The adherence and illness perception of patients diagnosed with asthma or chronic obstructive pulmonary disease treated with polytherapy using new generation Cyclohaler

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Abstract

Introduction: The factors influencing adherence of patients diagnosed with asthma and chronic obstructive pulmonary disease (COPD) include the complexity of the therapy, fear of side effects of drugs, method of taking the drug, dosage regimen, polypharmacy, adverse events, knowledge about the essence of the disease and its complications, illness perception and priorities in life, training on the use of the inhaler, the duration of treatment, social support, and drug availability.

Aim: To assess the adherence of patients diagnosed with asthma and COPD treated with polytherapy with fluticasone propionate and formoterol fumarate using the Fantasmino inhaler in relation to primary diagnosis and illness perception as well as patients’ and doctors’ opinion about this form of therapy.

Material and methods: A questionnaire survey covering adherence, illness perception and opinion about polytherapy using new generation Cyclohaler performed by pulmonologists, allergologists and general practitioners in 3,618 patients with asthma and 2,602 with COPD.

Results: On visit 1, a lower adherence rate was observed in COPD than in the asthma group (72.0% vs. 61.5%; p < 0.01). During the observation, the adherence rate increased significantly in the COPD group, only (61.5% vs. 73.0%; p < 0.01). A negative correlation between total MMAS-8 and BIPQ scores was observed in both study groups (R = –0.15; p < 0.001 and R = –0.24; p < 0.001, respectively). During the observation, a percentage of patients who believed that the administration of the two drugs in a single inhaler considerably facilitates their use increased significantly in both study groups. In addition, an increased percentage of doctors believed that this therapeutic option facilitated education of patients and decreased the number of errors made by the patients.

Conclusions: The illness perception, younger age, disease duration and severity are predictors of adherence to treatment with fluticasone propionate and formoterol fumarate using the Fantasmino inhaler among patients with asthma and COPD. The positive opinion of patients and doctors about administration of fluticasone propionate and formoterol fumarate using the Fantasmino inhaler increased during observation.

Key words: asthma, chronic obstructive pulmonary disease, adherence, polytherapy, new generation Cyclohaler.

Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are common diseases in the Polish population [1, 2]. Both are progressive diseases and their exacerbations are a threat to life. The appropriate pharmacotherapy slows the progression of these diseases, reduces the number of exacerbations and improves quality of life [3, 4]. Currently the preferred form of pharmacotherapy in asthma and COPD are drugs administered directly into the bronchial tree in the form of inhaled formulations. The benefit of this form of therapy over oral or parenteral use of drugs include rapid onset of action, high concentrations at the target site, the possibility of using lower doses and minimizing side effects. Polytherapy involves inhaled glucocorticosteroids and long-acting β₂-agonist acting on both key links of asthma and COPD pathogenesis – bronchoconstriction and inflammation [3, 4]. However, the effectiveness of pharmacotherapy depends
primarily on patient cooperation including adherence that consists of two components: compliance and persistence. Factors influencing the inclusion of the patient in the treatment process include attitude towards the disease (disease negation, underestimation of disease, exaggeration, adequate attitude), image of disease, the importance of the disease to the patient, doctor-patient communication [5]. Numerous studies revealed adherence of about 60% of patients diagnosed with asthma and COPD [6, 7]. The factors influencing adherence include the complexity of the therapy, fear of side effects of drugs, method of taking the drug, dosage regimen, polypharmacy, adverse events, knowledge about the essence of the disease and its complications, illness perception and priorities in life, training on the use of the inhaler, the duration of treatment, social support, and drug availability [8].

As mentioned above, asthma and COPD in most cases require polytherapy and the method of taking the drug is one of factors influencing adherence. Thus, possibility of administration of two formulations using one type of the inhaler may be the factor influencing adherence. It has been shown that the use of dry powder inhaler (DPIs) in the 1 generation inhaler (Cyclohaler and Diskhaler) is associated with a lower number of patients making mistakes during preparation and use of equipment for the same inhalation [9]. In addition, Pallen et al. [10] revealed that when using the Cyclohaler most of the maneuvers were performed correctly by 100% of patients. In 2006, the U.S. patented a new generation Cyclohaler, which is available on the Polish market under the name Fantasmino. This inhaler makes it possible to use two formulations: fluticasone propionate and formoterol fumarate. There are no studies assessing adherence and illness perception in patients with asthma or COPD treated with polytherapy using the Fantasmino inhaler as well as opinion of patients and doctors about this form of therapy.

**Aim**

Therefore, the aims of the study were:

1. to assess the adherence in patients diagnosed with asthma and COPD treated with polytherapy with fluticasone propionate and formoterol fumarate using the Fantasmino inhaler in relation to primary diagnosis and illness perception.
2. to assess patients’ and doctors’ opinion about this form of therapy.

**Material and methods**

In this observational survey, 3,618 patients diagnosed with asthma (56.9% of women) and 2,602 diagnosed with COPD (42.7% of women) were interviewed nationwide by 311 pulmonologists, allergologists and general practitioners in 2013–2014. Polish doctors participating in the study were recruited by medical representatives, and each of them conducted questionnaire interviews with a group of 6220 consecutive patients visiting the clinic for asthma or COPD treated with fluticasone propionate and formoterol fumarate using the Fantasmino inhaler during two successive visits resulting from the needs of therapy.

The inclusion criteria were age ≥ 18 years, diagnosis of asthma or COPD, current polytherapy with fluticasone propionate and formoterol fumarate using the Fantasmino inhaler at least 14 days prior to enrollment. The exclusion criteria included age below 18 years, inability to obtain the patient’s answers to the questions included in the survey, patient’s refusal. Characteristics of the surveyed population are summarized in Table 1.

The questionnaire consisted of several dichotomous and multiple choice questions.

