Iwona Florentyna Grzelewska-Rzymowska, Joanna Mikołajczyk, Jadwiga Kroczyńska-Bednarek, Paweł Górski

Departament of Pneumonology and Allergology, Medical University of Lodz, Poland

Association between asthma control test, pulmonary function tests and non-specific bronchial hyperresponsiveness in assessing the level of asthma control

The authors declare no finacial disclosure

Abstract

Introduction: Global Initiative for Asthma (GINA) reports emphasize the use of validated and simple tools in order to assess the level of asthma control, as the Asthma Control Test (ACT). However, an ACT does not include assessment of airway inflammation, which is better reflected when measuring nonspecific bronchial hyperresponsiveness (BHR). The authors aimed to find out if the level of asthma control quantified by an ACT correlates with BHR and pulmonary function tests.

Material and methods: 118 asthmatics participated in the study. All patients completed an ACT. The scores of the ACTs were compared with pulmonary function tests and BHR assessed with the methacholine challenge test and expressed as a provocative concentration of methacholine, inducing a 20% decline in the FEV_1 (PC_{20}M in mg/ml).

Results: Patients with controlled asthma amounted to 52 (44%) while those with uncontrolled asthma amounted to 66 (56%). In patients with controlled asthma (ACT score $\geq$ 20) the mean geometric value of PC_{20}M was 2.72 mg/ml (range from 0.25 to $>$ 8.0), whereas 0.94 mg/ml (range from 0.28 to 8.0) ($p = 0.02$) was observed in patients with uncontrolled asthma (ACT score $<$ 20). Almost 64% (21/33) of uncontrolled asthmatics achieved normal lung function ($FEV_1 > 80\%$ pred. value) while 19% (5/26) patients with controlled asthma presented an $FEV_1 < 80\%$ predicted value. Asthma duration in years in controlled asthmatics was significantly shorter than in uncontrolled patients (6.2 ± 8.9 vs. 12.0 ± 11.4, $p = 0.005$)

Conclusion: In determining the most accurate level of asthma control it is reasonable to use an ACT in conjunction with BHR, which provides more accurate assessment of bronchial inflammation than ventilatory parameters alone.

Key words: asthma, Asthma Control Test, pulmonary function tests, bronchial hyperresponsiveness

Pneumonol Alergol Pol 2015; 83: 266–274

Introduction

Recent GINA (Global Initiative for Asthma) guidelines recommend treating asthmatic patients towards assessing asthma control [1, 2]. The assessment of asthma control during a short period of time reflects the real nature of this chronic disease [1]. Control determines the degree to which the manifestations of asthma are minimized and, due to the multidimensional pathogenesis of the disease, it should refer not only to clinical manifestations but also to laboratory biomarkers of inflammation and pathophysiological features of the disease. According to the GINA report 2014, an assessment of asthma control as well as the effects of asthma treatment should be based on the evaluation of daytime and nocturnal symptoms, the limitation of physical activities and the use of rescue medication [3]. In practice GINA reports recommend the use of validated and simple tools in order to quantify the level of asthma control as with the Asthma Control Test (ACT), which pro-

Address for correspondence: Prof. Iwona Florentyna Grzelewska-Rzymowska, MD, PhD, Departament of Pneumonology and Allergology, Medical University of Lodz, ul. Kopcińskiego 22, 90–153 Łódź, Poland, e-mail: rzym@binar.pl

DOI: 10.5603/PiAPa2015.0044
Received: 25.11.2014

ISSN 0867–7077

vides a numerical value for control obtained by summing together responses for the 5 above-mentioned items [4]. However, ACT does not include an assessment of airway inflammation, this being the main pathogenic mechanism of asthma. This indicates that the use of an ACT alone cannot provide sufficient objective asthma control and may lead to an inappropriate clinical decision. Studies have shown that asthmatic patients with an adequate control of their symptoms might be still at risk of severe exacerbations associated with underlying airway inflammation [5]. As inflammation contributes to bronchial hyperresponsiveness, BHR is used to monitor asthma treatment [6–8]. It is also well-known that BHR is weakly associated with asthma symptoms, the need for medications and lung function [8]. However, there is no evidence confirming the relationship between BHR and nonspecific stimuli and the total ACT score. Due to the asthma control approach regarding asthma management, it was of interest to find if the level of asthma control assessing presented in an ACT correlates with the BHR and pulmonary function test.

