Pharmacotherapy, etiopathogenesis, and diagnostics

of bronchial asthma: assessment of the level of senior medical students' knowledge. Comparison of theASSA-I AND ASSA-II project results

Farmacoterapia, etiopatogénesis y diagnóstico del asma bronquial: evaluación del nivel de conocimiento de los estudiantes de medicina senior. Comparación de los resultados del proyecto ASSA-I y ASSA-II

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Abstract

Bronchial asthma (BA) is an incurable chronic disease that can become controlled after the appointment of rational and reasonable therapy. Due to the prevalence of this pathology, a patient with asthma can be met by a doctor of any specialty, so every clinician should have basic knowledge in the field of this nosology. We aimed to analyze the results of the first and second stages of the ASSA project and to determine the differences in the levels of senior students' knowledge in the field of BA.

Material and Methods. The article presents the results of an anonymous multicenter ASSA study (the full name of the project is "Assessment of senior medical students in the field of bronchial asthma", "ASSA" is a partial acronym) to assess the level of senior medical students' knowledge in the field of etiology, pathogenesis, diagnosis, and treatment of BA. The first stage of this study (2014-2016) involved 521 students from 7 cities in Russia. For the second stage (2017-2019), the results from 358 senior students from 6 cities of Russia and Ukraine were received and analyzed. The method of anonymous questioning was used in this study, for which an original questionnaire was developed based on current clinical guidelines.

Results and Discussion. Over the five years of the study, the level of students' knowledge remains above the average, without significant changes. The following questions in the two stages of the project caused the greatest difficulties in the respondents: question No.1 (the definition of BA), No.2 (a trigger of an asthma attack), No.3 (a key factor of asthma pathogenesis). Positive dynamics were observed on question No.11 (the basic treatment of moderate asthma), No.7 (the levels of BA control) and No.4 (the laboratory and instrumental markers of BA).

Keywords. Bronchial asthma, comparative analysis, students, level of knowledge, pharmacoepidemiological study.

Resumen

El asma bronquial (AB) es una enfermedad crónica incurable que se puede controlar después del nombramiento de una terapia racional y razonable. Debido a la prevalencia de esta patología, un médico de cualquier especialidad puede atender a un paciente con asma, por lo que cada médico debe tener conocimientos básicos en el campo de esta nosología. **El objetivo de la investigación** es analizar los resultados de la primera y segunda etapa del proyecto ASSA y determinar las diferencias en los niveles de conocimiento de los estudiantes de último año en el campo de AB.

Material y métodos. el artículo presenta los resultados de un estudio ASSA multicéntrico anónimo (el nombre completo del proyecto es "Evaluación de estudiantes de medicina de alto nivel en el campo del asma bronquial", "ASSA" es un acrónimo parcial) para evaluar el nivel de conocimiento de estudiantes de medicina senior en el campo de etiología, patogénesis, diagnóstico y tratamiento de AB. La primera etapa de este estudio (2014-2016) involucró a 521 estudiantes de 7 ciudades de Rusia. Para la segunda etapa (2017-2019), se recibieron y analizaron los resultados de 358 estudiantes de último año de 6 ciudades de Rusia y Ucrania. Este estudio se utilizó el método de cuestionario anónimo, para el cual se desarrolló un cuestionario original sobre la base de las guías clínicas actuales.

Resultados y discusión. Durante los cinco años del estudio, el nivel de conocimiento de los estudiantes permanece por encima del promedio, sin cambios significativos. Las siguientes preguntas en las dos etapas del proyecto causaron las mayores dificultades en los encuestados: pregunta No.1 (la definición de AB), No.2 (un desencadenante de un ataque de asma), No.3 (un factor clave la Patogénesis del asma). Se observó una dinámica positiva en la pregunta No.11 (el tratamiento básico del asma moderado), No.7 (los niveles de control de AB) y No.4 (los marcadores de laboratorio e instrumentales de AB).