The questionnaire on visit 1 consisted of four parts including demographic data (gender, age, place of residence, education and employment status), medical history (primary diagnosis, disease duration and severity, exacerbation of disease since the last visit, hospitalization due to exacerbation of primary disease since the last visit, the current treatment, duration of the therapy with fluticasone propionate and formoterol fumarate and duration of this therapy using the Fantasmino inhaler), the reasons for non-adherence. In the second part, similarity questions as at visit 1 were asked to assess patients’ and doctors’ opinions.

In addition, on both visits, Morisky 8-item medication adherence questionnaire (MMAS-8) and Brief Illness Perception Questionnaire (BIPO) Polish version were included in the study questionnaire. Each item of the BIPO assessed one dimension of IP such as the consequences, timeline, personal control, treatment control, identity, coherence, emotional representation and concern.

**Statistical analysis**

Statistical analysis was performed using the Statistica 10.0 PL software package. The adherence to the therapy of patients diagnosed with asthma or COPD treated with polytherapy with fluticasone propionate and formoterol fumarate using Fantasmino were analyzed according to illness perception as well as age, disease duration and severity.

The opinion of patients on the impact of the use of the Fantasmino inhaler on facilitation adherence and doctors’ opinion on facilitation of the patient education,
The adherence and illness perception of patients diagnosed with asthma or chronic obstructive pulmonary disease treated with polytherapy using new generation Cyclohaler

Table 1. Study group characteristics

| Parameter                        | Asthma $N = 3618$ | COPD $N = 2602$ | Asthma vs. COPD |
|----------------------------------|-------------------|-----------------|-----------------|
| Age, n (%) [years]:             |                   |                 |                 |
| 18–30                            | 46.7 ±15.0        | 60.0 ±13.5      | $p < 0.001$     |
| 31–40                            | 651 (18.0)        | 117 (4.5)       |                 |
| 41–50                            | 601 (16.6)        | 963.7           | $p < 0.001^*$   |
| 51–60                            | 905 (25.0)        | 300 (11.5)      |                 |
| > 60                             | 839 (23.2)        | 749 (28.8)      |                 |
|                                   | 622 (17.2)        | 1340 (51.5)     |                 |
|                                   |                   |                 |                 |
| Women, n (%)                     | 2059 (56.9)       | 1111 (42.7)     | $p < 0.01^*$    |
| Men, n (%)                       | 1559 (43.1)       | 1491 (52.3)     |                 |
| Education, n (%):                |                   |                 |                 |
| Primary                          | 318 (8.8)         | 528 (20.3)      | $p < 0.001^*$   |
| Vocational                       | 1631 (45.1)       | 921 (35.4)      |                 |
| Secondary                        | 948 (26.2)        | 932 (35.8)      |                 |
| Higher                           | 720 (19.9)        | 221 (8.5)       |                 |
| Labour activity, n (%):          |                   |                 |                 |
| Mental work                      | 1346 (37.2)       | 356 (13.7)      | $p < 0.001^*$   |
| Manual work                      | 821 (22.7)        | 533 (20.5)      |                 |
| Pensioner                        | 380 (10.5)        | 526 (20.2)      |                 |
| Retired                          | 474 (13.1)        | 982 (37.7)      |                 |
| Unemployed                        | 597 (16.5)        | 205 (7.9)       |                 |
| Place of residence, n (%):       |                   |                 |                 |
| Rural areas                      | 995 (27.5)        | 1241 (47.7)     | $p < 0.01^*$    |
| City                             | 2623 (72.5)       | 1361 (52.3)     |                 |
| Duration of the disease, n (%) [years]: |               |                 |                 |
| < 1                              | 293 (8.1)         | 177 (6.8)       | $p < 0.01^*$    |
| 1–2                             | 698 (19.3)        | 359 (13.8)      |                 |
| 3–5                             | 1133 (31.3)       | 682 (26.2)      |                 |
| > 5                             | 1494 (41.3)       | 1384 (53.2)     |                 |
| Severity of the disease, n (%):  |                   |                 |                 |
| Mild                             | 1071 (29.6)       | 723 (27.8)      | $p < 0.001^*$   |
| Moderate                         | 2308 (63.8)       | 21 (0.8)        |                 |
| Severe                           | 239 (6.6)         | 1673 (64.3)     |                 |
| Very severe                      | –                 | 185 (7.1)       |                 |
| Exacerbation of the disease between visit 1 and prior visit, n (%): | | | |
| Yes                              | 970 (26.8)        | 1160 (44.6)     | $p < 0.001^*$   |
| No                               | 2648 (73.2)       | 1442 (55.4)     |                 |
| Number of exacerbations, n (%):  |                   |                 |                 |
| 1–2                             | 3158 (87.3)       | 2259 (86.8)     | NS              |
| 2–5                             | 427 (11.8)        | 343 (13.2)      |                 |
| 5–10                            | 33 (0.9)          | 0               |                 |
| Hospitalization due to disease exacerbation between visit 1 and prior visit, n (%): | | | |
| Yes                              | 166 (4.6)         | 461 (17.7)      | $p < 0.01^*$    |
| No                               | 3452 (95.4)       | 2141 (82.3)     |                 |
| Number of hospitalizations, n (%): |               |                 |                 |
| 1                                | 3166 (87.5)       | 2339 (89.9)     | NS              |
| 2                                | 452 (12.5)        | 263 (10.1)      |                 |
| Currently used pharmacotherapy, n (%): |           |                 |                 |
| Short-acting $\beta_2$-agonist adrenergic receptor | 1910 (52.8)   | 1702 (65.4)     | $p < 0.01^*$    |
| Long-acting $\beta_2$-agonist adrenergic receptor | 3618 (100)     | 2602 (100)      |                 |
| Inhaled glucocorticosteroids     | 3618 (100)       | 2602 (100)      |                 |
| Oral glucocorticosteroids        | 362 (10.0)       | 396 (15.2)      |                 |
| Anti-leukotriene agents          | 1418 (39.2)      | 151 (5.8)       |                 |
| Theophylline                     | 496 (13.7)       | 1236 (47.5)     |                 |
| 4 phosphodiesterase inhibitor    | 94 (2.6)         | 91 (3.5)        |                 |
| Mucolytic drugs                  | 311 (8.6)        | 903 (34.7)      |                 |
reduction in the number of errors made during the inha-
lation, the treatment effectiveness were also assessed.

