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#### ORIGINAL RESEARCH



## Asthma patient satisfaction with different dry powder inhalers

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#### **ABSTRACT**

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**Background**: The preferences and opinions of patients are important when choosing the optimal inhaler device for asthma management. We compared patient satisfaction of three dry powder inhalers in patients with moderate to severe asthma.

**Methods**: We selected a group of patients treated with Easyhaler<sup>TM</sup> (n = 164) and a second group of patients treated with Turbuhaler<sup>TM</sup> (n = 100) or Diskus<sup>TM</sup> (Accuhaler<sup>TM</sup>) (n = 64) from the register of an observational, multicenter study. Data of patients were paired according to age, gender, and asthma severity. Patient satisfaction with the inhaler type was assessed with the specific 'Feeling of Satisfaction with Inhaler' (FSI-10) questionnaire.

**Results:** Specific satisfaction with inhaler was statistically significantly higher with Easyhaler<sup>TM</sup>, as well as the percentage of patients with high satisfaction with inhaler. (FSI-10 score ≥43). Scores for Easyhaler<sup>TM</sup> were also statistically significantly better for individual FSI-10 items such as learning how to use, inhaler preparation, inhaler use, weight and size, and portability. There were no significant differences in asthma control (ACT, Mini-AQLQ) and adherence (TAI global score).

**Conclusions:** Specific satisfaction with inhaler was higher with Easyhaler<sup>TM</sup> in a homogeneous population of patients with moderate to severe asthma. However, the relationship between satisfaction with the inhaler and adherence and asthma control deserves more investigation.

#### ARTICLE HISTORY

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#### **KEYWORDS**

Asthma; dry powder inhaler; patient satisfaction; adherence

## 1. Introduction

When choosing asthma inhaled therapy, taking into account the preferences and opinions of patients can improve adherence and asthma control [1,2]. Patient satisfaction with inhaler has been related to more favorable clinical outcomes [3], just as difficulties using the inhaler have been shown to contribute to poor adherence [2]. Thus, inhaler choice is considered key for asthma control [4].

Dry powder inhalers (DPIs) are used in asthma therapy [2]. However, they present different features that may have clinical implications [5]. Easyhaler<sup>TM</sup> (EH) (Orion Corporation, Finland), is a three-step, light, compact, and user-friendly DPI. It has advantages over older DPIs [6], including dose uniformity in different real-world conditions [7]. With regard to features such as perception of inhalation, size, discreetness, mouthpiece comfort, and dose counter, EH was rated higher than other inhaler devices by asthma patients [8]. In an observational, multicenter study, patient satisfaction with inhaler was higher in asthma patients treated with EH [9]. Here we present a *post-hoc* analysis of a homogeneous

subpopulation of this study. Our objective was to compare EH and other DPIs regarding patient satisfaction with inhaler and potential clinical differences.

## 2. Materials and methods

The method used in the ASCONA (Asthma Satisfaction, CONtrol and Adherence) study has been previously reported [9]. Briefly, the ASCONA scientific committee selected and invited the participating physicians. This selection aimed to achieve an appropriate geographical distribution across Spain, as well as involving centers providing different levels of healthcare. Seventy-three investigators (50.7% allergists and 49.3% pulmonologists) participated in the study. They selected 800 consecutive patients according to the inclusion criteria: age ≥ 18 years, physician-confirmed asthma diagnosis, moderate to severe asthma according to GINA guidelines [2], and in receipt of any kind of asthma medication with the same inhaler for at least 3 months prior to their inclusion in the study. This last criterion was intended to assure that patients were under steady treatment without

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Supplemental data for this article can be accessed here.

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recent changes. Prior and current medications were registered and analyzed. Patients with disabling comorbidities and/or cognitive dysfunction were excluded. All patients signed an informed consent form, no personal data were recorded, and neither physicians nor patients received any compensation for their participation.

