3. Maintenance treatment

3.1 Objectives

The main objective of asthma management is to achieve and maintain control of the disease as quick as possible, in addition to prevent exacerbations and chronic airflow obstruction and to maximally reduce mortality. With a properly designed treatment plan, therapeutic targets (Table 3.1) can be achieved in the majority of patients in terms of daily symptom control (current control domain) and prevention of both exacerbations and excessive loss of pulmonary function (future risk domain).

To attain these objectives a global and individualized long-term strategy must be followed based on an optimally adjusted pharmacological treatment along with supervision measures, environmental control and asthma education activities. Pharmacological treatment should be adjusted according to the degree of control, considering the most effective therapeutic options, safety and cost of the different alternatives, and taking into account the patient’s satisfaction with the degree of control achieved. Patients should be periodically evaluated to determine whether objectives are being met. Clinical inertia and causative factors on the part of the patient, the physician and the healthcare system should be avoided.

3.2 Pharmacological treatment

Asthma treatment should follow an overall plan, established by consensus of the physician and the patient (and eventually by the patient’s family), in which the goals, the interventions to achieve them and the criteria for their modification or adaptation according to changing disease circumstances must be made clear. Distinguishing between the ‘current control’ domain and the ‘future risk’ domain in the control of the disease is relevant, because it has been documented that these domains may respond differently to treatment. For example, some patients may have a good daily control of asthma symptoms and yet experience exacerbations, and vice-versa.

Treatment should be adjusted continuously, so that the patient remains always in a well-controlled status. This cyclic treatment adjustment means that asthma control should be objectively assessed (chapter 2.6), that the patient is being treated to achieve control and that treatment is periodically checked to maintain asthma control (Figure 3.1). That is, if a patient is not well controlled, treatment must be stepped up as needed in order to regain control, always taking into account non-pharmacological measures, treatment adherence and risk factors susceptible to be modified.

If asthma has been controlled for at least 3 months, maintenance therapy may be gradually decreased in order to determine minimum treatment needs that are required to maintain control. A simple scoring system that includes data of different clinical (ACT, previous exacerbations) and functional (spirometric values) variables has been developed, to determine the risk after stepping down treatment in patients with controlled asthma.

Drugs used to treat asthma are classified as controller or maintenance medications and reliever medication, also called “rescue” medication. Controller or maintenance medications should be administered continuously during prolonged periods of time, include inhaled glucocorticoids (IGC) or systemic glucocorticoids, leukotriene receptor antagonists (LTRA), long-acting β₂-agonists (LABA), tiotropium and monoclonal antibodies (omalizumab, mepolizumab, reslizumab and dupilumab). Chromones and sustained-release theophylline have fallen into disuse because of their lower efficacy. Reliever medications are used on-demand for rapid treatment or prevention of bronchoconstriction, and include

Table 3.1. Asthma treatment goals

<table>
<thead>
<tr>
<th>In the domain of current asthma control</th>
</tr>
</thead>
<tbody>
<tr>
<td>• To prevent daytime, nighttime and exercise-related symptoms.</td>
</tr>
<tr>
<td>• Use of short-acting β₂-agonists no more often than twice a month.</td>
</tr>
<tr>
<td>• To maintain a normal or near-normal pulmonary function.</td>
</tr>
<tr>
<td>• No restrictions on daily life activities and physical exercise.</td>
</tr>
<tr>
<td>• To fulfil the expectations of both patients and their families.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In the domain of future risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• To prevent exacerbations and mortality.</td>
</tr>
<tr>
<td>• To minimize progressive loss of pulmonary function.</td>
</tr>
<tr>
<td>• To avoid treatment-related adverse effects.</td>
</tr>
</tbody>
</table>

Avoid therapeutic inertia
Maintenance treatment

doi: 10.18176/jiaci.0664

Figure 3.1. Cyclic adjustment of treatment according to periodic assessment of control of asthma.

Table 3.2. Characteristics of inhaled β₂-adrenergic agonists

<table>
<thead>
<tr>
<th>Drug</th>
<th>Amount per puff (μg)</th>
<th>Time of effect (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pressurized inhaler</td>
<td>Dry powder</td>
</tr>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salbutamol</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Turbutaline</td>
<td>-</td>
<td>500</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formoterol</td>
<td>12</td>
<td>4.5 – 9 - 12</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Vilanterol</td>
<td>-</td>
<td>22</td>
</tr>
</tbody>
</table>

inhaled short-acting β₂-agonists (SABA) (Table 3.2) and inhaled short-acting anticholinergics (ipratropium bromide). Also, the combinations budesonide/formoterol, beclomethasone/formoterol or beclomethasone/salbutamol, used on-demand can be considered reliever medications.