Material and methods

A total of 118 asthma patients, 84 women and 34 men, with a mean (± SD) age of 44 ± 15 years (range 18–75 years) participated in this study. The subjects were recruited from the Medical University Out-patient Asthma Clinic in Lodz. The mean asthma duration was 10 ± 11 with a range from 3 to 43 years. As for all patients, the diagnosis of current asthma was made by a specialist and consistent with the GINA 2006 guideline [1]. All participants were interviewed regarding the use of antiasthmatic medications. Inhaled corticosteroids (ICSs) and long-acting β_2-agonists (LABA) combinations were the most common medication regimen used by approximately 60% of patients, either in a single inhaler or as two separate components. Twenty-four per cent (28/118) of subjects were treated with LABA and a low dose of ICSs (beclomethasone dipriopionate — BDP < 500 μg, budesonide ≤ 400 μg, ciclesonide ≤ 160 μg, fluticasone ≤ 250 μg). Twenty-nine per cent (34/118) of them were administered LABA with a medium ICS dose (BDP 500–1000 μg, budesonide 400–800 μg, ciclesonide 160–320 μg, fluticasone 250–500 μg). Eight per cent (10/118) of patients took separately ICSs in a dose exceeding 1000 μg of BDP, 800 μg budesonide, 320 μg ciclesonide and 500 μg fluticasone respectively. Furthermore, 15% of subjects used systemic corticosteroids in a daily dose equivalent to 5–10 mg prednisone, in addition of other controller medications, while the remaining 5 participants required no antiasthmatic treatment at the moment of being included into the study. Pulmonary function tests (PFTs) were performed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) consensus criteria of acceptability and reproducibility, using a volumetric storage spirometer (Vitalograph 2160, Vitalograph Ltd.) [9]. The forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC) were measured using a calibrated spirometer. Subjects were required to have abstained from using LABA for at least 48 hours and short-acting β_2-agonists (SABA) for 6 hours prior to tests. The best of three reproducible measurements for FEV_1 and FVC were recorded and expressed as a percentage of the predicted value [9]. In order to avoid any risk of serious adverse events of bronchial provocation, only subjects with stable asthma (N = 59; 26 patients with controlled asthma and 33 with uncontrolled asthma) and with a baseline of $FEV_1 \geq 50\%$ of that predicted and/or ≥ 1litre were included into the study. Nonspecific bronchial hyperresponsiveness (BHR) was assessed by the methacholine challenge test that was performed using a DeVilbiss nebulizer with an output of 0.26 ml/min and an air flow of 6 l/min, according to the method described previously by Cockcroft et al. [10] with some personal modifications. Subjects inhaled methacholine chloride (by Merck) via a mouthpiece wearing a nose clip in doubling concentrations from 0.015 mg/ml to 16 mg/ml for 2 minutes every 5 minutes. FEV_1 was recorded at 30 and 90 seconds after each inhalation. Bronchial responsiveness was expressed as the provocative concentration of methacholine that induces a 20% decline in the FEV_1 from baseline (PC_{20}). The $PC_{20}M$ was calculated by a linear interpolation from a dose-response curve between two points closest to a 20% fall of FEV_1. A positive response for methacholine was considered when at a value of $PC_{20} \leq 8$ mg/ml. BHR with a PC_{20} value ≤ 8 mg/ml and > 1 mg/ml was defined as mild, a value of $PC_{20} \leq 1$ m/ml and > 0.25 mg/ml as moderate, and as severe when a PC_{20} value was equal to or lower than 0.25 mg/ml.

The level of asthma control was measured using the Asthma Control Test (ACT), which was completed by each patient [4]. An ACT covers 5 items assessing limitations related to asthma on daily functions (question 1), the frequency of breathlessness (question 2), the presence of nocturnal awaking (question 3), the use of rescue

Table1. Value of $PC_{20}M$ in mg/ml in controlled and uncontrolled asthmatic patients

	Asthma			
	Controlled		Uncontrolled	
PC_{20} M in mg/ml	(n = 26)		(n = 33)	
	2.72*		0.94*	
	N	%	N	%
0–0.25	4	15%	10	30%
0.26–1	9	35%	14	43%
> 1–8	11	42%	9	27%
> 8	2	8%	0	0%

($PC_{20}M$ — provocative concentration of methacholine that induces a 20% decline in the FEV_1 from baseline); *$\bar{X}gPC_{20}M$ mg/ml, p = 0.02

medication (question 4) and the evaluation of the patient's subjective perception of their level of asthma control (question 5) over the previous 4 weeks. Each question included 5 response options from one to five with an increasing level of asthma control. A total score was obtained by summing up responses for 5 items ranging from 5 to 25 points. Three levels of asthma control were identified: scores from 5 to 19 indicated uncontrolled asthma, scores from 20 to 24 indicated well-controlled asthma while a score of 25 indicated total control. All participants were additionally requested to answer the following question: "Do you adhere to the treatment prescribed by the physician?" The answer was only yes or no.

