

4. Asthma Exacerbation

C Exacerbations (asthma attacks) are acute or subacute episodes, which are characterized by a progressive increase in one or more typical asthma symptoms (dyspnea, coughing, wheezing and tightness of the chest) accompanied by a decrease in expiratory flow (PEF or FEV₁). Depending on the speed with which crises ensue, there are two types: those that are slow to develop (normally over a period of days or weeks) and those that develop quickly (in less than three hours), and they must be identified in accordance with their different causes, pathogenesis and prognosis [160,195]. Exacerbations that are slow to develop (over 80% of the cases seen in ED) are often due to upper respiratory tract infections or to deficient control of the disease, as a result of poor therapeutic adherence; the basic mechanism underlying deterioration is inflammation and the response to treatment is also slow. Meanwhile, exacerbations that develop rapidly are due to inhaled allergens, the ingestion of drugs (NSAIDs or -blockers), foods (reactions to additives and preservatives) or emotional stress; the mechanism is bronchospasm and, although initially more serious (with a risk of intubation and death), the response to treatment is better and quicker. The intensity of exacerbations is variable. Sometimes the symptoms are mild and cannot be detected by the patient and other times they are very severe episodes that are lifethreatening. There are patients who have a greater risk of suffering life-threatening asthma crises (Table 4.1) [196-198].

4.1 Evaluation of Severity

D The severity of an exacerbation determines its treatment and, consequently, it is essential to make a quick initial assessment of the patient. The evaluation of an attack is performed in two stages [199]:

D – The initial (or static) stage. Its aims are: to identify patients with risk factors (Table 4.1), to identify life-threatening signs and symptoms (Table 4.2) and to objectively measure the extent of airflow obstruction by determining FEV₁ or PEF and its repercussion on gaseous exchange.

– The stage following response to treatment (or dynamic evaluation). Its objectives are: to compare the changes obtained in the degree of airflow obstruction with respect to initial values and to estimate the need to perform other diagnostic tests.

A brief initial medical history will give us an idea of the

Table 4.1. Pre-disposing factors for patients life-threatening asthma

- Previous ICU admissions or intubation/mechanical ventilation.
- Frequent hospitalizations during the previous year.
- Multiple visits to Accident and Emergency Services in the last year.
- Psychological traits (alexithymia) and disorders (attitudes of negation) or psychiatric diseases (depression) that make treatment adherence difficult.
- Cardiovascular comorbidity.
- Short-acting β_2 adrenergic agonist abuse.
- Abrupt crisis onset.
- Patients with no regular control of their disease.

ICU: Intensive Care Unit.

C
C cause of the asthma symptoms, the duration of the attacks and prior treatment. The presence of life-threatening signs or symptoms and the imminence of a cardio-respiratory attack (alteration of sensory perception or consciousness, bradycardia, hypotension, cyanosis, “silent” chest or psychomotor agitation) mean that intensive care units must be contacted. Other signs and symptoms (Table 4.2) are of little use, due to their poor correlation with the level of obstruction and wide variations in their interpretation [200]. The objective appraisal of the level of airflow obstruction using a spirometer (FEV₁) or a PEF meter permits initial severity and response to treatment to be determined. Depending on the values obtained, an exacerbation will be considered mild if the FEV₁ or PEF value is equivalent to or higher than 70% its theoretical or best previous personal value respectively, moderate if the FEV₁ or PEF measurement is between 70% to 50% and serious if these values are lower than 50%. It is estimated that the functional response to treatment is satisfactory when FEV₁ or PEF values are higher than 45% of the predetermined value and PEF increases at least 50 l/min 30 minutes after treatment is initiated [201]. The initial therapeutic airflow obstruction response is the key prognostic factor for assessing an attack.

