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## **Asthma therapy related problems in adult Mediterranean Croatian patients**

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### **ABSTRACT**

The aim of this study is to determine asthma treatment related problems, in cooperation with family medicine physicians. This study was conducted on a patient sample from Public Health Centre "Solin". The study included patients with a diagnosis of J45, who have agreed to participate while picking up their anti-asthmatic drug prescription in the pharmacy on a regular basis. Excluded were those patients who had just been diagnosed with asthma and patients who were less than 18 years old. The first part of the data required according to form for the analysis of therapy was taken from the patients' health records of a cooperative family medicine physician, while other necessary data was filled by the pharmacist in conversation with the patient. All participants were asked to examine and sign the informed consent about the purpose of the research conducted in accordance with ethical principles and the Declaration of Helsinki. Asthma Control Test (ACT) value identified 54% of the patients with uncontrolled asthma (ACT < 20). Adherence to GINA guidelines was identified in 32% of the patients. 40% of the patients experienced side effects from antiasthmatic drugs. 20% of the patients are declared as non-adherent to their asthma therapy at the present time and 66% of them were non-adherent at some time in the past. 42% of the patients demonstrated incorrect use of inhalers. Results of this study indicate the presence of significant asthma treatment-related problems in primary health care. These therapy-related problems in asthma and their number indicate the need for active integration of pharmacists into the process of monitoring and supervision of patients with asthma. It is imperative to educate the patients about the need for adherence, correct inhaler technique and how to avoid adverse drug reactions.

**Keywords:** asthma therapy related problems, ACT score, GINA guidelines, side effects, adherence, inhalers.



### **INTRODUCTION**

According to the World Health Organisation (WHO), asthma is a disease characterised by recurring attacks of difficult breathing and wheezing, which vary in frequency and severity from person to person [1]. Asthma is clinically manifested by repeated attacks of wheezing, breathlessness, chest tightness, and coughing, particularly at night and / or early in the morning. These attacks are usually associated with variable airway obstruction that is most often reversible, either spontaneously or with treatment. A number of inflammatory cells and their mediators play a role in the development of inflammation. Inflammation causes the airway hyper-reactivity to a variety of stimuli, and in some patients resulting in permanent morphological changes in the structure of the airways (remodelling), which

causes a certain degree of irreversible bronchial obstruction [2]. Asthma is a serious global health problem affecting all age groups. It is estimated that 300 million people have asthma. Its prevalence is increasing in many countries, especially among children. The aim of asthma treatment is now directed to achieving good, and if possible, complete control of the disease, over a longer period of time. Asthma control includes control of the symptoms above mentioned, but also includes risk reduction of the future adverse outcomes in a patient (exacerbations, rapid worsening of the lung function and adverse drug reactions) [3]. For the best outcomes, regular daily controller treatment should be initiated as soon as possible, primary inhaled corticosteroids (ICS), in a dose effective for each individual. This group of drugs is called the gold standard in the treatment of asthma. Controller medication is adjusted up or down in a

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stepwise approach for the best response [4]. On every step of asthma treatment, it is highly recommended to prescribe the patient with a symptom reliever medication (in most cases short-acting beta<sub>2</sub>-agonist - SABA). Frequent use of a short acting reliever medication indicates poor asthma control and this should result in a dose increase of the controller medications. In spite of laudable efforts to improve asthma care with better education of the patients and the greater availability of a large number of anti-asthmatic drugs, many patients globally have not benefited from advances in asthma treatment. Today asthma also imposes an unacceptable burden on health care systems because of its direct treatment costs, but also a burden on society, as indirect costs, through the loss of productivity in the workplace and disruption to the family [3]. The objectives of this study are to determine the most common therapy related problems in the treatment of asthma, but also to indicate the need for active integration of pharmacists into the process of monitoring and supervision of patients with asthma.

## PATIENTS AND METHODS

**Patients:** This observational study was conducted in Split-Dalmatian county pharmacy "Solin" which is a part of the Public Health Centre "Solin". The study included patients with a diagnosis of J45 (asthma) according to the International Classification of Diseases (ICD) [5], who have agreed to participate while picking up their anti-asthmatic drug prescription. The patients who were just diagnosed with asthma and who are picking up their anti-asthmatic drug from the pharmacy for the first time as well as the patients younger than 18 years of age were excluded from the study. All participants in the research were asked to examine and sign the informed consent about the purpose of the research conducted in accordance with ethical principles and the Declaration of Helsinki. The first part of data required according to form for the analysis of therapy was taken from the patients' health records of a cooperative family medicine physician, while the other necessary data was filled by the pharmacist in conversation with the patient.

