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ORIGINAL RESEARCH

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Multidisciplinary consensus on inhaled therapy in asthma

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ABSTRACT

Background: Asthma is managed by health professionals from different specialties. We aim to reach a consensus on the optimal use of inhaled therapy and the initial steps of asthma treatment, taking into account the opinions of the involved specialists.

Methods: A modified Delphi approach was used. A scientific committee provided 52 controversial statements, which were submitted to primary care physicians, allergists, and pulmonologists. Discrepancies among specialties were evaluated.

Results: A total of 209 specialists completed the questionnaire (20.2 ± 9.3 years of asthma management experience). A consensus was reached on 37 statements (71.1%), discrepancies among specialties were found in 14. The most recommended maintenance treatment for mild persistent asthma in adults/adolescents was low-dose-inhaled corticosteroids daily. MART (Maintenance and Reliever Therapy) was recommended as salvage treatment for moderate persistent asthma. Panelists agreed on the most frequent critical errors with pressurized Metered-Dose Inhalers or Dry-Powder Inhalers, and considered that Breath-Actuated Inhalers are a suitable option for all patients with the ability to inhale voluntarily.

Conclusions: The experts endorse the main guidelines recommendations; however, do not fully agree on recent GINA recommendations about the treatment of the initial steps of the disease. The experts value positively the differential characteristics of BAI over other devices.

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Asthma; breath-actuated inhalers; consensus

1. Introduction

Asthma is estimated to affect 235 million people worldwide [1]. Despite the advances in recent years in the pathophysiology of the disease, and especially in its treatment, it is estimated that less than 50% of asthmatic patients have their disease under control [2]. Among the causes of poor control are possible concomitant diseases and aggravating factors, lack of adherence, inadequate treatment or poor inhaler technique [3].

Inhaled therapy is the cornerstone of asthma treatment, however, it is associated with various disadvantages that may decrease its effectiveness. One of the main drawbacks lies in the difficulty that many patients have in using inhaler devices correctly [4]. Therefore, patients must be trained to use them correctly. In addition, many recent studies have shown that the level of knowledge of health professionals about the theoretical and practical aspects of inhaled therapy may be insufficient [5]. The existence of multiple devices for administration of inhaled therapy, each with its own particularities, can make it difficult for health professionals to know them in depth. Additionally, although there are rigorous evidence-based clinical guidelines for the management of asthma, not all of them are homogeneous in their recommendations, especially at the initial or intermediate stages of treatment, which account for the majority of patients [6–9]. Furthermore, asthma is a heterogeneous disease and is managed by various health professionals, such as primary care physicians, allergists, or pulmonologists. Although, the main asthma guidelines are similar for all health professionals, the views of the different specialists involved in the management of asthma may differ, since the type of patients they attend, and the available resources they have, are different.

Considering all these difficulties and disparities in asthma management, the objective of this work is to reach a multidisciplinary consensus on the optimal use of inhaled therapy in asthma and on the treatment of the initial and intermediate stages of the disease, taking into account the views of different specialties involved in the asthma patients care.

2. Patients and methods

In this project, a consensus methodology based on a modified Delphi technique has been used, following the UCLA/RAND recommendations [10,11].

As a first step, a scientific committee, consisting of 3 asthma experts (from primary care, allergy, and pulmonology), met to develop a Delphi questionnaire based on a non-

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Article highlights

- This multidisciplinary consensus brings together the opinion of a large number of specialists from different specialties on the optimal use of inhaled therapy and the initial steps of asthma treatment.
- This multidisciplinary group of experts endorsed the main recommendations on education and adherence proposed by national and international clinical practice guidelines but did not fully agree on recent GINA recommendations about the treatment of the initial steps of the disease (intermittent and mild persistent asthma) regarding the PRN use of low-dose ICS/formoterol combination as the preferred option.
- The most recommended maintenance treatment for mild persistent asthma in adults/adolescents was low-dose-inhaled corticosteroids daily.
- MART (Maintenance and Reliever Therapy) was recommended as salvage treatment for moderate persistent asthma.
- The experts valued very positively the diverse characteristics of BAI and their advantages over other inhaler devices.

