Research Article

Pharmacotherapy and other aspects of senior medical students' knowledge in community-acquired pneumonia: the final results of the KNOCAP II project

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Academic editor: Mikhail Korokin • Received 8 January 2020 • Accepted 24 February 2020 • Published 31 March 2020

Citation: Bontsevich RA, Gavrilova AA, Adonina AV, Vovk YR, Goncharova NY, Batisheva GA, Cherenkova OV, Myronenko OV, Luchinina EV, Barysheva VO, Ketova GG, Bochanova EN, Tilekeeva UM, Dauletbekov ND (2020) Pharmacotherapy and other aspects of senior medical students' knowledge in community-acquired pneumonia: the final results of the KNOCAP II project. Research Results in Pharmacology 6(1): 93–99. https://doi.org/10.3897/rrpharmacology.6.49977

Abstract

Introduction: Community-acquired pneumonia (CAP) remains an extensive medical and social problem. It is the most common human disease and one of the leading causes of death from infectious diseases. Increasing the level of senior medical students' knowledge of the diagnosis, treatment and prevention of CAP will improve the level of medical care to the population.

The aim of the study: to determine the level of senior medical students' basic knowledge of CAP prevention, diagnosis and treatment with the help of a pharmacoepidemiological study.

Materials and methods: The multicenter study "KNOCAP" (the full name of the project "The Assessment of Physicians' and Students' Knowledge of Community-acquired Pneumonia Basics") presents the results of an anonymous prospective survey aimed at assessing the knowledge and preferences of senior medical students in terms of the CAP pharmacotherapy. In the second stage of the project (2017–2019). The results from 394 senior students from 8 centers of Russia, Ukraine and Kyrgyzstan were received and analyzed. An original questionnaire was developed for this study on the basis of the current clinical guidelines.

Conclusion: The final results of a prospective survey revealed an insufficient level of students' basic knowledge of diagnosis, treatment and prevention of CAP. The study revealed a statistically significant heterogeneity of knowledge levels in different centers, which indicates the need for the introduction of unified and in-depth training programs in this area.

Keywords

survey, community-acquired pneumonia, clinical recommendations, knowledge level, pharmacotherapy, pharmacoepidemiology.

Introduction

Community-acquired pneumonia (CAP) is an acute disease that occurs under community-acquired conditions and is accompanied by the symptoms of a lower respiratory tract infection (fever, cough, sputum production, chest pain, labored breathing) and radiological signs of focal-infiltrative changes in the lungs in the absence of obvious diagnostic alternative (Chuchalin et al. 2010). Currently, the mortality rate from the above pathology remains high, despite a large number of research articles on the treatment of this disease and success in this area, which is associated with the developed pharmacotherapy schemes for CAP. Due to the prevalence of this disease throughout the world and the social and economic importance of CAP, the pharmacoepidemiological studies among senior students are especially relevant in order to further optimize their knowledge and, as a result, improve the implementation of clinical guidelines.

Materials and methods

The multicenter KNOCAP study (the full name of the project is "The Assessment of Physician' and Students' Knowledge of Community-acquired Pneumonia Basics") presents the results of an anonymous prospective survey on the assessment of senior medical students' knowledge in matters of the diagnosis, treatment, prevention of CAP and also their accordance with the modern clinical guidelines (Bontsevich et al. 2015, 2017; Russian Respiratory Society 2018). According to the outcomes of the second stage of this study (2017–2019), the results of a survey of 394 senior medical students from 8 centers of Russia, Ukraine and Kyrgyzstan were obtained and analyzed.