Introduction

Bronchial asthma (BA) is a common disease affecting up to 339 million people worldwide[1]. People of all ages are prone to the development of chronic inflammation of the respiratory tract, which can often occur in a severe form with an unfavorable outcome[2,3]. According to the Global Burden of Disease Study 2016 (GBD 2016) 420 000 people in the world were dying of asthma - more than 1 000 per day. Also in 2016, asthma ranked 23rd among the causes of premature death in the world. Although the fatal outcome of this disease is quite rare, it accounts for less than 1% of all cases in most countries, it causes concern, because it was in our power to avoid such an outcome. One of the life-threatening conditions in patients with BA in 30% of cases is the development of arterial hypertension (AH), which is possibly associated with the impact of pathological processes on the capillary endothelium and should be more widely reported in the literature[4-11].

To avoid the development of adverse outcomes or complications, it is necessary to achieve a high quality of medical care, first of all, timely diagnosis of this pathology, as well as to achieve an understanding medical management tactic of the patient in each case. The objective of this study is to conduct a comparative analysis of the results of the first and second stages of the ASSA project to determine differences in the levels of senior students' knowledge in BA.

Material and Methods

The ASSA project (the full name of the project is "Assessment of Senior Medical Students in the Field of Bronchial Asthma", "ASSA" is a partial acronym) is a multicenter pharmacoepidemiological study, which started in 2014 and aimed to assess the knowledge of specialists in the field of bronchial asthma. The study was conducted in compliance with the ethical principles of the World Medical Association's Declaration of Helsinki. Human rights were not violated.

The study took the form of a questionnaire; questions were based on the main provisions of the GINA leadership, at the first stage - GINA-2014[12], at the second stage - GINA-2017[13]. According to the changing provisions of the GINA, the questionnaire also underwent several amendments in 2017-2019, in particular concerning the definition of asthma.

The original questionnaire consisted of 12 questions with one correct answer. The respondent received 1 point for each correct answer, 0.5 point – for an incomplete answer (when choosing both correct and incorrect answers), and 0 points for the incorrect answer. Thus, 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 equivalent to 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[14]. The questionnaire used the anonymity method to obtain more independent results without the factor of possible evaluation influencing the respondents. For this purpose, the students were asked to specify their year of studies and/or major, indicating whether it was the first or second time when she/he had taken the questionnaire[37-39].

All the students were enrolled in standard educational programs. This method of knowledge evaluation is relative; it cannot fully reflect the general level of education quality at universities and it was specially developed for the ASSA project.

All the information on the questionnaire was entered into an electronic database and processed using the application programs of Microsoft Excel and IBM SPSS v26. Statistical data were processed through the analysis of the 2x2 contingency tables using the Pearson's chi-square (x^2) test (if necessary - with the Yates's correction and the calculation of the Fisher's exact test). The Mann–Whitney U-test was used to compare the two populations (ASSA I -ASSA II). The statistical significance of differences was recorded at a bilateral level of $p<0.05$.

The partial current results of the first stage of the ASSA project were reported at the Congress of the Asian Pacific Society of Respirology (2015) and published in the journal[15], and the results of this period of study were published in *Farmateka* (2019)[16]. The partial current results of the second phase of the project (ASSA-II) for 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 *Research Results in Pharmacology*[17,18]. The final results of ASSA-II are accepted for publication in *Farmateka* journal.

Results and Discussion

The first phase of the project - ASSA-I - was carried out in 2014-2016 among 521 students from 7 cities of Russia: Belgorod, Voronezh, Krasnodar, Saratov, Chelyabinsk, Vladivostok, and Samara. The second phase of the project(ASSA-II) involved 328 students from 6 centers of Russia and Ukraine: Belgorod, Voronezh, Chelyabinsk, Saratov, Dnipro, and Ufa.

