

Maintenance Inhalers for Asthma and COPD in Spain

Xavier Muñoz, Jordi Giner, Antoni Sicras, and Daniele Lo Re

BACKGROUND: This study aimed to describe the use of pressurized metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs) in Spanish subjects in terms of sociodemographic, clinical, and functional characteristics in subjects with asthma or COPD on maintenance treatment with inhaled therapy. **METHODS:** This was a retrospective, descriptive, national, multi-center, and observational study using a database with 1.8 million patients from hospitals and primary care centers as a secondary information source. **RESULTS:** The sample included 24,102 subjects with asthma on maintenance therapy (26.0% with pMDI, 55% with DPI, and 19.0% with a combination of DPI + pMDI inhalers) and 12,858 subjects with COPD on maintenance therapy (26% with pMDI; 39% with DPI; and 35% with a combination of pMDI + DPI inhalers, mostly extemporaneous triple therapy). In proportion, subjects ≥ 75 y old used more pMDI than DPI, while younger subjects (40–64 y old) used more DPI. An inhalation chamber was prescribed in 51.0% of subjects with asthma and 47.2% of subjects with COPD treated with pMDI. The use of an inhalation chamber increases with the degree of air-flow limitation by disease and age. In subjects with comorbidities, pMDI inhaler use increased in those ≥ 75 y old for subjects with asthma and subjects with COPD. Switching from pMDI to DPI and vice versa was relatively common: 25% of subjects with asthma and 21.6% of subjects with COPD treated with pMDI had switched from DPI in the previous year. On the contrary, 14.1% and 11.4% of subjects with asthma and subjects with COPD, respectively, treated with DPI had switched from pMDI the last year. **CONCLUSIONS:** The use of pMDI or DPI can vary according to age, both in asthma and COPD. Switching from pMDI to DPI and vice versa is relatively common. Despite the availability of dual- and triple-therapy inhalers on the market, a considerable number of subjects were treated with multiple devices. *Key words:* asthma; COPD; inhalation devices; dry powder inhaler; pressurized metered-dose inhaler; patient preference. [Respir Care 2024;69(12):1534–1542. © 2024 Daedalus Enterprises]

Introduction

Asthma is characterized by airway inflammation, hyper-responsiveness, and variable air-flow limitation for short periods.¹ The prevalence of asthma ranges between countries and cities, ranging from 4–12%.² COPD is a slow, progressive disease characterized by poorly reversible air-flow limitation due to chronic bronchitis and emphysema. The prevalence of COPD in Spain is currently 10.2% in people age ≥ 40 y, reaching 35% in males > 70 y of age.

Treatment of these 2 chronic respiratory disorders (asthma and COPD) involves inhaled medication delivered directly to the desired site, with reduced medication doses and minimized systemic adverse events compared to oral administration. It is a cornerstone for the treatment of both respiratory pathologies. Several inhaler devices are commercially available, each with specific characteristics to achieve the optimal inhalation and dose delivery of drugs. Challenges can range

from difficulties related to the degree of air-flow limitation by the disease and lung function to physical considerations, including manual dexterity and comorbidities such as arthritis.³ As each inhaler offers different technical properties, a personalized approach to selecting the most appropriate device for the patient is highly recommended to increase the likelihood of achieving better disease outcomes and improve treatment adherence. Poor adherence is associated with increased morbidity, mortality, and the incremental use of health services in patients with asthma and patients with COPD.⁴

Therefore, the patient must use a correct inhalation technique to be effective. A critical aspect of pressurized metered-dose inhaler (pMDI) technique is the coordination between inhalation and device activation; lack of coordination results in an inhalation^{5,6} with little or no drug reaching the lung. To avoid the lack of coordination between the patient and the device, patients should use inhalation

chambers, which could also reduce local adverse effects and increase the lung deposition of the drug.⁷ Despite the known benefits of using an inhalation chamber, a recent study highlights that most subjects with asthma used pMDIs without an inhalation chamber (63.4%).⁸

Another alternative is dry powder inhalers (DPIs).⁷ In these devices, the drug is in micronized (1–5 µm size range) and added to a much larger particle size vehicle (lactose), which separate from each other during the inhalation maneuver. This phenomenon is highly dependent on the flow of inspired air, device resistance, and lung capacity. This variability in inspiratory flow and inspiratory volume means that the inhaled dose can vary from patient to patient and, in some cases, be relatively low or nonexistent.^{9–11}

We postulated that sociodemographic, clinical, and functional attributes could influence the health care professional's choice between pMDIs and DPIs. Furthermore, we hypothesized that in routine clinical practice physicians switch between inhaler devices without altering the active pharmaceutical ingredient, transitioning from pMDIs to DPIs and vice versa.

Methods

Study Design

Data from this retrospective, descriptive, national, multi-center, and observational study were retrieved from a review of computerized medical records and other complementary databases with 1.8 million patients from hospitals and primary care centers (integrated areas) distributed in 7 autonomous communities in Spain. The study was conducted by protocol, the ethical principles of the Declaration of Helsinki, the standards of Good Clinical Practice, and the applicable legislation. It was approved by the local Ethics Committee for Research involving medicinal products of the Consorci Sanitari de Terrassa, Barcelona, Spain (CHI-RES-2021-01; FLASH study). Since the data used in this study have been previously anonymized and were dissociated data in which the subjects' identification data were wholly separated from the clinical care data, obtaining the subjects' informed consent was not necessary.