Values of variables were presented as percentages
and mean values with standard deviations (SD). Sepa-
rate groups were compared using the \( \chi^2 \) test and \( \chi^2 \) test
for trend and T test. The assessment of associations be-
 tween variables was done with Spearman correlation.
A \( p < 0.05 \) was considered as statistically significant.

Results

Discontinuation of therapy between visit 1 and 2

Between visit 1 and 2, 16.2% of patients with asthma
and 15.0% of patients with COPD discontinued therapy
with fluticasone propionate and formoterol fumarate us-

ing the Fantasmino inhaler. The most common reason for
 discontinuation in both groups was a conscious decision
to stop treatment (22.0% and 31.9%, respectively). An-
other reason for discontinuation of therapy was not pur-
chasing the prescription drugs for reasons independent
of the patient (13.5% and 14.9%, respectively). Patients
with COPD significantly more frequently than patients
with asthma discontinued treatment due to discomfort
associated with its use (24.5% vs. 11.3%, \( p < 0.01 \)) and
adverse events (13.8% vs. 7.1%, \( p < 0.01 \)). In turn, patients
with asthma significantly more frequently than with pa-
tients with COPD discontinued therapy due to the lack of
disease symptoms (14.2% vs. 5.3%, \( p < 0.01 \)) and influ-
enced by other people (12.1% vs. 4.3%, \( p < 0.001 \)) as well
as due to disappointment because of no improvement
(9.2% vs. 6.4%, \( p < 0.05 \)).

Illness perception in asthma and chronic
obstructive pulmonary disease groups

There were no differences in mean score of the ill-
ness perception between asthma and COPD groups on
visit 1. However, significantly higher mean scores of the
impact of the disease on patient’s life, opinion on the
duration of disease, assessment of disease severity and
the impact of the disease on the emotions were observed
in the COPD than in the asthma group. In turn, mean
scores of the sense of disease control, opinion that the
treatment can help in the disease, understanding the na-
ture of the disease and interest in knowledge about the
disease were significantly higher in the asthma than in
the COPD group (Table 2).

In both study groups, the mean scores of impact of
disease on patient’s life, assessment of disease severity
and impact of disease on the emotions decreased signifi-
cantly on visit 2. In turn, the mean score of disease con-
trol, and understanding of the disease increased signifi-
cantly. The mean score of opinion that the treatment can
help in the disease and interest in knowledge about the
disease increased significantly in the asthma group only.
In turn, the mean score of opinion on the duration of
disease in the asthma group increased and in the COPD
group decreased (Table 2).

Adherence and reasons for non-adherence

On visit 1, a lower adherence rate was observed in
the COPD than in the asthma group (72.0% vs. 61.5%;
\( p < 0.01 \)). During the observation, the adherence
rate in the asthma group did not change, while in the
COPD group, it increased significantly (61.5% vs. 73.0%;
\( p < 0.01 \)) – Table 3.

In both study groups, the more frequent reason for
non-adherence was the organizational causes – haste
and forgetfulness; well-being with the lack of conviction
about the need for a prescribed drug regimen and the
fear of side effects. However, these reasons were signifi-
cantly more rarely declared by patients diagnosed with
COPD than asthma (Table 3).

In the asthma group the non-adherence rate was the
highest among subjects aged 18–30 years (39.7%) and

| Parameter | Asthma | COPD | Asthma vs. COPD |
|-----------|--------|------|-----------------|
| Duration of use of polytherapy with inhaled glucocorticosteroids and long-acting \( \beta_2 \)-agonist adrenergic receptor, \( n \) (%): | | | |
| < 1 month | 499 (13.8) | 211 (8.1) | \( p < 0.01 \)* |
| 1–3 months | 355 (9.8) | 208 (8.0) |
| 3–6 months | 619 (17.1) | 396 (15.2) |
| 6–12 months | 311 (8.6) | 286 (11.0) |
| > 1 year | 1834 (50.7) | 1501 (57.7) |

*\( \chi^2 \) test for trend

| Parameter | Asthma | COPD | Asthma vs. COPD |
|-----------|--------|------|-----------------|
| Duration of use of inhaled glucocorticosteroids and \( \beta_2 \)-agonist adrenergic receptor with the Fantasmino inhaler, \( n \) (%): | | | |
| < 1 month | 857 (23.7) | 515 (19.8) | \( p < 0.01 \)* |
| 1–3 months | 913 (25.2) | 484 (18.6) |
| 3–6 months | 857 (23.7) | 677 (26.0) |
| 6–12 months | 398 (11.0) | 411 (15.8) |
| > 1 year | 593 (16.4) | 515 (19.8) |
## Table 2. Illness perception

