



Assessment of Nonadherence to Inhalation Therapy in Asthma and Chronic Obstructive Pulmonary Disease in Bulgaria

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Abstract

Introduction: Treatment for asthma and chronic obstructive pulmonary disease (COPD) is compromised, quality of life is negatively impacted, and significant financial losses result from nonadherence to the prescribed therapy.

Aim: To assess the nonadherence to inhaled therapy in patients with asthma and COPD in Bulgaria.

Materials and methods: A survey was conducted in 4020 asthma or COPD patients. Demographic data was collected, and a questionnaire was completed for assessing the adherence to inhalation therapy (using the Test of Adherence to Inhalers[®], TAI).

Results: We found some level of nonadherence to the therapy in 77.2% of the patients. Factors such as sex, education, and smoking did not influence the adherence. There were regional differences in the diagnoses of asthma and COPD concerning intentional or unintentional nonadherence. Erratic and intentional nonadherence occurred more frequently with longer disease duration. When pMDIs were used as opposed to DPI devices, unintentional nonadherence to treatment was more frequent. Using pMDI instead of DPI was associated with a higher likelihood of observing erratic or intentional nonadherence in some regions of the country. There was a positive link between erratic nonadherence to therapy and an intentional or unintentional nonadherences to it.

Conclusions: The rate of nonadherence to inhalation therapy for asthma and COPD in Bulgaria is very high and vary for the different regions. The TAI questionnaire allows a quick assessment and definition of the basic types of nonadherence. Correcting the causes of non-adherence to therapy reduces the frequency of exacerbations, improves quality of life, and prolongs the life expectancy of patients with asthma or COPD.

Keywords

erratic nonadherence, intentional nonadherence, obstructive pulmonary diseases, TAI test, unintentional nonadherence

INTRODUCTION

Asthma and chronic obstructive pulmonary disease (COPD) are two of the leading causes of morbidity, mor-

tality, and significant financial costs worldwide.^[1] If left untreated, both obstructive pulmonary diseases have a severe negative effect on the patients' quality of life, potentially resulting in significant disability and a reduction in

their lifespan. An effective therapy is needed to limit the progression, reduce the comorbidity, improve the quality of life and life expectancy in these patients.^[2] Different therapeutic options are available for patients with asthma and COPD; however, long-term adherence to therapy is required for their success.^[3,4] Poor patient adherence to inhalation therapy, irrespective of the reasons, compromises the treatment, deteriorates the quality of life, and causes major economic losses.^[2] There is evidence that the levels of adherence in asthma and COPD vary within a wide range of 22% to 78%, which determines the frequent unsuccessful treatment of these diseases.^[2,5,6]

AIM

To assess the nonadherence to inhaled therapy in patients with asthma and COPD in Bulgaria.

MATERIALS AND METHODS

A survey was conducted with 4020 patients diagnosed with asthma or COPD. The mean age of the patients was 59.43 ± 14.66 years. They were selected at random from the general lists of pulmonology and allergy specialists of the primary care units of all 28 major administrative territorial regions in Bulgaria, their distribution being proportional. The number of subjects by region is presented in **Table 1**. Sofia city had the highest percentage of patients in the survey (621; 15.4% of all patients), while Yambol region had the lowest percentage (52; 1.3% of all patients). Data regarding the region are not available for 29 of the patients (0.7%).

Data on sex, age, education, history of smoking (in years), type of disease (COPD or asthma) and its duration, and type of inhalation device used (Dry Powder Inhaler, DPI or pressurized Metered Dose Inhaler, pMDI) were collected for all patients.

To evaluate the level of adherence to inhaled therapy, a questionnaire was filled out (Test of Adherence to Inhalers[®], TAI). It consists of 12 questions allowing differentiation of the three types of nonadherence to the therapy: 'erratic nonadherence', 'unintentional nonadherence' and 'intentional nonadherence'.

The first 10 questions of the test are answered by the patient and scored from 1 to 5. A result of under 25 points to questions 1 through 5 including shows 'erratic nonadherence'. In responses with a result of under 25 points to questions 6 to 10 including, there is an 'intentional nonadherence' to inhaled therapy. Questions 11 and 12 are completed by the medical specialist conducting the survey. They are assessed from 1 or 2 points, and if the result is under 4 points, it is recorded as 'unintentional nonadherence' to the therapy by the patient.