systematic exhaustive literature search and their own expertise in the management of asthma. The three experts (VAL, TJA and PV) are prominent members of their respective scientific societies (the Spanish Society of General and Family Doctors [SEMG], the Spanish Society of Pulmonology and Thoracic Surgery [SEPAR], and the Spanish Society of Clinical Allergology and Immunology [SEAIC], respectively), and key members of the committee that develops the Spanish Asthma Guidelines (GEMA) [9]. Literature search included recent asthma management guidelines and the following terms in PubMed in the last 5 years: Asthma, Asthma/Therapy, Inhalers, Nebulizers, and Vaporizers, Dry Powder Inhalers, Metered Dose Inhalers, Breath-Actuated Inhalers, Treatment Adherence and Compliance, Patient education, Self-care, Self-management. After several meetings in person, the scientific committee reached an agreement on the content of the questionnaire. It included statements focused on controversial or unanswered questions about the optimal use of inhaled therapy in asthma, and on debatable recommendations given in the guidelines about the treatment of the initial or intermediate stages of the disease.

The questionnaire consisted of 52 items divided into 6 blocks: 1) general aspects of inhaled therapy in asthma, 2) selection of inhaled drugs, 3) pressurized metered-dose inhalers and spacers, 4) dry-powder inhalers, 5) breath-actuated inhalers, and 6) therapeutic adherence and educational aspects (Tables 1–4). The questionnaire was submitted to 210 specialists from 16 out of the 17 Spanish autonomous regions: 70 primary care physicians, 70 allergists, and 70 pulmonologists. Only one panelist (an allergist) did not complete the questionnaire, therefore, this panelist was excluded from the analysis.

In a second phase, the scientific committee selected the members of a panel of experts to evaluate the items of the questionnaire. The panelists were selected according to their experience and degree of knowledge or involvement in asthma. The inclusion criteria for the selection of the panel of experts were the following: (1) more than 10 years of experience managing asthma patients, (2) more than 50 follow-up consultations of asthma patients per month (more than 25 in the case of primary care physicians), (3) at least one asthma communication (in a journal or in a conference) or one training session on asthma as a tutor in the preceding year. The panelists were active members of scientific societies and were personally invited by the scientific committee.

The questionnaires were submitted to the panel online in two rounds (during November and December 2019, respectively). The items were evaluated using a 9-point Likert ordinal scale (1 = strongly disagree; 9 = fully agree). The responses were grouped into 3 categories (1–3 = disagree; 4–6 = neither agree nor disagree; 7–9 = agree). Consensus on an item was reached when (1) the median of the responses fell within the 7–9 category (consensus on agreement) or within the 1–3 category (consensus on disagreement); (2) less than one-third of the panelists voted outside these categories, and (3) the interquartile range of the responses (IQR) was lower than 4. Items for which an agreement was not reached in the first round were reevaluated in a second round of voting. Between rounds, panelists were informed of the detailed distribution of the responses from the first analysis. Panelists who did not respond to the first round were excluded from a subsequent questionnaire assessment.

Results are shown in tables as median and interquartile range (IQR) of the responses. Tables also show: (1) the percentage of panelists in the median region, which was defined as the percentage of panelists who voted within the category that included the median of the responses (1–3, 4–6, or 7–9), and (2) the final results of the consensus: agreement or disagreement in the 1st or 2nd round, or no consensus.

Once the general analysis was carried out, a post hoc analysis of the responses by specialties (primary care, allergy, and pulmonology) was performed to evaluate the degree of consensus amongst them.

3. Results

A total of 209 panelists answered the questionnaire. Panelists had a mean of 20.2 ± 9.3 years of experience in managing asthma patients. Mean number of follow-up of asthma consultations per month was 69.5 ± 68.6 (primary care physicians: 31.0 ± 24,1; allergists: 115.9 ± 67.9; pulmonologists: 62,2 ± 73,3).

Globally, 63 panelists (30.1%) had published at least one article about asthma in a journal, 90 (43.1%) had at least one communication in a conference, and 208 (99.5%) had conducted training sessions on asthma in the preceding year.