| Parameter                                      | Asthma | COPD  |
|------------------------------------------------|--------|-------|
|                                                | Visit 1| N = 3618 | Vis 1 | N = 2602 |
| Total score                                    | 54.3 ±9.7 | 54.0 ±9.2 | 54.3 ±10.0 | 51.9 ±10.7*** |
| Impact of asthma/COPD on patient’s life, n (%):| 6.2 ±2.5 | 5.5 ±2.7*** | 7.6 ±2.2*** | 6.7 ±2.4**** |
| None at all                                    | 300 (8.3) | 535 (14.8) | 49 (1.9) | 99 (3.8) |
| Slight                                         | 626 (17.3) | 879 (24.3) | 208 (8.0) | 416 (16.0) |
| Moderate                                       | 920 (25.4) | 763 (21.1) | 467 (17.9) | 656 (25.2) |
| Significant                                    | 1077 (29.8) | 891 (24.6) | 840 (32.3) | 721 (27.7) |
| Severe                                         | 695 (19.2) | 550 (15.2) | 1038 (39.9) | 710 (27.3) |
| Opinion on the duration of asthma/COPD, n (%): | 8.4 ±1.9 | 8.8 ±1.8*** | 8.8 ±1.7*** | 8.6 ±1.9* |
| Very short                                     | 18 (0.5) | 65 (1.8) | 13 (0.5) | 10 (0.4) |
| Short                                          | 141 (3.9) | 98 (2.7) | 49 (1.9) | 143 (5.5) |
| Moderately long                                | 496 (13.7) | 232 (6.4) | 273 (10.5) | 274 (10.5) |
| Long                                           | 854 (23.6) | 774 (21.4) | 442 (17.0) | 432 (16.6) |
| Forever                                        | 2109 (58.3) | 2449 (67.7) | 1825 (70.1) | 1743 (67.0) |
| Sense of disease control, n (%):               | 7.1 ±1.7 | 8.1 ±1.6*** | 7.1 ±1.7*** | 7.3 ±1.8*** |
| The total lack                                  | 58 (1.6) | 47 (1.3) | 75 (2.9) | 26 (1.0) |
| Lack                                           | 506 (14.0) | 283 (7.8) | 419 (16.1) | 284 (10.9) |
| Partially                                      | 988 (27.3) | 698 (19.3) | 804 (30.9) | 804 (30.9) |
| Significant                                    | 1368 (37.8) | 1436 (39.7) | 1026 (39.4) | 1132 (43.5) |
| Extreme                                        | 698 (19.3) | 1154 (31.9) | 278 (10.7) | 356 (13.7) |
| Opinion on the effects of treatment on asthma/ COPD, n (%): | 7.7 ±1.7 | 8.1 ±1.6*** | 7.1 ±1.7*** | 7.3 ±1.8*** |
| None at all                                     | 25 (0.7) | 36 (1.0) | 26 (1.0) | 26 (1.0) |
| Slight                                         | 174 (4.8) | 123 (3.4) | 146 (5.6) | 198 (7.6) |
| Moderate                                       | 514 (14.2) | 329 (9.1) | 715 (27.5) | 539 (20.7) |
| Significant                                    | 1650 (45.6) | 1397 (38.6) | 1145 (44.0) | 1103 (42.4) |
| Extreme                                        | 1255 (34.7) | 1733 (47.9) | 570 (21.9) | 736 (28.3) |
| Assessment of the severity of asthma/COPD symptoms, n (%): | 5.6 ±2.2 | 4.5 ±2.3*** | 6.7 ±1.9*** | 5.5 ±2.1**** |
| No symptoms                                     | 369 (10.2) | 897 (24.8) | 65 (2.5) | 190 (7.3) |
| Slight                                         | 734 (20.3) | 1071 (29.6) | 242 (9.3) | 682 (26.2) |
| Moderate                                       | 1111 (30.7) | 865 (23.9) | 757 (29.1) | 853 (32.8) |
| Significant                                    | 1111 (30.7) | 601 (16.6) | 1129 (43.4) | 677 (26.0) |
| Many severe symptoms                           | 293 (8.1) | 184 (5.1) | 409 (15.7) | 200 (7.7) |
| Interest in knowledge about the disease, n (%): | 7.8 ±2.1 | 8.0 ±2.0* | 6.7 ±2.4*** | 6.6 ±2.5*** |
| None at all                                     | 62 (1.7) | 40 (1.1) | 146 (5.6) | 148 (5.7) |
| Slight                                         | 188 (5.2) | 184 (5.1) | 333 (12.8) | 422 (16.2) |
| Moderate                                       | 771 (21.3) | 579 (16.0) | 713 (27.4) | 682 (26.2) |
| Great                                          | 933 (25.8) | 962 (26.6) | 744 (28.6) | 619 (23.8) |
| Extreme                                        | 1664 (46.0) | 1853 (51.2) | 666 (25.6) | 751 (28.1) |
| Understanding the nature of the disease, n (%): | 6.5 ±2.2 | 7.1 ±2.1*** | 5.4 ±2.2*** | 5.7 ±2.2*** |
| None at all                                     | 145 (4.0) | 90 (2.5) | 291 (11.2) | 250 (9.6) |
| A little                                       | 449 (13.8) | 318 (8.8) | 508 (19.5) | 468 (18.0) |
| Moderate                                       | 1158 (32.0) | 919 (25.4) | 1054 (40.5) | 856 (32.9) |
| Good                                           | 1035 (28.6) | 1274 (35.2) | 549 (21.1) | 763 (29.3) |
| Very good                                      | 781 (21.6) | 1017 (28.1) | 200 (7.7) | 265 (10.2) |
| The impact of asthma/COPD on the emotions, n (%): | 5.4 ±2.4 | 4.8 ±2.6*** | 5.7 ±2.3* | 5.1 ±2.3*** |
| Lack                                           | 535 (14.8) | 952 (26.3) | 265 (10.2) | 458 (17.6) |
| Slight                                         | 768 (21.2) | 800 (22.1) | 505 (19.4) | 619 (23.8) |
| Moderate                                       | 1020 (28.2) | 763 (21.1) | 864 (33.2) | 729 (28.0) |
| Significant                                    | 861 (23.8) | 810 (22.4) | 684 (26.3) | 635 (24.4) |
| Extreme                                        | 434 (12.0) | 293 (8.1) | 284 (10.9) | 161 (6.2) |

*p < 0.05; ***p < 0.001 asthma vs. COPD; p < 0.05; ****p < 0.001 visit 1 vs. visit 2
the lowest among subjects aged over 60 years (15.4%). In the COPD group, the non-adherence rate was the highest among subjects aged 31–40 years (56.5%) and the lowest among subjects aged 41–50 years (31.9%). Difficulties with the inhaler use as the cause of non-adherence in both study groups were most frequently reported by patients aged over 60 years (5.4% and 4.7%, respectively) – data not shown.