The study was carried out after approval of the Ethics Committee of the Medical University in Lodz. Prior to enrollment each subject provided written informed consent.

The summary of statistics includes median (min-max) values, mean ± standard deviation values and geometric mean values. The relationship between the hyperresponsiveness to methacholine, lung function and the ACT values were calculated using Pearson's correlation coefficient for continuous variables. An χ^2 analysis was used for comparison of the distribution of categorical variables. A value of $p < 0.05$ was considered statistically significant.

Results

According to the ACT, 56% of patients (66/118) were uncontrolled. The similar proportion of females and males with ACT score between 5 and 19 was seen and it was 55% (46/84) and 59% (20/34) respectively. Asthma was considered well-controlled in 36% (21/59) of subjects. Only 8% (10/118) of all participants reported total control during the last 4 weeks. Further analyses were performed considering two populations: controlled (ACT score ≥ 20) and uncontrolled (ACT score < 20). Of the patients with controlled asthma (N = 26) the geometric mean value of PC_{20} was 2.72 mg/ml and only 0.94 mg/ml in patients with uncontrolled asthma (N = 33) (Table 1). The mean geometric values of $PC_{20}M$ in controlled and uncontrolled patients were significant different (p = 0.02). Half of the patients with an ACT score ≥ 20 points had moderate or severe BHR with $PC_{20}M$ ≤ 1 mg/ml (Table 1).

Although there was a tendency towards a relationship between the fifth response on each question in the ACT and the $PC_{20}M$, a significant correlation was found only regarding the second ($R = 0.498$; $p < 0.001$) and fourth questions ($R = 0.27$; $p < 0.05$). A higher response option to questions 2 and 4 was correlated with a higher mean value of $PC_{20}M$ (Fig. 1). The estimation of dependence between FEV_1 values and ACT scores revealed that patients with an ACT score less or equal to 19 points had a significantly lower mean FEV_1 (85.7% ± 18%) compared to those with total and well-controlled asthma (96.1% pred. value ± 13.6%), (p = 0.017). At the same time, despite the significantly lower frequency of FEV_1 value over 100% of predicted, almost 64% (21/33) of uncontrolled asthmatics achieved normal lung function ($FEV_1 > 80\%$) (Table 2).

An evaluation of the influence of various analysed factors, including demographics on asthma control assessed by an ACT, did not identify any significant correlations. Adherence to treatment did not contribute to better ACT scores because the majority of controlled patients (85% — 22/26), as well as those uncontrolled (94% — 31/33) reported taking prescribed medications on a regular basis. Moreover, co-occurring rhini-

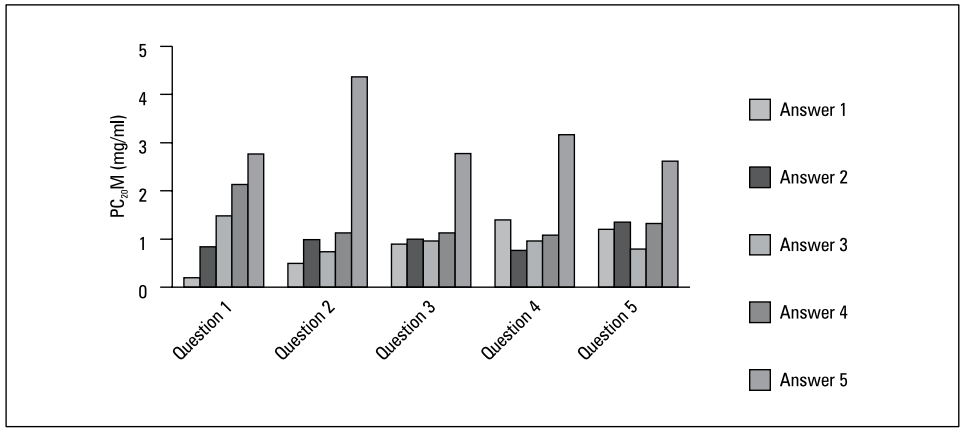

Figure 1. Relationship between choosing variant of answer regarding ACT and bronchial hyperresponsivenes

Table 2. Association between asthma control and FEV_1in% predicted value

	Asthma			
	Controlled		Uncontrolled	
FEV_1 (%pred. value)	(n = 26) 96.1 (± 13.6)*		(n = 33) 85.7 (± 18)*	
	N	%	N	%
≥ 100	14	54%	8	24%
80–100	7	27%	13	40%
< 80	5	19%	12	36%

