5. Treatment of childhood asthma

5.1 Education

The education of the child with asthma and his/her family increases the quality of life, reduces the risk of exacerbations and the cost of healthcare, the reasons for which education is one the fundamental pillars of treatment. Its objective is for the child to achieve a normal life for his/her age including physical exercise and sport activities. Education is essential to improve treatment adherence and to achieve control of the disease.

Education should be developed in all healthcare settings in which children with asthma are attended. Education will be primary addressed to the family during early childhood and, from 8-9 years, should be especially addressed to the child, in order to promote personal autonomy and to achieve the maximum degree of self-care.

Home education programs may be beneficial for children with poorly controlled asthma and are potentially profitable.

For education to be effective, it is essential to identify the educational needs and the factors that affect the behavior of the patient and/or his/her family.

Key aspects of education are shown in Table 5.1.

Table 5.1. Key aspects of the education of a child with asthma

<table>
<thead>
<tr>
<th>Topic area</th>
<th>Key aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>- Concept of asthma (chronic disease, variability)</td>
</tr>
<tr>
<td></td>
<td>- Symptoms exacerbation/between exacerbations</td>
</tr>
<tr>
<td></td>
<td>- Bronchoconstriction</td>
</tr>
<tr>
<td></td>
<td>- Inflammation</td>
</tr>
<tr>
<td>Environmental</td>
<td>- Counseling against smoking</td>
</tr>
<tr>
<td>measures</td>
<td>- Triggering factors (allergens, virus, exercise, etc.)</td>
</tr>
<tr>
<td></td>
<td>- How to identify and avoidance measures</td>
</tr>
<tr>
<td>Treatment</td>
<td>- Bronchodilators (rescue treatment)</td>
</tr>
<tr>
<td></td>
<td>- Anti-inflammatory drugs (maintenance treatment)</td>
</tr>
<tr>
<td></td>
<td>- Side-effects</td>
</tr>
<tr>
<td></td>
<td>- Exacerbation (how to recognize initial symptoms and early action)</td>
</tr>
<tr>
<td></td>
<td>- Immunotherapy</td>
</tr>
<tr>
<td>Inhalers</td>
<td>- Importance of inhaled medication</td>
</tr>
<tr>
<td></td>
<td>- Inhalation technique</td>
</tr>
<tr>
<td></td>
<td>- Maintenance of the system</td>
</tr>
<tr>
<td></td>
<td>- Errors/forgetfulness</td>
</tr>
<tr>
<td>Self-control</td>
<td>- PEF. Best personal value</td>
</tr>
<tr>
<td></td>
<td>- Symptoms registry</td>
</tr>
<tr>
<td></td>
<td>- Personalized written action plan</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>- School attendance</td>
</tr>
<tr>
<td></td>
<td>- Practice of sports</td>
</tr>
<tr>
<td></td>
<td>- Autonomy</td>
</tr>
</tbody>
</table>

PEF: peak expiratory flow.

5.2 Maintenance treatment

5.2.1 Drugs

Inhaled glucocorticoids (IGC). IGC are the first-line of treatment. In children older than 3 years of age, the efficacy of daily IGC is well established, with improvement of clinical and functional parameters, bronchial inflammation, better quality of life, and decrease in the risk of both exacerbations and hospitalizations.

Infants and preschool children treated with IGC daily experience fewer asthma/wheezing episodes, a better treatment response being obtained by those showing risk factors of developing persistent asthma (Asthma Predictive Index [API])

While viral-induced episodic wheezing shows limited response. A treatment trial followed by evaluation of response is recommended.
Treatment with IGC, either continuously or intermittently, does not modify the natural history of the disease\textsuperscript{21-25}.

In preschool and children, the use of controller drugs (IGC or montelukast) at regular doses or intermittently at the onset of symptoms is not recommended\textsuperscript{26-28}.