**Statistical Analysis:** In order to collect the data a form was designed for this research. The form consists of four sections. The first section includes general patient characteristics (gender, age, body weight, height, and body mass index), and the information subsequently taken from the health records of patients in collaboration with their family medicine physician, which include: the degree of asthma, the duration of illness, medications prescribed in treatment of asthma and their dosage. Data on the degree of asthma and

prescribed therapy was used to assess compliance of the prescribed therapy with GINA guidelines. ---

In the second section the patient answered questions about perceived side effects that may be associated with the use of anti-asthmatic drugs, and about the impact of these side effects on his attitude toward treatment as well as the impact of some other factors on the regularity of the use of prescribed anti-asthmatic drugs.

The third section is filled out by the patient with the help of a pharmacist in the form of ACT. ACT is a simple test consisting of 5 questions that may be filled out by the patients themselves, and serves to detect poorly controlled asthma. The test covers the period within 4 weeks before completing the questionnaire and through that period estimated are: frequency of shortness of breath and general symptoms of asthma, frequency of use of medications for quick relief of symptoms, the impact of asthma on daily activities and overall self-assessment of asthma control. Each question has 5 multiple choices that are scored (for symptoms and activities: 1-always to 5- never; for disease control itself: 1- no control to 5- totally under control). The range of the test results is from 5 (poor control of asthma) to 25 (complete control of asthma). Test results greater than 19 indicate good control of asthma [6, 7].

The fourth section is filled out by a pharmacist after the patient demonstrates the use of a prescribed inhaler (the propriety of using with a description of the observed errors). The pharmacist at the same time follows the pre-compiled summary of the proper use of different types of inhalers, in order to better detect errors that affect the most inefficiency of drugs administered and the occurrence of side effects. Summary of the proper use of inhalers is made according to the instructions for use of inhalers (from the patient information leaflet or via search engines available on the website of the Croatian Agency for Medicinal Products and Medical Devices) [8]. Summary contains descriptions of use divided by type of inhaler. All data collected was analysed using Microsoft Excel. The correlations between the relative values of ACT of compared groups were tested by Student's t-test and ANOVA test (multivariate analysis of variance) for testing the value of the difference between ACT among four degrees of asthma severity. The level of  $p < 0.05$  was considered statistically significant.

## RESULTS

The study included 50 patients, of whom 26 (52%) women. Distribution of age of patients was

negatively asymmetric, or shifted to an older age, and the average age of patients was  $52.78 \pm 17.80$  years. According to the calculated body mass index (BMI) [9] of patients tested, the average value of  $26.62 \pm 4.24$  was obtained, which indicates that for the most part included patients were overweight. BMI greater than 25 was present in 62% of subjects. Mean ACT value of the patients who are overweight is  $16.42 \pm 5.66$ , and of those with BMI under 25 is  $18.63 \pm 4.74$ . The difference between mean ACT values of groups above mentioned is not statistically significant (Student's t-test,  $p = 0.08$ ). Comorbidity with asthma is very common, found in 84% of the subjects, average 2.6 per patient. The most common comorbidity is allergic rhinitis (in 34% of the patients).

ACT results show that 54% of patients do not have adequately controlled asthma (ACT <20). Well-controlled asthma is found in 36% of patients (ACT = 20 - 24) and complete control in 10% of them (ACT = 25). The mean ACT value of all surveyed patients was  $17.26 \pm 5.39$ . The difference between ACT values of four groups divided by asthma level of severity, shown in Table 1, is statistically significant (ANOVA,  $p = 0.027$ ). 32% of the patients' therapies for asthma follow the GINA guidelines. In most patients, whose treatment is not in accordance with the GINA guidelines for a certain degree of asthma, it has been observed that drugs are prescribed in doses which, according to GINA guidelines, belong to one degree more severe asthma. The mean ACT value of patients with therapies in compliance with the guidelines is  $17.65 \pm 5.70$ , and of those who are not in compliance with the guidelines is  $16.76 \pm 5.19$ . The difference in mean ACT values between these two groups of patients was not statistically significant (t-test,  $p = 0.320$ ).