*FEV_1 in% pred. value (± SD), p = 0.017

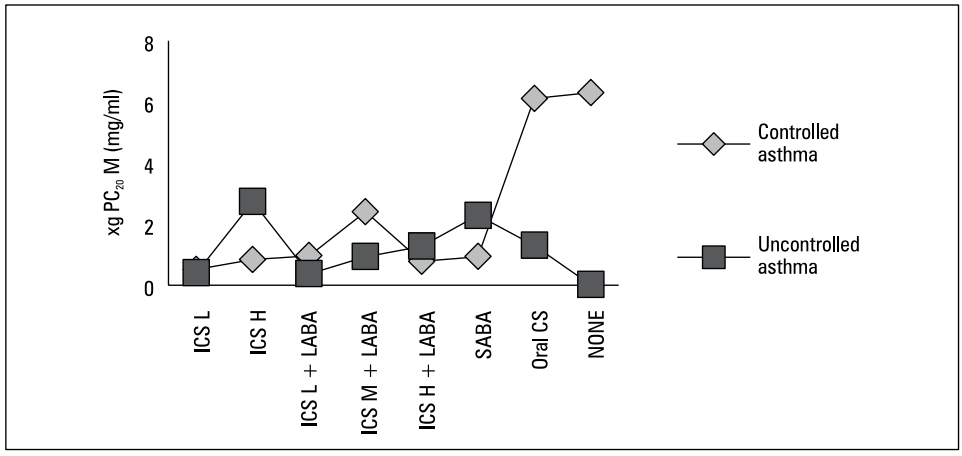

Figure 2. Relationship between $\overline{X}$g $PC_{20}M$ in mg/ml and asthma treatment; ICS L — low dose of ICS; ICS H — high dose of ICS; ICS M — medium dose of ICS; Oral CS — oral corticosteroids; SABA — short-acting beta-agonists; LABA — long-acting beta-agonists

tis and allergic sensitization were not related with poorer asthma control. Similarly, despite the fact that active smoking was more often observed in patients with uncontrolled asthma (12% — 4/33 vs. 4% — 1/26), current smoking did not significantly deteriorate one's control of asthma. Furthermore, the above-mentioned schemes of asthma treatment do not have a significant influence on the ACT score. In addition, no association was found between following any treatment regimen and the mean values of $PC_{20}M$ (Fig. 2) and FEV_1 values in patients with

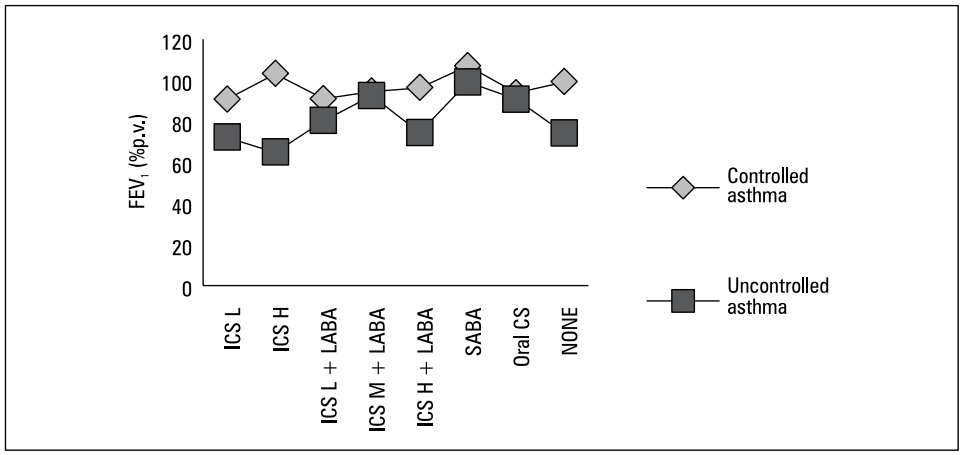

Figure 3. Relationship between FEV_1 (% pred.value) and asthma treatment; ICS L — low dose of ICS; ICS H — high dose of ICS; ICS M — medium dose of ICS; Oral CS — oral corticosteroids; SABA — short-acting beta-agonists; LABA — long-acting beta agonists

Table 3. Asthma duration, FEV_1 in% pred. value and $PC_{20}M$ in mg/ml in patients with controlled and uncontrolled asthma

	Asthma			
	Controlled		Uncontrolled	
Asthma duration (in years)	**(n = 26)**		**(n = 33)**	
	6.2 (± 8.9)*		**12.2 (± 11.4)***	
	FEV_1**	$PC_{20}M$***	FEV_1**	$PC_{20}M$***
≤ 1	99.2 (± 11.9)	1.7	85.8 (± 11)	0.7
> 1–10	91.3 (± 16.3)	4.75	91.4 (± 18.6)	1.28
> 10–20	101.2 (± 1.5)	1.41	75.4 (± 19.2)	0.62
> 20	94.4 (± 19.6)	1.65	82.8 (± 15.4)	0.59

*asthma duration in years, p = 0.005; **FEV_1 in% predicted value (± SD); ***$\bar{X}$g$PC_{20}M$ in mg/ml

or without asthma control (Fig. 3). Patients who did not require current antiasthmatic treatment but were well controlled had the lowest BHR ($PC_{20}M$ = 6.29 mg/ml) while those with uncontrolled asthma had the highest BHR ($PC_{20}M$ = 0.01 mg/ml).