The statistical analysis of data is performed using SPSS v. 19.0. A descriptive analysis was used: mean, median, mode, standard deviation. The chi-square test was used to search

Table 1. Patient distribution by administrative regions

Region	Number of patients	%
Blagoevgrad	177	4.4%
Burgas	205	5.1%
Varna	188	4.7%
Veliko Turnovo	130	3.2%
Vidin	77	1.9%
Vratsa	172	4.3%
Gabrovo	81	2.0%
Dobrich	111	2.8%
Kardzhali	88	2.2%
Kyustendil	81	2.0%
Lovech	94	2.3%
Montana	80	2.0%
Pazardzhik	135	3.4%
Pernik	78	1.5%
Pleven	192	4.8%
Plovdiv	319	7.9%
Razgrad	84	2.1%
Russe	86	2.1%
Silistra	92	2.3%
Sliven	129	3.2%
Smolyan	69	1.7%
Sofia city	621	20.4%
Sofia region	132	3.3%
Stara Zagora	211	5.2%
Targovishte	56	1.4%
Haskovo	150	3.7%
Shumen	102	2.5%
Yambol	52	1.3%
No information	29	0.7%
Total	4020	100%

for a statistically significant link between variables. We also used the Cramer exact test, logistic regression analysis, and correlation analysis. A value of $p \leq 0.05$ was considered statistically significant.

RESULTS

The subjects involved in the survey were allocated into two groups depending on their diagnosis: asthma or COPD: 51.4% (2066 patients) had asthma, and 46.8% (1880 patients) had COPD. There was no information about the diagnosis for 74 of the patients.

The average duration of the two diseases was similar without a statistically significant difference ($p > 0.05$). The duration of asthma was on average 13.5 ± 9.7 years, and that of COPD was 13.6 ± 10.0 years.

Of the subjects included in the study, 1765 (44.1%) were men, and 2235 (55.9%) were women. Twenty patients were excluded from the analyses because there was no information about their sex. In the group with COPD, there were more men than women (61.1% vs. 38.9%), while in the group with asthma, there were significantly more women than men (71.3% vs. 28.7%).

The mean age of the subjects involved in the study analysis (3946 patients) was 58.9 ± 14.8 years. The age of the asthma patients was lower compared to that of the COPD patients (51.8 ± 15.1 years vs. 66.7 ± 9.6 years). The age difference (standard deviation) between individual COPD patients was less than that in the asthma patients (Fig. 1).

Most of the survey participants (58.4%) were non-smokers. The data analysis found that a greater number of the asthma patients (71.3%) were also non-smokers. In the COPD group, the smokers prevailed, with only 44.1% being non-smokers.

Information about the survey participants' education was collected from 3965 of the patients. The majority of the study subjects (49.4%) had secondary education, while 26.4% of the patients had higher education and 19.5% had primary education. A statistically significant difference was found between the patients with different diagnoses and their education ($p < 0.05$) (Fig. 2). There was a prevalence of patients with secondary education in both groups – with

asthma and with COPD, respectively. In second place in terms of frequency in the COPD group are patients with primary education, and in the asthma group are those with higher education (Fig. 2).

There was valid data on the type of inhaler used for 3785 subjects. DPI were used more commonly: 53.3% of the cases versus 46.7% of the cases using pMDI (Fig. 3). A similar ratio of the inhaler devices was kept in the analysis of the disease groups (Fig. 3).

The results from the analysis of TAI show that 3102 patients (77.2% of all studied patients) had some type of non-adherence to therapy, either erratic, intentional or unintentional nonadherence (Fig. 4).

An analysis of the results reveals statistically significant differences in terms of total nonadherence to inhaled therapy by regions ($p < 0.001$) (Table 2). The highest nonadherence rates (of any type) were reported for the regions of Pernik (97.4%), Kyustendil (96.3%), Yambol (90.4%), and Pleven (89.6%). The lowest percentage of total nonadherence to inhaled therapy was found for the regions of Dobrich (60.4%), Varna (62.8%), Shumen (63.7%), and Plovdiv (64.9%).

The analysis of total nonadherence by sex does not reveal any statistically significant differences either for the country as a whole, or for the individual regions ($p > 0.05$). Nonadherence to the prescribed inhalation therapy was reported for 77.2% of men and 77.1% of women.