Physicians and patients completed electronic data collection forms in a single visit. We recorded sociodemographic and clinical data, including age at asthma diagnosis and at therapy onset, current asthma therapy, and asthma severity and control according to GINA [2]. We also included several questionnaires and tests. We assessed satisfaction with the specific Feeling of Satisfaction with Inhaler (FSI-10) questionnaire [10] and the more general Treatment Satisfaction Questionnaire for Medication (TSQM) [11]. For adherence, we used the Test of Adherence to Inhalers (TAI) to assess the specific adherence to inhalers [12] and the 4-item Morisky-Green scale for the general adherence to treatment (where 0 is no adherence and 4 is good adherence) [13]. We also used the Asthma Control Test (ACT) [14] and the reduced version of the Asthma Quality of Questionnaire (Mini-AQLQ) [15,16]. All these instruments have been validated in Spanish [10,12,17-20]. Furthermore, FSI-10 and TAI have been developed in Spain.

The specific FSI-10 questionnaire assesses the portability and usability of inhalers regardless of administered drugs. Patients answer ten questions, each with five options, using a Likert scale from 5 (very) to 1 (hardly at all). The FSI-10 maximum score is 50 (maximum satisfaction) [10] (see Supplementary file 1).

In turn, TAI consists of two complementary questionnaires. The 10-item TAI is completed by the patient and identifies the level of adherence: good (50 points), intermediate (46–49 points), and poor (≤ 45 points). In turn, the 12-item TAI suggests the pattern of non-compliance. It includes the 10-item TAI plus two items that are answered by the physician: knowledge of the dosing regimen by the patient (item #11) and performance of inhalation technique without critical errors (item #12) [12] (see Supplementary file 2).

The study was conducted according to the Declaration of Helsinki. The Clinical Research Ethics Committee of the Hospital Clinic in Barcelona (Spain) approved its protocol.

The more common DPIs in the ASCONA register were EH, Turbuhaler<sup>TM</sup> (TH) (AstraZeneca, Sweden) or Diskus<sup>TM</sup> (Accuhaler<sup>TM</sup>) (DKAH) (GSK, United Kingdom). They also were the only ones with an adequate number of patients to perform statistical analyses. In a prior analysis of the ASCONA registry, study investigators included 739 patients with moderate or severe asthma treated with EH, TH or DKAH. The comparison between these three DPIs showed a significant trend favorable to EH when compared both versus TH and versus AH individually in specific satisfaction to inhaler, satisfaction with treatment, quality of life, and asthma control [21] (see Supplementary file 3), without significant differences in other variables. However, because of non-systematic recruitment in the ASCONA registry, DPI groups were heterogeneous (in size and clinical profile) and therefore not directly comparable. For instance, percentage of patients with moderate asthma was higher in the EH group (p < 0.001). Therefore, we decided to perform a posthoc analysis using two randomized paired samples of patients matched according to age, gender and asthma severity, and treated with EH or with TH/DKAH. To explore whether this EH differences were relevant or not, we created homogeneous groups using paired matched samples approach, which will provide enough statistical power by unifying comparator groups (TH and AH) only under the assumption that they differ in a similar degree on the EH results.

#### 2.1. Statistical analysis

Statistical analysis was performed with SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). All statistical tests, tables and charts considered only the numbers of valid cases.

Categorical variables were described with number of valid cases and percentage, whereas mean and standard deviation (SD) were used for continuous variables. Dichotomous variables were created for each variable of interest using the median of the scores from the questionnaires and scales (FSI-10, TSQM, TAI and Mini-AQLQ) or a pre-established cut-off point (ACT [22] and Morisky-Green scale [13]).

Statistical tests included one-way analysis of variance (ANOVA) for group comparisons, Mann-Whitney test or Kruskal–Wallis test for continuous variables, and  $\chi^2$  test for categorical variables. Pearson and Spearman correlation tests were used to assess relationships between scale scores. Finally, multivariate analyses were performed to examine factors that influenced the study dependent variable (specific satisfaction with inhaler according to FSI-10).

## 3. Results

We included a group of patients treated with EH (n = 164)and a second group of patients treated with TH (n = 100) or DKAH (n = 64). Data were paired by gender, age, and asthma severity (Table 1). There were no statistically significant differences between groups in the forced expiratory volume in one second (FEV<sub>1</sub>) test (p = 0.443); daytime asthma symptoms more than twice/week (p = 0.664);

Table 1. Characteristics of study patients.

