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## Effectiveness of an educational program for children and their families on asthma control treatment adherence

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### ABSTRACT

**Objective:** To investigate the effect of an asthma care educational program for children and adolescents with asthma, on adherence to asthma control treatment and on clinical indices.

**Methods:** Individuals newly diagnosed with asthma, aged 4–16 years, randomized to the intervention and control group. The participants were monitored for 6 weeks. At baseline, before the initiation of inhaled corticosteroids/long-acting beta<sub>2</sub>-agonist (ICS/LABA), the intervention group attended the educational program; the control group received the usual care. Both groups were equipped with electronic monitoring devices for measuring adherence. Spirometry, exhaled nitric oxide fraction (FeNO), and asthma control test (ACT) score were measured in both groups in the pre and post-ICS/LABA initiation visit.

**Results:** Seventy-eight participants were enrolled in this study ( $n=39$  to each group). Median percentage of adherence was 73% for the total sample, and 80% and 68% in intervention and control group, respectively ( $p<0.001$ ). In multivariate analysis, the program was positively associated with improved adherence ( $p<0.001$ ). ICS/LABA had a positive effect on spirometric indices, FeNO, and ACT score, whilst the educational program did not improve significantly the above variables.

**Conclusions:** Establishing and increasing adherence is challenging. An asthma care educational program is associated with greater short-term adherence during a period of active monitoring.

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## Introduction

Asthma is a serious global health problem affecting all age groups; its prevalence has been increasing in many countries, especially among children [1]. This chronic disease is a frequent cause of emergency department visits and hospital admissions in the pediatric population [2]. Asthma management intends to achieve good control of symptoms, maintain activity levels, and minimize future risks of exacerbations [1]. Inhaled corticosteroids (ICS) are the cornerstone of maintenance treatment for asthma [3]. Sustained use of ICS reduces the underlying airway inflammation and ameliorates disease morbidity [4]. A combination of ICS and long-acting beta<sub>2</sub>-agonists (ICS/LABA) by inhaler is recommended for children with asthma which do not respond to the first line asthma control treatment with ICS [3].

Despite the long-term efficacy of ICS, adherence to this treatment remains suboptimal [5–7]. Almost 50% of adults and children with asthma on long-term

treatment do not use medication properly, at least part of the time [8]. Available data suggest that 24% of exacerbations and 60% of asthma-related hospitalizations are attributed to poor adherence [4], and that adherence must exceed 80% in order to achieve effective asthma control [9,10].

Low adherence rates emphasize the need for developing and establishing interventions for adherence improvement. Enhancing adherence to asthma medication is a complicated process. Education on its own can probably modify and promote adherence to some degree, whereas integrated programs providing information and incorporating behavioral components such as goal setting, reinforcement, monitoring, alarm setting, etc., appear more suitable to achieve this goal [11].

The aim of this study was to investigate the effect of an asthma care educational program on adherence to asthma control treatment and on clinical indices, in children, and adolescents newly diagnosed with asthma.

## Methods

### Study design and population

A convenience sample of children and adolescents, 4–16 years old, newly diagnosed with asthma on the basis of Global Initiative for Asthma (GINA) guidelines [1] were recruited in this randomized control trial from the pediatric asthma outpatient clinic of Attikon hospital, Athens, Greece, between January 2016 and July 2018. All participants had suffered at least two moderate/severe exacerbations that needed oral corticosteroids during the 12 months that preceded their referral in our clinic. No one had ever received any kind of prophylactic asthma treatment up to then. After physician's asthma diagnosis, all individuals commenced treatment with a combination of inhaled corticosteroids/long-acting beta<sub>2</sub>-agonist (ICS/LABA), in an effort to control asthma as efficiently and quickly as possible. Exclusion criteria comprised severe cardiovascular, neurological, or other respiratory comorbidities and insufficient understanding of Greek language.

