



Assessment of senior medical care majors' knowledge in antimicrobial chemotherapy

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Abstract

Introduction: The resistance of microorganisms to antimicrobials has been gradually increasing since 2011 and is now recognized by the World Health Organization as a global biological threat. Causes of antimicrobial resistance must be actively addressed. Healthcare workers' awareness of rational antimicrobial prescribing practices is of great importance. The increasing relevance of this issue is considered within this study, which started in 2014.

Materials and methods: The article represents the results of anonymous prospective surveys within the framework of the KANT multi-centered research project aimed at assessing students' knowledge of rational antimicrobial prescribing practices also known as "antimicrobial stewardship". The survey involved 309 Medical Care majors in their fifth- and sixth- years in two Russian regional centers: Belgorod and Voronezh. The answers to four main questions of the survey were analyzed in this work.

Results and discussion: According to the survey, 51.5% of the respondents properly identified a pharmacological group of an antimicrobial; 79.3% of the students would change an antibiotic if the desired therapeutic outcome was not achieved within two or three days of treatment; 29.8% of the students believed that an antimicrobial substitution was required even when a positive therapeutic outcome was achieved; and nobody could correctly identify all the proposed pharmacologically irrational combinations of antimicrobials.

Conclusions: The survey showed that senior medical students have insufficient knowledge in antimicrobial stewardship. Appropriate use of antibiotics and antimicrobial prescribing practices need to be considered more thoroughly in Pharmacology, Clinical Pharmacology and Medical Care curricula. Likewise, educational activities on antimicrobial stewardship and best prescribing practices are of great importance for students as they will help with improving the knowledge of future doctors.

Keywords

antimicrobial chemotherapy, rational antimicrobial prescribing, students, survey.

Introduction

Antibiotic resistance is one of the most acute problems in the XXI century (CDC 2014, Chellat et al. 2016). Strains of antimicrobial-resistant organisms are spreading not only across the Russian Federation, but also all over the world (Yakovlev et al. 2017, Akova 2016). According to the statistical forecasts, the number of deaths caused by them may reach 10 million annually by 2050 (Van de Sande-Bruinsma 2015). To put that into perspective, the world mortality rate caused by all infectious pathologies was about 13 million in 2012 (World Health Organization Documentation Center 2014), including 700 thousand of deaths caused by antimicrobial-resistant microorganisms (O'Neill 2014). Mass prescription of antimicrobials has led to a significant decrease in the sensitivity of microorganisms to the drugs (Theuretzbacher 2017). Meanwhile, the pipeline for new antimicrobials remains miserable (Kozlov 2015, Barber and Swaden-Lewis 2017).

The World Health Organization (WHO) recognized the antimicrobial resistance as one of the most significant global biological challenges in 2011. Its *Global Strategy for Containment of Antimicrobial Resistance*, developed in 2014, considers the following causes of antimicrobial resistance (Van de Sande-Bruinsma 2015):

- uncontrolled over-the-counter sale of antimicrobials;
- no common standards for infectious disease treatment;
- no programs for either disease prevention or infection control;
- use of antimicrobials in food-producing animals;
- low awareness of society and healthcare workers of rational antimicrobial chemotherapy.

The above-mentioned problems of antimicrobial resistance must be actively addressed. Rational antimicrobial prescribing depends on qualifications and expertise of future physicians (Abbo et al. 2013, Bontsevich et al. 2015). For this purpose, Pharmacology and Clinical Pharmacology disciplines have been introduced into the curriculum in higher medical educational institutions across Russia. Since the largest group of drugs is represented by antimicrobial agents, the greatest emphasize in education is placed on studying their characteristics, including classification, components and mechanism of action. During the course of Clinical Pharmacology, the following fundamentals are considered: practical use of antimicrobial agents, optimal doses, dosage interval and possible complications in treatment.