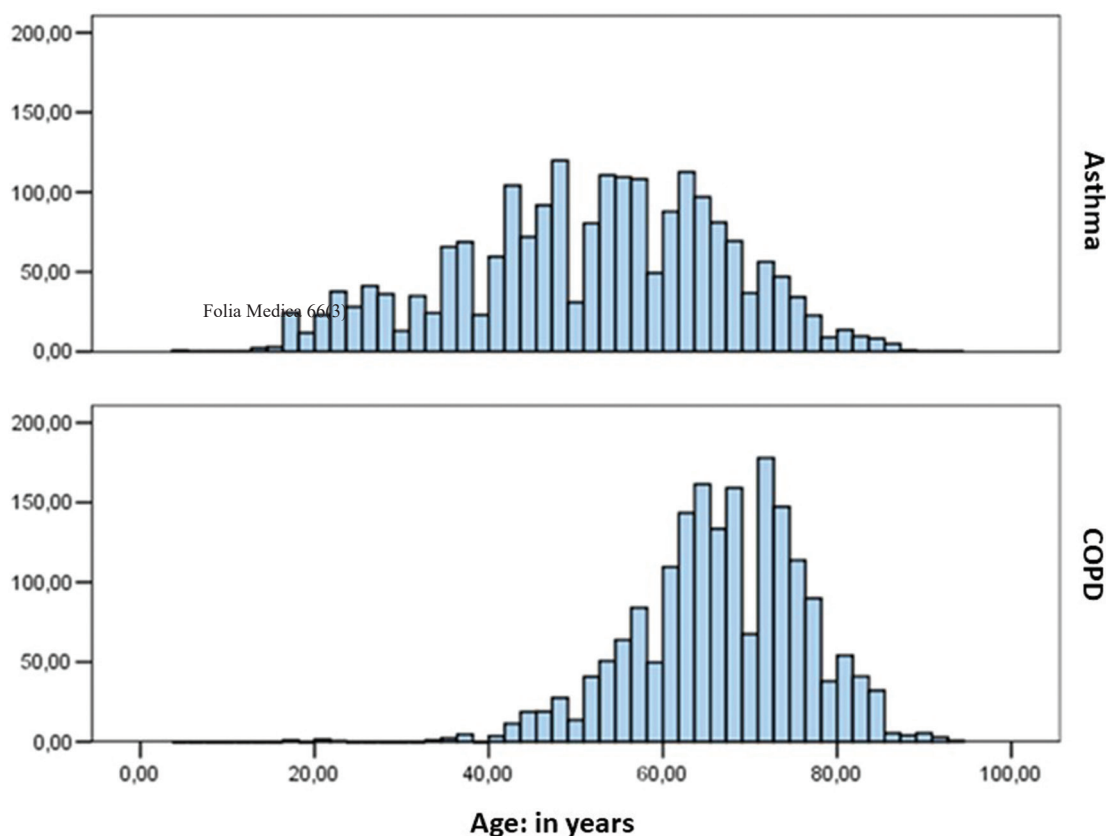


Figure 1. Distribution of patients by age.

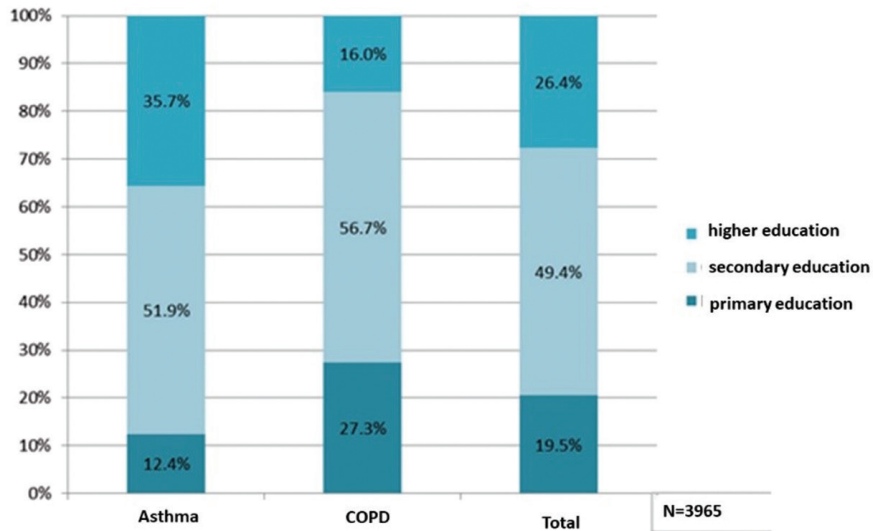


Figure 2. Distribution of patients by education.

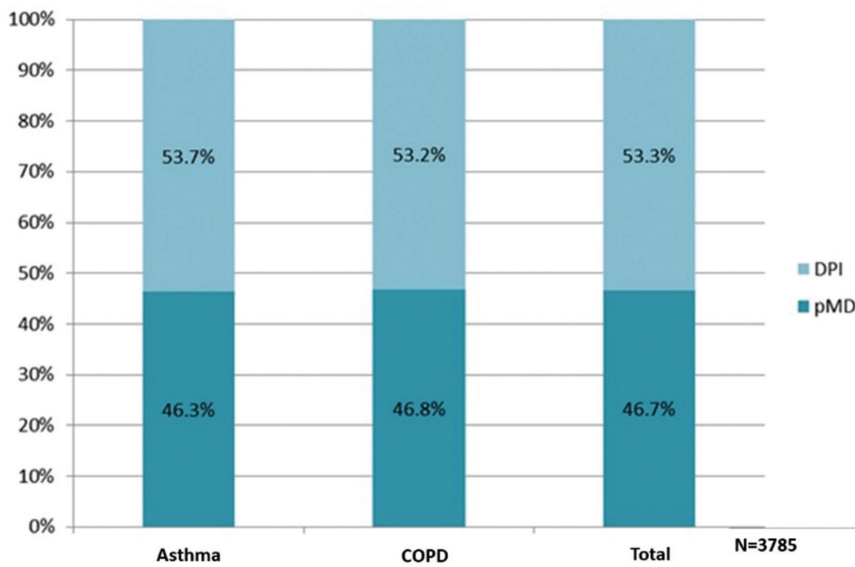


Figure 3. Distribution of patients by type of inhaler used.