Early intermittent therapy with IGC at high doses given to infants and preschool children with moderate-severe episodic wheezing and risk factors (API +) at the onset of symptoms have shown to be effective in reducing severity and duration of exacerbations\textsuperscript{16,29,30}, but further studies are needed to establish the recommendation of this therapy.

When administered at usual doses, IGC are safe drugs for the management of childhood asthma. There is usually a decrease in the growth rate at the beginning of treatment (1-3 years), although this is a transient effect and does not influence final growth or final height. However, the final height of children treated with IGC over prolonged periods is lower, an effect proved to be dose-dependent\textsuperscript{11,32}.

### Table 5.2. Components of a personalized action plan

#### Action plan for treating asthma exacerbation at home

- Recognize asthma symptoms and the onset of an exacerbation for using early short-acting bronchodilators and on-demand when symptoms appear.
- Recognize alarm signs and when to seek help from the doctor or go to the emergency department.

#### Self-controlled/family-controlled action plan

- Rules for avoiding specific asthma triggers in children.
- Daily use of preventive medication: doses, frequency and route of administration.
- Changes of preventive medication according to severity and frequency of symptoms (symptom diary) and/or measurement of peak expiratory flow (home PEF recording).
- When to go to his/her pediatrician because asthma is not controlled.
- Prevention and treatment of exertional asthma.

PEF: peak expiratory flow.

### Table 5.3. Written action plan to maintain asthma control

#### Your usual treatment (preventive):

Every day I take: __________________________________________________________

Before exercise I take ______________________________________________________

#### When to Increase Preventive Treatment

Assess your level of asthma control:

In the last week you have had:

<table>
<thead>
<tr>
<th>Question</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma symptoms more than twice a day?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activity or physican excersise limited by your asthma?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night awakenings due to asthma?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need of rescue medication more than twice a day?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If you measure (PEF), your PEF is lower than</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you have answered “Yes” to 3 or more questions, your asthma is not well controlled and to increase a step in your treatment may be necessary

#### How to Increase Treatment

Increase treatment from _______________________________________________________

to ____________________________________________________________________________

and assess improvement every day. Maintain this treatment for ________ days.

In case of an exacerbation, treatment in the action plan for the management of exacerbations will be started and will attend a medical consultation for a new assessment.

Modified from GINA www.ginasthma.com
It is difficult to establish the equivalent doses of the IGC mostly used in pediatric age. Comparable doses of IGC drugs for use in the pediatric age are tentatively shown in Table 5.5.

### Table 5.4. Action plan for treating an asthma exacerbation at home

**What is an ASTHMA EXACERBATION EPISODE and HOW TO ACT AT HOME?**

An asthma exacerbation episode is a sudden or progressive worsening of symptoms:
- Increased cough (continuous, nocturnal or with exercise).
- Whistling sound.
- Fatigue (difficult breathing).
- Feeling of chest tightness.
- Decrease of PEF (if you use the pek-flow meter).

There are **symptoms** that warn us that an exacerbation can be **severe** (warning signs):
- Bluish color of the lips.
- Ribs sink when breathing.
- Difficulty speaking.
- Numbness.

Warning signs indicate that medical assistance should be immediately requested!

**What to do at home in the presence of an exacerbation?**
- Keep calm.
- Treat symptoms as early as possible.
- Start medication at home.
- Never wait to see if symptoms disappear spontaneously.
- After starting medication, observe for 1 hour and assess response.

**USE OF MEDICATION:**

Take your rapid rescue medication: salbutamol with spacer, 2-4 puffs, separated by 30-60 seconds. This dose can be repeated every 20 minutes, up to a maximum of 3 times. If symptoms do not improve in 1 hour, start taking oral corticoids (1 mg/kg/day, maximum 40 mg/day), for 3-5 days.

Take your anti-inflammatory medication times a day, all days, according to the indications given by your pediatrician

**ASSESS RESPONSE TO TREATMENT**

If you improve in one hour and improvement is maintained for 4 hours, continue with salbutamol; 2-4 puffs every 4-6 hours (depending on symptoms) and visit your pediatrician in 24-48 hours.