By the fifth and sixth years of study, medical students should have appropriate knowledge of antimicrobials classification, rational drug combinations, and prevention of antimicrobial resistance development. Antibiotic resistance and antimicrobial stewardship issues are not covered sufficiently in the curricula of medical institutions, which results in the lack of proper understanding among future prescribers as for the significance of this problem (CDC 2014). The widespread practice of improper use of

antimicrobial agents and their combinations is one of the most threatening issues in Russia, as well as an overuse of parenteral route of administration and improper dosage regimens (Strachunskiy et al. 2007)

The increasing relevance of antimicrobial stewardship served as the basis for the study within the framework of KANT project started in 2014.

The **aim** of the study: to assess the senior Medical Care majors' knowledge in antimicrobial chemotherapy in medical institutions of Belgorod and Voronezh using the method of anonymous questioning.

Materials and methods

This article represents the results of a prospective survey of senior medical students, within the framework of the KANT multi-centered research project (the abbreviation of the project "The assessment of students' (physicians') knowledge in antimicrobials usage"), aimed at assessing the knowledge of rational antibacterial therapy. The survey was conducted in 2014–2018 at the Institute of Medicine of Belgorod State National Research University (BelsU) (Belgorod) and at Voronezh State Medical University named after N.N. Burdenko (Voronezh). Three hundred and nine Medical Care majors in their fifth and sixth years participated in the survey; 170 of them were from Belgorod and 139 – from Voronezh. All the students had completed Pharmacology and Clinical Pharmacology educational activities.

The method of anonymous questioning was used in this study, for which an original questionnaire had been developed on the basis of the current clinical guidelines (the questions can be found below in the "Results and discussion" section).

In the questionnaire, a respondent was to enter a year of studies and major, and then was required to answer several questions. The answers to four main issues of the survey were analyzed in this work (given without answer choices):

1. Determine the pharmacological group of the proposed antimicrobials;
2. Indicate pharmacologically irrational combinations of the proposed medications;
3. Specify the time for antimicrobial substitution when a positive therapeutic outcome is achieved;
4. Specify the time for antimicrobial substitution when a desired therapeutic outcome is not achieved.

The following score averages for each student were assessed: by question, by city and by the entire questionnaire. Since the question about determining an antimicrobial group (question No.1) required a mandatory written response, when none was provided, 0 points were assigned.

Since the question about pharmacologically irrational combinations (question No. 2) supposed a variety of possible answers, the following assessment system for a more detailed analysis was adopted. In case of an incomplete answer, the respondent was awarded 1 point for

each correctly chosen option, which corresponds to 33% of correct answers, and 1 point was deducted for each incorrectly selected drug combination, when a “difficult to answer” option was chosen, 0 points were assigned. Thus, in case of 100% correct answers, the maximum score was “3”, in case of selecting all the possible wrong options, the score was “minus 2”.

All the information collected through the questionnaires was entered to an electronic database and processed using Microsoft Excel applications. Statistical data were processed through the analysis of arbitrary contingency tables using the Pearson’s chi-square (χ^2) test.

It is necessary to emphasize that students majored in main therapeutic studies including Pharmacology and Clinical Pharmacology. The developed method of knowledge assessment is relative, and was specially created for this study, and cannot fully reflect the general level of education quality at university. It part, the primary and intermediate results of this study were presented in the article “Assessment of Senior Students’ Knowledge of Antimicrobial Chemotherapy Issues” (Bontsevich et al. 2016).

Results and discussion

In the first question of the questionnaire, the respondents were to classify the proposed antimicrobial agents according to pharmacological groups. The list of antibiotics was the following: amoxicillin/clavulanic acid, ceftriaxone, azithromycin, doxycycline, ciprofloxacin, levofloxacin.

The majority of students (53.6%) correctly identified all six pharmacological groups of drugs. The rest of the

students answered correctly the following number of questions out of six in such proportions: 15.3% – 5 answers; 11.8% – 4 answers, 6.8% – 3 answers, 4.7% – 2 answers, 3.4% – 1 answer, and 4.4% of the respondents did not give any correct answers ($p_{(Center1-2)} < 0.01$) (Fig. 1).

The best results were shown when determining the antibiotic of the cephalosporins group (91.3%) and protected aminopenicillins (84.9%). The group of macrolides was correctly identified by 77.3% of the students, fluoroquinolones of the 2nd and 3rd generation – by 76.9% and 73.2% of the respondents, respectively. The pharmacological group of tetracyclines was correctly specified by 69.6% of the students (Table 1).

