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Original Article

Management of Chronic Obstructive Pulmonary Disease

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Abstract

The relevance of the study of chronic obstructive pulmonary disease (COPD) can be explained by the persistence of unfavorable dynamics of the disease, even despite the achieved success in the pharmacotherapy of this pathology. In 2016, World Health Organization (WHO) ranked COPD as the third leading cause of death worldwide, far exceeding the experts' predictions, who believed that such an increase in the death rate would occur by 2030. This study aimed to determine the level of senior medical students' knowledge in the management of patients with COPD, based on the method of anonymous questioning. This research work describes the results of the second stage of the ASCO project (Assessment of Senior Medical Students in the Field of COPD) conducted in 2017-2019 among 338 senior medical students from six large cities of Russia and Ukraine. The survey revealed the average level of knowledge among senior medical students, based on the average level of correct answers (56.6%) obtained in the study. The best results were obtained for the questions about COPD risk factors, influenza vaccine prevention, and pneumococcal vaccine prevention in COPD patients. The worst results were recorded on the questions about the severity of COPD clinical symptoms, the choice of initial therapy for COPD with advanced symptoms, a high risk of exacerbations, and the moderate exacerbation of COPD. The obtained results indicated an insufficient level of students' basic knowledge in questions regarding etiopathogenesis, diagnosis, treatment, and prevention of COPD.

Keywords: Chronic obstructive Pulmonary disease, Level of knowledge, Pharmacoepidemiology, Questioning, Students

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease caused by the inhalation of harmful chemicals, mainly observed among people who smoke (1). These chemicals cause inflammation and damage to the lungs and increase mucus production in the lungs (2). This condition can lead to periods of shortness of breath and coughing called exacerbations of the disease. Exacerbation of pulmonary seizures makes it difficult for sufferers to perform daily tasks (3), and the severity of pulmonary attacks becomes more and more intensified over time. The severity of COPD varies in different people which may be related to differences in response to medication, as well as physical fitness and comorbidities (4). For most people, the only way to prevent further lung damage is to quit smoking (5). Moreover, COPD is a chronic disease associated with limited airflow in the airways (6). This disease is not completely reversible (7).

As a most common type of chronic disease, COPD is a major health problem and a major cause of disability in people (8). It presents as bronchitis and emphysema which are two chronic diseases (9). The prevalence of the disease, according to 2008 US statistics, was 13.5 million, or 1 in 20 people, of whom 12.1 million had chronic bronchitis and 2.3 million had emphysema (10). Based on the prediction of the World Chronic Pulmonary Respiratory Disease Plan, the disease would be the 6th most common cause of death in the world by 2020 (11).

Due to the progressive and chronic course of lung dysfunction and exacerbation of respiratory symptoms, COPD patients experience a gradual decline in health status and disruption of social life, physical function, and daily activities over the years (12). As a result, patients experience a reduction or loss of social roles and a variety of psychological problems, such as fear, anxiety, depression, isolation, and dependence on others, which ultimately lead to a reduction in quality of life, especially the health-related quality of life (13, 14).

According to some studies, the most common symptoms of this disease include lack of energy, dry mouth, fatigue, and feeling angry (15). Symptomatic seizures in these patients are associated with increased adoption of health care, progressive decline in lung function, increased hospitalization, and even death (15, 16). Recent studies have shown that the improvement of the quality of treatment can reduce mortality from chronic diseases (17, 18).

To date, the most important reasons for an increase in the incidence of COPD include social factors, such as the annual increase in the number of smokers, uncontrolled promotion of tobacco products by the media, and the lack of real preventive measures at the state level. According to the statistics, in 2019, more than 380 million people in the world had a confirmed diagnosis of COPD, and more than 3 million patients annually die from this pathology (19, 20), which is very alarming. The prognosis of the disease has also remained unfavorable. By 2030, despite the estimated global spread of HIV/AIDS, COPD will be the main cause of death among 7.8% of patients and the third after cancer (33%) and cardiovascular diseases (29%), the mortality from which is associated with smoking (27%) (21, 22).