After the first round of evaluation, consensus was reached on 35 out of the 52 statements (67.3%). Seventeen items on which there was no consensus were subjected to a second round of evaluation and a consensus was reached on 2 of them. Subsequently, after 2 rounds of evaluation, it was possible to reach a consensus on 37 out of the 52 proposed statements (71.1%) (Tables 1–4).

In the post hoc analysis of the results, for 14 out of the 52 statements evaluated (26.9%) there was divergence among specialties when reaching an agreement. In other words, consensus was reached by one specialty but not by the others during the 1st or 2nd round of voting. These divergences are shown in Table 5.

Table 1. Statements about general aspects of inhaled therapy in asthma and selection of inhaled drugs.

	Median (IQR)	Percentage of panelists in the median region*	Results
Block I. General aspects of inhaled therapy			
(1) In terms of clinical effectiveness, the inhaled device is more important than the active drug (s) included within the different therapeutic groups (e.g., LABA, ICS, etc.).	6 (3–7)	31.6%	No consensus
(2)In a patient with a good inhaler technique, the particle size determines the lung deposition.	8 (7–9)	88.5%	**Agreement in 1st round**
(3)In the asthmatic patient, there are no clinically significant efficacy differences when using inhalers that generate fine or extra-fine particles.	4 (3–7)	22.0%	No consensus
(4)A high lung deposition rate is the one that reaches at least 40% of the metered dose.	7 (7–8)	77.5%	**Agreement in 1st round**
(5)More than half of primary care physicians have inadequate knowledge in the inhaler technique of the inhalers they prescribe.	7 (6–9)	69.9%	**Agreement in 1st round**
(6)More than half of specialized physicians have inadequate knowledge in the inhaler technique of the inhalers they prescribe.	7 (3–8)	54.1%	No consensus
(7)Critical errors in the handling of inhaled devices associated with poor control and/or the presence of exacerbations are common amongst patients.	8 (7–9)	90.0%	**Agreement in 1st round**
The most common cause of poor asthma control is:			
(8)Inadequate inhaler technique.	7 (5.5–8)	65.6%	No consensus
(9)Poor therapeutic adherence.	8 (7–9)	90.0%	**Agreement in 1st round**
When deciding on which type of inhaler to prescribe, it is necessary to consider:			
(10)The level of severity of asthma.	8 (6–9)	72.2%	**Agreement in 1st round**
(11)The patient's degree of cognitive impairment.	9 (8–9)	92.8%	**Agreement in 1st round**
(12)The patient's social support.	8 (7–9)	78.5%	**Agreement in 1st round**
Block II. Selection of inhaled drugs			
The most recommended treatment for intermittent asthma in adults and adolescents is:			
(13)PRN low-dose ICS/formoterol.	7 (4–8)	62.7%	No consensus
(14)PRN low-dose ICS/salbutamol.	3 (2–7)	52.2%	No consensus
(15)PRN SABA monotherapy.	4 (2–7)	18.2%	No consensus
The most recommended maintenance treatment for mild persistent asthma in adults and adolescents is:			
(16)Daily low-dose ICS	7 (5–8)	68.4%	**Agreement in 1st round**
(17)PRN low-dose ICS/formoterol.	7 (3–8)	53.1%	No consensus
(18)The most recommended salvage treatment for moderate persistent asthma in adults and adolescents is MART	8 (7–9)	85.6%	**Agreement in 1st round**
(19)In a controlled patient, it is necessary to wait for 3 to 6 months before stepping down therapy.	8 (7–9)	82.3%	**Agreement in 1st round**
(20)In an uncontrolled patient, the patient's inhaler technique is usually checked before stepping up therapy.	9 (8–9)	85.6%	**Agreement in 1st round**

*It indicates the percentage of panelists who voted in the region where the median is (1–3; 4–6; 7–9).
ICS: Inhaled Corticosteroid; IQR: Interquartile Range; LABA: Long-Acting β2 Agonists; MART: Maintenance and Reliever Therapy; PRN: as needed; SABA: Short-Acting β2 Agonists.