A clinician should assess the quality of antimicrobial chemotherapy for a patient in dynamics as well as consider positive host responses in the form of improvement of the patient’s laboratory markers and his/her general well-being. In the second question of the questionnaire, a respondent was to specify the terms of an antibiotic substitution when a positive therapeutic outcome is achieved. Obviously, if there are adequate host responses to the antimicrobial therapy accompanied by the improvement of a patient’s general well-being, no antimicrobial substitution is required, of which only 69.3% of the students surveyed were aware. The difference between the centers totaled 25.9% ($p < 0.001$) (Fig. 2).

Treatment efficiency should be initially assessed within 48-72 hours after the start of the therapy, focusing on the dynamics of systemic inflammatory response syndrome and intoxication symptoms. Until that time, it is not recommended to change the initial empiric therapy (Eurasian Clinical Recommendations 2016). If the desired therapeutic outcome is not achieved or general well-

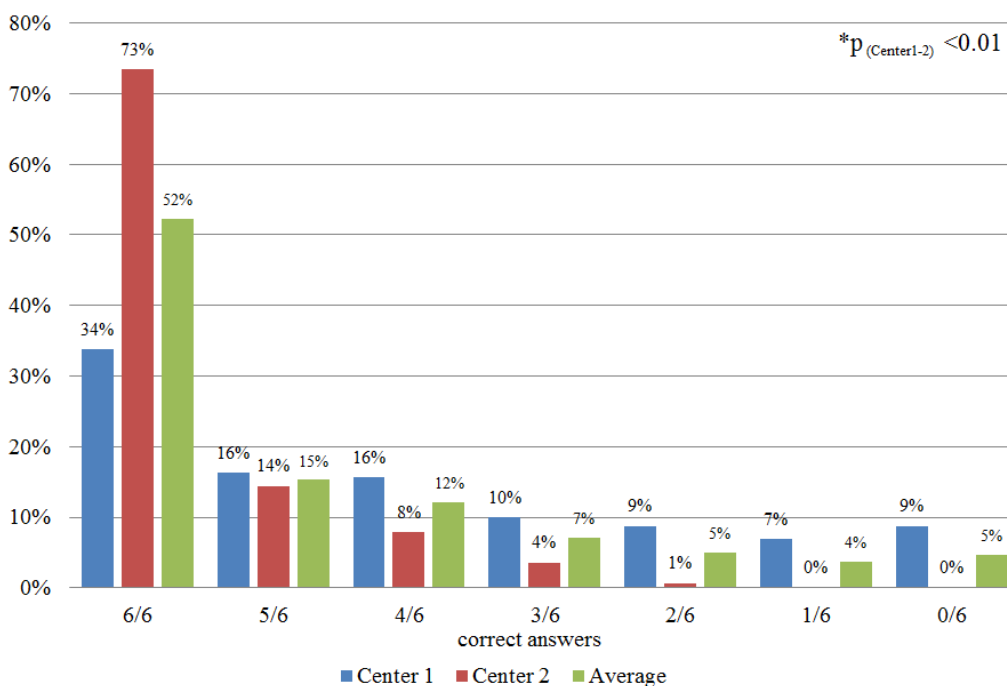


Figure 1. Distribution of correct answers to the question about pharmacological group of antimicrobials, %

Table 1. Distribution of Correct Answers by the Pharmacological Group of an Antimicrobial Agent

| Antimicrobial agent | Pharmacological group | Correct score averages, % | % Correct scores Center 1 | % Correct scores Center 2 |
|-------------------------------|--|---------------------------|---------------------------|---------------------------|
| amoxicillin / clavulanic acid | protected aminopenicillins | 84.9 | 73.6 | 97.8 |
| ceftriaxone | cephalosporins (3d gen) | 91.3 | 85 | 98.6 |
| azithromycin | macrolides | 77.3 | 66.3 | 89.9 |
| doxycycline | tetracyclines | 69.6 | 60 | 88.5 |
| ciprofloxacin | fluoroquinolones (2d gen) | 73.2 | 62.5 | 93.5 |
| levofloxacin | fluoroquinolones (3d gen), respiratory fluoroquinolones | 76.9 | 53.7 | 87.8 |