If you do not improve or the improvement is not maintained and you relapse again: go to an emergency department

If you know how to control exacerbations, the duration of symptoms will be lower and your quality of life will improve.

**Table 5.5. Comparable doses of inhaled glucocorticoids commonly used in pediatric age (mg/day)**

<table>
<thead>
<tr>
<th>Children under 12 years of age</th>
<th>Low doses</th>
<th>Medium doses</th>
<th>High doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide</td>
<td>100-200</td>
<td>&gt; 200-400</td>
<td>&gt; 400</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>50-100</td>
<td>&gt; 100-250</td>
<td>&gt; 250</td>
</tr>
</tbody>
</table>

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severe allergic asthma, omalizumab was found to improve asthma control, reduce exacerbation and hospital admission rates, and decrease IGC doses at the fifth month of treatment\(^8\).  

**Anti-IL5 monoclonal antibody (mepolizumab).** It is recommended in children from 6 years of age with severe eosinophilic asthma insufficiently controlled with high doses of IGC and LABA\(^51,52\). In children 6 to 11 years of age, the recommended dose is 40 mg subcutaneously every 4 weeks and 100 mg every 4 weeks from 12 years of age.  

**Immunotherapy (IT).** When biologically standardized extracts are used and sensitized patients are appropriately selected, immunotherapy has been shown to provide a beneficial effect by reducing symptoms, the need of reliever and maintenance medication, and decreasing bronchial hyperresponsiveness (both specific and non-specific)\(^53\). Also, IT prevents the development of new sensitizations and asthma in children with rhinitis\(^54,55\).  

### 5.2.2 Treatment according to the level of severity, control and future risk

In naïve patients, the choice of treatment is determined by the initial severity. Subsequently, modifications will be carried out in a stepwise approach, adjusting the medication according to the current degree of control, assessing future risk and taking into account the child's age (Figure 5.1).

Children with occasional episodic asthma should be prescribed bronchodilators on-demand without any maintenance treatment. Children with frequent episodic asthma should start treatment at step 2, whereas children with persistent symptoms and/or impairment of pulmonary function should start treatment at step 3 or 4. For children with severe asthma, treatment should preferably be started at step 5 with a further decrease to a lower step (step down) when control is reached and trying to find the minimum effective dose\(^38,56\). The degree of control and the treatment step should be assessed every three months.

### 5.3 Evaluation and treatment of exacerbations

#### 5.3.1 Evaluation of severity

The following factors should be considered: time course of the exacerbation episode, pharmacological treatment administered, presence of associated diseases and possible risk factors (previous intubation or ICU admission, hospitalizations in the preceding year, frequent need of admission to the emergency department in the previous year and/or use of oral glucocorticoids, excessive use of SABA in the preceding weeks).  

Severity assessment is mainly based on clinical criteria (respiratory rate, presence of wheezing and sternocleidomastoid retractions). Although no clinical scale is considered to be well validated\(^57,58\), the Pulmonary Score (Table 5.6)\(^59\) has been found

![Figure 5.1. Stepwise treatment of asthma in the pediatric age according to the level of control.](image)
Treatment of childhood asthma

Severity will be used.

Table 5.6. Pulmonary Score for the clinical assessment of asthma exacerbation in children*

<table>
<thead>
<tr>
<th>Score</th>
<th>Respiratory rate &lt; 6 years</th>
<th>Wheezing</th>
<th>Use of sternocleidomastoid muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 6 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>&lt; 30</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>1</td>
<td>31-45</td>
<td>End of expiration</td>
<td>Slight increase</td>
</tr>
<tr>
<td>2</td>
<td>46-60</td>
<td>Throughout expiration (stethoscope)</td>
<td>Increased</td>
</tr>
<tr>
<td>3</td>
<td>&gt; 60</td>
<td>Inspiration and expiration without stethoscope**</td>
<td>Maximum activity</td>
</tr>
</tbody>
</table>

SaO2: arterial oxygen saturation. In case of disagreement between clinical score and arterial oxygen saturation, the score indicating higher degree of severity will be used.