Taking into consideration asthma duration, we demonstrated that the mean duration of the disease was significantly shorter in patients with an ACT score ≥ 20 compared to those with uncontrolled asthma (6.2 ± 8.9 years and 12.2 ± 11.4 years respectively; $p < 0.001$). Irrespective of asthma duration, in both groups FEV_1 were over 80% of predictive value except for patients with a lack of asthma control and those with a ten to twenty-year history of disease, when FEV_1 was 75.4% of the normal value (Table 3). Subjects who were treated for asthma from 1 to 10 years had a significantly higher mean value of $PC_{20}M$ when compared to the group with longer duration of asthma symptoms (4.75 mg/ml vs 1.28 mg/ml; $p < 0.05$). In a group of uncontrolled patients $PC_{20}M$ values behaved similarly. The highest BHR was found in subjects with uncontrolled asthma and over a twenty-year history of asthma than in controlled patients ($PC_{20}M$ = 0.59 mg/ml vs 1.65 mg/ml; $p < 0.05$).

Disscussion

An accurate level of asthma control is fundamental for the initiation or modification of asthma pharmacotherapy. Currently, several parameters have been developed to quantify asthma control. The ideal measure of asthma control should reflect the multidimensionality of asthma, be easily interpreted, convenient to perform, quickly administered in clinical practice, responsive to changes in clinical status, valid and provide reliable assessment of asthma control [11, 12]. The ACT proposed by Nathan et al. [4], which was used in our study, has been developed to meet

these needs. Moreover, as the ACT scores were responsive to current asthma clinical status, it is a suitable survey to drive therapeutic decision making (step-up or step-down). A score of 19 on the ACT was considered as the best cut-off-point, at which the sensitivity and specificity of the ACT, whereas the point for classifying patients as poorly controlled or well-controlled was 71.3% and 70.8% respectively. The ACT proved to be a reliable instrument due to the presence of a significant correlation with FEV_1 values and the Asthma Control Questionnaire (ACQ) [13]. However, Stempel et al. [14] demonstrated that the combination of both ACT and FEV_1 values would better determine the patient asthma control than either of them alone. Therefore, in our study the level of asthma control assessed by a subjective numeric tool (ACT) was compared to the pulmonary function test and measurement of BHR. In the light of the above, we found significant differences in mean FEV_1 values across patients with uncontrolled and controlled asthma despite the level of mean FEV_1 indicating rather normal lung function and good asthma control in both groups of patients. Even more, a FEV_1 value less than 80% of that predicted, as one of the criteria of poor asthma control, was similarly frequent in patients with an ACT score $\geq$ 20 points, as well as in those with the ACT score < 20 points. It should be underlined that almost 20% of controlled subjects had FEV_1 less than 80% but 64% of patients with uncontrolled asthma had FEV_1 value within the normal range (i.e. $FEV_1 \geq 80\%$ predicted). This observation suggests that spirometry, which is an objective measurement of asthma control, does not confirm the ACT scores and consequently does not support the multidimensionality and the reliability of this test. These findings are consistent with previous studies that have revealed a weak correlation between pulmonary function and the level of asthma control [14]. It has also been shown that patients with intermittent and mild asthma have normal lung functioning, making spirometry less useful in accurate asthma control assessment. Moreover, subjective improvement in asthma symptoms may occur without any changes of airflow obstruction. Indeed, as others have previously reported, continuous FEV_1 measurements cannot be used as a marker for potential asthma exacerbations and cannot alone predict the loss of asthma control [15].

In order to provide a more comprehensive view of the overall level of asthma control it seems to be sensible to use composite measurements comprising different endpoints. Currently, there is no clear statement which parameter or its combination can be considered as the most relevant tool to evaluate asthma control. The ACT refers to clinical parameters (daily symptoms, nocturnal awaking, need for rescue medication, frequency of breathlessness), which are based on a patient's self-perception of symptoms. Although the assessment of symptoms is undoubtedly important, studies indicate that symptoms perception by asthmatic patients is often inaccurate, causing problems with its interpretation in clinical practice. Even more, the perception of dyspnoea intensity varies greatly among patients with asthma and therefore may not reflect the actual clinical status [16, 17]. Additionally, the ACT does not include an assessment of underlying airway inflammation which might be better reflected by the measuring of BHR.