The monitoring lasted 6 weeks and all participants attended a pre-ICS/LABA initiation visit and a post-ICS/LABA initiation visit, at the start and at the end of this period, respectively. During pre-ICS/LABA initiation visit, all participants underwent skin prick tests (SPT) to common aeroallergens (Timothy grass, Bermuda grass, Olea, Parietaria, Cypress, Chenopodium, Artemisia, Dermatophagoides pteronyssinus and farinae, Alternaria, Cladosporium, cat, and dog dander), spirometry, asthma control test (ACT), and measurement of exhaled nitric oxide (FeNO); also, the electronic monitoring devices (EMDs) were placed on inhalers and proper inhaler use instructions were given. The intervention group followed an asthma care educational program; the control group did not attend the educational program and they received the usual care. At the post-ICS/LABA initiation visit, spirometry, ACT, and FeNO measurement were performed in both groups and the electronic devices were collected in order to download and analyze their data.

The Attikon hospital ethics committee approved the study. Parents/carers of all participants gave written informed consent.

### Assessment of adherence

Adherence was monitored by the Smartinhalers (SmartTouch™ inhaler for salmeterol xinafoate/fluticasone propionate metered-dose inhaler, and

SmartDisk™ for salmeterol xinafoate/fluticasone propionate dry powder inhaler, Nexus6 Ltd, Auckland, New Zealand). Smartinhalers are validated EMDs that record the date, time, and number of actuations used daily [5,12]. Adherence was defined as the percentage of doses taken by total doses prescribed [13]. Adherence was further classified into 3 categories, i.e. good, moderate, and poor if it was  $\geq 80\%$ , 60–79%, and  $< 60\%$ , respectively [6]. Participants in moderate or poor category were collectively considered as having suboptimal adherence.

### Assessment of lung function, FeNO and asthma control

Percent predicted values of FEV<sub>1</sub> (ppFEV<sub>1</sub>) and FVC (ppFVC), and FEV<sub>1</sub>/FVC ratio, were measured using a spirometer (Flowscreen; Viasys Healthcare, Yorba Linda, USA) according to American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines [13].

FeNO measurements were performed with a single-breath, hand-held electrochemical analyzer (NIOX MINO; Aecroline, Solna, Sweden) at an expiratory time of 6 s [14].

Asthma control was assessed with the ACT score for children and adolescents  $\geq 12$  years or the corresponding childhood ACT score for children 4–11 years [15,16]. Good asthma control achieved when ACT  $\geq 20$  and poor control when ACT  $< 20$  [6].

### Intervention

Participants assigned to the intervention group, attended – along with their parents/carers – an asthma care educational program aiming at the development of self-management skills and the building of self-responsibility and self-efficacy in tackling with ensuing problems. The program was provided by a specialist nurse in a meeting conducted at the outpatient clinic through a 45–60 min interactive session. Its first part focused on understanding asthma symptoms, preventing triggers, recognizing early warnings, understanding the need of using reliever and controller medication, educating in proper inhaler use, and addressing exacerbations. The second part concentrated on increasing adherence through reinforcement (highlighting the benefits of asthma control in daily activities and in quality of life in general), setting medication “reminders” (linking medication with daily activities such as taking medication before teeth

brushing or before meal), and determining specific goals with rewards when achieved.

### Statistical analysis

The sample size was estimated on the assumption of a 25% difference in adherence between groups (60% vs. 85%, in the control and intervention group, respectively). The computation was performed with the use of likelihood-ratio test with type I error and power set at 0.05 and 0.80, respectively. The sample size was determined to be 42 individuals for each group. Assuming a loss to follow-up of 12%, the number chosen was 48 patients for each group (96 in total). Participants were randomly assigned to 2 groups with the use of block randomization with allocation 1:1, which resulted in equal sizes of 48.

The percent change (%Δ) between pretreatment and post-treatment values for spirometric indices (ppFEV<sub>1</sub>, ppFVC, FEV<sub>1</sub>/FVC ratio), FeNO, and ACT or cACT test, were calculated according to the formula: (post-treatment value – pretreatment value) × 100/pretreatment value.

Data are expressed as mean ± standard deviation (sd) if normally distributed or, as median with interquartile range (percentile25–percentile75) if their distribution deviates from normality. Univariate analysis

was performed with independent or paired-*t* tests, Wilcoxon rank-sum test, and chi-square test. Multivariate analysis was performed with linear regression models where adherence percentage, %ΔppFEV<sub>1</sub>, %ΔppFVC, %ΔFEV<sub>1</sub>/FVC ratio, %ΔFeNO, %ΔACT score, were sequentially used as response variables and intervention was used as the predictive variable. As covariates, in each of the aforementioned models, we used age, sex, family history of asthma or other atopic disorder, allergic sensitivity to aeroallergens, parent's education, parent's smoking, and type of inhaler device.