The average level of correct answers (ARC) to all questions at the first stage was 74.0%, at the second stage - 74.8% (Table 1). There is a slight tendency towards an increase in the level of respondents' knowledge between the stages of the study, however, it is not statistically significant ($p>0.05$) (Fig. 1).

| Table 1. Comparative analysis of the two phases of the project (ASSA I - ASSA II)			
Study phase	The average level of correct answers		P
	Me	Q_1-Q_3	
ASSA-I	0.74	0.71-0.76	>0.05
ASSA-II	0.75	0.73-0.77	

Figure 1. Distribution of ARC at the two stages of the project
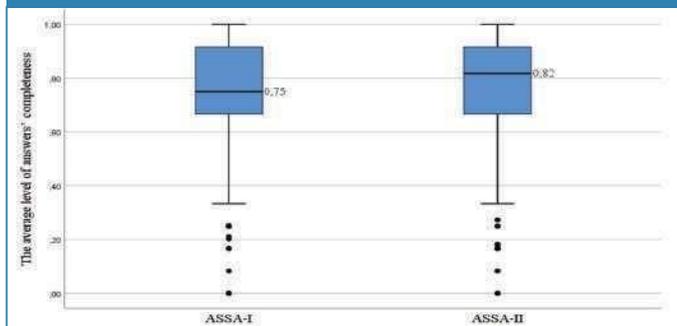
According to the results of comparative analysis, the indicator of the average level of correct answers among students for five years remained at the same level. The level of senior students' knowledge significantly increased on question No.11 (the basic treatment of moderate asthma) from 64.5% in the first stage to 78.7% in the second, on question No.7 (the levels of BA control) - from 67.4% to 73.8% and question No.4 (the laboratory and instrumental markers of BA) - from 65.6% to 69.9%. Lower results in dynamics are observed on question No. 1 (the definition of BA) - 56.8% in 2014-2016 and 46.5% in 2017-2019, question No. 2 (a trigger of an asthma attack) - 87.9% and 81.7% and question No. 3 (a key factor of asthma pathogenesis) - 70.8% and 67.6%, respectively. A summary of both stages is shown in Figure 2.

Figure 2. Comparative analysis of the dynamics of the average level of correct answers (ARC) of students for the periods 2014-2016 and 2017-2019
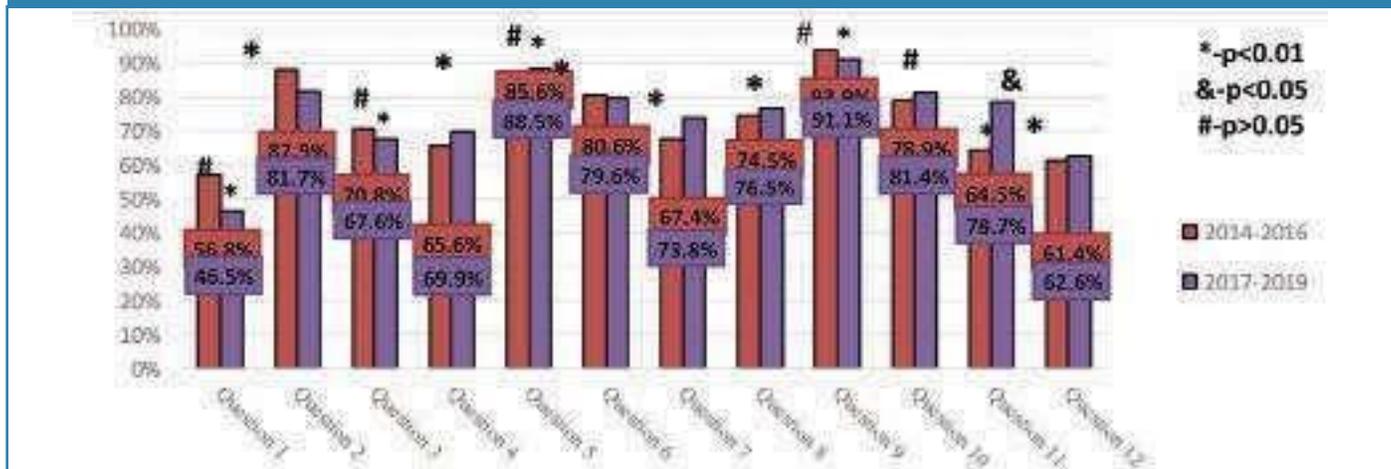
The first question of the questionnaire, both in the first and in the second stage of the project, was one of the most difficult for students. It required the respondents to choose the most correct definition of asthma in accordance with current clinical guidelines. During the study of this disease and the release of the new GINA guidelines, the wording was slightly changed according to GINA-2014, BA is "a chronic inflammatory disease with the development of bronchial hyperreactivity, which is manifested by a variable bronchial obstruction, which is reversible with the help of drug therapy"[12]. Over the past three years, according to the provisions of GINA-2017, bronchial asthma has been considered as «a heterogeneous disease, usually characterized by chronic airway inflammation, the presence of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity»[13]. During the two stages of the study, students showed a low level of knowledge on this question, the ARC did not exceed 60%, while at the first stage of the study, senior students were more informed than the participants of the second stage, which proves the ratio of ARC - 56.8% (from 12.5 to 66.7% among the different centers, p<0.01) and 46.5% (from 42.2 to 47.4%, p>0.05), respectively.