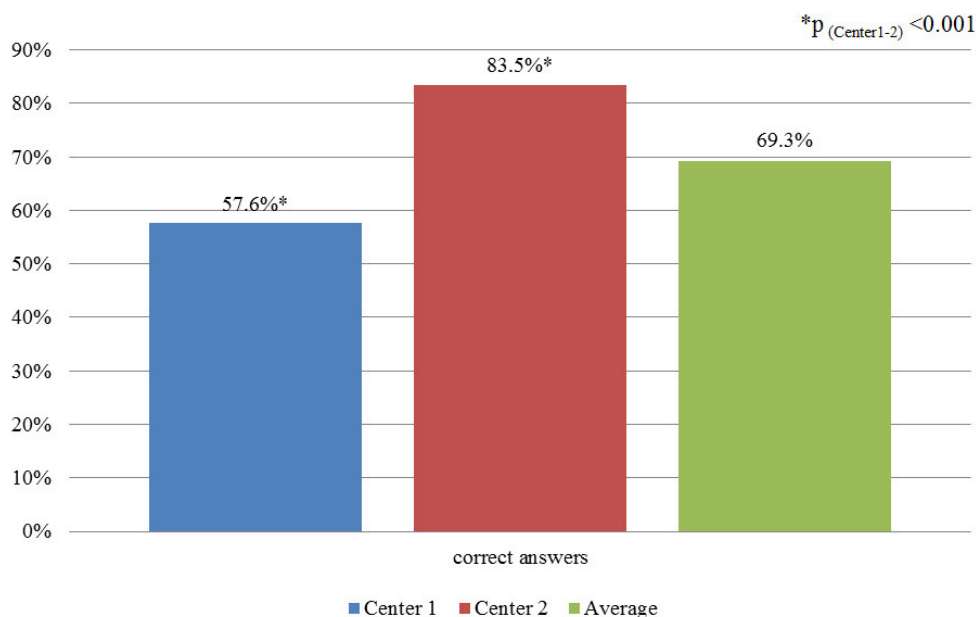
being is getting worse, antimicrobial substitution is required and should be made within 2-3 days after prescribing the medication. When there is no therapeutic outcome, an empiric treatment regimen has to be adjusted within 48-72 hours after the start of the therapy (Eurasian Clinical Recommendations 2016). The number of students who answered this question correctly totaled 79.3%, with the difference between the study sites being 13.8% ($p < 0.01$) (Fig. 3).

To date, antimicrobial resistance growth, cross-resistance and emergence of concurrent infections make a challenge for physicians when prescribing a rational antimicrobial therapy. At the same time, antimicrobials should not overlap in their mechanism of action and antibiotic coverage, enhance toxic effects, and should not be combined with incompatible medications prescribed to a patient. A synergistic action could be achieved by using drug combinations. On the other hand, it may cause adverse reactions in patients getting a concomitant pharmacotherapy. It should be noted that the bioavailability of oral medications may decrease due to the drug interactions (Strachunskiy et al. 2007).

The next question of the survey was aimed to assess the students' knowledge of rational drugs combinations. They were to specify pharmacologically irrational combinations of antimicrobials. The following drug combinations were offered to the respondents: ceftriaxone+amoxicillin; ofloxacin+doxycycline; levofloxacin+clarithromycin; ampicillin+gentamicin; and azithromycin+ampicillin+amikacin.

None of the students gave the correct answer (the first three options), which indicates the respondents' poor awareness of rational drug combinations.

Summarizing the results of all correctly and incorrectly chosen options, the largest number of students (124 people, 40.1%) scored 0% (0 points), with the difference between the sites being 17%. The majority of the respondents gave an incomplete correct answer: 43 students scored 2 points (67% of the correct answers), which was 13.9% of the total number of the respondents. Eighty-five students (27.5% of the respondents) scored 1 point (33% of the correct answers). Forty-eight majors (15.5%) scored "minus 33%" (-1 point) and 9 students (2.9%) gained "minus 66%" (-2 points) ($p < 0.001$) (Fig. 4).