The six treatment steps (Figure 3.2) aimed at achieving asthma control are the following:

3.2.1 Steps

Step 1

Different treatment options can currently be considered for this step. A correct clinical and functional assessment of the patient is required for an adequate selection of treatment. Inhaled SABA (salbutamol or terbutaline), exclusively on-demand, can be used in those patients with mild and occasional daytime symptoms (maximum twice a month) and without nighttime symptoms⁶⁷. The patient should remain asymptomatic between episodes, maintain a normal pulmonary function, and neither having had exacerbations in the previous year nor presenting risk factors for exacerbations (Table 2.7)⁸.

The association budesonide/formoterol on-demand can also be used⁹. In a randomized study on adult asthma patients with approximately half of patients having intermittent asthma and in which an open-label design was used to reflect clinical practice conditions⁹, the use of budesonide/formoterol on-demand was superior to salbutamol on-demand in the prevention of exacerbations. In a small study of patients with intermittent asthma and increased fractional exhaled nitric oxide (FE(NO) in which both budesonide/formoterol and formoterol on-demand were compared, the combination showed a higher reduction of FE(NO) levels¹¹. However, these indications are not included in the technical specifications of these drugs. In addition, cost-benefit studies have not been carried out.
The use of an inhaled SABA on-demand, more than twice a month, for the treatment of symptoms (excluding its preventive use before exercise), or having had exacerbations in the previous year, or a FEV$_1$ value < 80% indicates an inadequate asthma control and prompts the initiation of maintenance therapy.\textsuperscript{12-14}

Inhaled SABAs administered 10-15 minutes before exercise are the drugs of choice to prevent exercise-induced bronchoconstriction.\textsuperscript{15}

An inhaled anticholinergic is only recommended as a reliever medication in those rare cases of intolerance to SABA agents.\textsuperscript{8}

**Step 2**

The treatment of choice at this step is an inhaled glucocorticoid (IGC) (beclomethasone, budesonide, ciclesonide, fluticasone or mometasone) at low doses and administered daily.\textsuperscript{16-19} In general, this is the first step for most patients with persistent asthma who have not been previously treated. The usual dose ranges between 200 and 400 μg/day of budesonide or equivalent. Continuous administration of IGC is the most effective treatment for persistent asthma, both for the control of daily symptoms and to reduce the risk of exacerbations.\textsuperscript{13,19-21} The equipotent doses of the most common IGC are shown in Table 3.3.

**Table 3.3. Equipotent doses of inhaled glucocorticoids**

<table>
<thead>
<tr>
<th></th>
<th>Low dose (mg/day)</th>
<th>Medium dose (mg/day)</th>
<th>High dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide</td>
<td>200-400</td>
<td>401-800</td>
<td>801-1,600</td>
</tr>
<tr>
<td>Beclomethasone dipropionate</td>
<td>200-500</td>
<td>501-1000</td>
<td>1001-2000</td>
</tr>
<tr>
<td>Extrafine beclomethasone*</td>
<td>100-200</td>
<td>201-400</td>
<td>&gt; 400</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>80-160</td>
<td>161-320</td>
<td>321-1280</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>100-250</td>
<td>251-500</td>
<td>501-1000</td>
</tr>
<tr>
<td>Fluticasone furoate</td>
<td>-</td>
<td>92</td>
<td>184</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>100-200</td>
<td>201-400</td>
<td>401-800</td>
</tr>
</tbody>
</table>

*Extrafine beclomethasone dipropionate.
Two clinical trials showed that a strategy of using a combination of budesonide/formoterol in a single inhaler on-demand compared to continuous IGC treatment in mild persistent asthma, was not inferior in preventing exacerbations (the rate of which was similarly low); however, it was inferior in the maintenance of asthma control and in the increase of pulmonary function. In a randomized open-label study, budesonide twice a day plus salmeterol on-demand and budesonide/formoterol on-demand were similar regarding annualized exacerbation rates.

Also, a similar result with beclomethasone/salbutamol has been observed.

Results of the aforementioned studies may provide indirect evidence of a possible indication of the combinations of low dose IGC with LABA or SABA (e.g., budesonide/formoterol, beclomethasone/formoterol or beclomethasone/salbutamol), administered exclusively on-demand, in the treatment of step 2 in patients with low treatment adherence and in which specific educational interventions have been unsuccessful. However, no studies have been specifically designed to assess this therapeutic indication.

At this level, an alternative treatment includes leukotriene receptor antagonists (LTRA) or anti-leukotrienes (montelukast and zafirlukast), although IGC are more effective for long-term treatment. Patients who are well controlled on IGC at low doses fail to maintain the same level of asthma control with montelukast.

LTRA would be particularly indicated as alternative drug in patients who are unable or unwilling to receive IGC or have adverse effects with IGC, have difficulties with the inhaler technique, or suffer from concomitant allergic rhinitis.

In patients who have not previously received maintenance treatment with IGC, the combination of IGC at low doses and LABA as initial treatment as compared with IGC at low doses, improves symptoms and pulmonary function but has a higher cost and it does not reduce the risk of exacerbations.