Dr Muñoz is affiliated with Vall'd Hebrón Hospital, Department of Pneumology, Barcelona, Spain. Mr Giner is affiliated with Santa Creu i Sant Pau Hospital, Department of Asthma and Allergy Unit, Barcelona, Spain. Dr Sicras is affiliated with HEOR, Real-Life Data, Barcelona, Spain. Dr Re is affiliated with Department of Medicinal and Organic Chemistry, Faculty of Pharmacy, University of Granada, Campus de Cartuja, Granada, Spain.

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QUICK LOOK

Current knowledge

Inhaled medication is the cornerstone of the pharmacologic treatment of patients with asthma and patients with COPD. Appropriate selection and correct use of inhalation devices are an integral component in managing asthma and COPD. Patient characteristics, engagement, and satisfaction are also important factors.

What this paper contributes to our knowledge

The use of an inhalation chamber increased with the degree of air-flow limitation and with age. There was a preference for pressurized metered-dose inhalers use in subjects ≥ 75 y old, both male and female. Treatment adherence was increased in subjects with moderate-severe asthma and subjects with moderate COPD. It was demonstrated that patient characteristics are different and must be considered when prescribing an inhaler device to obtain the best possible results. We might conclude that the switch was guided by clinical reasons related to the subject's needs.

Data were retrieved between October 1, 2019–December 31, 2019. Information about the previous device for patients treated with a single pMDI or DPI inhaler on December 31, 2019, (index date) was retrieved from the last year.

Study Population

This study assessed females and males, ≥ 18 and ≥ 40 y old, objectively diagnosed with asthma or COPD on treatment with inhaled maintenance therapy with the last available prescription in the 3 months before the index date (December 31, 2019) and present on the chronic prescription program with at least 2 prescriptions. The sample included 24,102 subjects with asthma with maintenance therapy (6,270 with a single pMDI inhaler [inhaled corticosteroids [ICS]/long-acting β agonist [LABA]], 13,244 with a single DPI inhaler [ICS/LABA], and 4,588 with a combination of pMDI + DPI inhalers) with a percentage of females

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Dr Muñoz and Mr Giner contributed equally to this work.

Supplementary material related to this paper is available at <http://www.rcjournal.com>.

Correspondence: Xavier Muñoz MD, Department of Pneumology, Vall'd Hebrón Hospital, Passeig de la Vall d'Hebron, 119, 08035 Barcelona, Spain. E-mail: xavier.munoz@vallhebron.cat.

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of 61.3% and 12,858 subjects with COPD with maintenance therapy (3,350 with a single pMDI inhaler [ICS/LABA or ICS/LABA/long-acting muscarinic antagonist [LAMA]], 4,977 with a single DPI inhaler [ICS/LABA or ICS/LABA/LAMA], and 4,531 with a combination of pMDI + DPI inhalers) with a percentage of females of 33.4%.

Study Objectives

The main objective of this study was to describe the sociodemographic, clinical, and functional characteristics of subjects with asthma and subjects with COPD in treatment with inhaled maintenance therapy, depending on whether the treatment consisted of pMDIs, DPIs, or the combination of both devices. The principal end points included age, sex, body mass index, comorbidities, FEV₁, FVC, FEV₁/FVC, and use of inhalation chamber. Secondary end points included the type of drug used and concomitant medication. Exploratory end points included adherence to treatment and the type of the previous device (previous 1 y) only in the case of subjects treated with pMDI at the index date.

Study Definitions

In both asthma and COPD, we classify the degree of air-flow limitation of the pathology according to the air-flow obstruction values (based on post-bronchodilator FEV₁): normal (> 80%), mild (70–80%), moderate (60–70%), moderate/severe (50–60%), severe (35–50%), and very severe (< 35%). Due to the characteristics of the study, we have not been able to classify the degree of air-flow limitation of asthma and COPD as recommended by the guidelines (Global Initiative for Asthma or Spanish Guidelines for the Management of Asthma and Global Initiative for Chronic Obstructive Lung Disease for asthma and COPD, respectively) or as it is done in routine clinical practice.

High-maintenance treatment adherence was defined when the percentage of subjects who retrieved medication from the community pharmacy was $\geq 80\%$ in those without a change of device in the previous year before the index date. Change from pMDI to DPI and from DPI to pMDI was defined as subjects with asthma or subjects with COPD who have been treated with LABA/ICS in the previous year and who have experienced a change from pMDI to DPI or from DPI to pMDI. For subjects on triple therapy (LABA/LAMA/ICS), change of inhaler (from pMDI to DPI and vice versa) was defined as follows: subjects treated with fixed or extemporaneous (mixed devices pMDI and DPI) triple therapy in the previous year who have experienced a change from pMDI to DPI (or vice versa) or from extemporaneous to fixed triple therapy (both pMDI and DPI).

Statistical Analysis

The data were validated to ensure the quality of the records, and a descriptive-univariate statistical analysis was performed. Qualitative data were expressed as absolute and relative frequencies and quantitative data as mean and SD or medians and interquartile ranges. Confidence intervals were used for the estimation of population parameters. The normality of the distribution was tested using the Kolmogorov-Smirnov test. For the bivariate analysis, analysis of variance was used, as well as chi-square for linear correlation, and Student *t* test.

Results

Demographic Characteristics

Our final sample was 24,102 subjects diagnosed with asthma and 12,858 subjects diagnosed with COPD. In asthma, 20% of subjects were age 18–39 y, 44% were 40–64 y, 17% were 65–74 y, and 18.0% were ≥ 75 y old. In COPD, 39% of subjects were 40–64 y old, 27% were 65–74 y old, and 34% were ≥ 75 y old (Table 1). In the asthma group, the ratio of male/female was 0.63 and in COPD was 1.99. However, 11.1% and 10% of subjects included were current smokers in asthma and COPD, respectively.