GINA guidelines recommend that patients on all levels of asthma severity should be prescribed with a drug from the group of drugs called SABA, in most cases salbutamol. It is strongly advised that all patients should have this medication always on them in case of a sudden exacerbation. Despite of this, 24% of the patients are not prescribed with this drug at all. Over-prescribing and administration of drugs for quick relief of symptoms (rapid-acting inhaled  $\beta_2$ - agonists) were found in 24% of patients who have this group of drugs in their therapy, and in 18% of the total number of patients. Of those surveyed, 40% reported that they have noticed some of the side effects of anti-asthmatic drugs taken. In 11 cases hoarseness was reported, and in 5 thrush. Other side effects have occurred less frequently. Side effects caused change in attitude towards therapy in 11 patients. Different changes in the attitude

towards anti-asthmatic therapy of the patients are shown in Table 2. At the time of the survey 20% of patients stated that they were taking their therapy for asthma irregularly, and 66% of them stated that at some point of their treatment they were not taking their medication regularly. Patients who at the time of the survey stated that they were taking their medication regularly have a mean ACT value of  $17.41 \pm 5.60$ , and in those who do not use them regularly this value is  $16.55 \pm 5.28$ . There is no statistically significant difference between the two groups (t-test,  $p = 0.335$ ). The main causes of non-adherence, listed in the order of prevalence, are shown in Table 3.

Of all the patients, 42% use their inhalers incorrectly. Incidence of different inhaler technique errors is shown in Table 4. Mean ACT value in patients using their inhalers properly is  $17.41 \pm 5.62$ , and in those who use them incorrectly it is  $17.04 \pm 5.18$ . There was no significant difference in the ACT values among subjects who demonstrated proper use and those with incorrect inhalation technique (t-test,  $p = 0.473$ ).

## DISCUSSION

The goal of this study is to determine asthma therapy related problems in adult Mediterranean Croatian patients with asthma. For the purpose of this study a questionnaire was composed, filled by the patients from Public Health Centre „Solin“ and their family medicine physician with the help of a pharmacist. During data collection there were some limitations in the first part of the questionnaire, which is filled by the pharmacist in cooperation with family medicine physicians. Limitations are related to asthma severity level of certain patients, where it was observed that, in most cases, family medicine physicians do not keep records of their patients in a way that could allow simple assessment of asthma severity level. This is further contributed by the fact that only a small number of patients refer regularly to a pulmonary disease specialist. Marked levels of asthma severity are therefore a reflection of the existing situation in the medical data of the patients and as such can be only a partial indicator of GINA guidelines adherence.

It is a known fact that asthma is more common in overweight people. Lack of physical activity and lung volume reduction due to abdominal fat can lead to difficulty breathing. As shown in ACT results, overweight patients have a lower test value, which may be due to the reduced impact of inhaled corticosteroids in thicker persons. Weight loss improves asthma control and reduces the need for medication in obese people [4]. This study confirmed the presence of allergic rhinitis in 34%

of subjects. Chronic rhino sinusitis is usually associated with severe asthma, and if treated properly with intranasal corticosteroids, patients have less frequent exacerbations and fewer visits to the emergency room [4].

Test results indicate that more than half of the patients do not have adequately controlled asthma (54% of patients have ACT scores less than 20) while only 10% have completely controlled asthma (ACT is 25). Studies about the assessment of asthma control conducted in other countries yield very similar results [10, 11, 12]. By comparing the ACT results according to the severity of asthma a decrease of mean ACT value for every degree of asthma from mild intermittent to severe permanent can be seen. These results are expected because of the nature of the disease itself, whereas each more severe degree of asthma is characterised by the presence of a larger number of day and night symptoms and lower lung function, making it difficult to obtain the control of the disease. In 2009 study was conducted on 809 patients with asthma and the goal of this study was to assess which factors have an influence on asthma control. The results showed that patients of female gender, with greater severity of asthma and those treated by primary care physicians, without the guidance of pulmonary disease specialist, have a greater risk of poor asthma control [13].

By comparing the prescribed patients therapy with recommended therapies for certain degree of asthma, 32% of patients did not have treatment in compliance with GINA guidelines. GINA guidelines recommend a stepwise approach to the treatment of asthma, allowing the scaling up or reducing the doses of medicines, depending on the presence of symptoms it allows the transition to a higher level of treatment or in the absence of symptoms it allows the transition to a lower level of treatment. For this reason it can be said that in the majority of cases the treatment of patients observed still follows the guidelines. The main problem when stepping up to a higher level of treatment is not implementing assessment of new therapy and failure to solve very common problems, such as checking the inhalation technique, poor adherence and presence of comorbidities (such as allergic rhinitis), which can make asthma control difficult [4].