The second question of the questionnaire also showed negative dynamics in assessing the level of knowledge. The students had to select a possible trigger of an asthma attack. A

larger number of students at the first stage of the study chose the correct answer "all the above" (indoor allergens, physical stress, cold, administration of non-steroidal anti-inflammatory drugs) than at the second stage, ARC 87.9% (from 75.0% to 100.0%, p<0.01) and 81.7% (from 75.3% to 95.3%, p<0.01), respectively[13,19,20].

For five years, the respondents have had difficulty with the third question of the questionnaire. The students were to choose a key factor of asthma pathogenesis from the proposed options. The pathogenesis of the disease is based on bronchial hyperreactivity triggered by irritants ranks, after which an anaphylactic type of allergic reaction develops, manifested by the release of the various inflammatory mediators from mast cells. The influence of biologically active substances (BAS), as well as prostaglandins (GD2) and leukotrienes (LTC4), cause an increase in vascular permeability, and edema of the respiratory tract mucosa, a bronchial smooth muscle spasm, strengthen bronchial secretions and infiltration of tissue with eosinophils[13,21-29]. During the two stages of the study, students did not show a knowledge level above 71.0% on this question.

At the ASSA-I stage the ARC was 70.8% (from 63.1% to 87.5%, p>0.05), at the ASSA-II stage the indicator is slightly lower - 67.6% (from 64.8% to 84.1%, p<0.01).

The students demonstrated positive changes in the fourth question of the questionnaire. In 2014-2016 only 65.6% (from 53.2% to 80.9%, p<0.01) were considered the main laboratory and instrumental markers to diagnose asthma are a decreased forced expiratory volume within the 1st second (FEV1), increased IgE and eosinophilia[13,19,21,30], however, in 2017-2019 the level of knowledge increased to 69.9% (from 61.3% to 86.8%, p<0.01).

The next question was about the main asthma diagnostic method. The students were presented with the following options: radiography, bronchography, bronchoscopy, and pulmonary function test (correct answer)[13]. The difference between the project participants in different years is only 2.9%, the respondents of the second stage did a little better, where the ARC is 88.5% (from 85.9% to 94.2%, p>0.05), at the first stage, the ARC is slightly less - 85.6% (from 70.0% to 94.2%, p<0.01).

The existing classification of BA is currently relevant and recommended for use, even though the severity of the disease does not always objectively assess the patient's condition and prognosis. Over the five years of the study, on the question of BA severity according to the classification (intermittent, mild persistent, moderate persistent and severe persistent[13,19]), the students' knowledge remains practically the same: in 2014-2016 - 80.6% (from 54.6% to 95.8%, p<0.01) and in 2017-2019 - 79.6% (from 65.9% to 96.2%, p<0.01).