Clinical Characteristics

Charlson comorbidity index; years since diagnosis; and the results obtained for FEV₁, FVC, and FEV₁/FVC are shown in Table S1 (see related supplementary materials at <http://www.rcjournal.com>). Arterial hypertension, dyslipidemia, obesity, and diabetes mellitus were the most common comorbidities both in asthma and COPD (Table S2). The use of pMDI and DPI in subjects with arterial hypertension, obesity, and diabetes was studied according to age and sex (Tables S3 and S4, see related supplementary materials at <http://www.rcjournal.com>).

Functional Characteristics

In the asthma group, 12,846 subjects (53.3%) had moderate asthma; 7,260 (30.1%) had moderate-severe asthma; and 3,190 subjects (13.2%) had mild asthma while 692 (2.9%) and 114 subjects (0.5%) had severe and very severe asthma, respectively (Table 1). In the COPD group, 6,637 subjects (51.6%) had moderate COPD; 4,835 subjects (37.6%) had moderate-severe COPD; and 591 subjects (4.6%) had mild COPD while 633 (4.9%) and 162 subjects (1.3%) showed severe and very severe COPD, respectively (Table 1). In asthma and COPD, the degree of air-flow limitation by

DPI AND pMDI USE IN SPAIN

Table 1. Demographic and Functional Characteristics of Subjects With Asthma and Subjects With COPD According to the Inhaler Prescribed

Asthma					
Characteristic	pMDI Single Device*	DPI Single Device*	<i>P</i> DPI vs pMDI	Multiple Devices: pMDI + DPI†	<i>P</i> Multiple Devices vs pMDI+DPI
Subjects	6,270 (26)	13,244 (55)		4,588 (19)	
Age, y	55 (19.0)	53.1 (17.2)	< .001	65.5 (15.0)	< .001
Age range, y					
18–39	1,512 (24.1)	3,194 (24.1)	> .99	232 (5.1)	< .001
40–64	2,616 (41.7)	6,448 (48.7)	< .001	1,642 (35.8)	< .001
65–74	956 (15.2)	2,008 (15.2)	> .99	1,154 (25.2)	< .001
≥ 75	1,186 (18.9)	1,594 (12.0)	< .001	1,560 (34.0)	< .001
Sex					
Male	2,310 (36.8)	5,368 (40.5)	< .001	1,658 (36.1)	< .001
Female	3,960 (63.2)	7,876 (59.5)	< .001	2,930 (63.9)	< .001
Degree of air-flow limitation					
Mild, 70–80	966 (15.4)	1,938 (14.6)	.34	286 (6.2)	< .001
Moderate, 60–70	3,382 (53.9)	7,080 (53.5)		2,384 (52.0)	
Moderate/severe, 50–60	1,760 (28.1)	3,874 (29.3)		1,626 (35.4)	
Severe, 35–50	152 (2.4)	324 (2.4)		216 (4.7)	
Very severe, < 35	10 (0.2)	28 (0.2)		76 (1.7)	
Current smoker	678 (10.8)	1,464 (11.1)	.62	542 (11.8)	.24
Treatment adherence > 80%	3,168 (50.5)	6,986 (52.7)	.004	3,352 (73.1)	< .001
Inhalation chamber	3,196 (51.0)			244 (10.6)	
COPD					
Characteristic	pMDI Single Device‡	DPI Single Device‡	<i>P</i> DPI vs pMDI	Multiple Devices: pMDI + DPI§	<i>P</i> Multiple Devices vs pMDI+DPI
Subjects	3,350 (26)	4,977 (39)		4,531 (35)	
Age, y	66 (16.9)	63.3 (16.4)	< .001	71.8 (12.8)	< .001
Age range, y					
18–39					
40–64	1,375 (41.0)	2,380 (47.8)	< .001	1,236 (27.3)	< .001
65–74	836 (25.0)	1,317 (26.5)	.13	1,297 (28.6)	< .001
≥ 75	1,139 (34.0)	1,280 (25.7)	< .001	1,998 (44.1)	< .001
Sex					
Male	2,317 (69.2)	3,306 (66.4)	.009	2,939 (64.9)	.041
Female	1,033 (30.8)	1,671 (33.6)		1,592 (35.1)	
Degree of air-flow limitation					
Mild, 70–80	231 (6.9)	338 (6.8)	.80	22 (0.5)	< .001
Moderate, 60–70	1,822 (54.4)	2,700 (54.2)		2,115 (46.7)	
Moderate/severe, 50–60	1,209 (36.1)	1,804 (36.2)		1,822 (40.2)	
Severe, 35–50	81 (2.4)	117 (2.4)		435 (9.6)	
Very severe, < 35	7 (0.2)	18 (0.4)		137 (3)	
Current smoker	341 (10.2)	525 (10.5)	.59	444 (9.8)	.27
Adherence to treatment > 80%	1,620 (48.4)	2,520 (50.6)	.042	3,564 (78.7)	< .001
Inhalation chamber	1,581 (47.2)			1,134 (12.8)	