4. Discussion

In this multidisciplinary consensus, carried out using a modified Delphi technique, a large group of experts from primary care, allergy and pulmonology reached consensus on numerous issues related to inhaled therapy and management of patients with asthma.

Regarding general aspects of inhaled therapy (Table 1), the panel members agreed that critical errors in the handling of inhaled devices are frequent among the patients, and underlined poor adherence as a major factor related to poor control.

Critical errors are associated with uncontrolled asthma and/or increased rates of exacerbations [5]. Although poor inhaler technique is an integral component of adherence, the scientific committee differentiated these two concepts in the questionnaire (items 8 and 9) considering adherence as the extent to which a patient follows the prescribed interval and dosing regimen. These two factors, inhaler mishandling and poor adherence, are common causes of poor disease control in many studies [12–15] and may undermine all the efforts made in the development of new inhaled drugs or in the rigorous updating of guidelines. Furthermore, a large part of the panel believed that many prescribers do not have adequate knowledge in the inhaler technique. This perception is in line with a recent systematic review that evaluated the inhaler technique knowledge of health care professionals (HCP) [5]. This review included data from 55 studies involving 6,304 HCPs who performed nearly 10,000 tests to demonstrate their inhaler technique proficiency. Overall, the inhaler technique was considered correct in only 15.5% of the cases. Surprisingly, the proficiency decreased over time from 20.5%, in studies conducted from 1975 to1995, to 10.8% in studies conducted from 1996 to 2014. Our panelists' opinion and these results highlight the urgent need to design efficient strategies to improve the training of HCP in the appropriate use of inhalers or the development of more user friendly inhalers.

Considering the size of the particles, the experts considered that in a patient with a good inhaler technique, the size of the particles determines the lung deposition. The size of the particles is indeed an important factor in pulmonary deposition, although there are many other factors such as the plume speed, the airways geometry, the degree of humidity, the mechanisms of clearance of the respiratory tract, etc [16]. Our panelists considered that a high pulmonary deposition rate is the one that reaches at least 40% of the measured dose. This percentage is important since there are studies indicating that with the classic pressurized metered dose inhaler (pMDI) only 9–10% of the administered drug particles reach the bronchial tree, mainly due to two factors: the particles velocity is too high in pMDI, and the turbulent flow may favor deposition in the oropharynx [17]. The use of the so-called 'extrafine' aerosols could increase pulmonary deposition [18] but the panel did not reach a consensus on the clinical importance of the use of inhalers that generate fine or extrafine particles.

The statement with the highest score, in the section about general aspects of inhaled therapy, is the one considering the importance of taking into account patients' degree of cognitive impairment when choosing which type of inhaler should be prescribed. Probably, devices that omit the need for patient coordination between inhalation and actuation, may be particularly useful for those patients with cognitive impairment [19]. In addition, the panel members agreed that when deciding on which type of inhaler to prescribe, it is necessary to consider the patient's social support. By social support, we mean that patients have family or close friends or providers who can provide practical support and helps patients cope better with the medication administration.

Considering the selection of inhaled drugs (Table 1), the questionnaire tried to settle some controversies in the treatment of intermittent and mild persistent asthma [20]. These are the two types of asthma that affect the majority of patients and are predominantly attended by primary care physicians.

The use of short-acting ß2-agonists (SABA) in intermittent asthma is open to debate. All guidelines and most physicians usually recommend salvage therapy with SABAs as needed (PRN) [6–9,20]. However, the primary pathogenic mechanism of asthma is inflammation and SABAs neither treat inflammation nor reduce the risk of exacerbations [20]. Some authors argue that adding an inhaled corticosteroid (ICS) PRN in all patients with intermittent asthma may help to relieve symptoms and reduce the frequency of exercise-induced bronchial constriction, as well as the risk of serious exacerbations and subsequent decline in lung function [4,20]. Based on indirect evidence, the 2019 Global Initiative for Asthma (GINA) guidelines now recommend low-dose ICS/formoterol PRN as preferred controller in step 1 in adults and adolescents. This combination is also one of the preferred options in step 2 together with daily low-dose ICS plus PRN SABA. In this regard, our panelists agreed on considering daily low-dose ICS as the preferred maintenance treatment for mild persistent asthma in adults and adolescents. However, they did not reach an agreement on the most recommended treatment for intermittent asthma (statements 13–15). Nevertheless, it is noteworthy that treatment with low-dose ICS/formoterol PRN (statement 13) was by far the panelists' preferred option over other options (low-dose ICS/salbutamol PRN or monotherapy with SABA PRN), but it did not reach consensus by a narrow margin. In fact, in the post hoc analysis (Table 5), we observed that pulmonologists reached an agreement in the 2nd round and considered low-dose ICS/formoterol PRN as the most recommended treatment for intermittent asthma in adults and adolescents. So it is possible that this treatment option will become more commonly used in the future for this population.