From 2008 until now, the experts of the international organization GINA offer to approach the tactics of treating bronchial asthma from the position of continuous monitoring of the disease. The guidelines for determining the level of monitoring are clinical symptoms, the need for drugs to relieve symptoms, the number of night attacks, and any limitation of daily activity due to BA[13,19,21,30,31]. In the seventh question, it was necessary to indicate the existing levels of disease control, such as controlled, partly controlled, uncontrolled bronchial asthma. In this question, there is a positive dynamic in the level of students' knowledge, the ARC increased from 67.4% (from 52.1% to 75.0%, p<0.01) according to the results of the first stage to 73.8% (from 59.6% to 92.3%, p<0.01) according to the results of the second stage.

In the eighth question, it was required to indicate the correct option of asthma self-control at home. In 2017-2019 76.5% (from 66.0% to 90.4%, p <0.01) of students considered peak flowmetry based on the peak expiratory flow rate (PEF) measurements[19,21]. In 2014-2016 the indicator was slightly lower - 74.5% (from 50.0% to 87.2%, p<0.01), but in general, at two stages of the study, the level of knowledge on this question is kept at the same level.

A fairly high level of knowledge is recorded in the ninth question of the questionnaire for five years. It concerns the choice of a definition for asthma exacerbations (synonyms: BA attacks, or acute BA). According to GINA international guidelines, exacerbations are changes in the patient's normal condition that are severe enough to require a change in therapy. With an adverse course of asthma exacerbation, the status

asthmaticus – an episode of an acute respiratory failure (life-threatening asthma; nearly fatal asthma) – is highly likely to develop[13,21]. The students were right when choosing the answer option with this definition for asthma exacerbation. At all stages of the study respondents completed this task: at the first stage the ARC is 93.9% (from 89.1% to 100.0%, p>0.05), at the second is a little lower - 91.1% (from 88.6% to 97.1%, p>0.05).

A positive increase in the level of knowledge among senior students is recorded when assessing the dynamics in the tenth question. In this question, it was necessary to indicate a drug to use first of all in asthma attack treatment: 1) mechanical lung ventilation, 2) β2 short-acting agonists (correct answer)[13,32,33], 3) inhaled glucocorticoids, 4) systemic hormones, 5) aminophylline, 6) not sure. The correct answer at the first stage of the study was chosen by 78.9% (from 70.8% to 81.0%, p>0.05) of students, and at the second stage –by 81.4% (from 75.6% to 96.2%, p<0.01).

In recent years, students have become more informed in the field of treatment of bronchial asthma, therefore, in the eleventh question it was necessary to specify the right option for the basic treatment of moderate asthma, and there is a significant positive jump in the level of knowledge. In 2014-2016 only 64.5% (from 40.0% to 86.9%, p<0.01) of students knew that the combination of inhaled glucocorticoid + long-acting β2-agonist is correct[13,19,34], however, in 2017-2019 the ARC increased to 78.7% (69.6% to 90.6%, p <0.05).

Among the wrong answers, which make up 35.5% in the first stage of the project and 21.3% in the second, there is no trend towards diversity. Of the error rate, 39.2% in ASSA-I and 43.4% in ASSA-II are the choice of the combination of aminophylline + short-acting β2-agonist; 41.2% and 39.5%, respectively, - the combination of M-anticholinergic + short-acting β2-agonist; 15.7% and 10.5% - the combination of inhaled glucocorticoid + aminophylline.A small part of students, namely 5.9% and 6.6% in the ASSA-I and ASSA-II stages, respectively, chose «Not sure» and/or left the field empty (Fig.3).