Data are presented as *n* (%) or mean (SD).
 For asthma:
 *Inhaled corticosteroids/long-acting β agonist.
 †Inhaled corticosteroids(ICS)+long-acting β agonist (LABA)+long-acting muscarinic antagonist (LAMA) or ICS/LABA+LAMA: mix of devices dry powder inhaler+pressurized metered-dose inhaler.
 For COPD:
 ‡Inhaled corticosteroids (ICS)/long-acting β agonist (LABA) or ICS/LABA/long-acting muscarinic antagonist.
 §Long-acting muscarinic antagonist (LAMA)/long-acting β agonist (LABA)+inhaled corticosteroids (ICS); LABA/ICS+LAMA; LAMA+LABA+ICS; ICS+LABA; ICS+LAMA; LAMA+LABA: mix of devices DPI +pMDI.
 pMDI = pressurized metered-dose inhaler
 DPI = dry powder inhaler

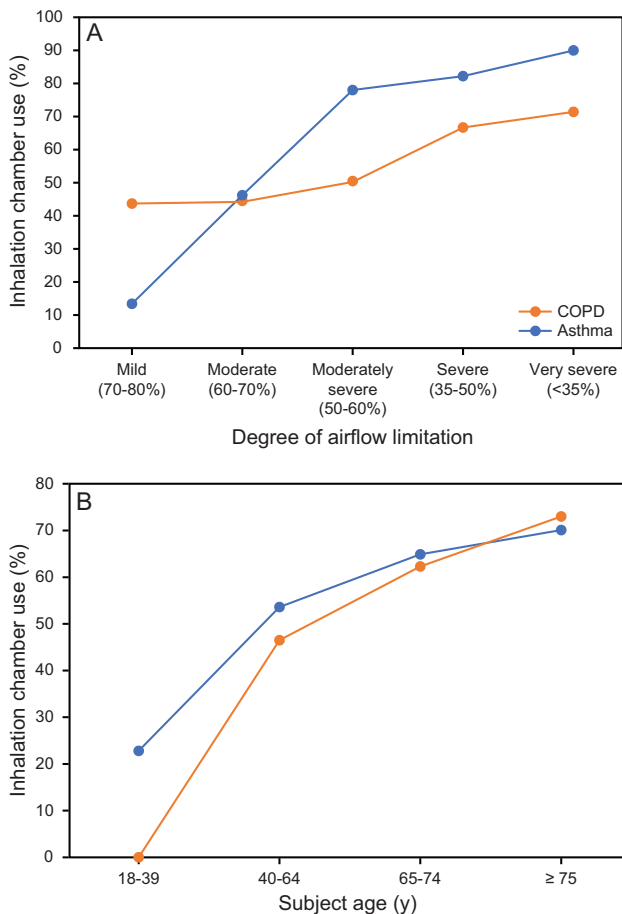


Fig. 1. Use of inhalation chamber according to (A) degree of air-flow limitation and (B) age.

the disease has been established using FEV₁ values (see study definition).

Use of pMDI and DPI According to Age

The use of pMDI increased in the elderly population (≥ 75 y old group, both sexes) when compared with DPI (18.9% vs 12.0%, *P* < .001, subjects with asthma; and 34.0% vs 25.7%, *P* < .001, subjects with COPD). However, the use of pMDI in the subgroup of subjects age 40–60 y (both sexes) was < the use of DPI (41.7% vs 48.7% *P* < .001, subjects with asthma; and 41.0% vs 47.8% *P* < .001, subjects with COPD). No differences were observed between the use of pMDI and DPI in the subgroup of subjects age 65–74 y (both sexes) for asthma and COPD (Table 1). When males and females were compared separately, the results were similar.

Use of Multiple Devices

In asthma, 19% of subjects were treated with a mix of DPI and pMDI inhalers (ICS+LABA+LAMA or ICS/LABA +

LAMA). In the COPD group, this percentage rose to 35% (LAMA/LABA+ICS, LABA/ICS+LAMA, ICS+LABA, ICS+LAMA, and LAMA+LABA) (Table 1). A significant proportion of elderly subjects (≥ 75 y old group) were treated with mixed devices (asthma 34%, COPD 44.1%). In addition, the percentage of subjects treated with mixed devices increased as a function of age in the group of subjects with COPD.

Use of Inhalation Chamber in Subjects Treated With pMDI

The physician recommended inhalation chamber in 51% of subjects in the asthma group and 47% of subjects in the COPD group using only a pMDI device and 10.6% of subjects in the asthma group and 12.8% of subjects in the COPD group using a combination of pMDI and DPI devices. In both asthma and COPD groups, the recommendation of an inhalation chamber by the physician increased accordingly with the degree of air-flow limitation by the disease, age, and Charlson index (Table S5, see related supplementary materials at <http://www.rcjournal.com>).

In the asthma group, the recommendation by the physician of an inhalation chamber increased with the degree of air-flow limitation by the disease (13.4% mild asthma, 46.2% moderate asthma, 78.0% moderate/severe, 82.2% severe, and 90% very serious) and with age (22.8%, 18–39 y age group; 53.6%, 40–64 y age group; 64.9%, 65–74 y age group; and 70.1%, ≥ 75 y old) (Fig. 1).

Similarly, in the COPD group, the recommendation by the physician of an inhalation chamber increased with the degree of air-flow limitation by the disease (43.7% mild, 44.5% moderate, 50.5% moderate/severe, 66.7% severe, and 71.4% very serious) and with age (47.4%, 40–64 y age group; 62.3%, 65–74 y age group; and 73%, ≥ 75 y old group) (Fig. 1).