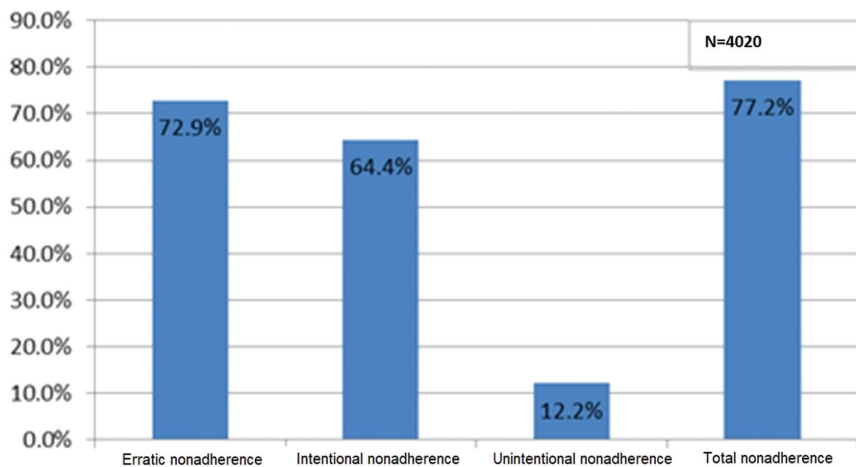


Figure 4. Types of nonadherence to inhalation therapy.

Table 2. Nonadherence by administrative region

Region	Base = 3991			
	Some nonadherence	Erratic nonadherence	Intentional nonadherence	Unintentional nonadherence
Blagoevgrad	83.6% *	77.4%	65.7%	18.5% *
Burgas	80.4%	77.9%	73.2% *	16.1%
Varna	62.8% †	59.0% †	49.5% †	17.6% *
Veliko Turnovo	82.4%	80.0%	66.2%	20.8%*
Vidin	77.9%	75.6%	64.9%	13.0%
Vratza	72.7%	70.9%	62.8%	9.9%
Gabrovo	82.7%	55.8%	72.8%	12.3%
Dobrich	60.4% †	59.1% †	49.5% †	2.7% †
Kardzhali	73.0%	62.9% †	52.3% †	20.5% *
Kyustendil	96.3% *	96.3% *	91.3% *	5.0%
Lovech	85.1%	76.6%	77.7% *	3.2% †
Montana	77.2%	76.3%	69.6%	3.8% †
Pazardzhik	85.9% *	81.5% *	60.7%	5.9% †
Pernik	97.4% *	96.2% *	91.0% *	6.4%
Pleven	89.6% *	84.8% *	74.3% *	31.4% *
Plovdiv	64.9% †	60.5% †	52.2% †	9.1%
Razgrad	78.6%	76.2%	61.9%	16.7%
Ruse	88.5% *	87.4% *	88.5% *	29.1% *
Silistra	72.8%	70.7%	50.0%	12.0%
Sliven	77.5%	75.2%	69.8%	6.9%
Smolyan	84.1%	71.0%	79.7% *	12.9%
Sofia city	74.9%	68.1% †	63.4%	9.7% †
Sofia region	77.9%	77.1%	47.7% †	4.5% †
Stara Zagora	72.5%	68.7%	63.0%	16.6%
Targovishte	87.5%	78.6%	71.4%	7.1%
Haskovo	82.0%	78.0%	65.3%	0.7% †
Shumen	63.7% †	58.8% †	52.0% †	10.8%
Yambol	90.4% *	88.2% *	80.8% *	13.5%
Total	77.2%	73.0%	64.4%	12.2%

*: have a significantly higher proportion vs. the total levels; †: have a significantly lower proportion manifestation vs. the total levels

A diagnosis of asthma or COPD does not affect the general nonadherence to the prescribed inhalation therapy. Asthma patients were nonadherent in 76.2% of the cases, whereas COPD patients – in 78.1%, the differences between the two patient groups being statistically non-significant ($p>0.05$).

The analysis of disease duration reveals that it does not affect statistically the total nonadherence to the prescribed inhalation therapy ($p>0.05$). No statistically significant relationship was identified between tobacco smoking and some of the types of nonadherence to therapy, considering that 41.1% of the interviewed patients showing some nonadherence to the therapy were smokers, and 58.9% were non-smokers ($p>0.05$).

Education does not impact the overall nonadherence to therapy. Some nonadherence was observed in 20.1% of the patients with basic education, 53.7% of those with secondary education, and 26.2% of those with higher education ($p>0.05$).

Of the patients using pMDI device, 47.1% were nonadherent to therapy. For those using DPI, general nonadherence was a little higher (52.9%), but the difference between the two groups could not reach statistical significance ($p>0.05$).