In the asthma group the non-adherence rate was the highest among subjects with disease duration over 5 years (43.9%) and in the COPD group, among subjects with disease duration of less than 1 year (43.5%). However, difficulties with the inhaler use as the cause of non-adherence in the asthma group were most frequently reported by subjects with disease duration of less than 5 years and in the COPD group by subjects with disease duration over 5 years (2.9% and 4.9%, respectively) – data not shown.

In the asthma group, the non-adherence rate was the lowest among patients with mild disease severity and in the COPD group among patients with very severe disease (16.6% and 35.3%, respectively). Difficulties with the inhaler use as the cause of non-adherence in the asthma group were most frequently reported by subjects with moderate disease severity and in the COPD group by subjects with mild disease severity (5.0% and 3.2%, respectively) – data not shown.

### Table 3. Adherence during the observation period and factors influencing non-adherence

| Parameter | Asthma N = 3618 | COPD N = 2602 |
|-----------|----------------|--------------|
|           | Visit 1 | Visit 2 | Visit 1 | Visit 2 |
| Results of Morisky questionnaire, n (%):  |  |  |  |  |
| Adherence (≤ 4 points) | 2605 (72.0) | 2551 (70.5) | 1600 (61.5)^^^ | 1899 (73.0) |
| Non-adherence (> 4 points) | 1013 (28.0) | 1067 (29.5) | 1002 (38.5) | 703 (27.0) |
| Reasons for non-adherence [%]:  |  |  |  |  |
| Organizational causes – haste, forgetfulness | 2012 (55.6)*** | 806 (22.3)*** | 965 (37.1)^^^ | 492 (18.9)^^^ |
| Well-being – the lack of conviction about the need for a prescribed drug regimen | 1324 (36.6)*** | 637 (17.6)*** | 565 (21.7)^^^ | 263 (10.1)***^^ |
| Fear of side effects | 802 (22.2)*** | 340 (9.4)*** | 346 (13.3)^^^ | 94 (3.6)****^ |
| Desire to reduce the number of drugs used daily | 626 (17.3)*** | 83 (2.3)*** | 606 (23.3)^^ | 138 (5.3)*****^ |
| Difficulties in the use of the inhaler | 90 (2.5) | 0 | 206 (7.9) | 0 |
| A conscious decision not to purchase a prescribed drug | 90 (2.5) | 0 | 86 (3.3) | 31 (1.2) |
| Non-purchase of prescribed drugs for reasons beyond the patient | 119 (3.3) | 28 (0.8) | 140 (5.4) | 0 |
| Poor understanding of instructions from the doctor | 119 (3.3) | 0 | 109 (4.2) | 31 (1.2) |
| The method of taking the drug is complicated | 14 (0.4) | 0 | 55 (2.1) | 0 |
| Disappointment with the lack of improvement | 192 (5.3) | 65 (1.8) | 229 (8.8) | 0 |
| The high cost of treatment (less frequent use of the drug will bring savings) | 90 (2.5) | 14 (0.4) | 140 (5.4) | 0 |
| Frequent trips and forgetting to take the drug with the patient | 253 (7.0) | 72 (2.0) | 86 (3.3) | 31 (1.2) |
| Shift work system | 329 (9.1) | 58 (1.6) | 185 (7.1) | 47 (1.8) |
| Lack of medicine, long waiting time for a visit to get a prescription | 148 (4.1) | 83 (2.3) | 130 (5.0) | 0 |
| Other | 0 | 0 | 21 (0.8) | 0 |

**p < 0.01; ***p < 0.001 visit 1 vs. visit 2; ^^p < 0.01; ^^^p < 0.001 asthma vs. COPD

### Adherence and illness perception

On visit 1, the mean total score of illness perception in both study groups was significantly higher in adherence than non-adherence subgroups, while, on visit 2, this difference was observed in the asthma group only (Table 4).

There were no differences in mean score of the impact of the disease on patient’s life between adherence and non-adherence asthma subgroups on visit 1 and on visit 2, the impact was significantly higher in non-adherence than adherence subgroups. In turn, in the COPD group on both visits the impact of the disease did not differ between adherence and non-adherence subgroups (Table 4).

The mean score of the opinion on the duration of the disease on visit 1 was significantly higher in adherence than non-adherence subgroups in both asthma and COPD groups, while, on visit 2, this difference was observed in the COPD group only (Table 4).

The mean score of sense of disease control was significantly higher in adherence than non-adherence subgroup on both visits and in both study groups (Table 4).

The mean score of opinion on the effect of treatment on both visits in both study groups was significantly higher in the adherence than non-adherence subgroup (Table 4).
### Table 4. Adherence and illness perception