	Easyhaler <sup>TM</sup> (n = 164)	Turbuhaler <sup>TM</sup> / Diskus <sup>TM</sup> (Accuhaler <sup>TM</sup> ) (n = 164)	
V	N (%) or	N (%) or	
Variab <b>l</b> e	mean ± SD	mean ± SD	р
Socio-demographic and clinical data			
Age (y)	48.9 (16.16)	47.6 (15.9)	ns
Gender (female)	104 (63.4)	104 (63.4)	1
Age at asthma diagnosis (y)	$32.7 \pm 18.6$	29.6 ± 18.8	ns
Age at onset of asthma therapy (y)	34,34 ± 18,18	31,4 ± 18,3	ns
Asthma severity (GINA)			1
Moderate	120 (73.2)	120 (73.2)	
Severe	44 (26.8)	44 (26.8)	

ns, non-statistically significant; GINA, Global Initiative for Asthma.

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night waking due to asthma (p = 0.861); need for rescue medication (p = 0.975); and activity limitation due to asthma (p = 0.823). No prior or current medication affected satisfaction with inhaler.

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Table 2 shows the differences between groups in terms of patient satisfaction and adherence. Specific satisfaction with the inhaler (global score of FSI-10) was statistically significantly higher with EH compared with TH/DKAH (p < 0.01). With regard to individual FSI-10 items, patients considered EH to be easier to learn to use (p = 0.025), easier to prepare for inhalation (p = 0.01), easier to use (p = 0.012), and easier to carry (p = 0.018). Patients found EH easier to continue with regular activities (p = 0.038), and its weight and size were more convenient (p < 0.001). In addition, = they felt they had used it correctly after inhalation (p = 0.02). Overall, patients noted greater satisfaction with the device (p = 0.001). No statistically significant difference was found for device cleaning and maintenance, or for mouthpiece comfort. Moreover, the percentage of patients with high satisfaction with inhaler was statistically significantly higher with EH (p = 0.01).

Regarding general satisfaction with therapy (TSQM), there were no statistically significant differences in global scores between DPIs. However, patients in EH group reported that it was easier to take their medication in its current form (p = 0.018) and to plan when they will use the medication each time (p = 0.004). Patients using EH also found it more convenient to take the medication as instructed (p = 0.042). Furthermore, all items of adverse event subscale showed a trend to be lower for EH group, but without statistical significance; this result is based on questionnaire answers, not on patient-reported adverse events of administered drugs. Moreover, convenience was statistically significantly higher in EH group

Table 2. Comparison of questionnaire results between groups.

	Easyhaler <sup>TM</sup> (n = 164)	Turbuhaler <sup>TM</sup> / Diskus <sup>TM</sup> (Accuhaler <sup>TM</sup> ) (n = 164)			
Variab <b>l</b> e	N (%) or mean ± SD	N (%) or mean ± SD			
	mean ± 3D	mean ± 3D	р		
Specific satisfaction with inhaler (FSI-10)					
FSI-10 score	$43.8 \pm 7.1$	$41.3 \pm 7.6$	< 0.01		
High satisfaction (score ≥ 43)	92 (62.4)	68 (43)	0.01		
General satisfaction with medication (TSQM)					
Effectiveness	$71.4 \pm 20.6$	$70.9 \pm 18.4$	ns		
Adverse events	$97.1 \pm 9.7$	94.1 ± 14.3	< 0.05		
Convenience	79.7 ± 14.2	75.75 ± 16.1	< 0.01		
Global satisfaction	$74.6 \pm 16.1$	$72.3 \pm 17.7$	ns		
High global satisfaction (score ≥ 75) Adherence TAI	102 (63.4)	84 (51.2)	< 0.05		
Score	47.1 ± 4.4	46.4 ± 5.1	ns		
Good adherence (score ≥ 50)	64 (40.8)	59 (37.1)	ns		
Non-adherence pattern	04 (40.0)	37 (37.1)	113		
Erratic	$23.1 \pm 2.7$	$22.4 \pm 3.4$	< 0.05		
Deliberate	$24.1 \pm 2.2$	$24.24 \pm 2.2$	ns		
Unwitting	$3.9 \pm 0.4$	$3.8 \pm 0.4$	< 0.05		
Morisky-Green scale					
Score	$3.1 \pm 1.1$	$2.9 \pm 1.1$	ns		
Good adherence (score = 4)	75 (45.1)	59 (36.0)	ns		

ns, non-statistically significant; FSI-10, Feeling of Satisfaction with Inhaler guestionnaire; TSQM, Treatment Satisfaction Questionnaire for Medication; TAI, Test of the Adherence to Inhalers.