### Results

Ninety-six children and adolescents (48 in each group) were originally enrolled in the study and randomly assigned to the 2 groups. However, 5 participants did not attend the follow-up visit and 13 more did not recharge their devices leading to data loss (Figure 1). Hence, the analysis was based on the rest of the children (78 in total, 39 to each group). The baseline characteristics of participants by groups are depicted in Table 1. No differences between the two groups were found on demographics.

Median (percentile25–percentile75) percentage of adherence was 73 (66–82)% for the total sample, and

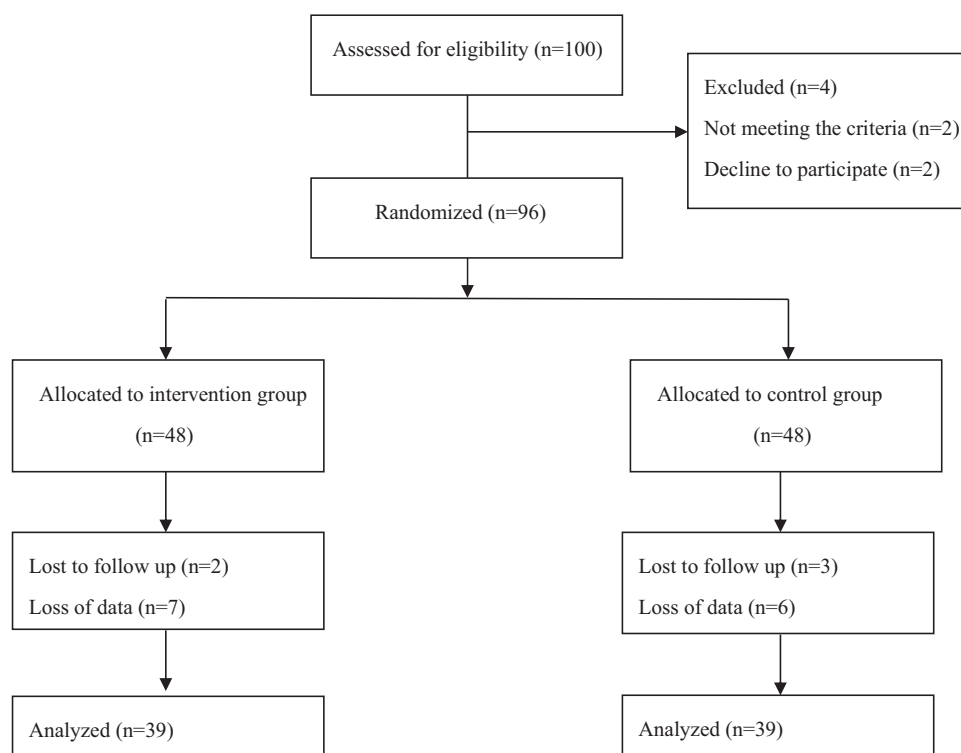


**Figure 1.** Consort flow chart of the study participants.

**Table 1.** Baseline characteristics of participants by groups.

|                                                | Intervention ( <i>n</i> = 39) | Control ( <i>n</i> = 39) | <i>p</i> -value |
|------------------------------------------------|-------------------------------|--------------------------|-----------------|
| Sex (male/female)                              | 23/16                         | 27/12                    | 0.79            |
| Age (years)                                    | 8.4 ± 2.8                     | 8.3 ± 2.7                | 0.81            |
| Parental education (years)                     | 13.3 ± 2.6                    | 14.3 ± 2.2               | 0.10            |
| Parental smoking (yes/no)                      | 21/18                         | 18/21                    | 0.49            |
| Family history of asthma and/or atopy (yes/no) | 17/22                         | 15/24                    | 0.64            |
| Type of inhaler device (MDI/DPI)               | 34/5                          | 36/3                     | 0.45            |
| SPT (positive/negative)                        | 16/23                         | 14/25                    | 0.64            |

MDI: metered-dose inhaler.