Since COPD is one of the leading causes of death worldwide, it is important to prevent and detect this pathology in time and control its development. This study aimed to determine the level of senior medical students' basic knowledge in the management of patients with COPD using the method of anonymous questioning.

2. Materials and Methods

The survey was carried out as part of the Assessment of Senior Medical Students in the Field of COPD (ASCO) project beginning in 2015. The second stage of this project (ASCO-II) was launched in 2017 at Belgorod State National Research University, Belgorod, Russia; Voronezh State Medical University, Voronezh, Russia (named after N.N. Burdenko); Kuban State Medical University, Krasnodar, Russia; Saratov State Medical University, Saratov, Russia (named after V.I. Razumovsky); South Ural State Medical University, Chelyabinsk, Russia; and Dnepropetrovsk State Medical Academy, Dnipro, Dnipropetrovsk Oblast, Ukraine.

The study is based on the use of the method of anonymous questioning, for which an original questionnaire was developed based on the main provisions of the current clinical guidelines (23). The students were asked to indicate their course and specialty without revealing personal information. The anonymity of the project provides more reliable results. It should be noted that this method of knowledge evaluation is relative and was developed especially for this study; therefore, it cannot fully reflect the level of education quality of the respondents.

This questionnaire included 19 multiple-choice questions to assess the basic knowledge of senior students on etiology, pathogenesis, diagnosis, treatment and prevention of COPD. The respondents had to

choose only one correct answer from the proposed options. Each correct answer was scored 1, incomplete answers (the correct answer with the wrong answer) were scored 0.2, 0.33, or 0.5 points (depending on the number of erroneous answers), and incorrect answers were scored 0. Therefore, with all correct answers, the total score of the questionnaire would be 19.

The average values of each respondent, the average value of individual questions, the average value of the centers (cities), and the entire questionnaire were estimated in this study. The average value of correct, partially correct, and incorrect answers were characterized as the average level of response completeness (ARC), representing the average level of correct answers.

2.1. Ethical Considerations

This study is a continuation of the first stage of the "ASCO" project, the final results of which were published in the journal "Farmateca" No. 8 (2018). Partial current results of the ASCO-II project (2017-2018) were presented at the Congress of the European Respiratory Society (Madrid, 2019) and published in the supplement to the "European Respiratory Journal" and in the journal "Research Results in Pharmacology" (24, 25).

2.2. Statistical Analysis

All questionnaire information was entered, analyzed, and processed using application programs Microsoft Excel and SPSS software (Version 26). The normal distribution of variables was assessed using a nonparametric Kruskal-Wallis test. In addition, the analysis of nominal variables was carried out using arbitrary contingency tables using the Pearson's chi-square ($\chi 2$) test. Fisher's exact test was calculated in cases where the expected number of observations was less than 5 in more than 20% of the cells of multi-field tables. The Cramer's V was used to assess the strength of the association between the categorical variables (26). A p-value less than 0.05 ($P<0.05$) was considered statistically significant.

Considering the conditions and restrictions on the use of arbitrary contingency tables, the centers with a small number of respondents (Dnipro, Saratov, and Krasnodar) were considered statistically insignificant ($P<0.05$) and combined for the correct calculation of the statistical significance.

3. Results

The survey included 338 senior students from six cities of Russia and Ukraine (40.9% from Belgorod, 22.2% from Voronezh, 20.1% from Chelyabinsk, 16.8% from the joint center (Dnipro, Saratov, Krasnodar). At the time of the study, all the respondents were trained in standard educational programs, including courses in pulmonology and clinical pharmacology.

The average level of correct answers to all questions of the questionnaire was 56.6% (between 52.9% and 63.3% for different centers). At the same time, the differences in answers to individual questions ranged from 10.0% to 85.6% on average throughout the study, and from 2.2% to 95.6% for various questions in different centers.