Sustained-release theophylline is not recommended for use at this step since it has been shown to be modestly effective as both bronchodilator and anti-inflammatory drug and may cause mild to serious adverse events.

Chromones (disodium cromoglycate and nedocromil sodium) show low efficacy, although they have a good tolerability. Currently, they are not commercialized in Spain for this indication.

**Step 3**

First-line treatment at this step is a combined inhaled treatment with IGC at low doses and a LABA (salmeterol or formoterol or vilanterol), which can be administered using a single device (preferred option) or separate inhalers. By using this combination a more pronounced reduction of symptoms, improvement of pulmonary function, and reduction of exacerbations and use of reliever medications is obtained as compared to increasing the dose of IGC. However, an appropriate individualized risk/benefit assessment for both strategies is required.

Treatment with LABA should always been accompanied by an IGC. LABA agents must never be used as monotherapy because of a higher risk of hospitalizations and life-threatening exacerbations. IGC/LABA combinations commercialized in Spain include fluticasone propionate with salmeterol, budesonide with formoterol, beclomethasone dipropionate with formoterol, and fluticasone furoate with vilanterol.

**Formoterol** is a rapid-onset LABA. For this reason, if budesonide/formoterol or beclomethasone/formoterol combinations are chosen, they can be used as both maintenance and reliever therapy (MART strategy). This strategy leads to reduced exacerbations and a better asthma control, despite requiring a lesser amount of IGC. It may be assumed that other IGC combinations (fluticasone propionate) with formoterol may be effective as MART strategy, although there is no evidence of its use as maintenance and on-demand treatment and the indication is not included their technical specifications.

In any case, MART therapy always should be administered using a single inhaler device.

A further option at this step includes increasing IGC doses up to medium doses, but this approach is less effective than adding a LABA. Alternatively, IGC at low doses associated with a LTRA may be used. This option has been found to be superior to IGS monotherapy and although it is not as effective as the IGS and LABA combination, has an excellent safety profile. However, the addition of an LTRA does not appear allowing to reduce the IGC dose.

**Step 4**

The first-line treatment at this step is the combination a IGC at medium doses with a LABA.

For patients who have had at least one exacerbation in the previous year, the combination of a IGC at low doses (budesonide or beclomethasone) and formoterol, using the MART strategy, is more effective in reducing exacerbations than the same dose of an IGC and LABA in a fixed schedule, or higher doses of IGC.

Alternatively, the combination of an IGC at medium doses with a LABA can be used, although the addition of LABA to the IGC is more effective in preventing exacerbations, control of daily symptoms and improving pulmonary function.

**Step 5**

The next step consists of up-titrating IGC dosage and using it in combination with LABA. IGC at medium and high doses are usually administered twice daily, although a greater therapeutic efficacy can be achieved with budesonide by increasing the dosing frequency up to 4 times a day.

Other drugs can be added for maintenance therapy, with a subgroup of patients improving with the addition of LTRA or sustained-release theophylline.

In patients not well controlled with the combination of an IGC at low doses and a LABA, who show post-bronchodilator FEV1/FVC ≤ 70 %, the addition of tiotropium as maintenance therapy has shown to improve pulmonary function and to reduce exacerbations.

Macrolide antibiotics, particularly azithromycin administered 3 days/week for several months, may play a role as an add-on medication in patients with severe non-eosinophilic asthma and frequent exacerbations, as well as in eosinophilic asthma (see chapter 7).

**Step 6**

For asthma patients who remain uncontrolled and with frequent exacerbations, the addition of biologic drugs should
be considered after a specialized evaluation and according to the endophenotype of the patient.

In cases of uncontrolled severe allergic asthma (USAA), the anti-IgE monoclonal antibody (omalizumab) by the subcutaneous route can be added, which improves daily symptoms and decreases exacerbations\textsuperscript{70-73}, increasing the overall control of the disease (see chapter 7).

In patients with eosinophilic USAA, independently of the presence of allergy, biologic drugs targeting interleukin-5 (IL-5) pathway can be used. Currently, anti-IL-5 monoclonal antibodies, nkelizumab and reslizumab, and the anti-IL-5 receptor α chain (IL-5Ra), benralizumab, are approved as additional treatment of eosinophilic USAA (severe refractory eosinophilic asthma)\textsuperscript{74-80} (see chapter 7).

Dupilumab, a human monoclonal antibody directed against the interleukin-4 receptor subunit α (IL-4Ra) of IL-4 that blocks the effects of IL-4 and IL-13 is approved as additional treatment in patients older than 12 years of age with USAA with increased eosinophils and/or FE\textsubscript{NO} (see chapter 7).

In cases in which the administration of biologic agents has failed, the indication of enbronchial thermoplasty may be considered\textsuperscript{83} (see chapter 7).