Switching from DPI to pMDI

In the asthma group, 25.0% of subjects treated with pMDI (LABA/ICS) at the index date had experienced a switch of inhaler (from DPI to pMDI) the previous year. In the COPD group, 21.6% of subjects treated with pMDI (LABA/ICS) at the index date had experienced a switch of inhaler (from DPI to pMDI) in the previous year (Fig. 2). On the other hand, 42.1% of subjects treated with triple therapy using a pMDI inhaler (LABA/LAMA/ICS) at the index date had experienced a change of inhaler (24.2% from DPI to pMDI and 17.9% from multiple devices) (Fig. 2).

Switching from pMDI to DPI

In the asthma group, 14.1% of subjects treated with DPI (LABA/ICS) at the index date had experienced a switch of inhalers in the previous year (from pMDI to DPI). In

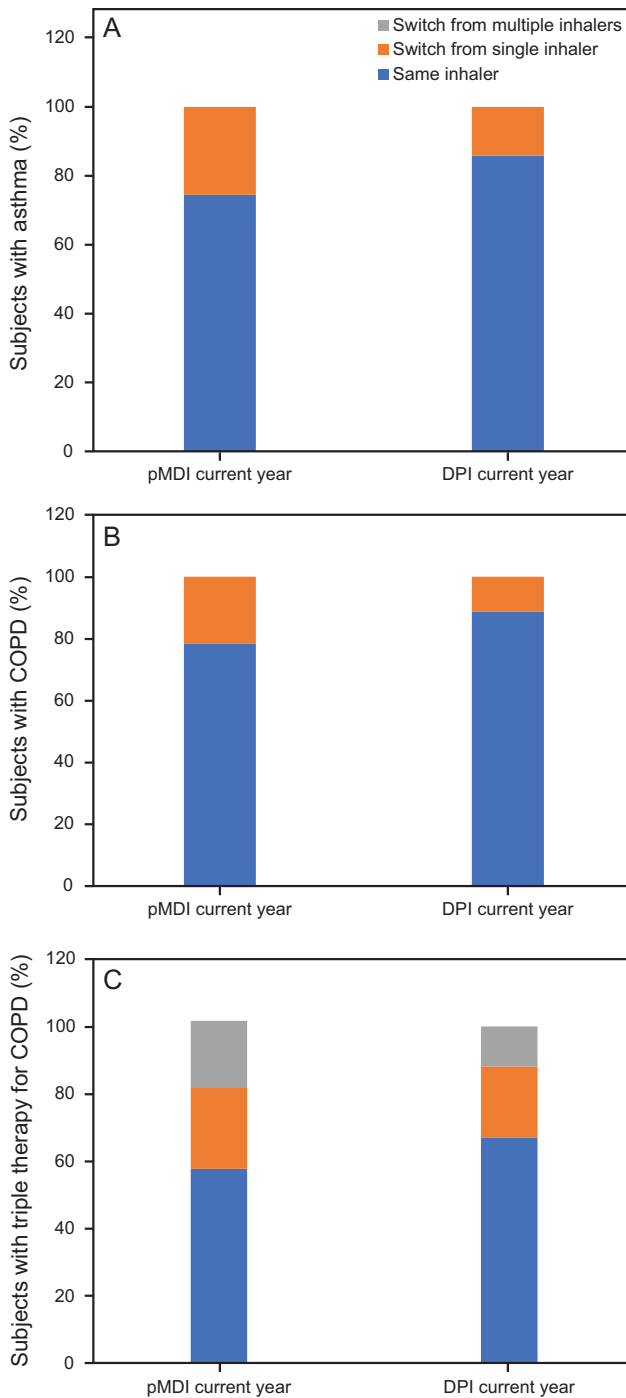


Fig. 2. Change in inhalers in asthma and COPD. A: Switch from pressurized metered-dose inhaler (pMDI) and dry powder inhaler (DPI) in subjects with asthma in the previous year; B: switch from pMDI to DPI and vice versa in subjects with COPD; C: switch from single pMDI to DPI and vice versa and from multiple inhalers in subjects treated with triple therapy in COPD.

the COPD group, 11.4% of subjects treated with DPI (LABA/ICS) at the index date had experienced a switch of inhaler (from pMDI to DPI) in the previous year (Fig. 2). On the other hand, 33% of subjects treated with triple

therapy using a DPI inhaler (LABA/LAMA/ICS) at the index date had experienced a change of inhaler (21.2% from pMDI to DPI and 11.8% from multiple devices) (Fig. 2).

Adherence to Maintenance Treatment

The results show that adherence to maintenance treatment was significantly increased according to the degree of air-flow limitation by the disease ranging from 46 (moderate asthma)–90% (severe asthma) in subjects treated with pMDI and from 48 (moderate asthma)–79% (severe asthma) in those treated with DPI. A similar pattern was observed in COPD, where the adherence ranged from 46 (moderate COPD)–71% (severe COPD) in subjects treated with pMDI and from 49 (moderate COPD)–83% (severe COPD) in those treated with DPI. Adherence also increased as a function of age in both COPD and asthma, regardless of the type of device (Fig. 3).

In terms of rescue medication, short-acting β_2 agonists (SABAs), such as salbutamol, were widely prescribed for subjects with asthma and subjects with COPD: 88% and 93.7% in subjects treated with a single pMDI maintenance inhaler, respectively; 87.1% and 93.3% in subjects treated with a single DPI maintenance inhaler, respectively; and 88.1% and 93% in subjects treated with a mix of devices, respectively.