DPI: dry powder inhaler.

SPT: skin prick tests to common aeroallergens.

80 (73–85)% and 68 (56–76)% for the intervention and control group, respectively ( $p < 0.001$ ). Distribution of participants in the 3 categories of adherence differed significantly between groups ( $p < 0.001$ , Table 2); suboptimal adherence was significantly higher in the control group compared to the intervention group (82.0% vs. 48.7% of patients, respectively,  $p < 0.001$ ).

Spirometric indices (ppFEV<sub>1</sub>, ppFVC, and FEV<sub>1</sub>/FVC ratio), FeNO values, and ACT scores for the total number of participants, before and 6 weeks after the ICS/LABA initiation, are presented in Table 3. All the above variables showed significant improvement after ICS/LABA initiation ( $p < 0.001$ ), in both groups. Although ICS/LABA had a positive effect on the above variables, improvement did not differ significantly between the 2 groups (Table 4).

In the multivariate analysis it was demonstrated that the educational program was positively associated with greater adherence ( $p < 0.001$ ). In the rest of the multivariate models, intervention was not associated with any of the examined response variables, namely, %ΔppFEV<sub>1</sub>, %ΔppFVC, %ΔFEV<sub>1</sub>/FVC ratio, %ΔFeNO, %ΔACT.

## Discussion

The present study highlights the key role of an asthma care educational program in increasing adherence to asthma control treatment, in children and adolescents with asthma. This finding is in accordance with previous studies that applied an integrated care program, or an asthma tailored, home-based, family treatment approach [17,18].

A systematic review of interventions on adherence in children with severe asthma concluded that individualized care programs improve adherence [19]. In another systematic review and meta-analysis it was demonstrated that patients education on adherence to medication, electronic trackers/reminders, and simplified regimens, could improve adherence by 20%, 19%, and 4%, respectively [20].

**Table 2.** Number and percentage of patients in each one of the 3 adherence groups.

|                                     | Adherence   |                   |             |
|-------------------------------------|-------------|-------------------|-------------|
|                                     | Good (≥80%) | Moderate (60–79%) | Poor (<60%) |
| Without intervention ( <i>N</i> /%) | 6/15.3%     | 21/51.3%          | 12/30.7%    |
| With intervention ( <i>N</i> /%)    | 20/51.3%    | 17/43.6%          | 2/5.1%      |
| Total ( <i>N</i> /%)                | 26/33.3%    | 38/48.7%          | 14/17.9%    |

**Table 3.** Spirometric, FeNO, and asthma control test values, before and after 6 weeks from ICS/LABA commencement for the total number of participants.

|                       | Before ICS/LABA<br>Total ( <i>n</i> = 78) | After ICS/LABA<br>Total ( <i>n</i> = 78) | <i>p</i> -value |
|-----------------------|-------------------------------------------|------------------------------------------|-----------------|
| ppFEV <sub>1</sub>    | 97.1 ± 13.0                               | 105.5 ± 13.0                             | <0.001          |
| ppFVC                 | 95.0 ± 11.9                               | 99.4 ± 12.4                              | <0.001          |
| FEV <sub>1</sub> /FVC | 87.1 ± 7.7                                | 92.6 ± 7.5                               | <0.001          |
| FeNO (ppb)            | 22.8 ± 12.8                               | 14.1 ± 9.9                               | <0.001          |
| ACT                   | 19.3 ± 2.6                                | 23.3 ± 2.5                               | <0.001          |

ppFEV<sub>1</sub>: Percent predicted FEV<sub>1</sub>.

ppFVC: Percent predicted FVC.

FeNO: Exhaled nitric oxide fraction.

ppb: parts per billion.

ACT: Asthma control test.

Interventions to increase adherence represent a much valuable tool in achieving satisfactory asthma control, which could be quite difficult to be accomplished otherwise. The complexity of the issue becomes obvious from the many factors that are involved such as parental education, parental beliefs about medication necessity, and environmental triggers, whereas it is further aggravated from the disparity between physicians' and patients' expectations leading either to overestimation or underestimation of control level [21–24].