The last therapeutic option when all other alternatives have failed is the administration of systemic glucocorticoids (always used at the lowest effective dose and for the minimum period of time possible)\textsuperscript{84,85} even though they are also associated with adverse effects, occasionally serious (see chapter 7).

3.2.2 Inhalers and nebulizers

Inhaled therapy is the preferred administration route for the treatment of asthma as it acts directly on the lungs, delivers a greater amount of drug into the airways, elicits a rapid response and is associated with few or no systemic effects\textsuperscript{86-91}.

The main disadvantage of this route is the difficulty of the inhalation technique of the different devices\textsuperscript{92-95}.

<table>
<thead>
<tr>
<th>Table 3.4. Aerodynamic properties provided by inhalers (based in part on Giner 2013)\textsuperscript{96}</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary deposition (%)</strong></td>
</tr>
<tr>
<td><strong>in vivo</strong></td>
</tr>
<tr>
<td>pMDI</td>
</tr>
<tr>
<td>Conventional pMDI</td>
</tr>
<tr>
<td>Conventional pMDI with spacer</td>
</tr>
<tr>
<td>Breath-actuated pMDI</td>
</tr>
<tr>
<td>Modulite®</td>
</tr>
<tr>
<td>Alvesco®</td>
</tr>
<tr>
<td>BAI</td>
</tr>
<tr>
<td>k-haler®</td>
</tr>
<tr>
<td>SMI</td>
</tr>
<tr>
<td>Respimat®</td>
</tr>
<tr>
<td>DPI (by alphabetical order)</td>
</tr>
<tr>
<td>Accuhaler®</td>
</tr>
<tr>
<td>Aerolizer®</td>
</tr>
<tr>
<td>Breezhaler®</td>
</tr>
<tr>
<td>Easyhaler®</td>
</tr>
<tr>
<td>Ellipta®</td>
</tr>
<tr>
<td>Genuair®</td>
</tr>
<tr>
<td>Handihaler®</td>
</tr>
<tr>
<td>Ingelheim® inhaler</td>
</tr>
<tr>
<td>Nexthaler®</td>
</tr>
<tr>
<td>Spinhaler®</td>
</tr>
<tr>
<td>Turbohaler®</td>
</tr>
<tr>
<td>Twisthaler®</td>
</tr>
</tbody>
</table>

MADM: mean aerodynamic diameter mass; BAI: breath-actuated inhaler; DPI: dry powder inhaler; pMDI: pressurized metered-dose inhaler; SMI: soft mist inhaler. The comparison of values among devices should be considered with caution because of differences in the methods and drugs used for estimating the corresponding values, as well as differences in human studies, which were performed in diverse clinical settings (healthy and ill subjects with different diseases and degrees of severity), inspiratory flows and ages.
Currently available inhalation devices include: the conventional pressurized inhaler (pMDI) and the dry Modulite® system, which can be used with or without a spacer, the breath-actuated inhaler (BAI) k-haler® and Easy-breathe®, the soft mist inhaler (SMI) Respimat®, the dry powder inhalers (DPI) (Accuhaler®, Aerolizer®, Breezhaler®, Easyhaler®, Ellipta®, Forspiro®, Genuine®, Handihaler®, Nexthaler®, Spiromax®, Turbuhaler®, Twishaler® and Zonda®) and the nebulizers (jet, ultrasonic or vibrating mesh). Each of these has their own technical characteristics that should be considered when prescribed (Table 3.4)90.

All inhaler devices if correctly used provide an efficient deposition of the drug in the lung88. The use of spacers is recommended for pMDI. Spacers circumvent coordination issues, improve the distribution and the amount of drug reaching the bronchial tree, reduce the deposition of drug particles in the oropharynx, decrease cough and the possibility of oral candidiasis (that may be associated with the use of IGC), decrease systemic bioavailability and, hence, the risk of systemic effects99-102.

Healthcare professionals involved in the care of patients with asthma should know the inhalation techniques of each of the devices; knowledge, however, is still insufficient103-104. Given that the proper use of inhalers is a crucial aspect in the treatment of patients with asthma, all healthcare professionals involved, doctors, nurses and pharmacists especially those from the community due to their accessibility, should be involved in the instruction and review of the inhalation technique105-112. The patient should be periodically trained and controlled in the use of the prescribed inhaler device, explaining its characteristics, the appropriate technique, demonstrating how it is used, then asking the patient to perform the maneuvers (with a placebo device) and correcting the possible mistakes91,113-115. Whenever pharmacologically possible, a single type of inhaler device should be used116,117. After the instruction in the use of the device, the patient should be given a brochure with description of the technique and receive information on how to find demonstration videos showing the correct technique89,90,92,114,115. It is important to take advantage of control visits, performance of pulmonary function tests and admissions to the hospital to check the patient’s inhalation technique114.