Table 5.7. Overall evaluation of the severity of asthma exacerbation in children by integrating the Pulmonary Score and the arterial oxygen saturation

<table>
<thead>
<tr>
<th>Pulmonary Score</th>
<th>SaO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&gt;94%</td>
</tr>
<tr>
<td>Moderate</td>
<td>91-94%</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;91%</td>
</tr>
</tbody>
</table>

SaO2: arterial oxygen saturation. In case of disagreement between clinical score and arterial oxygen saturation, the score indicating higher degree of severity will be used.

5.3.2 Drugs

Inhaled short-acting β2-adrenergic agonists (SABA). These agents constitute the first-line treatment due to their higher effectiveness and lower incidence of side effects60. They should preferably be administered via a pressurized inhaler with a spacer chamber, since this way of administration is as effective as nebulizers for treating an acute asthma episode61-64.

Recommended doses and dosing intervals depend on the severity of the exacerbation episode and the response to the initial doses65. The most commonly used drug is salbutamol, which is available as a solution for use with a nebulizer and a pressurized inhaler. The latter must be administered in sequences of 2-10 puffs of 100 μg until response is obtained. For mild attacks, a series of 2-4 puffs may be sufficient, although up to 10 puffs may be necessary for severe exacerbations.

Nebulized SABA should be restricted to those cases in which the patient requires oxygen supply for SaO2 normalization, although a recent randomized clinical trial showed that even in severe exacerbations, the administration of salbutamol and ipratropium bromide with spacer chamber and faci mask with oxygen by means of a nasal cannula was more effective than using a nebulizer66.

Continuous nebulization does not offer greater advantages compared to intermittent nebulization at the same total administered doses67,68.

Ipratropium bromide. The use of frequent doses, every 20 minutes, of ipratropium bromide for the first 2 hours in case of severe asthma exacerbations or moderate exacerbations not responding to initial treatment with SABA, has been shown to be effective and safe69,70. The nebulized dose is 250 μg for children weighing less than 30 kg, 70 for those weighing more than 30 kg. The dose for inhaled use with a spacer chamber is 40-80 μg (2-4 puffs). The maximum effect, which tends to decrease gradually, is observed with the first doses, so this agent should only be used during the initial 24-48 hours71.

In infants, the use of ipratropium bromide combined use with inhaled SABA has been shown to be effective in treating more severe exacerbations72. The effect of this association using an inhaler seems to be superior than that administered by nebulization66.

Systemic glucocorticoids. The efficacy of systemic glucocorticoids in preschool children with mild to moderate acute episodes of wheezing induced by viral infections has been questioned; hence, its use should be restricted to more severe exacerbations (1-2 mg/kg/day)73,74. In children aged over 5 years, these agents have shown benefit after early use75, with the oral route being preferred over intravenous or intramuscular routes, except for circumstances in which oral intake may be inappropriate76,77. Systemic glucocorticoids should be administered in moderate-severe exacerbations, and may be considered for mild exacerbations when sufficient improvement with bronchodilators has not been achieved or the child has a history of severe attacks. Prednisolone at doses of 1-2 mg/kg/day (maximum 40 mg) for 3 to 5 days until resolution is commonly administered78,79.

Dexamethasone is being used as an alternative. The effect of administering a single dose of dexamethasone orally (at 0.3 mg/kg) is not inferior to that of administering prednisolone orally (at 1 mg/kg/day) during 3 days of treatment80-83.

Inhaled glucocorticoids. There is insufficient evidence to recommend the use of IGC as an alternative84 or additional treatment to systemic glucocorticoids85,86 in the management of asthma exacerbations. Larger studies are required, with better methodological quality and cost-effectiveness analysis87, as well as safety studies88.