(p < 0.01). In addition, the percentage of patients with high satisfaction with treatment was statistically significantly higher in the EH group (p = 0.027).

In respect of specific adherence to inhaler (TAI), there was no statistically significant difference in TAI global scores between groups. Nevertheless, mean scores of erratic and unwitting non-adherence patterns were higher in the EH group (p < 0.05 for both patterns), reflecting that these nonadherence patterns were less frequent with EH. There was no statistically significant difference between groups for general adherence in global scores of the Morisky-Green scale.

With regard to asthma control, there was no statistically significant difference in ACT global score or in the percentage of patients with controlled asthma (ACT score  $\geq$  20). Finally, there was no statistically significant difference in healthrelated quality of life (Mini-AQLQ).

We performed a logistic regression analysis with specific satisfaction with inhaler (FSI-10) as a dependent variable (Figure 1). The most important factor leading to high satisfaction was the use of EH (odds ratio [OR] 1.705; 95% CI 1.056-2.755). Moreover, male gender slightly inclined towards high satisfaction with inhaler (OR 1.245; 95% CI 0.756-2.051). Conversely, factors that led to low satisfaction with inhaler were severe asthma (OR 1.186; 95% CI 0.663-2.120) and noncontrolled asthma (OR 0.390; 95% CI 0.236 -0.643).

#### 4. Discussion

In our real-world study, patient satisfaction with inhaler was higher with EH than with TH/DKAH. Among other features, ease of use, convenient weight and size, and ease of portability contributed to higher satisfaction with EH. These results confirm the findings in the whole ASCONA population, where patient satisfaction was also higher with EH than with TH or DKAH [9]. Moreover, although the aim of our study was not to prove the clinical relevance of differences in FSI-10 score, results of ASCONA main analysis [9] showed that these differences are clinically relevant.

The preference for EH has been found in other studies in patients with asthma. Ahonen et al. [23] performed a metaanalysis of nine clinical trials (n = 802) of EH and metereddose inhalers (MDIs) with and without a spacer, TH, and Diskhaler<sup>TM</sup> in patients with asthma. Ease of use was statistically significantly better for EH vs. the pooled data (p < 0.001) and for almost all individual studies. Inhalation through the device was also easier with EH, as was learning how to use it. Patients preferred EH to the MDI and spacer (p < 0.001) and to TH (p < 0.01) [23]. Preference of patients for EH has also been shown in other randomized clinical trials in patients with asthma. Jäger et al. [24] compared EH and TH; almost 59% of patients preferred EH and scores of device acceptability were higher for EH (p = 0.001). Similarly, in a study by Tukiainen et al. [25] again 59% of patients preferred EH vs. TH. Moreover, overall acceptability was higher for EH (p < 0.0001). In a study by Giner et al. [8], nine aspects of the inhalers were rated from 0 to 10 for each device. The overall score was higher for EH vs. TH (p = 0.015) and vs. DKAH (p = 0.003). When patients were asked to rank the inhalers in order of preference, EH was

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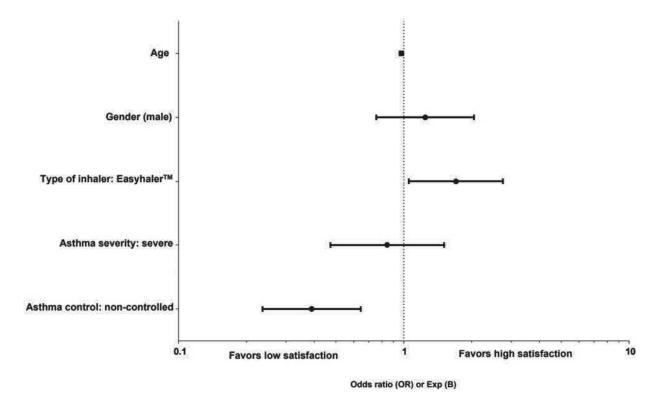