3.3 Other treatments

3.3.1 Smoking and environmental control

Smokers with asthma have more severe symptoms, a poorer response to IGC treatment, even in patients with mild asthma119, and an accelerated loss of pulmonary function119,120, so that a step-up in treatment is often required121. The proportion of asthmatic smokers is high and similar to that in the general population. Moreover, since longitudinal studies have found a relationship between tobacco use and asthma in both adults and adolescents122, the main objective in environmental control is getting the patient to stop smoking. To this end, smokers should receive full information of the most appropriate quit smoking methods123. Exposure to both tobacco smoke and second-hand smoke is a risk factor for asthma development and constitutes a risk factor for asthma development in childhood124. Administrative regulations banning smoking in public spaces are being having a highly positive impact125,126. Also, passive exposure to smoke of electronic cigarettes has been related with a higher risk for exacerbations and asthma symptoms127,128, and active exposure to severe effects of respiratory health129, so that vaping cannot be recommended as a method to quit.

Some asthma patients, particularly those with sinusitis polyposis, may experience exacerbations when administered acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAID). Many of these reactions are serious or even fatal130, so that it is necessary that patients are correctly diagnosed based on evident data in the medical history (several reactions to different NSAID) or by means of an oral challenge test which, in severe cases, can be replaced with bronchial or nasal inhalation challenge testing131,132. This issue is more comprehensively explained in chapter 8.5 (acetylsalicylic acid-exacerbated respiratory disease). These patients, however, among their environmental measures, should avoid the use of analgesic or anti-inflammatory treatments with drugs of the NSAID therapeutic class.

Specific recommendations should be considered in allergic asthma, once sensitizations to different allergens had been confirmed in each patient. The most effective measures are those enabling a dramatic decrease of exposure levels, such as those applicable to many patients with occupational asthma (job change) or asthma due to animal dander (removal of animals from the patient’s home) or cockroach allergy (wise use of pesticides)133-138. Isolated individual interventions, such as the use of mattress covers or acaricides have not shown to be effective, not even in reducing exposure levels139-141.

However, in a recent randomized study, the use of impermeable bed covers was effective for preventing exacerbations in children and adolescents with allergic asthma triggered by dust mites142. The use of combined specific measures has been associated with a significant reduction in the level of allergen exposure and, in consequence, of benefits in clinical efficacy133,143,144. In a randomized trial of 937 patients with uncontrolled moderate to severe asthma and sensitization to at least one domestic allergen, in which combined measures were applied (impermeable covers, vacuum cleaners and air purifiers in the bedroom both with HEPA filters, cockroach disinsection plans), associated with a general education program, for one year, obtained a significant reduction in symptoms and unscheduled medical visits133.

Finally, the two more recent systematic reviews of the effect of combined interventions showed favorable outcomes137,145.

3.3.2 Allergen immunotherapy

Subcutaneous immunotherapy with allergen extracts is an effective treatment in well-controlled allergic asthma with low or medium treatment levels (steps 2 to 4), provided that a clinically relevant IgE-mediated sensitization against common aeroallergens has been demonstrated and well-characterized and standardized allergen extracts are used146,147, avoiding complex mixtures148,149. However, many patients with mild intermittent asthma (step 1) suffer from moderate or severe allergic rhinitis concomitantly, which would justify the
prescription of immunotherapy. Immunotherapy should not be prescribed to patients with uncontrolled severe asthma, because its efficacy is not well documented and entails a high risk of serious, even fatal, adverse reactions. For this reason, subcutaneous immunotherapy should only be prescribed by specialist physicians with experience in this type of treatment and administered in centers equipped with the basic resources for the immediate treatment of a possible adverse reaction.

The search for safer and more convenient options for the patient has led to investigate the efficacy of sublingual immunotherapy. Some systematic reviews conclude that oral immunotherapy with capsules or lyophilized extracts can significantly reduce clinical manifestations and the use of rescue medication in children, adolescents and adults with allergic asthma. Most clinical trials showing clinical efficacy were performed with well-characterized extracts at much higher doses than those usually prescribed for subcutaneous immunotherapy. The tolerability profile of sublingual immunotherapy is optimal and fatal reactions have not been reported.

Sublingual immunotherapy with an oral lyophilized mite extract when added to regular pharmacological maintenance treatment is able to reduce the number of moderate to severe exacerbations and to improve control of the disease, with a very favorable safety profile. Therefore, its use is recommendable for adult patients with moderately controlled asthma. Because its efficacy is not well documented and entails a high risk of serious, even fatal, adverse reactions, it should not be prescribed to patients with uncontrolled severe asthma, because its efficacy is not well documented and entails a high risk of serious, even fatal, adverse reactions. Therefore, its use is recommendable for adult patients with moderately controlled asthma. Because its efficacy is not well documented and entails a high risk of serious, even fatal, adverse reactions, it should not be prescribed to patients with uncontrolled severe asthma.