GINA guidelines for each level of severity of asthma recommend prescribing medication from the group of short-acting beta agonists (salbutamol) that patients should always have on hand in case of a sudden onset of symptoms, but 24% of patients do not have this drug prescribed. At the time of the study, 18% of patients were over-using medications

for quick relief of symptoms, either due to ignorance and lack of understanding of how these drugs are properly used or due to real need because their asthma has worsened. In similar studies excessive use of medications for quick relief of asthma symptoms was found [14]. 40% of patients say that they have noticed some of the side effects of anti-asthmatic drugs (usually hoarseness and thrush). Side effects, in more than half of the patients who observed them, caused a change in attitude towards the treatment resulting in taking medication irregularly or in total discontinuation of therapy. The fear of drugs is the most common cause of reduced adherence of patients [15]. Pharmacists should keep in mind the existence of this problem in patients with asthma when issuing anti-asthmatic drugs and advise them on how to use their medicine.

Most of the patients, 66% of them, said that at some point of their treatment they did not take their medication as prescribed. This percentage is somewhat higher than those specified in the GINA guidelines which say that about 50% of people with asthma at some point in the treatment do not take medication as instructed by the physician [16]. Although most of the patients stated that the reasons for their poor compliance are unintentional, the research shows that these unintentional reasons for taking medication irregularly are not random and that in this case, non-adherence was also caused by their beliefs about the medicines they use and by the fact that they suffer from a chronic disease. After all, an unintentional non-adherence can switch to a deliberate one [17].

According to GINA guidelines almost 70 - 80% of patients are not using their inhalers properly. Many doctors and other health care professionals, including pharmacists, do not exactly know how to demonstrate the use of prescribed inhalers to their patients [18]. Patients are often unaware of their problems with taking the drug, a poor inhalation technique can lead to worse asthma control, increasing the risk of exacerbations and the number of side effects (stomach pain due to drug deposition in the mouth and its ingestion, thrush due to not using procedure of rinsing their mouth after inhalation of certain types of drugs) [4]. The study found that 42% of patients do not use their inhalers properly. Results of correctness of inhalation technique and frequency of improper use of the inhaler may vary due to parameters monitored during the assessment. Poor inhalation technique in most cases leads to poorer disease control [12, 19]. In this study, the difference in ACT results between subjects who demonstrated proper inhalation technique and those who have demonstrated incorrect technique was minimal.

Research results of therapeutic problems in asthma suggest that there is a wide range of activity of the pharmacist in patients with asthma. It involves collaboration with patients, but also family medicine physicians. Since trained pharmacists are among the most accessible members of the health care team, they may be involved in the daily monitoring of patients with asthma and during every picking up of anti-asthmatic drug prescription they may advise the patients about the importance of adherence and correct inhalation techniques. Pharmacists can conduct additional education about the importance of correct treatment of comorbidities, about the importance of reducing body weight and avoidance of allergens in people with allergic asthma. As a part of everyday work in a pharmacy filling ACT should be included. This would allow easy detection of patients who do not have adequate control of the disease. Cooperation of pharmacists with patients and family physicians could contribute to a better treatment outcome to a

significant extent, which would ultimately lead to a reduction in healthcare costs.

## CONCLUSIONS

Results of this study indicate the presence of significant asthma treatment-related problems in primary health care. More than half of the patients in this study have uncontrolled asthma, two-thirds do not have anti-asthmatic drugs prescribed in adherence to GINA guidelines, adverse drug reactions are present in 40% of them, 66% are non-adherent in some level and a large number of them demonstrated inadequate inhaler technique. Significant therapy-related problems in asthma and their number indicate the need for active integration of pharmacists into the process of monitoring and supervision of patients with asthma. It is imperative to educate the patients about the need for adherence, correct inhaler technique and how to avoid adverse drug reactions.