The minimum level of correct answers received for questions No. 8 (criteria for severe symptoms of COPD), No. 12 (drugs for initial therapy of COPD with advanced symptoms and a high risk of exacerbations), and No. 9 (respondents' attitude to influenza vaccination as an effective measure to reduce mortality in COPD) was 10.0% (2.2% -21.6% in different centers, $P<0.001$), 19.4% (15.2%-23.3%, in different centers, $P=0.782$), and - 22.9% (16.4%-27.0%, $P=0.083$), respectively.

The maximum level of correct answers registered for questions No. 2 (risk factors for COPD), No. 19 (positive attitude to vaccine prevention of pneumococcal infection in patients with COPD), and No. 18 (approval of seasonal influenza vaccine prevention in patients with COPD) were 85.6% (ARC: 67.0%- 95.6%, $P<0.001$), 83.5% (ARC: 65.9-93.2% in

different centers, *P*<0.001), and 83.4% (ARC: 71.0%-89.8%, *P*=0.017), respectively.

The summary data on the levels of correct answers to all questions of the questionnaire are presented in figures 1 and 2.

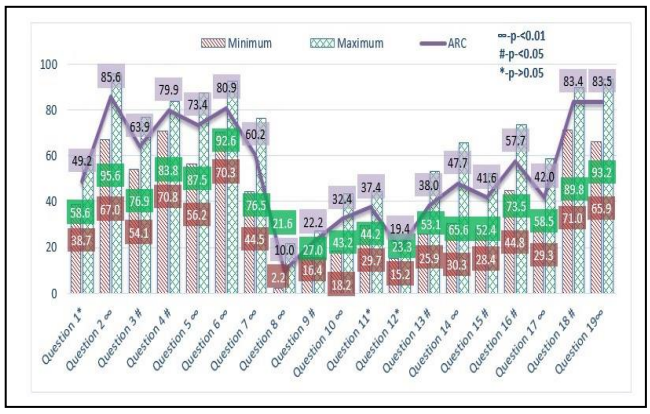

Figure 1. Maximum, average, and minimum levels of complete answers to individual items of the questionnaire in different centers (%)

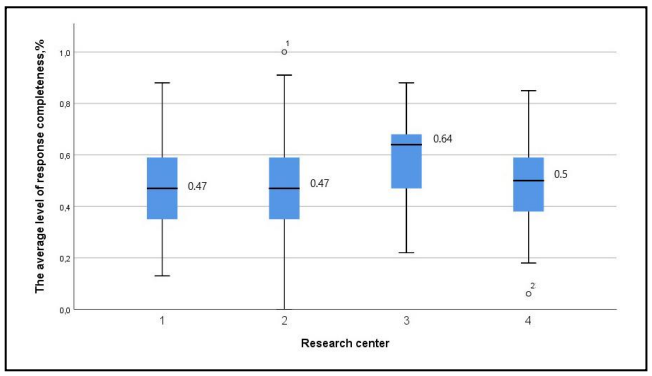

Figure 2. Average levels of complete answers to all items of the questionnaire in the centers

Considering the selection of the option "all of the above", which includes all the above risk factors, 85.6% of students gave the right answer (ARC: 67.0-95.6% in different cities, *P*<0.001; Cramer's V=0.244).

Of all the proposed pathogenetic associations in the third item of the questionnaire, 63.9% of the surveyed students chose the correct answer (inflammation of the airways and destruction of lung parenchyma) (ARC: 4.1% -76.9% in different centers, *P*=0.021; Cramer's V=0.125).

This question was answered correctly by 79.9% of the respondents (ARC: 70.8- 83.8% in the centers, *P*=0.077, Cramer's V=0.146).

In item 6, students had to choose the main method for the diagnosis of COPD from the proposed options (i.e., bronchoscopy, bronchography, spirometry, chest X-ray, and computer tomography). In total, 60.2% of the respondents correctly indicated the severity of bronchial obstruction in COPD (ARC: 44.5% -76.5% in different centers, *P*<0.001; Cramer's V=0.207).