An original questionnaire was developed for this study. It consisted of multiple choice questions and openend questions. This questionnaire is based on the current clinical guidelines for managing patients with CAP (Chuchalin et al. 2010). The following point system was used to calculate the results of the survey: the respondent received 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 points; for the correct 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 skippings were allowed. No answer to open-end questions rendered 0 points. The main questions of the questionnaire are presented below (without answers):

- 1. Indicate the main pathogen(s) of CAP.
- 2. Choose the most effective way to prevent CAP.
- 3. Indicate the main diagnostic sign of CAP when examining a patient.
- 4. Determine the diagnostic minimum of a mild form of CAP.
- Choose criteria without which the diagnosis of CAP cannot be confirmed
- Indicate the rational time for a repeated X-ray examination with positive dynamics in the treatment of CAP.
- 7. Indicate possible reasons for delaying an antimicrobial therapy (AMT).
- 8. Choose a key criterion for terminating AMT.
- 9. Indicate the correct definition of the "sequential therapy" in the management of patients with CAP.
- 10. Indicate typical mistakes in the initial AMT for a non-severe CAP.
- Write a drug/treatment regimen for a mild form of CAP without risk factors and/or concomitant diseases, indicating the dosage, frequency and mode of administration.
- Write a drug/treatment regimen for a mild form of CAP with risk factors and/or concomitant diseases, indicating the dosage, frequency and mode of administration.

All the information of the questionnaire was entered into an electronic database and processed using the application programs of Microsoft Excel and Statistica 10. Statistical processing showed that the analyzed distribution of data from the sample of the senior medical students was expectedly normal: Kolmogorov-Smirnov test d=0.04982, p>0.20; Lilliefors test p<0.05. The statistical significance of the differences when comparing these samples were recorded at a bilateral level of p<0.05 based on the analysis of arbitrary contingency tables, using the Pearson's chi-square (×2) test.

The centers from the Ukraine (Dnipro and Kiev) were combined to correctly calculate the statistical significance.

This method of knowledge evaluation was specially developed for the KNOCAP project and cannot fully reflect the general level of education quality at universities.

Results and discussion

The survey involved 394 senior medical students (23.6% from Belgorod, 7.6% from Bishkek, 29.0% from Voronezh, 10.5% from the Dnipro and Kiev (the united center of the Ukraine), 5.3% – from Krasnoyarsk, 6.8% – from Saratov and 1.2% – from Chelyabinsk). The average completeness rate for all the questionnaires was 43.7%, from 33.1% to 51.9% for different centers (p<0.05). The minimum level of correct answers was received to questions No.6 (time for a repeated X-ray examination) – 24.4% (from 10.0 to 40.0% among centers, p<0.01), No.10 (typical mistakes in the initial AMT) – less than 1% (from 19.0 to 40.0%, p<0.01), No.12 (treatment regimen for patients with risk factors and/ or concomitant diseases) -6% (from 0 to 25.0%, p<0.01). The maximum average level of correct answers was received to questions No.2 (the most effective way to prevent CAP) – 63.7% (from 31.0 to 90.0%, p<0.01), No.7 (the reasons for delaying an AMT) -63.2% (from 52.0 to 79.0%, p > 0.05), and No.9 ("sequential therapy" of CAP) -61.6%(from 48.0 to 90.0%, p<0.01). The major results are presented in Fig. 1. A detailed analysis with comments on each question of the questionnaire is presented below.

At the beginning of the questionnaire, the students had to choose the preferred regulatory documents when managing patients with CAP. The following answers were offered: "order", "standard", "guidelines", "treatment based on own experience", "neither agree nor disagree" and "other", where the respondents could provide their own answer option. The majority of the respondents preferred to use a standard as a regulatory document (25.0%), 19.5% choose 2 or more regulatory documents for the treatment of CAP, the order was chosen by 10.5% of the respondents, 4.6% choose the category "other", 27.0% preferred guidelines, and 13.4% of senior students found it difficult to answer. The answer "treatment based on own experience" was not chosen by any of the respondents, which may be due to the lack of experience in practical healthcare among the respondents. It is important to note that there is no correct answer to this question; therefore it was possible to assess the level of senior students' awareness of the use of the regulatory framework only indirectly.