**Table 1. ACT values of four levels of asthma severity.**

ASTHMA SEVERITY LEVEL	NUMBER OF PATIENTS	ACT SCORE
Mild intermittent	11	20.45 ± 4.52
Mild persistent	17	17.18 ± 5.35
Moderate persistent	16	16.94 ± 5.11
Severe persistent	6	12.50 ± 4.85

**Table 2. The influence of side effects on patients attitude towards prescribed antiasthmatic therapy.**

CHANGE IN ATTITUDE TOWARDS THERAPY AFTER OBSERVED SIDE EFFECTS	NUMBER OF PATIENTS
The implementation of all the steps of proper use of the drug to reduce the side effects to a minimum	11
Irregular drug taking	3
Discontinuation of therapy	3

**Table 3. Causes of non-adherence (patients could choose more than one answer).**

THE CAUSE OF NON-ADHERENCE	NUMBER OF PATIENTS
Sometimes I forget to take my medication(s)	13
I'm taking anti-asthmatic(s) only when I am not feeling well	7
I am not exactly clear how I should take my medication(s)	6
I am convinced that inhaled corticosteroids are harmful	6
My illness is not that serious	4
Other	13

**Table 4. Incidence of different inhaler technique errors.**

THE DESCRIPTION OF INHALER TECHNIQUE ERROR	INCIDENCE OF ERROR PREVALENCE IN THE GROUP WHO DEMONSTRATED INCORRECT INHALATION TECHNIQUE (%)
Incorrect expiration before using the drug	72
Incorrect inspiration of powdered drug	62
Absence of breath holding after removing the inhaler from the mouth	38
Irregular coverage of the mouthpiece of the inhaler	14
Other irregularities	19

## REFERENCES

- [1] World Health Organisation (WHO). Chronic Respiratory Diseases. Asthma. 2014. <http://www.who.int/respiratory/asthma/en/> (Accessed March 03, 2014).
- [2] Tudorić N et al. Guidelines for diagnosis and management of asthma in adults of the Croatian Respiratory Society. *Liječ Vjesn* 2007; 129: 315-21.
- [3] Vuknić Dugac A. Correct use of inhalers- the path to asthma control. *Medicus* 2013; 22(1): 25-31.
- [4] Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2014. <http://www.ginaastma.org/> (Accessed June 11, 2014).
- [5] World Health Organisation (WHO): ICD-10 Version: 2010. <http://apps.who.int/classifications/apps/icd/icd10online/> (Accessed October 27, 2014).
- [6] Nathan RA et al. Development of the asthma control test: A survey for assessing asthma control. *J Allergy Clin Immunol* 2004; 113: 59-65.
- [7] Schatz M et al. Asthma Control Test: reliability, validity and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol* 2006; 117: 549-56.
- [8] Agencija za lijekove i medicinske proizvode (HALMED): Drugs. <http://www.almp.hr/?in=hr&w=lijekovi/> (Accessed September 27, 2014).
- [9] National Heart, Lung, and Blood Institute, U.S. Department of Health & Human Services, Bethesda. <http://www.nhlbi.nih.gov/.../BMI/bmicalc.htm> (Accessed September 28, 2014).
- [10] Olaguibel JM et al. Measurement of asthma control according to Global Initiative for Asthma guidelines: a comparison with the Asthma Control Questionnaire. *Respir Res* 2012; 13: 50.
- [11] Price D, Fletcher M, van der Molen T. Asthma control and management in 8000 European patients: the REcognise Asthma and LInk to Symptoms and Experience (REALISE) survey. *NPJ Prim Care Respir Med* 2014; 24: 14009.
- [12] Baddar S et al. Asthma control: importance of compliance and inhaler technique assessments. *J Asthma* 2014; 51(4): 429-34.
- [13] Badiola C et al. Women, patients with severe asthma, and patients attended by primary care physicians, are at higher risk of suffering from poorly controlled asthma. *Prim Care Respir J* 2009; 18(4): 294-9.
- [14] Slejko JF et al. Asthma control in the United States, 2008-2010: Indicators of poor asthma control. *J Allergy Clin Immunol* 2014; 133(6): 1579-87.
- [15] Haugbølle LS, Sørensen EW. Drug-related problems in patients with angina pectoris, type 2 diabetes and asthma-interviewing patients at home. *Pharm World Sci* 2006; 28(4): 239-47.
- [16] Boulet L-P et al. Adherence: the goal to control asthma. *Clin Chest Med* 2012; 33: 405-17.
- [17] Gadkari AS, McHorney CA. Unintentional non-adherence to chronic prescription medications: how unintentional is it really? *BMC Health Serv Res* 2012; 12: 98.
- [18] Fink JB, Rubin BK. Problems with inhaler use: a call for improved clinician and patient education. *Respir Care* 2005; 50: 1360-74.
- [19] Dalcin Pde T. Factors related to the incorrect use of inhalers by asthma patients. *J Bras Pneumol* 2014; 40(1): 13-20.