The correct answer (i.e., CAT≥10, mMRC≥2) was chosen by 10.0% of senior students, indicating a low level of respondents' awareness about these scales for assessing symptoms and severity of a disease. Preference was given to various non-specific instrumental and laboratory markers (ARC: 2.2%-21.6%, *P*<0.001; Cramer's V=0.19).

In item 9 of the questionnaire, it was necessary to select an appropriate statement regarding the improvement of treatment or control options for COPD. Only 22.2% of respondents coped with the task (ARC: 16.4% -27.0% in different centers, *P*=0.011; Cramer's V= 0.162).

In item 11, the students were asked to select an inhalation device for a patient with poor coordination and low inspiratory rate (> 30 L/min). The optimal device for such patients is a nebulizer or a Respimat inhaler, and only 37.4% of the respondents knew about it (ARC: 29.7-44.2% among centers, *P*=0.267, Cramer's V= 0.111).

Items 12 and 13 questioned the selection of drug therapy considering the severity of symptoms and the risk of exacerbations. It should be noted that in the newest GOLD guidelines for some patients in group D (with fewer symptoms, CAT<20), it is possible to start monotherapy with LAMA. Only 19.4% of students were able to select the proper dose of medicine (ARC: 15.2%- 23.3% in different centers, *P*=0.828; Cramer's V= 0.08).

In item 19, the respondents were asked to choose medicines for basic therapy in a patient with advanced

symptoms of COPD and a low risk of exacerbation.

In item14 of the questionnaire, students had to choose a clinical group (type) of COPD with FEV1=60%, one exacerbation per year, mMRC-1, and CAT-9. The correct answer to this item (i.e., group /type A) was chosen by 47.7% of the respondents (ARC: 30.3-65.6%, $P<0.001$, Cramer's V=0.228).

In item 15 of the questionnaire, students had to choose a drug for moderate exacerbation of COPD. The correct combination (short-acting β2 -agonist + antimicrobial drug and/or systemic GCS) was chosen by 41.6% of the respondents (ARC: 28.4-52.4%, $P=0.014$, Cramer's V=0.172).

After analyzing the students' responses to this question, the authors concluded that the majority (58.9%) of responses presented erroneous judgments about the treatment of moderate exacerbation of COPD (ARC: 40.1%-70.6% in different centers). According to the analysis of erroneous answers, 39.4%, 25.3%, and 24.0% of respondents considered the combinations "β2-agonist + methylxanthine + antimicrobial drug + systemic GCS", "short-range anticholinergic ± β2-agonist", and "methylxanthine + systemic corticosteroids + mucolytic" to be the correct response, respectively. Moreover, 5.7% of respondents found it difficult to answer this question and left the item unanswered (Figure 3).

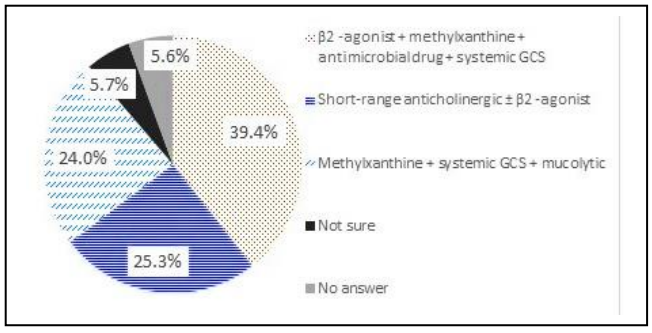

Figure 3. Distribution of respondents' erroneous responses to the item on proper medicines for moderate exacerbation of COPD

4. Discussion

In the first item of the questionnaire, the students were asked to select the most appropriate definition of COPD from five suggested options. According to the current version of the GOLD guidelines, COPD is a common preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation associated with airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles and gases (20, 23). This question was answered correctly by 48.9% of the respondents (ARC: 38.7-58.6% in different centers, $P=0.105$; Cramer's V=0.135).