Discussion

Several studies in subjects with asthma and subjects with COPD have analyzed subject satisfaction with inhalers, adherence to treatment, and subject characteristics. In most cases, these studies were designed to identify subjects’ errors during inhaler use. As expected, these errors can directly impact treatment adherence and, therefore, treatment effectiveness.^{1,4,12} There are over 230 different types of inhalers on the market. To date, no universal device can adapt to every patient. A personalized approach is, therefore, extremely important since choosing the correct inhaler must consider the needs, characteristics, and preferences of patients with asthma or patients with COPD.^{3,13,14} Recommendations in asthma and COPD guidelines presuppose that practitioners have the evidence, information, knowledge, and tools to select inhaler devices appropriate for individual patients.

In this observational retrospective study, we analyzed the prescription of pMDI and DPI in a real-world setting. Our findings indicate that there may be differences in the prescription of pMDI or DPI depending on demographic factors and show that physicians routinely switch from pMDI to DPI and vice versa. Whereas results of randomized controlled trials indicate little difference in the effectiveness of inhaler devices when used correctly and predominantly

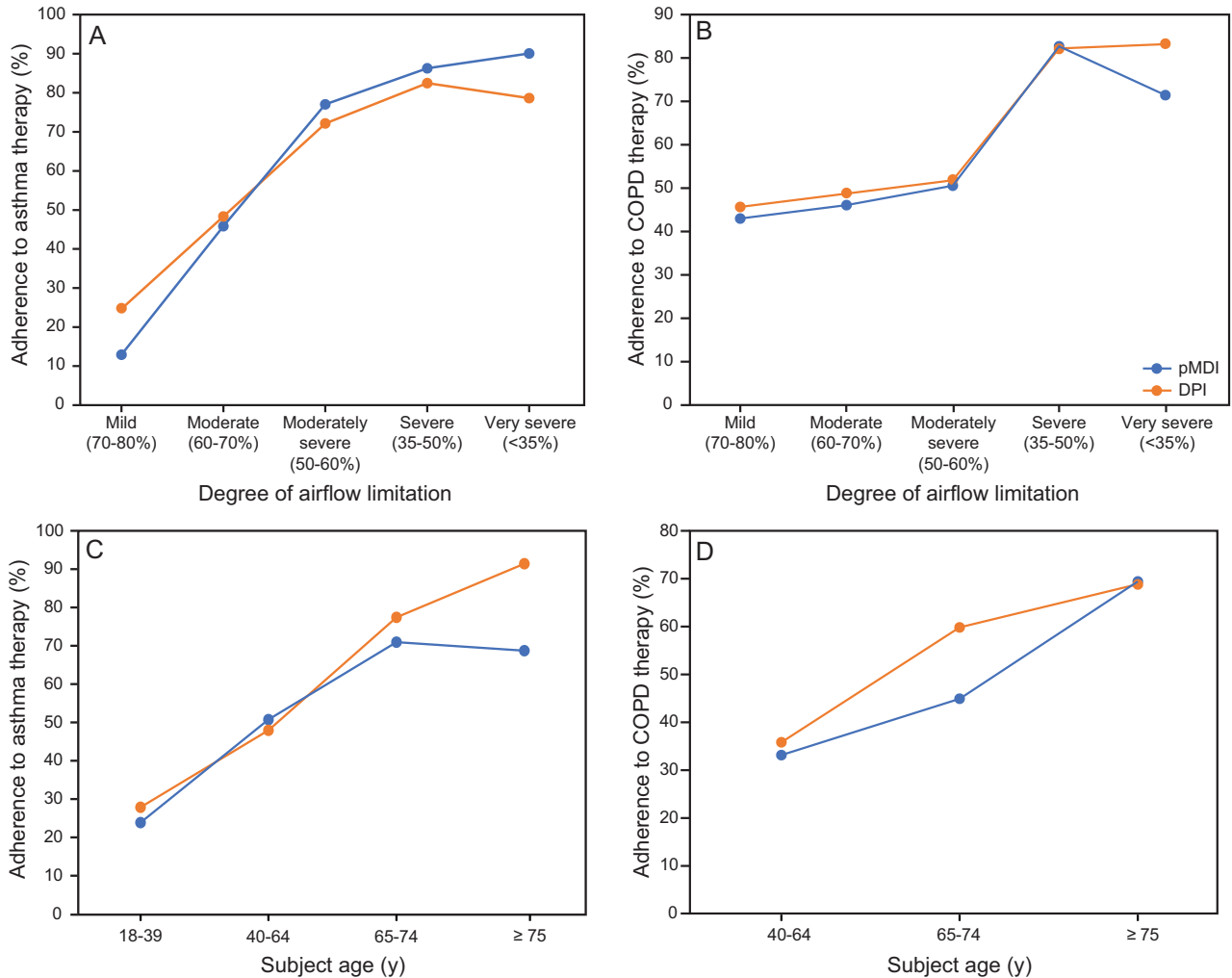


Fig. 3. Adherence to treatment in subjects treated with pressurized metered-dose inhalers (pMDI) and dry powder inhalers (DPI) in asthma and COPD. A: Adherence to treatment according to severity in subjects with asthma; B: adherence to treatment according to severity in subjects with COPD; C: adherence to treatment according to age in subjects with asthma; and D: adherence to treatment according to age in subjects with COPD.

over the short term,^{15,16} our findings suggested that real-world factors influence the effectiveness of these devices. Correct inhaler use is integral to the effectiveness of inhaled therapy, and for proper use, it could be essential to consider the patients' sociodemographic, clinical, and functional characteristics. Other factors that could influence the effectiveness of therapy include patient preferences and physician knowledge of the device. It has been suggested before that an optimal match between patient and device may be achieved by applying a simple 4-model question approach: Who-What-Where-How (Who: consider asthma and COPD disease characteristics; What: consider the type of drug to use; Where: targeting the medication; and How: matching patient, molecule, dose, and device).¹²

As reflected in the results of this study, DPIs are the most prescribed inhaler devices in the analyzed population, for both subjects with asthma and subjects with COPD.