| Parameter                                      | Adherence                | Asthma, N = 3618 | COPD, N = 2602 |
|------------------------------------------------|--------------------------|------------------|-----------------|
|                                                | Visit 1: N = 2344/64.8   | Visit 2: N = 3036/83.9 | Visit 1: N = 1274/35.2 | Visit 2: N = 582/16.1 | Visit 1: N = 1280/49.2 | Visit 2: N = 2225/85.5 | Visit 1: N = 1322/50.8 | Visit 2: N = 377/14.5 |
|                                                | Adherence                | Non-adherence    | Adherence       | Non-adherence |
| Total score (%)                                | 55.5 ± 9.0               | 54.3 ± 9.6       | 52.2 ± 10.4***  | 52.1 ± 7.3*  |
| The impact of asthma/COPD on patient’s life (%)| 6.3 ± 2.5                | 5.5 ± 2.6        | 6.0 ± 2.5       | 6.8 ± 1.7*** |
| None at all (%)                                | 162 (6.9)                | 401 (13.2)       | 138 (10.8)      | 0             |
| Slight (%)                                     | 424 (18.1)               | 835 (27.5)       | 200 (15.7)      | 50 (8.6)      |
| Moderate (%)                                   | 579 (24.7)               | 637 (21.0)       | 341 (26.8)      | 166 (28.4)   |
| Significant (%)                                | 696 (29.7)               | 683 (22.3)       | 387 (30.4)      | 280 (48.2)   |
| Severe (%)                                     | 483 (20.6)               | 480 (15.8)       | 208 (16.3)      | 86 (14.8)    |
| Visit 1: N = 1274/35.2                         |                          |                  |                |              |
| N                                               | 1322/50.8                |                  |                |              |
| N (%)                                          | 50.8 ± 9.4*              |                  |                |              |
| Opinion on the duration of asthma/COPD (%)     | 8.6 ± 1.8                | 8.7 ± 1.9        | 8.1 ± 2.1***   | 8.5 ± 1.2    |
| Very short (%)                                 | 5 (0.2)                  | 64 (2.1)         | 11 (0.9)       | 0             |
| Short (%)                                      | 84 (3.6)                 | 99 (3.2)         | 59 (4.6)       | 0             |
| Moderately long (%)                            | 253 (10.8)               | 163 (5.4)        | 243 (19.0)     | 29 (4.9)     |
| Long (%)                                       | 553 (23.6)               | 539 (17.8)       | 299 (23.5)     | 302 (51.9)   |
| Forever (%)                                    | 1449 (61.8)              | 2171 (71.5)      | 662 (52.0)     | 251 (43.2)   |
| Sense of disease control (%)                   | 7.0 ± 1.9                | 7.5 ± 1.9        | 6.3 ± 2.1***   | 6.0 ± 1.3*** |
| The total lack (%)                             | 26 (1.1)                 | 45 (1.5)         | 33 (2.6)       | 0             |
| Lack (%)                                       | 284 (12.1)               | 237 (7.8)        | 224 (17.6)     | 58 (9.9)     |
| Partial (%)                                    | 546 (23.3)               | 460 (15.1)       | 443 (34.7)     | 323 (55.6)   |
| Significant (%)                                | 986 (42.1)               | 1280 (42.2)      | 378 (29.7)     | 201 (34.5)   |
| EXTREME (%)                                    | 502 (21.4)               | 1014 (33.4)      | 196 (15.4)     | 246 (19.2)   |
| Opinion on the effects of treatment on asthma/| 7.9 ± 1.5                | 8.1 ± 1.6        | 7.3 ± 1.9***   | 7.1 ± 1.3*** |
| COPD, n (%)                                    | 7 (0.3)                  | 34 (1.1)         | 17 (1.3)       | 0             |
| None at all (%)                                | 70 (3.0)                 | 103 (3.4)        | 104 (8.2)      | 29 (4.9)     |
| Slight (%)                                     | 272 (11.6)               | 182 (6.0)        | 242 (19.0)     | 129 (22.2)   |
| Moderate (%)                                   | 1090 (46.5)              | 1186 (39.0)      | 558 (43.8)     | 323 (55.6)   |
| Significant (%)                                | 905 (38.6)               | 1531 (50.5)      | 353 (27.7)     | 101 (17.3)   |
| Assessment of the severity of asthma/COPD     | 5.6 ± 2.2                | 4.5 ± 2.3        | 5.6 ± 2.3      | 5.7 ± 1.6*** |
| symptoms, n (%)                                | 188 (8.0)                | 732 (24.1)       | 182 (14.3)     | 28 (4.9)     |
| No symptoms (%)                                | 584 (24.9)               | 969 (31.9)       | 150 (11.8)     | 101 (17.3)   |
| Moderate (%)                                   | 696 (29.7)               | 677 (22.1)       | 417 (32.7)     | 259 (44.4)   |
| Significant (%)                                | 688 (29.4)               | 485 (16.0)       | 420 (33.0)     | 165 (28.4)   |
| Many severe symptoms (%)                       | 188 (8.0)                | 178 (5.9)        | 104 (8.2)      | 29 (5.0)     |
| Interest in knowledge about the disease, n (%) | 8.0 ± 2.0                | 8.1 ± 2.0        | 7.4 ± 2.3***   | 6.3 ± 1.7*** |
| None at all (%)                                | 26 (1.1)                 | 40 (1.3)         | 37 (2.9)       | 0             |
| Slight (%)                                     | 117 (5.0)                | 168 (5.5)        | 71 (5.6)       | 22 (3.7)     |
| Moderate (%)                                   | 408 (17.4)               | 341 (11.2)       | 363 (28.5)     | 33 (5.6)     |
| Great (%)                                      | 649 (27.7)               | 845 (27.9)       | 287 (22.5)     | 136 (23.5)   |
| Extreme (%)                                    | 1144 (48.8)              | 1642 (54.1)      | 516 (40.5)     | 93 (16.0)    |
The mean score of patient assessment of the severity of the disease on visit 1 did not differ between asthma adherence and non-adherence subgroups and on visit 2 was significantly higher in the non-adherence subgroup. In turn, in the COPD group, on visit 1, it was significantly higher in the non-adherence than adherence subgroup and on visit 2, it did not differ (Table 4).

On both visits, the mean score of the understanding of the nature and interest in knowledge about the disease was significantly higher in asthma adherence than non-adherence subgroup and did not differ between COPD subgroups (Table 4).

On both visits, the mean score of the impact of the disease on the emotions was significantly higher in COPD non-adherence than adherence subgroup and on visit 2, it was also higher in asthma non-adherence than adherence subgroups (Table 4).

A significant negative correlation between total MMAS-8 and BIPQ scores was observed in both asthma and COPD groups ($R = -0.15; p < 0.001$, and $R = -0.24; p < 0.001$, respectively).