Another controversial issue concerns the best salvage treatment option for moderate persistent asthma since the guidelines include the use of SABA or the use of the maintenance and reliever therapy (MART), which is the use of low-dose ICS/formoterol for both maintenance and salvage therapy [7,8,21]. Various studies suggest that MART may be associated with a reduction in asthma exacerbations, despite requiring a lower amount of ICS in both adults and adolescents [22–30]. In line with this evidence, most panelists overwhelmingly consider that the most recommended rescue treatment for moderate persistent asthma in adults and adolescents is MART (statement 18).

Table 2. Statements about pressurized metered-dose inhalers and spacers, and about dry-powder inhalers.

	Median (IQR)	Percentage of panelists in the median region*	Results
Block III. Pressurized metered dose inhalers and spacers			
(21)The most frequent critical error of patients on pMDI treatment is the lack of coordination between actuation and inhalation.	9 (8–9)	99.0%	**Agreement in 1st round**
(22)In pMDI, slower plume speed implies less oropharyngeal deposition.	7 (6–8)	68.4%	**Agreement in 1st round**
(23)In acute asthma exacerbations attended in Primary Care, the use of pMDI with spacers is preferred to the use of nebulizers for the administration of short-acting bronchodilators.	8 (5–9)	68.4%	**Agreement in 1st round**
(24)In acute asthma exacerbations attended in a hospital setting, the use of pMDI with spacers is preferred to the use of nebulizers for the administration of short-acting bronchodilators.	7 (3–8)	55.5%	No consensus
(25)In your specialty consultations, the spacer is prescribed for more than 30% of patients on maintenance treatment with pMDI.	7 (3–8)	56.0%	No consensus
(26)It is recommended to use spacers when pMDI are prescribed as maintenance treatment for elderly patients	9 (8–9)	89.0%	**Agreement in 1st round**
When a patient performs the inhaler technique with a pMDI poorly, the most common approach is:			
(27)To switch to a non-pMDI device.	7 (4–8)	59.3%	No consensus
(28)To add a spacer to the pMDI.	8 (7–9)	81.3%	**Agreement in 1st round**
Block IV. Dry-powder inhalers			
(29)The most frequent critical error of the patients on treatment with DPI is not to perform a forceful inhalation.	8 (7–9)	83.7%	**Agreement in 1st round**
(30)Before prescribing a DPI, the ability of the patient to inhale forcefully is not checked.	7 (3,5–8)	62.2%	No consensus
(31)DPI requires a higher inspiratory flow than pMDI and BAI.	9 (8–9)	94.3%	**Agreement in 1st round**
(32)DPI produces more oropharyngeal side effects than pMDI and BAI.	7 (6–8)	67.5%	**Agreement in 1st round**
When a patient performs the inhaler technique with a DPI poorly, the most common approach is:			
(33)To switch to another DPI.	4 (2–7)	15.3%	No consensus
(34)To switch to a of non-DPI device	7 (6–8)	71.3%	**Agreement in 1st round**

* It indicates the percentage of panelists who voted in the region where the median is (1–3; 4–6; 7–9). BAI: Breath-Actuated Inhaler; DPI: Dry-Powder Inhaler; IQR: Interquartile Range; pMDI: pressurized Metered-Dose Inhaler.

Table 3. Statements about breath-actuated inhalers.