A preference for pMDI inhalers is observed in subjects ≥ 75 y old with asthma and subjects with COPD, while a preference for DPI is observed in subjects age 40–60. In elderly subjects (≥ 75 y old) with hypertension, obesity, and diabetes mellitus comorbidities, pMDI inhaler use also increased for both subjects with asthma and subjects with COPD. However, this observation could be related to the advanced age of the subjects; and therefore, this result needs to be taken with caution.

Clinical guidelines¹⁷ for asthma treatment indicate that pMDIs should preferably be used with an inhalation chamber as their use slows down the aerosolized particles emitted from the pMDI and, therefore, can increase lung deposition and reduce oropharyngeal deposit.¹⁸ However, our results indicate that this happens only for 51% of subjects in the asthma group and 47% of those in the COPD group. Importantly, the recommendation of an inhalation

chamber increases with degree of air-flow limitation by the disease and age.

Interestingly, a considerable number of subjects were using a mix of devices, DPI and pMDI (19% for asthma and 35.2% for COPD). Using multiple devices could confuse patients and increase errors that could also have a tremendous impact on treatment adherence. This can be reduced by using the same inhaler device; therefore, using multiple devices should be avoided when possible.¹⁹ The use of mixed devices, both in asthma and COPD, increases with age and severity, meaning that an important proportion of elderly and patients with severe disease are using a mixed combination of devices. On the other hand, a consistent number (4,097 subjects, 89.4%) of subjects with COPD receiving maintenance inhalation medication with mixed devices are treated with triple therapy, and only 842 subjects (17.0% of the total population with triple therapy) are treated with fixed triple therapy. At the time of the study, access to this class of drugs was limited by the health care system, resulting in a therapeutic approach that does not seem to follow the clinical recommendations of guidelines.²⁰ On the other hand, it is worth noting that fixed triple therapy had been on the Spanish market for 1.5 y (pMDI) and 6 months (DPI); and therefore, these results should be analyzed with care.

As expected, adherence to maintenance treatment (defined as $\geq 80\%$ of retrieved medication from the community pharmacy) increased with age and degree of air-flow limitation by the disease in both subjects with asthma and subjects with COPD, regardless of the type of inhaler (DPI or pMDI). In terms of sex, adherence was similar in females with asthma and males with COPD.

Interestingly, there was a considerable percentage of subjects who switched from DPIs to pMDIs (and vice versa) in the previous year. The design of this study does not allow us to identify the main reasons for these switches; however, we could assume that the switch was guided by clinical reasons related to the subject's needs.

This study also confirms the wide use of SABAs, such as salbutamol, as rescue medication for subjects with asthma and subjects with COPD. Both asthma^{2,17} and COPD^{21,22} guidelines consider the use of SABAs as an important parameter to consider assessing poor control of the disease. Moreover, Nwaru et al²³ have recently argued that SABAs overuse was associated with increased risks of exacerbation and mortality in asthma.

Strengths and Limitations

This study was based on real-life data, which are of great value for understanding patients' characteristics, uses, and preferences regarding prescribed treatments. Our study limitations include those inherent to any observational study using retrospective data. First, the data collected were limited to the information recorded in the database and, second,

because data were collected for a specific period (between October 1, 2019–December 31, 2019), which does not fully reflect reality. Third, the classification of asthma and COPD degree of air-flow limitation according to FEV₁ is not recommended by the guidelines; and therefore, this should be considered when interpreting the results.

During the study period, access to fixed triple therapy was limited, as it had recently entered the Spanish market (1.5 y for pMDI and 6 months for DPI), warranting caution in interpreting the results. Patients with asthma and patients with COPD treated with a drug in monotherapy were not included since we decided to focus exclusively on subjects receiving fixed ICS+LABA maintenance combinations (or fixed triple therapy in COPD) for comparison between pMDI and DPI devices (groups 1 and 2). In the third group, subjects with asthma on a combination of device types were considered.

Conclusions

The multitude of available inhalation devices could present a considerable challenge in selecting the appropriate inhaler for individual patients. When selecting a device, patients have a range of characteristics, such as age, cognitive status, manual dexterity, visual acuity, inspiratory capacity, ability to coordinate actuation of the inhaler with inhalation, and comorbidities, and some of these characteristics seem to determine the type of device (pMDI or DPI) recommended by the physician.

The use of an inhalation chamber when pMDI is recommended is still not optimal and should be encouraged as reflected in international guidelines. Despite the availability of dual- and triple-therapy inhalers on the market, many patients are still treated with multiple devices (pMDI + DPI). In a real-world environment, DPI and pMDI are likely not always interchangeable as it will depend on the optimal use that the patient can make of one or the other device. In our study, a considerable percentage switched from DPIs to pMDIs and vice versa in the previous year. Even if our data cannot explain the reason for the switch, we can probably assume that the change was motivated by clinical decisions based on subject needs, highlighting that both therapeutic options are important to meet the needs and preferences of patients.