Previous studies have shown that the threshold value of histamine appears to be a more sensitive determinant of airway responsiveness than changes in FEV_1 values after allergen exposure [18, 19]. Moreover, it was found that both in seasonal or persistent asthma BHR may be present even though FEV_1 was within normal range [20]. BHR correlates with markers of persistent inflammation including sputum eosinophilia and/or exhaled nitric oxide (eNO) [21]. Sont et al. [22] documented that patients treated with inhaled corticosteroids (ICSs) guided by the degree of BHR, had a lower exacerbation rate, improved lung function and reduced remodeling, compared to those treated based only on asthma management guidelines. Linked to this fact, BHR normalizing may be important in order to improve asthma control. In this study we demonstrated the lack of association between the level of asthma control as assessed by the ACT and the degree of BHR. In a group of controlled asthma patients, approximately half had severe or moderate BHR while only 2 subjects achieved $PC_{20}M$ values exceeding 8mg/ml, which is regarded as normal airway responsiveness. Furthermore, the significant difference between the geometric mean of $PC_{20}M$ in controlled and uncontrolled patients observed in our study weakens seriously the usefulness of the ACT as a tool providing sufficient information about asthma control. These data do not support the multidimensionality of the ACT, but suggest that BHR may occur irrespective of the clinical level of asthma control. With regard to these, we conclude that a total ACT score and BHR measurement do not gauge the same aspect of asthma. Thus, an ACT without an assessment of BHR, which reflects and provides additional information about di-

sease activity and the risk of exacerbation, may lead one to establish an inappropriate level of asthma control. Our results confirm the findings of Bora et al. [23] who demonstrated that although ACT can be used in clinical practice, it does not correlate with airway inflammation. Similarly Melosini et al. [24] found that although an ACT can be a valid tool to assess the current level of asthma control in terms of symptoms, rescue medication use, and PEF variability, in cases of pulmonary function and biomarkers of airway inflammation they are not related to the clinical asthma control. BHR is improving with treatment in the long-term, in contrast with achieving control of lung function and symptoms. Earlier Lündback et al. [25] showed that asthma control improvement demonstrated as BHR reduction is achievable with adequate anti-inflammatory pharmacotherapy. Decreasing BHR with treatment requires months or even years, while symptoms and lung function have been shown to improve relatively quickly. In our study, normalizing of BHR was not associated with longer asthma duration and the use of asthma medication. We found that with increasing years of asthma duration patients were scored lower on the ACT. Moreover, a longer asthma duration in patients with uncontrolled asthma was not related to greater BHR and with no meaningful changes in FEV_1 values. In accordance with these observations, we could suggest that BHR is a more sensitive marker in asthma control assessment than FEV_1. In addition, our results indicated that asthma treatment had no significant influence on BHR level and achieving optimal asthma control. A combination of ICSs and long-acting β_2-agonists (LABAs) was used by the majority of patients from both groups: controlled and uncontrolled. However, several studies have shown that ICSs reduce airway inflammation and persistent treatment with ICSs ameliorates BHR [22, 25]. Bateman et al. [26] proved that addition LABA to ICSs provides obtaining clinical control in more patients, immediately and at lower doses of ICSs than the application of ICSs alone. Our data revealed no agreement with these findings and suggest that the most effective therapy reflected by ACT scores ranged from 20 to 25 and that the lowest BHR value was assured by taking oral corticosteroids as an additional asthma treatment. In this case, following guidelines to achieve asthma control step-down therapy should be reconsidered. The highest value of $PC_{20}M$ was observed in controlled patients but those not having been treated by any asthma medication. Even more, patients with poor asthma control who had not been treated with antiasthmatic medications had the severest BHR. On the basis of mean FEV_1 results we could not reach similar conclusions as the FEV_1 values obtained in both groups did not identify what kind of medications may improve or worsen asthma control. In line with the above, determining the most accurate level of asthma control and obtaining the more objective ACT scores, it seems reasonably to use an ACT in conjunction with an assessment of BHR instead of spirometry parameters. Moreover, lung function tests alone should not be recommended in the evaluation of asthma control and decision making regarding optimal pharmacotherapy without including measures of the extent of airway inflammation or BHR since, lung function tests, as well as symptoms, might provide a different assessment, one not the reflecting inflammatory process which characterizes asthma. Laprice et al. [27] found that airway inflammation and remodeling are more intense in more symptomatic patients. Our study showed that more symptomatic patients expressed in a numerical ACT score also had a lower $PC_{20}M$ value that corresponded with moderate to severe BHR. In contrast, lower BHR significantly correlated with less intensified breathlessness and the infrequent use of rescue medication.