3.3.3 Influenza and pneumococcal vaccinations

Influenza and pneumococcal vaccines have not been shown to be effective in preventing asthma exacerbations. However, since it is a cost-effective approach, and due to the high risk of complications in patients with chronic diseases and a higher risk of therapeutic failure in children, annual influenza vaccination should be considered in patients with moderate and severe asthma, both in adults and children. Similarly, and given that asthma population has a high risk of invasive pneumococcal disease and different international and national consensus documents as well as the National Healthcare System recommend the administration of pneumococcal vaccine in patients with severe asthma.

3.4 Education

3.4.1 Objectives

Education of asthma patients is an essential component of treatment, because reduces the risk of exacerbations, improves quality of life and decreases healthcare costs, thus becoming an indispensable part of the overall management of asthma. The main goal of education is to provide patients with the knowledge and skills they need to improve self-care and treatment compliance. This results in a better adherence to treatment and, in consequence, in an optimal control of the disease. In addition, education promotes patient's self-control of asthma. Self-control is the situation in which the patient monitors their symptoms and applies self-management following a plan agreed with his/her doctor. Self-control supported by a healthcare professional reduces the number of consultations and exacerbations, and improves quality of life without increasing costs.

3.4.2 Knowledge and skills

From a practical point of view, education should consider two major aspects: transmission of knowledge and acquisition of skills and competences (Table 3.5).

Regarding the information that the patient should receive about asthma, their needs, previous knowledge, beliefs, age, severity of asthma, and the degree of involvement necessary in their self-control and treatment should be considered.

These interventions should include: symptom self-management or PEF monitoring, written action plans, and regular assessments of asthma control, asthma treatment and abilities of the healthcare personnel.

Interventions without written action plans are less effective. Actions that are exclusively informative are ineffective.

Regarding the skills to be developed, patients will be trained in taking the prescribed medication, particularly in the technique of their inhalation devices, in the recognition of exacerbations and how to act early, and in the avoidance of allergenic triggers.

Table 3.5. In information and basic skills that should be learned by a patient with asthma

1. To know that asthma is a chronic disease requiring continuous treatment even if symptoms are absent.
2. To know the differences between inflammation and bronchoconstriction.
3. To be able to differentiate between inflammation “controller” drugs and obstruction “reliever” drugs.
4. To recognize the symptoms of the disease.
5. To use inhalers correctly.
6. To identify triggers and avoid triggering factors as much as possible.
7. To monitor symptoms and peak expiratory flow (PEF).
8. To recognize the signs and symptoms of asthma worsening (loss of control).
9. To act in case of asthma worsening in order to prevent an attack or exacerbation.
Table 3.6. Asthma action plan

A. Standard

I. USUAL TREATMENT

1. Take daily ____________________________

2. Before Exercise, take ____________________________

II. WHEN SHOULD YOUR TREATMENT BE INCREASED

1. Assessment of the degree of asthma control

   Do your asthma symptoms occur more than twice a day? No/Yes

   Do your activity of physical exercise is limited by asthma? No/Yes

   Do you wake up at night because of asthma? No/Yes

   Do you need to take your bronchodilator more than twice a day? No/Yes

   If you use a peak flow meter (PEF), are PEF values lower than ___? No/Yes

   If your answers have been Yes to three or more questions, your asthma is not well controlled and your usual treatment needs to be increased.

2. How to increase treatment

   Increase your treatment as follows and assess your improvement daily:

   ____________________________ (Write down the increase of your new treatment)

   Maintain this treatment for _______ days (specify the number).

3. When should I call the doctor/hospital for help

   Call your doctor/hospital _______________ (Provide phone numbers)

   If your asthma does not improve __________ days (specify the number)

   ____________________________ (lines for Complementary instructions)

4. EMERGENCY: severe loss of asthma control

   If you have a severe breathlessness attack that your can only speak short sentences.

   If you have a severe breathlessness or asthma attack.

   If you have to use your reliever or rescue bronchodilator every 4 hours without any improvement.

   1. Take 2 to 4 puffs ________________ (rescue bronchodilator)
   2. Take ___ mg of ____________ (oral glucocorticoids)
   3. Ask for medical assistance: go to ________________: Address _________:  Call phone number _________________
   4. Continue using your _________________ (rescue bronchodilator) until you get medical help

B. REDUCED (mini-action plan), based in part on Plaza 2015*©

FRONT

Name ______________________________

Date _______________________________

If your asthma has worsened in the last 24 hours due to having:

- Difficult breath or whistling more than twice or
- Difficult breath or whistling in the last night or
- Need to take your rescue inhaler more than twice

Increase treatment as follows:

1. Increase _______ and maintain for ___ days

2. If no improvement start _______ (prednisone)
   30 mg. 1 tablet a day, and maintain for ___ days (maximum 3-5).*

3. If no improvement, ask for a visit with your doctor.

*Review and put notes to avoid overdosing or uncontrolled repeated treatment.