The assessment of the results by region shows significant differences in terms of any nonadherence to inhaler therapy depending on the type of inhaler used. The analyses in which the region of Yambol was used as a relevant cat-

egory revealed that for the regions of Burgas (OR=5.265; $p=0.001$), Sliven (OR=5.123; $p=0.001$), Stara Zagora (OR=2.116; $p=0.036$), Shumen (OR=0.394; $p=0.037$), and Haskovo (OR=0.373; $p=0.029$) there was a statistically higher probability for the occurrence of some nonadherence when using pMDI vs. DPI device.

Erratic nonadherence to the prescribed inhaled therapy was identified in 2930 patients (72.9%). Intentional nonadherence to therapy was found in 2588 of the participant subjects (64.4%). The number of patients showing unintentional nonadherence was significantly lower (489 patients, 12.2%) (Fig. 4).

Erratic nonadherence is reported in 73.3% of the male and 72.5% of the female patients. Intentional nonadherence was present in 64.1% of the male and 64.4% of the female subjects. Unintentional nonadherence was found in 11.4% of the male and 12.7% of the female subjects. The results demonstrate an absence of a statistically significant difference between the sexes in terms of erratic, intentional or unintentional nonadherences to therapy ($p>0.05$ for all).

No statistically significant differences were found in the patients' age and erratic, intentional, or unintentional nonadherences to the therapy both as a whole for the country and for the regions ($p>0.05$ for all).

Overall for the country, the types of nonadherence to inhaled therapy are not influenced by diagnosis. Erratic nonadherence was present in 71.7% of the asthma patients and in 74.0% of the COPD patients. Intentional nonadherence was found in 63.0% of the asthma patients and 65.6% of the COPD patients. Unintentional nonadherence was observed in 12.3% of the asthma patients and in 11.8% of the COPD patients ($p>0.05$ for all). The multiple logistic regression analysis of the results by region shows absence of a statistically significant difference in terms of erratic nonadherence to inhaled therapy, depending on diagnosis. In terms of intentional and unintentional types of nonadherence, however, significant differences were identified by regions. The region of Silistra had the highest percentage of intentional nonadherence among the asthma patients (91.2%), followed by the regions of Pernik and Pleven (89.4% for each, respectively). The lowest percentage of intentional nonadherence was identified in the regions of Kardzhali and Shumen: 41.2% for both regions.

For the COPD patients, the highest intentional nonadherence was found in the region of Kyustendil (95.6%), followed by Pernik and Pleven (92.9% for each of the two regions, respectively). The lowest percentage of intentional nonadherence was found in the regions of Razgrad (46.5%), Varna (47.6%), and Dobrich (49.0%).

Unintentional nonadherence to inhaled therapy in the asthma patients was reported mostly for the regions of Pleven (25.9%), Russe (23.5%), Kardzhali (20.8%), and Varna (20.5%). The lowest percentage of unintentional nonadherence to inhaled therapy prescribed for asthma treatment was identified in Targovishte and Haskovo, where no patient shows unintentional nonadherence.

Unintentional nonadherence in COPD patients was observed most often in the regions of Russe (38.2%) and Pleven (36.5%). The lowest percentage of unintentional nonadherence was found in the regions of Haskovo (1%) and Dobrich (1.8%). No COPD patients in the region of Kyustendil showed unintentional nonadherence to the prescribed inhaled therapy.

The duration of the disease does not statistically affect the unintentional nonadherence to the prescribed inhaled therapy ($p>0.05$). The erratic nonadherence to therapy, and the intentional nonadherence, however, are influenced by the duration of the disease. One year of increased COPD or asthma increases the likelihood of erratic nonadherence to inhaled therapy by a factor of 1.010 (OR=1.010; $p=0.006$). In case of an increase of one year in the duration of COPD, the probability of intentional nonadherence to therapy increases by a factor of 0.012 (OR=1.012; $p=0.001$).

No statistically significant relationship was found between smoking, educational degree, and the erratic, unintentional, or intentional types of nonadherence to inhaled therapy ($p>0.05$ for all).

The significant relationship between the type of inhaler and the manifestation of unintentional nonadherence was confirmed, the difference between the two inhalers being statistically significant ($p<0.001$). With pMDI, the manifestations of unintentional nonadherence are considerably higher (55.9%), and with DPI – significantly less than expected (44.1%). Data analysis by region shows that the statistically significantly higher percentage of unintentional nonadherence is retained in using pMDI versus DPI.