In the first question, potential pathogens of CAP were presented – staphylococcus (including *S. aureus* and others); streptococcus – *S. pyogenes* π *S. haemoliticus*; *S. pneumoniae*; *Enterobacteriaceae*; *Haemophilus influenza*; viruses, fungi; and atypical microorganisms. The students had to choose one or more pathogens, which, in their opinion, are the most common pathogens of CAP or write their own version. According to the current clinical guidelines (Russian Respiratory Society 2018; Bontsevich et al. 2019b), the most common causative agent of CAP is *S. pneumoniae*, this answer was the only true one. The correct answer was given by 33.5% of the respondents, 47.7% answered partially correctly, indicating several pathogens along with *S. pneumonia*, 18.8% answered incorrectly. ARC among the centers was from 48.0 to 68.0%, p<0.01.

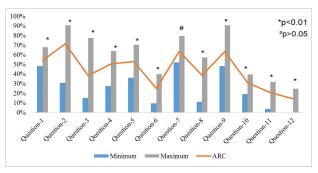


Figure 1. The minimum, maximum and average levels of response completeness of knowledge in CAP among the centers. Note: ARC – average response completeness rate.

Today the most effective way to prevent CAP is pneumococcal and influenza vaccines (Chuchalin et al. 2010; McLaughlin et al. 2018; Russian Respiratory Society 2018). The second question of the questionnaire suggested choosing the highly efficient methods of CAP prevention from the proposed options: cold water treatment, homeopathic and immunomodulatory therapy, vaccination with pneumococcal and influenza vaccines. The majority of the respondents (63.7%) chose the correct answer, indicating vaccinal prevention, 16.6% answered partially correctly, and 19.7% of the respondents did not complete the task. ARC was from 31.0 to 90.0% at different centers (p<0.01).

In the third question, the students had to indicate the main diagnostic sign of CAP when examining a patient. Classic objective symptoms are: dullness of percussion sound over the affected areas of the lung, bronchial breathing, rhonchi crackles, or crepitation, increased bronchophony and vocal trembling. All of these clinical manifestations are the main components of the syndrome of pulmonary consolidation. One-third (32.1%) of the students chose the correct answer, 14.8% gave a partially correct answer, and 53.2% answered incorrectly. ARC among the centers was from 15.0 to 77.0%, p<0.01.

In the fourth question of the questionnaire, the students were asked to determine the diagnostic minimum of a mild form of CAP. The following answer options were suggested:

- Single-plane radiography;
- Biplane radiography;
- Biochemical blood assay;
- Complete blood count;
- · Clinical analysis of sputum;
- Microbiological analysis of sputum.

The correct answer (biplane radiography, complete blood count) was given by 10.2% of the respondents, partially correct answers – by 73.9%, and 15.9% of the students answered incorrectly. ARC among the centers was from 28.0 to 64.0% (p<0.01).

It must be remembered that the diagnosis of CAP is determined if the patient has an X-ray confirmation of focal lung infiltration and at least two clinical signs from

among the following: acute fever at the onset of the disease (t° > 38.0 °C), wet cough, physical symptoms (rhonchi crackles or crepitation, bronchial breathing, dullness of percussion sound), leukocytosis >10*10°/L and/or shift to the stab neutrophils (>10.0%) (Chuchalin et al. 2010; Russian Respiratory Society 2018).

In the next question, the respondents had to choose the criteria without which the diagnosis of CAP could not be confirmed. Fewer than half of the respondents (42.9%) chose the correct answer, indicating the absence of X-ray confirmation of focal lung infiltration as the main reason of problems with CAP diagnosing, 21.1% of the respondents answered partially correct, 36.0% of the students gave the wrong answer. ARC was from 36.0 to 70.0% at the different centers, p<0.01.