	Median (IQR)	Percentage of panelists in the median region*	Results
Block V. Breath-actuated inhalers			
(35)The fact that the BAI require neither coordination, nor a forceful inhalation, makes them a suitable option for all those patients with the ability to inhale voluntarily.	9 (8–9)	98.6%	**Agreement in 1st round**
(36)It is easier to train patients to use BAI than pMDI.	9 (8–9)	92.3%	**Agreement in 1st round**
(37)It is easier to train patients to use BAI than DPI.	8 (6–9)	74.6%	**Agreement in 1st round**
(38)It is easier for patients to use a BAI than a pMDI.	9 (8–9)	95.7%	**Agreement in 1st round**
(39)It is easier for patients to use a BAI than a DPI.	8 (7–9)	80.4%	**Agreement in 1st round**
(40)To activate the BAI, only minimal inspiratory effort is required.	8 (8–9)	94.3%	**Agreement in 1st round**
(41)The low error rate observed with BAI devices helps to improve asthma control.	8 (8–9)	94.3%	**Agreement in 1st round**
(42)The low error rate observed with BAI helps to reduce the overall cost of treatment (healthcare and non-healthcare related costs).	8 (7–9)	81.3%	**Agreement in 1st round**

* It indicates the percentage of panelists who voted in the region where the median is (1–3; 4–6; 7–9). BAI: Breath-Actuated Inhaler; DPI: Dry-Powder Inhaler; IQR: Interquartile range; pMDI: Pressurized Metered Dose Inhalers.

Table 4. Statements about therapeutic adherence and educational aspects.

	Median (IQR)	Percentage of panelists in the median region*	Results
Block VI. Therapeutic adherence and educational aspects			
(43)Patients need to get involved in the choice of inhaler device.	9 (8–9)	92.3%	**Agreement in 1st round**
(44)The ease of use of inhaler devices is the most important factor in promoting therapeutic adherence.	8 (7–9)	85.2%	**Agreement in 1st round**
(45)The instructions on how to use the inhaler in the package leaflets are difficult for patients to read and understand.	7 (6–8)	71.3%	**Agreement in 1st round**
(46)In check-up visits it is common that the inhaler technique is NOT checked periodically.	7 (6–8)	69.4%	**Agreement in 1st round**
(47)In check-up visits, a reevaluation of the inhaler technique should be carried out.	9 (8–9)	98.1%	**Agreement in 1st round**
(48)In check-up visits, adherence must be verified with a validated method.	9 (8–9)	92.3%	**Agreement in 1st round**
(49)In check-up visits, therapeutic adherence is verified with a validated method before stepping-up therapies.	6 (3–8)	17.7%	No consensus
(50)In check-up visits, the patient is given a written Action Plan.	7 (3–8)	53.6%	No consensus
(51)Nursing professionals are capable to assess therapeutic adherence and correct errors of the inhaler technique.	8 (7–9)	76.6%	**Agreement in 2nd round**
(52)The use of software applications helps to improve adherence to treatment and control of the disease.	7 (6–8)	70,8%	**Agreement in 2nd round**

* It indicates the percentage of panelists who voted in the region where the median is (1–3; 4–6; 7–9). IQR: Interquartile range.

In the section centered in pMDI (Table 2), the panelists agreed on some weaknesses of these devices. The panelists considered that the most frequent critical error of patients on pMDI treatment is the lack of coordination between actuation and inhalation (statement 21). In fact, this item reached the highest degree of consensus of the entire questionnaire and is in line with the results of many studies [12–15]. To solve this problem, there was agreement on the option of incorporating a spacer (statement 28), especially in emergencies in the outpatient setting (statement 23) and for the elderly (statement 26). However, the use of the spacer does not seem to happen frequently either in the emergencies attended in the hospital, where nebulizers are preferred (statement 24), or paradoxically, in the follow-up visits of patients on maintenance treatment with pMDI (statement 25). The limited use of the spacers during consultations may be due to their disadvantages [31]. They are not very manageable and transportable due to their large size, there are incompatibilities between the spacers holes and the different models of pMDI in the market, they may reduce the perception of inhalation, or, in Spain, some are not financed [32]. Additionally, it is noteworthy that, when a patient performs the inhaler technique poorly with a pMDI, the most common approach slightly differs among specialties because, globally, the best options seem to be the addition of a spacer. However, in the post hoc analysis, allergists agreed in 2nd round on the option to switch to a non-pMDI device.