Overall for the country, it was found that a similar percentage of patients using pMDI or DPI inhalers show erratic or intentional nonadherence to the prescribed inhalation therapy ($p>0.05$ for all). The analysis of the individual regions, however, demonstrated a statistically significant higher probability of erratic nonadherence when using pMDI versus DPI inhalers (versus the region of Yambol as reference) for the regions of Kardzhali (OR=3.485; $p=0.042$), Burgas (OR=3.357; $p=0.004$), Sliven (OR=3.048; $p=0.012$), Haskovo (OR=0.425; $p=0.041$), and Shumen (OR=0.305; $p=0.007$). Statistically significant, it was more likely to have intentional nonadherence when using pMDI than when using DPI inhaler for the regions of Sliven (OR=3.658; $p=0.002$), Burgas (OR=2.432; $p=0.016$), and Varna (OR=0.511; $p=0.026$) vs. the region of Yambol.

There was a moderately high, statistically significant correlation between the erratic nonadherence to inhaled therapy, and the intentional nonadherence for asthma and COPD patients in Bulgaria ($r_s=0.632$; $p<0.001$). This dependence is also retained by region (Table 3). The correlation dependence is the lowest between the erratic nonadherence and the intentional nonadherence to therapy in the region of Targovishte ($r_s=0.345$; $p<0.001$), and the highest – in the region of Russe ($r_s=0.955$; $p<0.001$) (Table 3).

There is a low positive correlation between erratic nonadherence and unintentional nonadherence to inhaled therapy ($r_s=0.181$; $p<0.001$).

Table 3. Correlation between erratic nonadherence and intentional nonadherence

Region	Spearman's rank correlation coefficient	p	n
Blagoevgrad	0.437	<0.001	145
Burgas	0.760	<0.001	240
Varna	0.764	<0.001	240
Veliko Turnovo	0.539	<0.001	191
Vidin	0.698	<0.001	49
Vratza	0.729	<0.001	160
Gabrovo	0.682	<0.001	75
Dobrich	0.795	<0.001	112
Kardzhali	0.444	<0.001	129
Kyustendil	0.690	<0.001	90
Lovech	0.538	<0.001	118
Montana	0.875	<0.001	47
Pazardzhik	0.350	<0.001	150
Pernik	0.541	<0.001	120
Pleven	0.409	<0.001	140
Plovdiv	0.695	<0.001	250
Razgrad	0.597	<0.001	130
Ruse	0.955	<0.001	102
Silistra	0.568	<0.001	120
Sliven	0.756	<0.001	120
Smolyan	0.596	<0.001	110
Sofia - the city of Sofia	0.604	<0.001	710
Sofia - the region of Sofia	0.490	<0.001	123
Stara Zagora	0.744	<0.001	188
Targovishte	0.345	<0.001	80
Haskovo	0.560	<0.001	150
Shumen	0.629	<0.001	118
Yambol	0.761	<0.001	46
Total level	0.632	<0.001	4249

DISCUSSION

There are multiple reasons why asthma and COPD patients fail to adhere to their inhalation therapy regimens. But what is undeniably confirmed is that poor adherence is closely linked to poor disease management.^[2]

The respondents to the survey were roughly equal numbers of patients with asthma or COPD, proportionately distributed by administrative regions in the country. Both diseases had a similar duration of roughly 13 years. The analysis of the patients by sex shows some differences. The findings showed that while women made up the majority

of subjects in the asthma group, men outnumbered women in the COPD group. This difference in the sex distribution is not surprising and is due to the different incidence of the two diseases in both sexes: men are more likely than women to have COPD, while women over the age of 18 are more likely to have asthma.^[3,4]

According to the survey, individuals with asthma are significantly younger than those with COPD (51.8±15.1 and 66.7±9.6 years, respectively); however, among asthma patients, the age difference between the youngest and oldest subject is significantly larger. These findings are to be expected, as the diagnosis of asthma typically occurs in younger patients, while COPD typically affects those over 40.^[3,4]

Asthma is a heterogeneous disease characterized by various geno- and phenotypes. There are many distinct and varied etiological factors that lead to the disease, with smoking generally exacerbating the disease's progression and causing the pulmonary function to deteriorate more quickly.^[7] Smoking, on the other hand, increases the risk of developing COPD when combined with dust particle exposure.^[4] This also can account for the fact that in the survey, a great number of patients in the asthma group were non-smokers (71.3%) while the percentage of smokers in the COPD group was higher (55.9%).

A good number of drug products are available to treat asthma and COPD, primarily through inhalation; however, the key to the therapy's effectiveness is the patient's compliance with the prescribed course of action. The overall adherence of asthma and COPD patients to the therapy is worse compared to other patients with chronic diseases.^[8,9] The main reasons for this are the wide range of symptoms, the frequent comorbidities, and the inhalation route of medication administration.^[8,9]

The survey shows that 77.2% of all respondents demonstrate some type of nonadherence to the therapy. More than half of the subjects involved in the survey were either erratically or intentionally nonadherent to the prescribed therapy. Unintentional nonadherence to inhaled therapy was found in a small number of the patients. Data analysis shows significant differences in terms of consistency in the adherence to therapy and the type of nonadherence, i.e. intentional or unintentional, in the different administrative regions of the country. This is most likely due to the regions' differences in age and education of the patients, as well as the duration of asthma or COPD. It is possible that some other factors also have influence, such as differences in the economic status or the access to pharmacies in the different regions of the country.