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REFERENCES

1. Darbà J, Ramírez G, Sicras A, García-Bujalance L, Torvinen S, Sánchez-de la Rosa R. Identification of factors involved in medication compliance: incorrect inhaler technique of asthma treatment leads to poor compliance. *Patient Prefer Adherence* 2016;10:135-145.

2. GEMA 5.2. Actualización de la Guía de Manejo de Asma. Available at: <https://se-fc.org/wp-content/uploads/2022/05/GEMA-5.2-Final.pdf>. Accessed August 31, 2022.
3. Usmani OS. Choosing the right inhaler for your asthma or COPD patient. *Ther Clin Risk Manag* 2019;15:461-472.
4. Donaire JG, Pérez DD, Hernández C, Cabestre R. Study to evaluate satisfaction with the inhalation device used by patients with asthma or chronic obstructive pulmonary disease and the association with adherence and disease control. *J Aerosol Med Pulm Drug Deliv* 2020;33(3):153-160.
5. Newman SP, Pavia D, Clarke SW. Simple instructions for using pressurized aerosol bronchodilators. *J R Soc Med* 1980;73(11):776-779.
6. Crompton GK. Problems patients have using pressurized aerosol inhalers. *Eur J Respir Dis Suppl* 1982;119:101-104.
7. Fernández Tena A, Casan Clarà P. Deposition of inhaled particles in the lungs. *Arch Bronconeumol* 2012;48(7):240-246.
8. Valladales-Restrepo LF, Saavedra-Navia JC, Montezuma-Casanova CA, Montañez-Díaz V, González-Ospina JA, Caballero-Martínez LM, et al. Satisfaction with and use of inhalation devices in patients with bronchial asthma. *J Aerosol Med Pulm Drug Deliv* 2022;35(6):313-320.
9. Meakin BJ, Ganderton D, Panza I, Ventura P. The effect of flow rate on drug delivery from the Pulvinal, a high-resistance dry powder inhaler. *J Aerosol Med* 1998;11(3):143-152.
10. Price DB, Román-Rodríguez M, McQueen RB, Bosnic-Anticevich S, Carter V, Gruffydd-Jones K, et al. Inhaler errors in the CRITIKAL study: type, frequency, and association with asthma outcomes. *J Allergy Clin Immunol Pract* 2017;5(4):1071-1081.e9.
11. Corradi M, Chrystyn H, Cosio BG, Pirozynski M, Loukides S, Louis R, et al. NEXThaler, an innovative dry powder inhaler delivering an extra-fine fixed combination of beclometasone and formoterol to treat large and small airways in asthma. *Expert Opin Drug Deliv* 2014;11(9):1497-1506.
12. Dekhuijzen PN, Vincken W, Virchow JC, Roche N, Agusti A, Lavorini F, et al. Prescription of inhalers in asthma and COPD: toward a rational, rapid, and effective approach. *Respir Med* 2013;107(12):1817-1821.
13. Lavorini F, Janson C, Braido F, Stratelis G, Løkke A. What to consider before prescribing inhaled medications: a pragmatic approach for evaluating the current inhaler landscape. *Ther Adv Respir Dis* 2019;13:1753466619884532.
14. Cataldo D, Hanon S, Peché RV, Schuermans DJ, Degryse JM, De Wulf IA, et al. How to choose the right inhaler using a patient-centric approach? *Adv Ther* 2022;39(3):1149-1163.
15. Dolovich MB, Ahrens RC, Hess DR, Anderson P, Dhand R, Rau JL, et al; American College of Asthma, Allergy, and Immunology; American College of Chest Physicians. Device selection and outcomes of aerosol therapy: evidence-based guidelines: American College of Chest Physicians/American College of Asthma, Allergy, and Immunology. *Chest* 2005;127(1):335-371.
16. Brocklebank D, Wright J, Cates C. Systematic review of clinical effectiveness of pressurized metered-dose inhalers versus other handheld inhaler devices for delivering corticosteroids in asthma. *BMJ* 2001;323(7318):896-900.
17. Levy ML, Bacharier LB, Bateman E, Boulet LP, Brightling C, Buhl R, et al. Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. *NPJ Prim Care Respir Med* 2023;33(1):7.
18. Vincken W, Levy ML, Scullion J, Usmani OS, Dekhuijzen PNR, Corrigan CJ. Spacer devices for inhaled therapy: why use them, and how? *ERJ Open Res* 2018;4(2):00065-02018.
19. Usmani OS, Hickey AJ, Guranlioglu D, Rawson K, Stjepanovic N, Siddiqui S, Dhand R. The impact of inhaler device regimen in patients with asthma or COPD. *J Allergy Clin Immunol Pract* 2021;9(8):3033-3040.e1.
20. Plaza V, Alobid I, Alvarez C, Blanco M, Ferreira J, García G, et al. Spanish Asthma Management Guidelines (GEMA) Version 5.1. Highlights and controversies. *Arch Bronconeumol* 2022;58(2):150-158.
21. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Eur Respir J* 2023;61(4):2300239.
22. Miravittles M, Calle M, Molina J, Almagro P, Gómez JT, Trigueros JA, et al. Spanish COPD guidelines (GesEPOC) 2021: updated pharmacological treatment of stable COPD. *Arch Bronconeumol* 2022;58(1):69-81.
23. Nwaru BI, Ekström M, Hasvold P, Wiklund F, Telg G, Janson C. Overuse of short-acting β_2 agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA program. *Eur Respir J* 2020;55(4):1901872.