The development and progression of COPD are directly associated with risk factors, especially smoking, exposure to occupational air pollutants (dust, vapors of acids and alkalis, NO_2), and atmospheric air pollution. In addition, pathology can develop in the presence of a genetic predisposition - Alpha-1 antitrypsin deficiency - a protein produced in the liver and protecting lung tissue from the damaging action of the enzyme elastase (23, 27, 28).

The main mechanisms of COPD development include chronic inflammatory process, oxidative stress, imbalance in the proteinase-antiproteinase system, among which inflammation plays a leading role in the development of the disease from the early stages (29, 30).

In item 4 of the questionnaire, students were asked to select signs that would allow them to suspect COPD. As a rule, the early symptoms of COPD (cough, often with sputum, and/or shortness of breath) are underestimated by patients and perceived as expected consequences of smoking or exposure to occupational hazards. However, these symptoms are significant for the early diagnosis of the disease since patients visit the doctor with these early complaints (28).

In item 5 of the questionnaire, respondents were asked to choose appropriate instrumental and

laboratory markers for COPD. In total, 73.4% of the respondents gave the correct answer (by choosing a decrease in the post-bronchodilator ratio of FEV1/FVC<0.7 as the main diagnostic criterion for the disease) to this item (ARC: 56.2%-87.5% in different centers, $P<0.001$; Cramer's V=0.198) (30).

The correct answer (i.e., spirometry) (23) was successfully selected by 80.9% of respondents (ARC: 70.3-92.6% in centers, $P= 0.001$, Cramer's V= 0.161).

Item 7 of the questionnaire was devoted to the spirometric component of the modern COPD classification used since 2011. This principle of distribution is based on indicators of the functional state of the lungs, namely, the assessment of the severity of bronchial patency impairment, which varies from mild to severe (30).

In item 8 of the questionnaire, the students had to choose the diagnostic criteria that indicate advanced symptoms of COPD (23).

The correct answer was that "vaccination against influenza reduces mortality in COPD patients" (20). According to 12.3% of senior students, in case of m-anticholinergic intolerance, phosphodiesterase-4 inhibitor (roflumilast) can be used in case of mild COPD, and roflumilast is a drug that, according to the current recommendations, should be used as an adjunctive therapy drug in the most severe category of the disease (group D) (20, 31, 32).

Long-term monotherapy with oral corticosteroids significantly increases the risk of developing adverse events (AE), which is steroid myopathy in the case of COPD. However, this fact was not considered by 5.1% of respondents who selected this option as the correct response (33).

Among the analyzed responses, 76.2% were erroneous, most of which (43.4%) accounted for the selection of the option "Monotherapy with ICS is no less effective than the combination of ICS + long-acting β2-agonist", even though a therapy containing ICS is used only in certain clinical situations and is not the therapy of choice for most patients (31). Another 4.2% of students found it difficult to answer this question and/or left it unanswered. The remaining 11.2% of incorrect options selected various combinations of two or even three options.

In item 10 of the questionnaire, respondents were asked to choose an existing combination of β2-agonists with one or more of the proposed drugs in one delivery device for the treatment of COPD. Before the revision of the GOLD guidelines in 2014, the only possible option was the combination of β2-agonists with ICS. However, according to the current guidelines, a combination of a β2-agonist with an m-anticholinergic drug is considered relevant. In addition, a "triple" combination in one delivery device has appeared on the market (20, 33). The correct answer - "there are combinations of a β2-agonist with ICS and with an m-anticholinergic" - was indicated by 32.4% of the respondents (ARC:18.2% -43.2%, $P<0.007$; Cramer's V= 0.189).

An equally important factor in the successful treatment of COPD, in addition to the selection of the appropriate drug, is the selection of the "correct" inhalation device. Despite the modern variety of metered-dose inhalers used for broncho-obstructive diseases, none of them was completely suitable for all patients, indicating the need for an individual approach to the choice of a delivery device in each case (33, 34).

According to the description of the patient's status, the respondent had to establish the appropriate clinical type of COPD ("A", "B", "C" or "D") and select the initial basic therapy, considering the GOLD recommendations (20, 23).