Adherence to inhaled therapy in case of asthma and COPD reported in literature varies within wide range. Tabyshova et al. observe poor adherence in 80.7% of the patients with asthma and COPD. According to the results they obtained, both intentional and erratic types of nonadherence (89.7% and 88.0%, respectively) predominate followed by unintentional nonadherence (31.3%) to inhaled therapy.^[10] Most authors gather around this high incidence of nonadherence.^[9,11] Adherence to therapy is especial-

ly low in COPD patients, with reported levels of nonadherence varying from 50% to 80%.^[12-14] Other authors indicate wider limits, approximately from 22% to 78%, of patients with asthma or COPD who do not adhere to the prescribed treatment.^[2]

Nazareth et al. assess the adherence to inhaled therapy in 150 patients with asthma (70 patients, 46.7%) and COPD (80 patients, 53.3%) with mean age of the subjects 54.7 ± 13.5 years. The researchers found that 64.7% of the patients did not adhere to the inhalation therapy. In an analysis of the patients by group (COPD or asthma), the percentage of nonadherence is similar (COPD – 68.7%, asthma – 64.2%).^[15] In a retrospective analysis, Humenberger et al. found that the adherence to inhalation therapy in patients with COPD was poor as a whole. Complete adherence to inhalation therapy was observed only in 33.6%. The factors associated with better adherence were age, tobacco smoking in the past, and more serious limiting of the air flow.^[13]

According to other authors, however, the adherence to inhalation therapy in asthma and COPD is comparatively good. In their study, Kardas et al. report low levels of nonadherence to inhalation therapy. They identify nonadherence to therapy in 15.3% of asthma or COPD cases.^[16] In a meta-analysis conducted by Cheen et al., the levels of primary nonadherence to the therapy for asthma/COPD are in the range of 9% to 25%, on average 14.0%.^[17]

One of the key instruments to assess the adherence to inhaled therapy is the TAI questionnaire, which is also employed in this survey. Using this questionnaire, a research on asthma patients' nonadherence to inhaled medication in a reference hospital in Ethiopia reported that 18.3% of patients showed nonadherence to inhalation therapy, whereas 49.4% of patients showed strong adherence.^[18]

Plaza et al., defined the difference in adherence to inhaled therapy in patients with COPD and asthma using the TAI questionnaire. The study included 910 patients (55% with asthma, 45% with COPD). The asthma patients had a statistically lower level of adherence versus those with COPD, respectively 140 (28%) and 201 (49%). The patients with asthma showed more often erratic nonadherence (66.8% of the asthma patients vs. 47.8% of the COPD patients) or intentional nonadherence (47.2% vs. 34.1%, respectively). On the other hand, the COPD patients more often demonstrated unintentional nonadherence to therapy versus those with asthma (31.2% vs. 22.8%).^[19] According to the results of this study, patients younger than 50 years (OR 1.88; 95% CI: 1.26-2.81; $p=0.0020$) and working people (OR 1.45; 95% CI: 1.00-2.09; $p=0.0457$) are among the main risk factors for nonadherence to inhaled therapy whereas asthma diagnosis has a border acceptance limit as a risk factor (OR 1.44; 95% CI: 0.97-2.14; $p=0.0697$).^[19]

Various authors have contradicting opinions about how age and sex affect adherence to therapy. Kardas et al. do not identify any relationship between sex and adherence to inhaled therapy. They identify, however, statistically significant differences between age and adherence.^[16] The analysis of nonadherence shows significant differences between age

groups. The highest percent of nonadherence (18.0%) is reported in the group of patients aged 65-74 years, whereas the highest level of adherence is observed in the patient group over 75 years old (89.2%).^[16] According to other authors, however, it is the female sex rather than age that is associated with poorer adherence to therapy in case of asthma.^[11] There are also studies that do not demonstrate the effect of sex and age on the adherence to inhaled therapy.^[18] Similar results are also provided in the present survey, according to which nonadherence to therapy is not associated with either sex, age or type of diagnosis (asthma or COPD).

The results of some studies indicate that nonadherence to therapy in COPD patients is more likely to occur in young patients, current smokers, patients with more severe COPD, and those receiving a number of different inhaler devices.^[20,21] The adherence of asthma patients is better in men, in patients who have been prescribed higher drug doses, those with comorbidities, and those of more advanced age.^[22]

According to the results we obtained, the duration of the disease has no statistically significant influence on the general or unintentional nonadherence to the prescribed inhaled therapy ($p>0.05$ for both). Erratic and intentional types of nonadherence, however, are influenced by the duration of the disease. The longer the duration of asthma or COPD, the higher the probability of erratic or intentional nonadherence. This is most likely because of the possibility of as-needed therapy in asthma patients, the fear of long-term drug use's negative effects, and the hassle of using multiple inhalers to maintain compliance.