Regarding the use of dry-powder inhalers (DPI) (Table 2), the panelists agreed that the most frequent critical error of patients on treatment with DPI is failure to perform a forceful inhalation. Furthermore, they considered that the use of DPI requires a higher inspiratory flow and produces more oropharyngeal side effects than pMDI and breath-actuated inhalers (BAI) (statements 29, 31, and 32). Inspiratory flow required for most DPI ranges between 30 and 60 l/min, which is higher than the necessary for a pMDI [33]. This fact can make their use by patients who are not capable of generating these flows difficult, such as elderly, people with severe bronchial obstruction or young children. Evidence shows that up to 32–38% of

Table 5. Discrepancies in the consensus among specialties in the post hoc analysis.

Statements	Global*	Primary care physicians	Allergists	Pulmonologists
Block I. General aspects of inhaled therapy				
5. More than half of primary care physicians have inadequate knowledge in the inhaler technique of the inhalers they prescribe.	**AG 1st R**	NC 1st R	NC 1st R	**AG 1st R**
8. The most common cause of poor asthma control is: Inadequate inhaler technique.	NC 1st R	**AG 1st R**	NC 1st R	NC 1st R
	NC 2nd R	**AG 2nd R**	NC 2nd R	NC 2nd R
10. When deciding on which type of inhaler to prescribe, it is necessary to consider: The level of severity of asthma.	**AG 1st R**	**AG 1st R**	**AG 1st R**	NC 1st R
Block II. Selection of inhaled drugs				
13. The most recommended treatment for intermittent asthma in adults and adolescents is: PRN low-dose ICS/formoterol.	NC 1st R	NC 1st R	NC 1st R	NC 1st R
	NC 2nd R	NC 2nd R	NC 2nd R	**AG 2nd R**
16. The most recommended maintenance treatment for mild persistent asthma in adults and adolescents is: Daily low-dose ICS	**AG 1st R**	**AG 1st R**	NC 1st R	**AG 1st R**
Block III. Pressurized metered dose inhalers and spacers				
22. In pMDI, slower plume speed implies less oropharyngeal deposition.	**AG 1st R**	NC 1st R	**AG 1st R**	**AG 1st R**
25. In your specialty consultations, the spacer is prescribed for more than 30% of patients on maintenance treatment with pMDI.	NC 1st R	NC 1st R	NC 1st R	NC 1st R
	NC 2nd R	NC 2nd R	NC 2nd R	**AG 2nd R**
27. When a patient performs the inhaler technique with a pMDI poorly, the most common approach is: To switch to a non-pMDI device.	NC 1st R	NC 1st R	NC 1st R	NC 1st R
	NC 2nd R	NC 2nd R	**AG 2nd R**	NC 2nd R
Block IV. Dry-powder inhalers				
30. Before prescribing a DPI, the ability of the patient to inhale forcefully is not checked.	NC 1st R	**AG 1st R**	NC 1st R	NC 1st R
	NC 2nd R	**AG 2nd R**	NC 2nd R	NC 2nd R
32. DPI produces more oropharyngeal side effects than pMDI and BAI.	**AG 1st R**	**AG 1st R**	NC 1st R	**AG 1st R**
34. When a patient performs the inhaler technique with a DPI poorly, the most common approach is: To switch to a non-DPI device.	**AG 1st R**	**AG 1st R**	NC 1st R	**AG 1st R**
Block VI. Therapeutic adherence and educational aspects.				
45. The instructions on how to use the inhaler in the package leaflets are difficult for patients to read and understand.	**AG 1st R**	**AG 1st R**	NC 1st R	**AG 1st R**
46. In check-up visits it is common that the inhaler technique is NOT checked periodically.	**AG 1st R**	**AG 1st R**	**AG 1st R**	NC 1st R
50. In check-up visits, the patient is given a written Action Plan.	NC 1st R	NC 1st R	**AG 1st R**	NC 1st R
	NC 2nd R	NC 2nd R	**AG 2nd R**	NC 2nd R