BACK

The 4 basic advices

1. Asthma is a chronic inflammatory disease.

   For this reason, do not stop taking daily your maintenance or usual treatment. It is the best way to prevent crisis or asthma attacks.

2. Do not smoke, or be in the presence of other people smoking.

3. If you lose control of your asthma, take action! If your have an action plan, implement it; if not, seek for medical help.

4. If you have allergy (mites, pets, pollens, etc..), avoid exposure.

5. If you repeat the use of cortisone* ...
Minimal educational interventions reduced to the essentials (mini-action plan, avoidance behaviors and revision of inhalation technique) have shown efficacy if they are administered repeatedly at follow-up visits190.

3.4.3 Action plan

The education program should consider setting up an action plan, which consists of a set of individualized written instructions in which asthma severity, disease control and the usually prescribed treatment are taken into account. The main objective of the education program is the early detection of asthma worsening and the rapid adoption of measures to achieve quick remission. Depending on the patient’s and the physician’s preferences191-193, the level of control on which the action plan should be based can be assessed in terms of severity and frequency of asthma symptoms, as well as through daily home recording of PEF. This plan should include two basic components194-196: usual treatment in situation of clinical severity and frequency of asthma symptoms, as well as through the action plan should be based can be assessed in terms of adherence in asthma patients is lower than 50% 198,199. Low achieving and maintaining disease control. It is estimated that 3.4.4 Treatment adherence

Patient’s adherence to treatment is a critical factor for achieving and maintaining disease control. It is estimated that adherence in asthma patients is lower than 50%198,199. Low adherence is associated with increased morbimortality as well as with a greater use of healthcare resources200,201.

Three types of patients with low adherence or non-adherence have been described: erratic (due to forgetfulness to take medication), deliberated (or intentionally non-adherence where the patient decides not to take medications) and involuntary or unwitting (due to failure in understanding the disease and/or its treatment)202,203.

Treatment adherence should be evaluated at each medical visit using a reasonably validated method, such as the Test of Adherence to Inhalers (TAI), pharmacy dispensing medication, or the combination of both204-206.

The education program should include the assessment of the level of adherence, promoting the appropriate corrective measures in case of low adherence and adapting them to the patient’s pattern of non-adherence.

Participation of the patient in the choice of the inhaler provides greater therapeutic adherence and control of the disease. Therefore, patients should be involved in the selection of the inhaler device102,104,116,117,207-210.

Non-adherence to control medication in severe asthma can be detected by the FE(NO) suppression test211.

3.4.5 Other aspects to be considered

For education to be effective, a confidence relationship between the healthcare team and the patients should be established, so that patients can raise their doubts, concerns and fears. The healthcare provider should use a simple and understandable language towards both the patients and their relatives, ensure that all concepts have been understood and encourage the patients to put forward their doubts and queries.

Also, written personalized goals shared by patients and physicians must be established.

An appropriate agreement between the patient’s opinions and expectations and his/her physician is one of the factors related to asthma control212.

Patients and their families should be encouraged to raise doubts and queries regarding the information received or emerging from the medical interview, and sufficient time should be allocated so that they can be sorted out at the next visit.

Since education is a continuous process and not an isolated event, each visit should give the opportunity to review, strengthen and increase patients’ knowledge and skills; hence, it is indispensable that education should be agreed on and accepted by the whole team213.

Table 3.7 describes the educational tasks that should be undertaken at each visit. Once properly trained, the nursing and pharmacy staff should actively participate in the organization and management of education programs106,213-215.

<table>
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<tr>
<th>Communication</th>
<th>Information</th>
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<tr>
<td><strong>Initial visit</strong></td>
<td>Assess expectations</td>
<td>Basic concepts on asthma and its treatment</td>
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<td>Agree on common targets</td>
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<tr>
<td></td>
<td>Discuss adherence issues</td>
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<td><strong>Control visits</strong></td>
<td>Evaluate achievements concerning expectations and objectives</td>
<td>Reinforce information provided at the initial visit, Inform about environmental avoidance measures</td>
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<tr>
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<td>Discuss adherence issues</td>
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<td><strong>Reviews</strong></td>
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<td></td>
<td>Discuss adherence to treatment and environmental avoidance measures</td>
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Table 3.7. Educational tasks to be implemented at each visit
Individualized discharge programs assisted by trained nursing personnel prevent readmissions for exacerbations\textsuperscript{216}. Educational interventions carried out in the primary care setting reduce unscheduled visits and the inappropriate use of drugs, such as antibiotics\textsuperscript{217}.

In the interventions to potentiate self-care, sociocultural differences of the patients should be considered\textsuperscript{184}. Educational interventions cannot exclusively develop in the clinical setting. Interventions of self-care in schools or by other patients with asthma provide a better control, a reduction of exacerbations and a better quality of life. Also, they can positively influence on adolescents to quit smoking\textsuperscript{218,219}.