The sixth question of the questionnaire asked the respondents to indicate the rational time for repeated X-ray examination with positive dynamics in the treatment of CAP. Only 24.4% of the students answered the question correctly, choosing "at least 14 days later", 1.0% answered partially correctly, and 74.6% did not complete the task. ARC in the centers was from 10.0 to 40.0% (p<0.01).

In the seventh question, the students were asked to choose the possible reasons for delaying an antimicrobial therapy (AMT). The majority (62.3%) of the respondents coped with this task, indicating that there were no reasons for the delay of AMT with a confirmed diagnosis of CAP, 35.4% gave an incorrect answer, and 2.3% gave an incomplete answer. ARC in the different centers was from 52.0 to 79.0%, p> 0.05.

The leading indication for terminating AMT for a non-severe CAP is a stable normalization of body temperature over a period of 48–72 hours, combined with both a positive clinical picture and the absence of signs of clinical instability (Pertseva and Sanina 2013; Rachina et al. 2016; Sinopalnikov 2018,2019). This question was answered correctly by 33.2% of students, 12.0% of the respondents answered partially correctly, and 54.7% answered incorrectly. ARC among the centers was from 11.0 to 57.0%, p<0.01.

The ninth question of the questionnaire concerned the "sequential therapy" for CAP. This type of AMT involves the consistent administration of two dosage forms (for parenteral and oral administration) of the same antibacterial drug. The best option for this type of AMT is a two-stage administration of antimicrobial drugs: first, the use of parenteral form and then the transition to the oral administration right after the stabilization of the patient's condition, normalization of the body temperature and the improvement of the CAP clinical picture (Pertseva and Avramenko 2017; Spichak 2019). The correct answer was given by 61.6% of the respondents, 3.3% answered partially correctly, and 35.1% did not cope with the question. ARC among the centers was from 48.0 to 90.0%, p<0.01.

In the next question, the students had to indicate typical mistakes in the initial AMT for a non-severe CAP. The following answers were proposed: the use of ampicillin/oxacillin (Ampiox); the use of ciprofloxacin; the use of

cefazolin; the use of ampicillin per os; the use of respiratory fluoroquinolones in patients without risk factors and a "not sure" option. According to the clinical guidelines (Chuchalin et al. 2010), all the options referred to an erroneous strategy in managing non-severe CAP patients: the use of ampicillin per os is accompanied by low bioavailability (40.0%) in comparison with amoxicillin (75-93.0%); cefazolin has a low activity against pneumococci, as well as the absence of clinically significant activity against H. influenzae; ciprofloxacin is low-active against S. pneumoniae and M. pneumonia; it is inappropriate to prescribe respiratory fluoroquinolones as drugs to patients without risk factors; ampicillin/oxacillin (Ampiox) should not be used in medical practice because of an irrational combination of antibiotics (Çilli et al. 2018; Cillóniz et al. 2018). The majority of students gave an incomplete correct answer – 90.5%, fewer than 1.0% of the respondents were able to give the correct answer, and 9.3% of the respondents gave a wrong answer. ARC among the centers was from 19.0 to 40.0%, p<0.01.

The next two questions required a "written" answer from each student. In the first question, it was necessary to indicate the optimal starting therapy for a non-severe CAP in patients without risk factors and/or concomitant diseases (diabetes, chronic renal insufficiency, congestive heart failure, COPD, chronic alcoholism, cachexy, drug addiction, liver cirrhosis) and/or in patients who had been taking systemic antimicrobial drugs (AMD) in the previous 3 months for more than 2 days. In this case, according to the clinical guidelines, the drugs of choice are amoxicillin or macrolides. Despite the fact that in vitro aminopenicillins do not cover the full range of potential pathogens, clinical trials did not reveal differences in the effectiveness of these antibiotics in comparison with macrolides and respiratory fluoroquinolones (McLaughlin et al. 2018; Wicha et al. 2019). Macrolides should be preferred if it is impossible to use aminopenicillins (idiosyncrasy, allergy), and also with a suspected "atypical" etiology of the disease (S. pneumoniae and M. pneumoniae) (Breitling et al. 2018; Lee et al. 2018). It is worth noting that parenteral forms of drugs during out-patient treatment do not have proven advantages over oral ones, at the same time, they pose a threat to the development of post-injection complications in the form of abscesses and require additional costs for administration (Chuchalin et al. 2010; Bontsevich et al. 2019a). Only 9.1% of the senior students answered this question correctly, 27.2% of the students answered partially correctly, and 63.7% gave the wrong answer. ARC among the centers was from 4.0 to 32.0%, p<0.01.