*Statements agreed on 1st round were not submitted to a 2nd round of voting.
AG: Agreement; NC: No Consensus; 1st R: first round of voting; 2nd R: second round of voting.
BAI: Breath-Actuated Inhaler; DPI: Dry-Powder Inhaler; ICS: Inhaled Corticosteroid; pMDI: Pressurized Metered Dose Inhaler; PRN: as needed.

patients on DPI treatment may perform insufficient inspiratory effort when using this type of device, and this error is associated with poor asthma control and a higher rate of exacerbations [34]. In addition, DPI produce higher oropharyngeal impact than other devices [17], which would explain why the panelists agreed that DPI produces more oropharyngeal side effects than pMDI and BAI.

The last type of device evaluated by the panel was the breath-actuated inhaler (BAI) one (Table 3). The panelist agreed on the eight statements related to this device with no discordances between specialties. Panelists considered the BAI a suitable option for all those patients with the ability to inhale voluntarily, because they require neither coordination nor a vigorous inhalation (statement 35). The primary focus on the BAI development was indeed to overcome the disadvantage of pMDI, namely the lack of coordination and the inability of patients to synchronize actuation with inhalation [35]. Additionally, these devices require a minimum activation flow (30 l/min), which means that 99% of patients can activate them on their first attempt, regardless of their forced expiratory volume in the first second (FEV_1) or age [36]. Furthermore, evidence suggests that almost all patients can be trained quickly to use BAI, with 93% of them being capable of using the device correctly after 1 or 2 attempts [36]. In line with these findings, the panelists considered that it is easier to use BAI than pMDI or DPI and, moreover, it is easier to train patients to use the BAI than the pMDI or the DPI (statements 36–39). The panelists also considered that the low error rate observed with the BAI might help to improve asthma control and reduce the overall cost of treatment, although these statements would need to be verified in clinical studies.

Regarding the last section about therapeutic adherence and educational aspects (Table 4), the panelists agreed on various statements that can be considered as opportunities for improvement in the management of asthma patients and are in line with the current guideline recommendations [7–9]. During checkups, it would be advisable to reevaluate the inhaler technique and check adherence with a validated method. Furthermore, it would be necessary to involve patients in the choice of the inhaler device and to simplify the instructions contained in the package leaflets. Finally, the experts valued the easiness of using inhaler devices as the most important factor to promote therapeutic adherence, and supported the role of nursing professionals and the use of new technologies, such as software applications, to improve adherence and disease control.

Interestingly, in the post hoc analysis, the divergence among specialties when reaching an agreement is not very high (14 out of the 52 statements evaluated). Taking into account the differences between specialists (allergists and pulmonologists) and primary care, only in three statements (items 8, 22 and 30) primary care doctors' opinions differ from specialists' opinions (Table 5). This finding suggests that the primary care doctors, who were very carefully selected, are real asthma experts and their opinion is valuable.

Limitations of this study include those inherent to a Delphi consensus, mainly the inability to include the panelists' opinions or more details into the proposed statements. The panelist selection may be another limitation of the methodology although we consider that the expertise of the panelists is contrasted given the strict criteria used to select the panel. Possible influence of the scientific committee on the consensus is limited since they did not participate in the voting.

5. Conclusions

This multidisciplinary consensus brings together the opinion of a large number of specialists with vast experience in asthma management. This multidisciplinary group of experts endorsed the main recommendations on education and adherence proposed by national and international clinical practice guidelines. However, the panelists did not fully agree on recent GINA recommendations about the treatment of the initial steps of the disease (intermittent and mild persistent asthma) regarding the PRN use of low-dose ICS/formoterol combination as the preferred option. The experts valued very positively the diverse characteristics of BAI and their advantages over other inhaler devices. These agreements might be taken into consideration for the next version of the Spanish Asthma Guidelines (GEMA).

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