Figure 1. Binary logistic regression analysis using specific satisfaction with inhaler (FSI-10) as dependent variable. Use of Easyhaler<sup>TM</sup> led to high specific satisfaction with inhaler.

placed first by 53% of patients, TH by 27% and DKAH by 20%. In two real-world multicenter studies by Gálffy et al. [26], patients considered that EH was easy to learn and use, and 95% were satisfied or very satisfied with this inhaler.

Erratic and unwitting non-adherence patterns were less frequent in patients using EH. With respect to erratic nonadherence, we could not find a direct relationship between forgetting to take the dose and the different inhaler devices. Regarding the lower unwitting nonadherence with EH, we suggest that it was due to its ease of use, with only three steps and therefore fewer technical errors. There were no statistically significant differences between groups in terms of global adherence scores. Similarly, asthma control was comparable in both groups. A relationship between satisfaction and adherence has been found in other studies [3,27], but these did not compare different inhalers. In the main analysis of ASCONA, high patient satisfaction with inhaler was related to adherence and asthma control [9]. However, because of the sample size in our subanalysis, the difference in satisfaction was insufficient to be reflected in adherence and asthma control.

The main strengths of our study are the population homogeneity and the use of validated and specific scales and questionnaires. Regarding potential limitations, adherence was self-reported except for items 11 and 12 of TAI. However, these two physician-reported items define the unwitting non-adherence pattern. Another potential limitation could be that different drug combinations may affect results.

## 5. Conclusions

Physicians should keep in mind patient satisfaction with asthma therapy, and especially specific satisfaction with the inhaler. In this setting, EH is well valued by patients. In our homogeneous population of patients with moderate to severe asthma, specific satisfaction with the inhaler was higher with EH.

However, the relationship between satisfaction with the inhaler and adherence and asthma control deserves more investigation.

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## Key issues

- Physicians should keep in mind patient satisfaction with asthma therapy, and especially specific satisfaction with the inhaler.
- Dry powder inhalers (DPIs) present different features that may have clinical implications.
- Easyhaler<sup>TM</sup> has been shown to have advantages over older DPIs in prior studies.
- In a homogeneous population of patients with moderate to severe asthma, specific satisfaction with inhaler (measured with the FSI-10 questionnaire) was statistically significantly higher with Easyhaler<sup>TM</sup> (43.8 ± 7.1) compared with Turbuhaler<sup>TM</sup> or Diskus<sup>TM</sup> (Accuhaler<sup>TM</sup>) (41.3 ± 7.6) (p < 0.01).</li>
- Moreover, high satisfaction with inhaler was statistically significantly higher with Easyhaler<sup>TM</sup> (62.4% of patients) than with Turbuhaler<sup>TM</sup> or Diskus<sup>TM</sup> (Accuhaler<sup>TM</sup>) (43% of patients) (p = 0.01).

• This preference for EH has been found in other studies in patients with asthma.

## **Acknowledgments**

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#### **Author contribution**

320 All authors have contributed significantly to conception, design and execution of the study. All authors have participated in drafting, reviewing, and/or revising the manuscript, and have approved its submission.

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A.V. has previously received honoraria for speaking at sponsored meetings from AstraZeneca, Chiesi and Novartis, and is a consultant for Astrazeneca and Sanofi.

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V.P. previously received honoraria for speaking at sponsored meetings from AstraZeneca, Chiesi, GlaxoSmithKline and Novartis. They also received assistance in traveling to meetings from Chiesi and Novartis. They act as a consultant for ALK, AstraZeneca, Boehringer, MundiPharma and Sanofi. They have also received funding/grant support for research projects from a variety of government agencies and not-for-profit foundations, as well as AstraZeneca, Chiesi and Menarini.

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#### **Reviewers Disclosure** 350

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- Patients with asthma found Easyhaler<sup>TM</sup> easy to use and they had high satisfaction with the device.

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