**Figure 2.** Distribution of correct answers concerning the necessity and terms of antimicrobial substitution when a positive therapeutic outcome is achieved, %

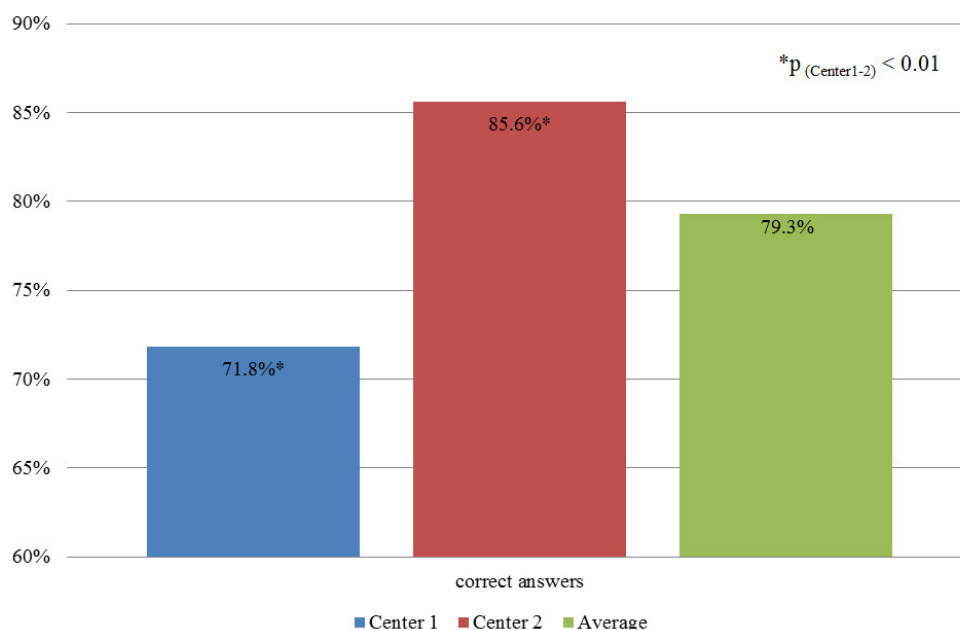


Figure 3. Distribution of answers to the question about the necessity and terms of antimicrobial substitution when a desired therapeutic outcome is not achieved, %

The best result was recorded when choosing the irrational combination “ceftriaxone+amoxicillin” (38.5% of correct answers, the difference between the centers is 16.3%), the options “ofloxacin+doxycycline” and “levofloxacin+clarithromycin” were correctly chosen by 21% and 18.1% of the respondents, respectively (Table 2).

Almost a third of the respondents (30.7%, the difference between the centers is 1.6%) considered the rational combination of “azithromycin+ampicillin+amikacin” as “irrational”. The rational combination of “ampicillin+gentamicin” was chosen as incorrect by 12.9% of the respondents (Table 3).