Although, as some authors believe, there is an association between smoking and adherence to inhaled therapy in COPD and asthma, its role remains questionable.^[11] The interesting part is that smoking (active, past, or passive) is associated with good adherence to therapy according only to the study results conducted in Europe (RR=1.32; $p=0.50$).^[11] According to the results we obtained, smoking has no effect on adherence to therapy.

In the present survey, education is not a factor that may influence the adherence to inhalation therapy. The results we obtained differ from those of other authors, who suggest that strict adherence to the recommended treatment is dependent on education. According to a study by Ayele et al., asthma patients with only a primary education have a 2.71-fold higher tendency than those with a higher education to not follow their treatment plan.^[18] A study of Kebede et al. shows that illiterate patients are more likely to be nonadherent to treatment than patients who attended higher schools (OR=2.9; $p=0.02$).^[23]

The role of inhalation devices has been discussed many times both in asthma and COPD treatment. The findings of our survey suggest that DPI is the inhalation device that is used more frequently than pMDI. With pMDI, the nonadherence to therapy is more commonly unintentional. A similar percentage of patients tend to have either erratic or intentional nonadherence to therapy when they use both types of inhalers. There is, however, a greater probability of

erratic or intentional nonadherence in using pMDI vs. DPI in specified areas. Kardas et al. find in their study that non-adherence to MDIs vs. DPIs is 13.4% vs. 17.0%^[16], whereas other authors do not find any association between nonadherence and the type of inhaler used^[24].

The findings in the present survey clearly indicate that factors such as sex, education, and tobacco smoking do not affect adherence to inhaled therapy. Both diseases (asthma and COPD) demonstrate differences in terms of intentional or unintentional nonadherence to the therapy by regions. The erratic and intentional types of nonadherence increase with the duration of the diseases. Unintentional nonadherence to therapy occurs more often with the use of pMDI vs. DPI device. There are significant differences by regions in terms of erratic or intentional nonadherence to the therapy depending on the inhaler used, with an increased probability of their occurrence resulting from the use of pMDI vs. DPI. There is a positive association between erratic nonadherence to inhaled therapy and the intentional or unintentional nonadherence to it.

CONCLUSIONS

Nonadherence to inhaled therapy in asthma and COPD patients in Bulgaria is very high and varying in the different regions. The TAI questionnaire allows us to make a rapid assessment and determine the main types of nonadherence to therapy. The correction of the causes leading to nonadherence to the therapy improves the quality of life, reduces the incidence of exacerbations, decreases financial losses, and improves the life expectancy of asthma or COPD patients.

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Competing Interests

The authors have declared that no competing interests exist.

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Оценка несоблюдения ингаляционной терапии при астме и хронической обструктивной болезни лёгких в Болгарии

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Резюме

Введение: Лечение астмы и хронической обструктивной болезни лёгких (ХОБЛ) ставится под угрозу, качество жизни ухудшается, а несоблюдение назначенной терапии приводит к значительным финансовым потерям.

Цель: Оценить несоблюдение ингаляционной терапии у пациентов с астмой и ХОБЛ в Болгарии.

Материалы и методы: Было проведено обследование 4020 пациентов с астмой или ХОБЛ. Были собраны демографические данные и заполнена анкета для оценки приверженности ингаляционной терапии (с использованием Теста на соблюдение требований к использованию ингаляторов®, ТАИ).

Результаты: Мы обнаружили определённый уровень несоблюдения терапии у 77.2% пациентов. Такие факторы, как пол, образование и курение, не влияли на приверженность. Были региональные различия в диагностике астмы и ХОБЛ относительно преднамеренного или непреднамеренного несоблюдения. Нерегулярное и преднамеренное несоблюдение наблюдалось чаще при большей продолжительности заболевания. При использовании ингаляторов с дозируемой подачей воздуха под давлением (pMDI) вместо ингаляторов сухого порошка (устройства DPI) непреднамеренное несоблюдение лечения наблюдалось чаще. Использование pMDI вместо DPI было связано с более высокой вероятностью наблюдения нерегулярного или преднамеренного несоблюдения в некоторых регионах страны. Была выявлена положительная связь между нерегулярным несоблюдением терапии и преднамеренным или непреднамеренным несоблюдением её.

Заключение: Уровень несоблюдения ингаляционной терапии астмы и ХОБЛ в Болгарии очень высок и различается в разных регионах. Анкета ТАИ позволяет быстро оценить и определить основные типы несоблюдения. Устранение причин несоблюдения терапии снижает частоту обострений, улучшает качество жизни и продлевает продолжительность жизни пациентов с астмой или ХОБЛ.

Ключевые слова

нерегулярное несоблюдение, намеренное несоблюдение, обструктивные заболевания лёгких, тест ТАИ, непреднамеренное несоблюдение