These observations are consistent with previous findings indicating that in real-life assessments of asthma control, by means of an ACT incorporating a measurement of BHR, allow one to obtain the proper level of asthma control and, in particular, can provide the relevant information for treatment decisions.

The current study shows the possibility of inadequate assessment of asthma control as evaluated by an ACT. Inadequate suppression of airway inflammation follows when its extent in guiding anti-inflammatory medications is not considered. Unfortunately, despite of the availability of highly effective pharmacotherapy, this problem occurs extensively. The ACT scores distinguishing uncontrolled patients from those with asthma control seem to be uncertain. Asthma control in an ACT is assessed on the basis of subjective intensity of symptoms, limitation in daily activity or the need for rescue medication. This generally results in overestimating the level of control because of poor recognition of symptoms, treating them as unavoidable consequences of disease [28]. Boulet et al. [29] demonstrated that two thirds of patients with mildly and moderately uncontrolled asthma, as measured according to

asthma guidelines, reported proper control. Furthermore, patients might not realize that there is a possibility of improving their quality of life by suitable pharmacotherapy. Although the adherence to prescribed medications is vital to achieve therapeutic success in asthma, other determinants may also impact on disease control. This is consistent with our observation, which indicated that even though almost all patients were in compliance with the prescribed treatment, 56% reported uncontrolled asthma. For effective asthma management, GINA reports have recommended developing a partnership between the physician and the patient, especially in the case of asthma as a condition which demands continuous monitoring over long period of time and, if necessary, individually adjusting one's treatment. Recently, the importance of education in asthma, ensuring essential knowledge about recognizing worsening asthma control and skills in the proper use or modification of medication, has been highlighted. According to the INSPIRE (International Asthma Patient Insight Research) study only 29% of patients with asthma are instructed how to increase their ICS dose in case of crisis or exacerbation while 88% reported a willingness to acquire similar knowledge [30]. More surprising results were presented by the GAPP (Global Asthma Physician and Patient Survey) project that showed a huge disproportion between the patient's and physician's awareness of implementing education being crucial in the self-management of asthma [31]. To avoid therapeutic failure of asthma treatment and to improve the anti-inflammatory effect of ICSs, training in the right technique for inhaler device usage should be an integral part of every visit [1, 2, 32]. Studies have demonstrated that approximately 50% of patients admit not having sufficient ability to use their inhaler device [32]. Indeed, almost 30% misuse their pressured metered-dose inhalers (pMDI), a phenomenon which is due to poor coordination between inhaler activation and inspiration [33]. The results of this study demonstrate that half of patients with controlled asthma had severe or moderate BHR. The single use of an ACT does not provide a full picture of asthma control because the total ACT score and BHR measurements do not measure the same aspect of asthma. BHR is a more sensitive marker in asthma control assessment than FEV_1. Therefore, better solution is to combine the objective parameters assessing asthma control. Thus, a BHR measurement which reflects underlying disease activity, should be combined with subjective parameters such as an ACT.

Conflict of interest

The authors declare no conflict of interest.