The next question required to indicate the optimal starting therapy for a non-severe CAP in patients with risk factors and/or concomitant diseases (diabetes, chronic renal insufficiency, congestive heart failure, COPD, chronic alcoholism, cachexy, drug addiction, liver cirrhosis) and/or in patients who had been taking systemic antimicrobial drugs (AMD) in the previous 3 months for more than 2 days. It is recommended to prescribe tableted forms of

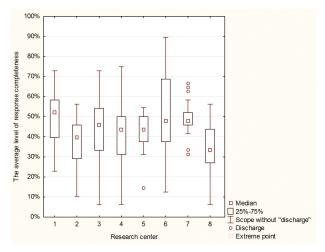


Figure 2. Variability of ARC for the studied centers.

AMD to such patients, but the therapy strategy in these patients is different, because the probability of the etiological role of gram-negative flora increases (Ewig et al. 2009; Sligl et al. 2014). Combined AMD is recommended as a starting therapy: amoxicillin + clavulanic acid. If there is a risk factor of "atypical" microflora, a combination of β -lactam and macrolide may be prescribed. An alternative to the combined therapy is the administration of respiratory fluoroquinolones (levofloxacin, moxifloxacin, gemifloxacin) or oral cephalosporins (cefditoren) (Chuchalin et al. 2010; Russian Respiratory Society 2018).

Fewer than half of the students answered partially correctly -21.6%, 72.4% gave the wrong answer and only 6.0% of the respondents gave a correct answer. ARC among the centers was from 0% to 25.0% (p<0.01).

In conclusion of the study, the variability of the ARC range was analyzed among the centers which participated in the study. The maximum value of ARC was 51.9%, and it was registered in center No. 6, whereas the minimum value of ARC -33.1% was registered in center No. 8. These results are presented in Fig. 2.

Summarizing this study, in order to optimize pharmacotherapy and other aspects of senior students' knowledge in community-acquired pneumonia, the following algorithms for mastering the material to form the professional competence of future doctors should be considered:

- acquiring basic scientific, theoretical and practical knowledge to solve theoretical and practical problems:
- mastering the technology of pharmacoepidemiological research;
- improving professional skills throughout professional career;
- · learning to work independently;
- having skills associated with the use of modern information on clinical guidelines and treatment standards for community-acquired pneumonia;
- · using a computer;
- · having research skills.

Conclusions

A survey of the senior medical students within the framework of the KNOCAP multicenter study showed that there are significant gaps in knowledge of the correct management of patients with CAP. The greatest difficulties for students were caused by open-end questions, which involved determining the starting AMT in the treatment of a non-severe CAP in patients with or without risk factors and concomitant diseases, the question of determining the "typical mistakes" in the initial AMT for a non-severe CAP, as well as the question that suggested setting the rational time for a repeated X-ray examination with positive dynamics in the treatment of CAP.

Therefore there is a need for educational activities among senior students: additional seminars, lectures, development of educational materials for self-training in clinical pharmacology. And the therapeutic disciplines should comply with current regulatory documents developed for the diagnosis and treatment of various nosological forms, and an increasing number of academic hours will help to solve the problem of insufficient awareness of future doctors of basic issues of managing patients with CAP.

Conflict of interest

The authors have no conflict of interest to declare.

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