In the asthma group, a significant negative correlation has been observed between total MMAS-8 score and the score of BIPQ such as sense of disease control, opinion on the effect of treatment on the disease, understanding the nature of the disease and interest in knowledge about the disease ($R = -0.30; p < 0.001$, and $R = -0.23; p < 0.0001$, and $R = -0.32; p < 0.0001$ and $R = -0.15; p < 0.001$, respectively).

In the COPD group, a significant negative correlation has also been shown between total MMAS-8 score and the score of BIPQ such as opinion on the duration of disease, sense of disease control and opinion on the effect of treatment on the disease ($R = -0.20; p < 0.001$, $R = -0.39; p < 0.0001$ and $R = -0.33; p < 0.001$, respectively).

### Patients' and doctors' opinion about the use of two drugs in a single inhaler

During the observation, the percentage of patients who believed that the administration of the two drugs in a single inhaler considerably facilitates their use increased significantly in both asthma and COPD groups (Table 5).

There have also been significant changes in the opinions of doctors. On visit 1, all doctors believed that the possibility of administration of the two drugs in a single inhaler does not facilitate education of patients diagnosed with asthma and COPD at all, while on visit 2, 82.0% of doctors believed that this option significantly facilitates education of patients diagnosed with asthma and 75.2% that patients with COPD. During the observation, there was also a significant increase in the percentage of doctors expressing an opinion that administration of the two drugs in a single inhaler significantly decreased the number of errors made by the patients with asthma and COPD. However, the percentage of doc-
### Table 5. Opinions of patients and physicians regarding the use of the two drugs in one inhaler

| Variables                                                                 | Asthma | Value of p | COPD  | Value of p |
|--------------------------------------------------------------------------|--------|------------|-------|------------|
| The degree of ease of treatment when two drugs may be taken using a single inhaler in the patient’s opinion, n (%): |        |            |       |            |
| Not at all                                                               | 145 (4.0) | 14 (4.4) | 114 (4.4) | 34 (1.3) |
| Slightly                                                                 | 257 (7.1) | 213 (5.9) | 429 (16.5) | 122 (4.7) |
| Moderately                                                               | 1176 (32.5) | 938 (25.9) | 950 (36.5) | 794 (30.5) |
| Significantly                                                            | 2040 (56.4) | 2453 (67.8) | 1109 (42.6) | 1652 (63.5) |
| **It facilitates patient education if the two drugs can be administered using a single inhaler in the opinion of the physician, n (%):** |        |            |       |            |
| Not at all                                                               | 311 (100) | 0 | 311 (100) | 1 (0.3) |
| Slightly                                                                 | 0 | 11 (3.6) | 0 | 7 (2.3) |
| Moderately                                                               | 0 | 45 (14.4) | 0 | 69 (22.2) |
| Significantly                                                            | 0 | 255 (82.0) | 0 | 234 (75.2) |
| Reduction in the number of errors made by the patient if the two drugs can be administered using a single inhaler, n (%): |        |            |       |            |
| None at all                                                              | 5 (1.7) | 1 (0.3) | 10 (3.1) | 1 (0.3) |
| Slight                                                                   | 14 (4.6) | 8 (2.6) | 30 (9.6) | 7 (2.3) |
| Moderate                                                                 | 52 (16.5) | 39 (12.3) | 84 (27.2) | 63 (20.3) |
| Significant                                                               | 240 (77.2) | 263 (84.7) | 187 (60.1) | 240 (77.1) |
| Doctor’s opinion on the impact of the use of the patient’s Fantasmino inhaler on the treatment effect, n (%): |        |            |       |            |
| Yes                                                                      | 266 (85.4) | 237 (76.1) | 266 (85.4) | 244 (78.4) |
| No                                                                       | 45 (14.6) | 74 (23.9) | 45 (14.6) | 67 (21.6) |
| Opinion of physicians about how the use of the Fantasmino inhaler affects the treatment effect, n (%): |        |            |       |            |
| Reduces the frequency of use of rescue medication                        | 237 (69.9) | 217 (69.7) | 198 (63.6) | 214 (68.8) |
| Reduces the frequency of exacerbations                                   | 135 (3.3) | 5 (1.6) | 169 (54.4) | 6 (2.0) |
| Other including:                                                        | 2 (0.6) | 5 (1.6) | 10 (3.2) | 8 (2.6) |
| Good tolerance                                                          | 104 (33.3) | 0 | 19 (5.9) | 0 |
| Low cost of the treatment                                               | 155 (50.0) | 28 (9.0) | 73 (23.5) | 48 (15.4) |
| Good exercise tolerance                                                 | 52 (16.7) | 0 | 0 | 0 |
| Ease of use of the inhaler                                               | 0 | 113 (36.4) | 0 | 68 (22.0) |
| General improvement                                                     | 0 | 57 (18.2) | 0 | 0 |
| No dyspea                                                               | 0 | 28 (9.0) | 18 (5.9) | 24 (7.7) |
| Improvement of the respiratory function                                  | 0 | 28 (9.0) | 0 | 0 |
| No sick leave                                                           | 0 | 28 (9.0) | 0 | 0 |
| Improved daily functioning                                               | 0 | 28 (9.0) | 73 (23.5) | 24 (7.7) |
| Better cooperation                                                      | 0 | 0 | 37 (11.8) | 72 (23.1) |
| Patient satisfaction                                                    | 0 | 0 | 18 (5.9) | 0 |
| Improvement of mental work                                              | 0 | 0 | 18 (5.9) | 0 |
| Improved quality of life                                                | 0 | 0 | 18 (5.9) | 48 (15.4) |
| Marked improvement in spirometry                                        | 0 | 0 | 18 (5.9) | 24 (7.7) |

*χ² test for trend
Discussion

The presented study is the first large survey performed in the Polish population. The analysis of study group characteristics has shown that its structure is representative of Polish patients with asthma [11, 12]. However, the group of patients with COPD does not seem to be representative of the Polish population, due to greater than expected participation of women and rural residents. It is in contrast with previously published studies showing that men develop COPD almost twice as often as women [13] and that COPD is more common among urban dwellers [14, 15]. However, it should be noted that these studies were performed more than a decade ago and COPD’s major risk factors such as smoking and environmental pollution have changed in the meantime. Thus, it cannot be excluded that the group of patients with COPD is now representative of the Polish population.