References

1. Bateman ED, Hurd SS, Barnes PJ. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 2006; 31: 143–178.
2. GINA 2014. http://www.ginasthma.org/local/uploads/files/GINA_Report_2014_Aug12.pdf; 15.03.2015.
3. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma — Summary Report J. Allergy Clin Immunol 2007; 120 (Suppl 5): S94−S138.
4. Nathan RA, Sorkness CA, Kosinski M et al. Development of Asthma Control Test: a survey for assessing asthma control. J Allergy Clin Immunol 2004; 113: 59−65.
5. Tattarsfield A, Postma D, Barnes P et al. Exacerbations of asthma: a descriptive study of 425 severe exacerbations. The FACET International Study Group. Am J Respir Crit Care Med 1999; 160: 594−599.
6. Currie GP, Jackson CM, Lipworth BJ. Does bronchial hyperresponsiveness in asthma matter? J Asthma 2004: 41: 247−258.
7. Busse WW. The relationship of airway hyperresponsiveness and airway inflammation. CHEST 2010; 138: 4S–10S.
8. Brannan JD. Bronchial hyperresponsiveness in the assessment of asthma control. Chest 2010; 138: 11S–17S.
9. Miller MR, Hankinson J, Brusasco V et al. ATS/ERS Task Force. Standardisation of spirometry. Eur Respir J 2005; 26: 319−338.
10. Cockroft DW, Davis BE, Todd DC, Smycniuk AJ. Methacholine challenge: comparison of two methods. Chest 2005; 127: 839−844.
11. Magnan A. Tools to assess (and achieve?) long-term asthma control. Respir Med 2004; 98: S16−S21.
12. Cloutier MM, Schatz M, Castro M et al. Asthma outcomes: composite scores of asthma control. J Allergy Clin Immunol 2012;129: S24−33.
13. Schatz M, Sorkness CA, James T et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. J Allergy Clin Immunol 2006; 117: 549−556.
14. Stempel DA, Williamson A, Stanford RH. Comparative assessment of asthma control with both ACT and spirometry in subjects attending community events. J Allergy Clin Immunol 2005; 115: S216.
15. Jatakanon A, Lim S, Barnes P. Changes in sputum eosinophils predict loss of asthma control. Am J Respir Crit Care Med 2000; 161: 64−72.
16. Kroczyńska-Bednarek J, Kwiatkowska S, Zięba M et al. The relationship between lung ventilation and nonspecific bronchial hyperresponsiveness in mild and moderate asthma. Cur Pneumonol 2000; 4: 53−60.
17. Rietveld S. Symptom perception in asthma: a multidisciplinary review. J Asthma1998; 35: 137−146.
18. Kroczyńska-Bednarek J, Grzelewska-Rzymowska I, Tymińska K. Nieswoista nadreaktywność oskrzeli u chorych na sezonową astmę oskrzelową obserwowanych przez 2 kolejne lata. Pol Arch Med Wewn 1997; 97: 216−223.
19. Grzelewska-Rzymowska I, Pietrzkowicz M, Kroczyńska-Bednarek J. Zależności między stężeniem czynnika martwicy nowotworu alfa w surowicy a przebiegiem klinicznym, wentylacją i nieswoistą nadreaktywnością oskrzeli u chorych na izolowany sezonowy nieżyt nosa i sezonową astmę. Pol Merk Lek 2005; 107: 530−535.
20. Ward C, Pais M, Bish R et al. Airway inflammation, basement membrane thickening and bronchial hyperresponsiveness in asthma. Thorax 2002; 57: 309−316.
21. Jatakanon A, Lim S, Kharitonow SA, Chung KF, Barnes PJ. Correlation between exhaled nitric oxide, sputum eosinophils and methacholine responsiveness in patient with mild asthma. Thorax 1998; 53: 91−95.

22. Sont J, Willems L, Bel E et al. Clinical control and histopathologic outcome of asthma when using airway hyperresponsiveness as an additional guide to long-term treatment, The AMPUL Study Group. Am J Respir Crit Care Med 1999; 159: 1043–1051.
23. Bora M, Alpaydin AO, Yorgancioglu A et al. Does asthma control assessed by asthma control test reflect inflammation? Multidiscip Resp Med 2011; 6: 291–298.
24. Melosini L, Dente FL, Bacci E et al. Asthma control test (ACT): comparison with clinical, functional, and biological markers of asthma control. J Asthma 2012; 49: 317–323.
25. Lundbäck B, Rönmark E, Lindberg A et al. Asthma control over 3 years in a real-life study. Respir Med 2009; 103: 348–355.
26. Bateman ED, Boushey HA, Bousquet J, et al. Can guideline-defined asthma control be achieved? Am J Respir Crit Care Med 2004; 170: 836–844.
27. Laprice C, Laviolette M, Boutet M et al. Asymptomatic airway hyperresponsiveness: relationships with airway inflammation and remodeling. Eur Respir J 1999; 14: 63–73.
28. Rabe KF, Vermeire PA, Soriano JB et al. Clinical management of asthma in 1999; the Asthma Insights and Reality in Europe (AIRE) study. J Allergy Clin Immunol 2004; 114: 40–47.
29. Boulet LP, Philips R, O'Byrne P, Becker A. Evaluation of asthma control by physicians and patients: comparison with current guidelines. Can Respir J 2002; 9: 417–423.
30. Partridge MR, van der Molen T, Myrseth SE et al. Attitudes and action of asthma patients on regular maintenance therapy: the INSPIRE study. BMC Pulm Med 2006; 6: 13–22.
31. Canonica GW, Baena-Cagnani CE, Blaiss MS et al. GAPP Survey Working Group. Unmet Leeds in asthma: Global Asthma Physician and Patient (GAPP) Survey: global adult findings. Allergy 2007; 6: 668–674.
32. Crompton GK, Barnes PJ, Broeders M et al. Aerosol Drug Management Improvement Team. The need to improve inhalation technique in Europe: a report from the aerosol Drug Management Improvement Team. Respir Med 2006; 9: 1479–1494.
33. Giraud V, Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. Eur Respir J 2002; 2: 246–225.