Our asthma care educational program was provided by a specialist nurse through an interactive with participant/caregiver session. Nurses play a pivotal role in providing education to the patient with asthma and caregiver, in eliciting patients' view on treatment and in promoting treatment adherence [25].

In our study, we avoided the use of subjective estimations of adherence. Instead, we used EMDs in order to increase the validity and reliability of our results [5,10,26]. EMDs record the exact date and

**Table 4.** Percent change (%Δ) between pre and post-ICS/LABA initiation values.

|                        | Patients with intervention (n = 39) | Patients without intervention (n = 39) | p-value |
|------------------------|-------------------------------------|----------------------------------------|---------|
| %Δ FEV1                | 8.7 ± 2.2                           | 10.0 ± 1.5                             | 0.63    |
| %Δ FVC                 | 3.8 ± 9.7                           | 6.3 ± 8.2                              | 0.22    |
| %Δ FEV1/FVC ratio      | 8.1 ± 8.5                           | 5.0 ± 6.1                              | 0.07    |
| %Δ FeNO                | 39.1 ± 17.5                         | 35.2 ± 33.7                            | 0.67    |
| %Δ Asthma control test | 25.4 ± 23.6                         | 19.7 ± 13.9                            | 0.20    |

time that an inhaler is activated, and provide detailed information about patterns of medication use [10]. Because of this, they are considered as the gold standard in adherence monitoring [5]. Whilst there are a few reports indicating substantial malfunction rates [26,27] or doubts about the correct way of drug delivery [28], EMDs remain the best available objective method to estimate adherence [29].

In the present study, the median adherence to treatment for the whole study population was 73%, a finding consistent with other pediatric studies where the median adherence ranged from 34% to 73% [10,30,31]. Suboptimal adherence (<80%) was observed in almost 67% of participants even though they were aware about the monitoring. However, suboptimal adherence was far more prevalent amongst patients in the control group with a rate close to 2 times higher than the intervention group (82.0% vs. 48.7%).

Treatment improved spirometric indices, FeNO values, and ACT score in both groups. However, despite the intervention having enhanced the adherence of patients, the improvement of the above variables was similar in both groups. This phenomenally surprising finding has also been observed in some other studies where the improved adherence various interventions did not result in measurable responses in asthma control markers [7,18,32]. A plausible explanation may be the fact that all participants had at least 2 asthma exacerbations but had not been diagnosed with asthma by the time they were referred in our clinic. This may imply that our population represented, at least in their majority, one of the asthma phenotypes with normal spirometry and/or near normal FeNO values between exacerbations [33,34]. Furthermore, our study design and the sample size selection were based on demonstrating a difference in adherence and not in the asthma severity indices.

A limitation of our study was the higher than expected number of participants that either dropped out the study, or simply did not recharge the device according to instructions. Another drawback was due to the limited period of our study. Because of this what was actually found was the short-term adherence that most likely was better than the long-term

adherence since participants knew that they were monitored and that the date of their scheduled follow-up visit was in a few weeks time. However, since this drawback affected equally both groups it is likely that no bias was introduced in our results.

Another limitation was the fact that this study was conducted at an asthma outpatient clinic. Parents/caregivers that visit the clinic are much more likely to be adherent and may be also more likely to be educated and informed about asthma. Presumably, they are knowledgeable of other factors that can impact the morbidity in their children not related with the use of ICS/LABA. Furthermore, the parents/caregivers that are motivated to visit an asthma clinic, likely have inherently higher tendency towards adherence at baseline and so perhaps the effect of the educational program on this population is not the same as on a different one.

## Conclusions/key findings

The results of this study have shown a benefit in increasing short-term adherence to ICS/LABA after the implementation of an asthma care educational program. Adherence is difficult to establish, but our study demonstrated that it is possible to make gains with education. There was no evidence of better clinical indices due to the program. From our data, we cannot define to what extent this may improve long-term clinical outcomes since the duration of population's attendance was relatively short. Evidently, there is a need for well-designed intervention studies in children and adolescents with asthma, targeting greater long-term adherence and being tailored to detect improvement in clinical outcomes.

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## Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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