In both study groups, most patients had a diagnosis of the disease for more than 5 years prior to enrollment. However, the study groups differ in terms of disease severity. In the asthma group, only 6.6% of patients have severe disease and in the COPD group, 64.3% of patients have severe and 7.1% very severe disease. 50.7% of the asthma group and 57.7% of the COPD group were treated with fluticasone propionate and formoterol fumarate for more than a year. However, this therapy using the Fantasmino inhaler for more than a year was conducted only in 16.4% and 19.8%, respectively, and for not more than 3 months in 48.8% and 38.4%, respectively. A recently published review showed that this type of therapy in patients with asthma is effective in terms of the lung function and symptom control and highlights the dose flexibility, safety and tolerability of this new inhaled combination [16]. In addition, the TORCH study revealed that this therapy decreased the number of exacerbations and improved the health status as well as spirometry measurements. In addition, it also reduced the risk of death in patients with COPD by 17.5% [17].

The general illness perception was similar in both study groups. However, significantly higher mean scores of the impact of the disease on the patient’s life, opinion on the duration of disease, assessment of disease severity and the impact of the disease on the emotions were observed in COPD than in the asthma group. In turn, mean scores of the sense of disease control, opinion that the treatment can help in the disease, understanding the nature of the disease and interest in knowledge about the disease were significantly higher in asthma than in the COPD group. It should be emphasized that during observation there have been positive changes in the illness perception in both study groups. The results of a recently published study showed that health-related quality of life (HRQoL) of COPD patients is associated with illness perception as well as with the severity of dyspnea as experienced by patients. It has also been suggested that interventions focusing on illness perception helped to support COPD patients in their disease management and to improve HRQoL [18]. The present study did not assess the education process during observation but the positive changes in illness perception suggest a greater focus of the doctor on the patient in connection with his participation in the study has a positive effect on the process.

The non-adherence rate on visit 1 was lower in asthma than in the COPD group. It should be noted that adherence in the asthma group (72.0%) was higher than reported in recently published meta-analysis (from 22.0% to 63%) [19]. As suggested, the results of this meta-analysis may be a result of polytherapy with inhaled glucocorticosteroids and long-acting β2 agonists used in the present study. In turn, the adherence in the COPD group (61.5%) was similar to that previously reported [7]. However, it should be emphasized that during observation the adherence increased significantly in the COPD group only. This may be the effect of changes in the illness perception. Positive changes have also been observed in the asthma group though. On the other hand, impact of disease duration and its severity may be factors partially explaining these differences. Further studies are necessary to explain the differences in the impact of illness perception on adherence between patients with asthma and COPD.

On visit 1, the mean total score of illness perception in both study groups was significantly higher in adherence than non-adherence subgroups. In turn, on visit 2, this difference was observed in the asthma group only. In addition, a negative correlation between total MMAS-8 and BIPQ scores was observed in both asthma and COPD groups. Moreover, in both asthma and COPD groups non-adherence was inversely proportional to the sense of disease control and opinion on the effect of treatment on the disease. The association between belief that treatment is ineffective in controlling symptoms and poor adherence has also been described previously among patients with asthma and COPD [20–22]. In turn, the association between sense of disease control has not been previously observed. It should be also noted that this association requires confirmation in studies with other questionnaires assessing sense of disease control. The present study has also shown that adherence was inversely proportional to understanding the nature of the disease and interest in knowledge about the disease. This study did not assess the levels of knowledge about disease. In turn, in the GAPP study, 23.0% of patients thought that education is not conducted at all [23]. Thus, further studies should be performed to assess the association between education levels about disease and adherence.
The adherence and illness perception of patients diagnosed with asthma or chronic obstructive pulmonary disease treated with polytherapy using new generation Cyclohaler

The additional assessment in this study was opinions of patients and doctors on the Fantasmino inhaler use. During the observation, the percentage of patients who believed that the administration of the two drugs in a single inhaler considerably facilitates their use increased significantly in both asthma and COPD groups. There have also been significant changes in the opinions of doctors. On visit 1, all doctors, contrary to a previously published study [24], believed that the possibility of administration of the two drugs in a single inhaler does not facilitate education of patients diagnosed with asthma and COPD at all. In turn, on visit 2, 82.0% of doctors believed that this option significantly facilitates education of patients diagnosed with asthma and 75.2% that it facilitates education of patients with COPD. In accordance to previously published studies [10, 24] during observation, there was a significant increase in the percentage of doctors expressing an opinion that administration of the two drugs in a single inhaler significantly decreased the number of errors made by the patients with asthma and COPD.

The study has several limitations. The most important is the lack of a control group treated with fluticasone propionate and formoterol fumarate without using the Fantasmino inhaler. The second limitation is the self-reported assessment of adherence. The factors influencing the results may be also the patient’s education during observation and the level of knowledge about disease before enrolment. In addition, the differences in duration of disease and therapy with the Fantasmino inhaler may influence the results of this study. Moreover, in this study the impact of comorbidities and use of other drugs on the illness perception and adherence was not analyzed.

However, the strength of the study is a large study group representative of the Polish population and multicenter nature of the study.

Conclusions

The illness perception, younger age, disease duration and severity are predictors of adherence to treatment with fluticasone propionate and formoterol fumarate using the Fantasmino inhaler among patients with asthma and COPD. The positive opinions of patients and doctors about administration of fluticasone propionate and formoterol fumarate using the Fantasmino inhaler increased during observation.

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