Figure 3. Comparison of the distribution structure of students' erroneous answers to the question of the choice of drugs for the basic treatment of moderate asthma
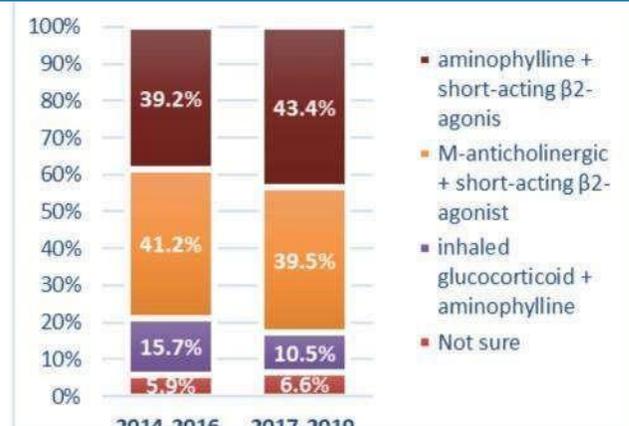
A slight increase in awareness was observed among the participants at different stages of the study in question No.12, where students had to determine the correct combination of drugs in one delivery device. The introduction into clinical practice of the "single inhaler" regimen, combining fixed doses of inhaled glucocorticoid and a long-acting β2-agonist in one delivery device, has helped to achieve a better level of disease control and also reduce the risk of exacerbations[13,21,33,35,36]. The positive increase in the ARC on this question is only 1.2%, at both stages of the study more than half of the students chose the right combination of drugs, at the first - 61.4% (from 41.7% to 77.5%, p<0.01), at the second - 62.6% (from 46.4% to 73.4%, p<0.01).

The wrong answers in ASSA-I and ASSA-II are 37.6 and 37.4%, respectively, while their distribution among the variants has the same structure. During the two stages of the study, the majority of the incorrect answers were attributed to the irrational combination M-anticholinergic + β-blocker (40.8% in 2014-2016 and 56.0% in 2017-2019), the next most common mistake was the combination of aminophylline + long-acting β2-agonist (34.7% and 17.4%, respectively), some of the incorrect options were indicated for a complex of inhaled glucocorticoid + aminophylline (17.4% in the first stage and 16.7% in the second stage). Also, up to 10.0% of students (6.1% in ASSA-I and 9.9% in ASSA-II) in both stages of the study chose «Not sure» and/or left the field empty (Fig.4).

Figure 4. Comparison of the distribution of students' wrong answers to the question of the choice of the correct combination of drugs in one delivery device for the treatment of BA
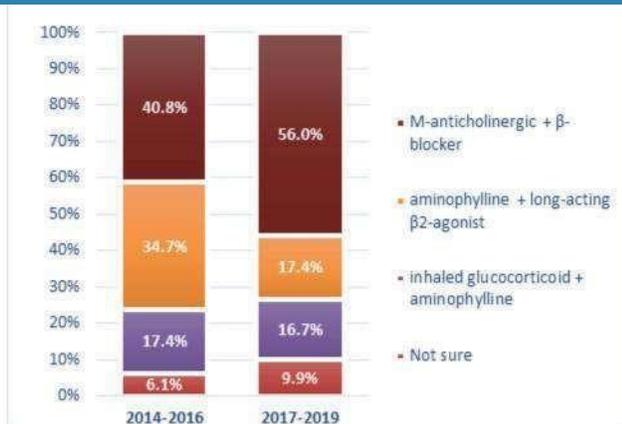
Conclusion

A comparison of the results of two stages of the study within the ASSA project showed that the basic knowledge of respondents in key questions of etiology, pathogenesis, and diagnosis of BA is above average. During the project from 2014 to 2019 the level of knowledge of senior students has not undergone significant dynamic changes for better or worse, except for several questions. Throughout the study, the issues of the definition of BA, a trigger of an asthma attack, a key factor of asthma pathogenesis were traditionally "difficult" for students. On these questions, the participants showed a

negative dynamic in the level of basic knowledge. The senior students became more informed about the appointment of basic treatment of moderate asthma, the designation of the levels of BA control, and the definition of the laboratory and instrumental markers of BA.

Based on the foregoing, we consider it is necessary to conduct this and similar studies among current and future healthcare professionals, primarily to optimize the education process, to identify shortcomings in the study of various nosologies and their timely elimination. In addition, conducting pharmaco-epidemiological studies allows moving away from the usual system of organizing the educational process and focusing the attention of respondents on the main aspects of any disease.

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