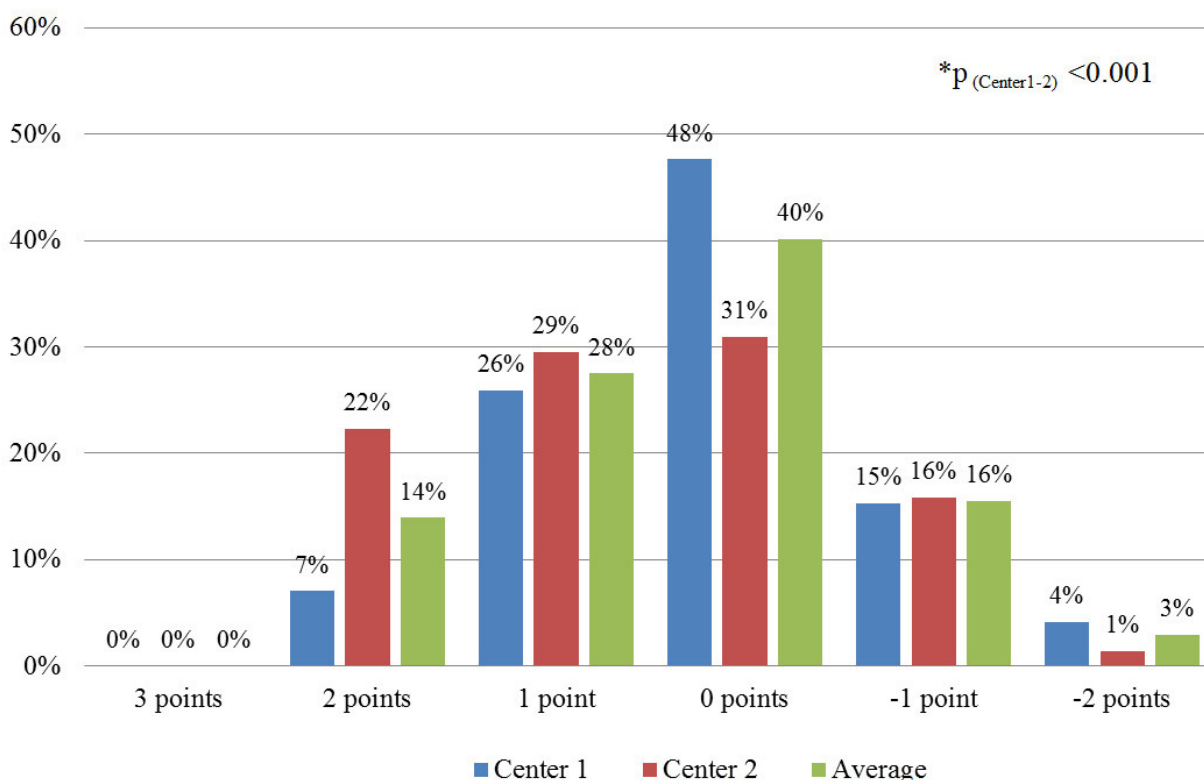


Figure 4. Distribution of students by knowledge scores when answering about rational drug combinations, %

Table 2. The Correct Answers to the Question of Irrational Drug Combinations, %.

| Irrational drug combinations | Students majoring in Medical Care (n=309) – average | Center 1 | Center 2 |
|------------------------------|--|----------|----------|
| Ceftriaxone+amoxicillin | 38.5 | 31.2 | 47.5 |
| Ofloxacin+doxycycline | 21.0 | 15.3 | 28.1 |
| Levofloxacin+clarithromycin | 18.1 | 17.1 | 19.4 |

Table 3. Wrong Answers to the Question of Irrational Drug Combinations, %

| Drug combinations | Students majoring in Medical Care (n=309) – average | Center 1 | Center 2 |
|----------------------------------|--|----------|----------|
| Ampicillin+gentamicin | 12.9 | 17.1 | 7.9 |
| Azithromycin+ampicillin+amikacin | 30.7 | 30 | 31.6 |

Conclusions

This survey of the fifth- and sixth-year Medical Care majors showed a low level of preparedness in antimicrobial stewardship. More than a half of the graduates gave wrong (or not completely correct) answers to the fundamental questions. The most difficult question was about the choice of pharmacologically rational and irrational combinations of drugs: none of the students gave a completely correct answer, 13,9% of the respondents scored 2/3 of the correct answers.

According to the authors, to date, rational antimicrobial use is not sufficiently covered in the curricula of higher medical schools in Russia, which undermines the level of future prescribers' knowledge. One of the possible reasons for the irrational tactics of infectious diseases treatment is the low level of doctors' preparedness, including insufficient knowledge of either the etiological structure of infections or the fundamentals of clinical pharmacology of antibiotics (Strachunskiy et al. 2007).

This study gives an opportunity to identify strengths and weaknesses and draw attention to those points that cause maximum difficulties. The survey showed that the growing problem of antimicrobial resistance should be addressed by an increase in the number of practical class hours for training future doctors in the principles and practices of appropriate use of antibiotics and antimicrobial stewardship.

Conflict of interests

The authors have no conflict of interest to declare. The study was conducted without the participation of sponsors.

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