Magnesium sulfate. It can be used in severe exacerbations failing to respond to initial treatment89,90. The drug is administered intravenously as a single dose of 40 mg/kg (up to 2 g) over 20 minutes.
Nebulized magnesium sulfate together with a β2-adrenergic agonist in the treatment of an asthma exacerbation seems to have benefits in the improvement of pulmonary function90,91.

### 5.3.3 Therapeutic regimens

Treatment of an asthma exacerbation episode depends on its severity and follows the scheme shown in Figure 5.2. Doses of drugs and duration of administration should be modified according to the severity of the exacerbation and the response to treatment.

When SaO2 is below 94%, oxygen therapy is required to maintain SaO2 between 94-98%92,93. An SaO2 < 92 % after initial treatment with inhaled bronchodilators can be used as a marker to select the more severely ill patients who should be hospitalized for starting intensive treatment92,94.

In children with moderate/severe exacerbations refractory to first-line treatment, high-flow nasal cannula oxygen therapy appears to be superior to conventional oxygen therapy to reduce breathing difficulty95,96. However, more studies are needed to show its general efficacy for treating asthma and respiratory failure in the emergency setting97.

Regarding non-invasive ventilation (NIV), the current available evidence does not allow us to confirm or exclude its use in exacerbation episodes refractory to the usual treatment98.

Mild and moderate exacerbations can be treated in the primary care setting.

In the presence of severe exacerbation or suspicion of complications, history of high-risk exacerbations or lack of response to treatment, patients should be referred to the hospital in a medicalized ambulance.

**Follow-up.** It is necessary to evaluate the degree of the control of symptoms in the previous weeks, the presence of risk factors, possible triggering factors and previous treatment. Also, it is important to assess the level of therapeutic adherence and to supervise that the inhalation technique is correct. A written action plan must be reviewed or provided and a follow-up visit arranged10.

Figure 5.2. Treatment of asthma exacerbation in children.
## RECOMMENDATIONS

1. The education of the child with asthma and his/her family is recommended because increases the quality of life and reduces the risk of exacerbations and healthcare costs.

2. In the education of children with asthma, it is recommended to include written personalized management action plans, addressing maintenance treatment and how to treat exacerbations.

3. Inhaled IGC is recommended as first-line treatment for the control of persistent asthma in children of all ages.

4. Montelukast can be tried as an alternative to IGC for maintenance therapy.

5. Treatment with LABA can be considered in children older than 4 years of age but always combined with IGC. LABA monotherapy should never be administered.

6. In the treatment of children with allergic asthma, immunotherapy should be considered provided that biologically standardized extracts are used and patients are appropriately selected.

7. In children aged 6 years or older with insufficiently controlled severe persistent asthma with high doses of IGC and LABA and/or LTRA and/or tiotropium, the use of biological agents or monoclonal antibodies is recommended.

8. Before considering that an asthma patient is poorly controlled and stepping up treatment, the diagnosis of asthma should be confirmed, treatment adherence and inhalation technique should be evaluated, and other comorbidities excluded.

9. Early and repeated administration of SABA at high doses is the first-line of treatment of asthma exacerbations in children.

10. It is recommended to individualize drug doses according to severity of exacerbations and the response to treatment.

11. Early use of systemic glucocorticoids is recommended in moderate and severe exacerbations; in mild exacerbation, an individualized assessment is recommended.

12. In the presence of SaO2 < 92 % after an initial treatment with inhaled bronchodilators, admission to the hospital to start intensive therapy is recommended.

13. A pMDI with spacer chamber is recommended for the administration of bronchodilators, particularly in mild-moderate exacerbations.

14. It is necessary to evaluate the degree of control, risk factors, adherence to treatment and inhalation technique, as well as to offer a written action plan and guarantee the follow-up of children with exacerbations.
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Treatment of childhood asthma


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