In item 12 of the questionnaire, the students had to choose the appropriate combination of drugs for basic therapy of COPD patients with advanced symptoms and a high risk of exacerbation. Regarding the fact that this category of patients belongs to clinical group D, the correct combination of first-line therapy includes a combination of a long-acting m-anticholinergic drug with a long-acting β2-agonist for a long time (20, 23, 31, 33).

Considering that the patient belongs to the "B" group of COPD, the correct option for drug therapy is LAMA

or LABA, or their combination for a long time (20, 23, 33). The correct response was selected by 38.0% of students (ARC: 25.9% -53.1% in different centers, *P*= 0.018; Cramer's V= 0.144).

An exacerbation of COPD is defined as an acute worsening of respiratory symptoms that requires additional therapy (20).

Treatment is determined primarily by the severity of the condition, which corresponds to the severity of clinical symptoms. Therefore, a moderate exacerbation of COPD is accompanied by at least two of the three main symptoms, including increased dyspnea, increased sputum volume, and increased sputum purulence (30, 33).

Exacerbations of COPD are not always caused by bacterial agents, meaning that there must be signs for the adoption of antibiotic therapy. Such defining signs include increased shortness of breath, an increase in the volume and degree of purulence of sputum, or a combination of two of the three listed symptoms, as well as a severe exacerbation of the disease (23, 35, 36).

In item 16 of the questionnaire, the respondents had to indicate the drugs of choice for empiric antibiotic therapy of infectious exacerbation of COPD (20, 31). The correct response (amoxicillin/clavulanate and macrolide or doxycycline) was given by 57.7% of the students (ARC: 44.8%-73.5% in different cities, P= 0.011, Cramer's V=0.147).

In case of ineffectiveness of antibiotic therapy for the exacerbation of an infectious COPD using drugs of the first line, a reserve group was provided, the drugs for which had to be selected by students in item 17 of the questionnaire (31). A smaller number of correct answers were given to this item (42.0% of respondents chose the correct option, i.e., moxifloxacin and levofloxacin), compared to the previous one (ARC: 29.3% -58.5%, *P*=0.004; Cramer's V= 0.167).

The last two items were included in the questionnaire to determine the students' level of knowledge on the immunization of influenza and pneumococcal infection in patients with COPD. Items 18 and 19 were about influenza vaccination and pneumococcal vaccination, respectively. It should be noted that vaccine prevention of these infectious diseases is the most effective method of combating them, based on the standards for managing patients with COPD (20, 33, 37, 38).

Immunization against influenza and pneumococcus for patients with COPD was recommended by 83.4% (ARC: 71.0% -89.8%, *P*= 0.016; Cramer's V=0.199) and 83.5% of respondents (ARC: 65.9%- 93.2%, *P* <0.001; Cramer's V=0.21).

5. Conclusion

According to the results of the conducted survey, senior medical students had an average level of basic knowledge of etiopathogenesis, diagnosis, treatment, and prevention of COPD. The respondents showed high awareness of the prevention of the disease, determination of risk factors for pathology, vaccine prevention of influenza, and pneumococcal infection in patients with COPD, indicating that future doctors would be less competent in the diagnosis and treatment of this nosology.

An insufficient level of knowledge about COPD may lead to the provision of ineffective medical care for this serious and socially significant pathology in the future by the respondents. The solution to this problem, according to the authors, may lay in the optimization of educational activities and an increase in the number of academic hours in universities in key clinical subjects.

Authors' Contribution

Study concept and design: R. A. B. and E. V. L.
Acquisition of data: A. V. A. and T. G. P.
Analysis and interpretation of data: Y. R. V.
Drafting of the manuscript: G. A. B.
Critical revision of the manuscript for important intellectual content: O. V. C. and G. G. K.
Statistical analysis: V. O. B.
Administrative, technical, and material support: R. A. B.

Ethics

The current study was conducted following the ethical principles of the Helsinki Declaration by the World Medical Association.

Conflict of Interest

The authors declare that they have no conflict of interest.

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