additional educational courses to improve their awareness of modern antimicrobial chemotherapy, the quality of medical care and reducing the risk of developing antibiotic resistance.

Conflict of interest

The authors declare no conflict of interests. This study was not sponsored.

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