The use of telemedicine improved adherence to treatment\textsuperscript{220} through inhaler monitoring devices\textsuperscript{221} or reminder alarms\textsuperscript{222}. It also improves symptoms and decreases the use of medical care\textsuperscript{223}. Teleconsultation improves asthma control and quality of life\textsuperscript{224} (see section 9.4).

The effectiveness of the patient's self-control in asthma is very positive. For interventions on the patient's self-management to be effective, it is necessary to combine the active participation of the patient, with training and motivation of professionals integrated into a healthcare system that values the self-control in asthma patients\textsuperscript{225}.

Educational workshops are a useful tool as a complement to individualized care, being more profitable when performed during the periods of time when patients present more symptoms\textsuperscript{226}.

The community pharmacist, due to its accessibility and frequent use by the patient, can identify poorly controlled patients especially those who abuse SABA agents or have low adherence to anti-inflammatory maintenance treatment. The community pharmacist can offer health education improving adherence, asthma control and obtaining better clinical and economic outcomes. If necessary, he/she can refer the patient to medical consultation\textsuperscript{112,227-230}. 

\textsuperscript{A} A \textsuperscript{C} C \textsuperscript{B} B \textsuperscript{A} A
**RECOMMENDATIONS**

3.1. SABAs, when administered 10-15 min before the exercise, are the drugs of choice to prevent exercise-induced bronchoconstriction.

3.2. In step 1 budesonide/formoterol, beclomethasone/formoterol or beclomethasone/salbutamol on-demand can be used, although this strategy is not approved in technical specifications and the cost-effectiveness is unknown.

3.3. First-choice treatment **(step 2)** is an IGC at low doses used on a daily basis. LTRA can be considered as alternative treatment.

3.4. In step 2, an alternative could be the use of IGC at low doses with LABA or SABA (e.g. budesonide/formoterol, beclomethasone/formoterol, or beclomethasone/salbutamol) on-demand in patients with low adherence to treatment in whom a specific education had previously failed. However, this strategy is not approved in the products technical specifications and the cost-effectiveness is unknown.

3.5. For moderate persistent asthma, the first-line treatment is the combination of an IGC at low doses **(step 3)** or medium doses **(step 4)** with inhaled LABA.

3.6. For moderate persistent asthma, an IGC at low doses **(step 3)** or medium doses **(step 4)** associated with an LTRA can be considered as an alternative treatment.

3.7. The combination of budesonide/formoterol or beclomethasone/formoterol can be used as maintenance and on-demand (reliever) treatment.

3.8. In severe persistent asthma **(step 5)** first-line treatment is an IGC at high doses in combination with a LABA.

3.9. In patients with severe persistent asthma **(step 5 or 6)** uncontrolled with the combination of an IGC at high doses and a LABA, with post-bronchodilation FEV1/FVC ≤ 70 %, the addition of tiotropium has shown to improve pulmonary function and reduce exacerbations.

3.10. SABA, budesonide/formoterol or beclomethasone/formoterol combinations and, in selected cases, short-acting anticholinergics (ipratropium bromide), are the drugs that can be used as reliever medications (in all therapeutic steps).

3.11. Inhalation is the route of choice in the management of asthma.

3.12. All healthcare professionals taking care of asthma patients should be involved in the instruction and control of inhaled therapy.

3.13. The patient should participate in the selection of the inhaler device.

3.14. It is recomendable the use of a single type of inhaler or at least similar inhalers.

3.15. Patients should be trained on the inhalation technique of inhaler devices and their technique should be periodically supervised.

3.16. Smoking cessation is recommended in smokers with asthma.

3.17. In allergic asthma, specific combined measures of **environmental control according to sensitization of the patient** are recommended.

3.18. In well-controlled allergic asthma with low or medium treatment levels **(steps 1 to 4)**, **allergen immunotherapy** is recommended when clinically relevant IgE-mediated sensitization against common aeroallergens has been demonstrate, and well standardized extracts are used.

3.19. **Allergen immunotherapy** should be prescribed by experienced specialized physicians. All administration of subcutaneous immunotherapy and the first of sublingual immunotherapy should be carried out in centers with available basic resources for immediate treatment of a possible adverse reaction.

3.20. When differente alternatives of **immunotherapy** are available, the use of those that have the consideration of registered medicines with well established efficacy, safety and quality should be prioritized.

3.21. Patients with asthma should follow a **fomal education program** of their disease. Informative actions alone have not been shown to be effective.

3.22. Patients with asthma should be provided with a **written action plan** in order to detect early asthma worsening and to be able to implement actions for rapid remission.

3.23. It is indispensable to determine the level of adherence to treatment in each individual patient. To this purpose, the use of validated methods such as the TAI questionnaire or electronic registry of pharmacy dispensing medicines is recommended.

3.24. Sel-control interventions to be effective should combine the active participation of the patient, the healthcare profesional and the healthcare system.
References


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