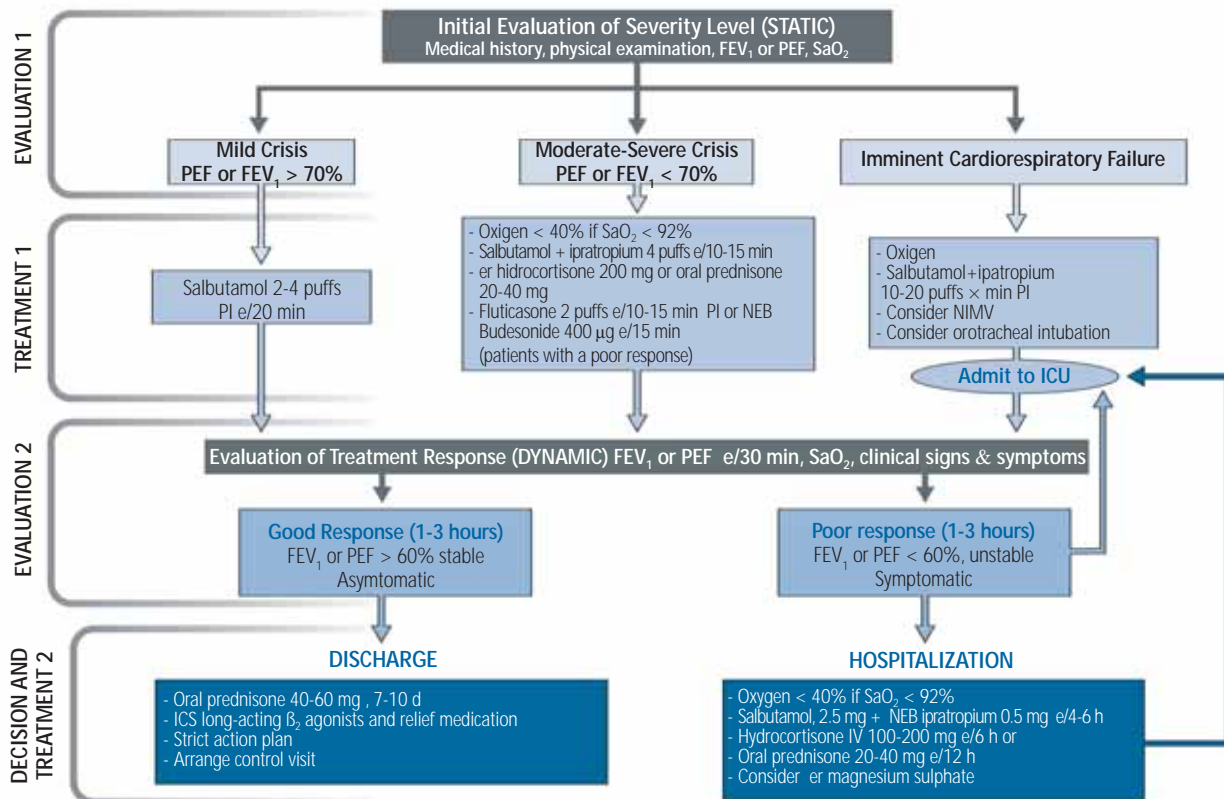
D The measurement of oxygen saturation by pulseoximetry is required in all patients with a FEV₁ or PEF reading of less than 50% of its theoretical value in order to rule out hypoxemia. Arterial gasometry is useful in patients whose saturation cannot be maintained above 90% despite oxygenotherapy [202].

D Other complementary tests may be performed at the outset, such as chest X-rays and ECG. They are usually performed

Table 4.2. Assessment of the severity of asthmatic exacerbation

	Mild Crisis	Moderate-severe Crisis	Imminent Respiratory Failure
Dyspnea	Mild	Moderate-intense	Very intense
Speech	Paragraphs	Sentences-words	
Respiratory rate (x')	Increased	> 20-30	
Heart rate (x')	< 100	> 100-120	Bradycardia
Use of accessory muscles	Absent	Present	Paradoxical thoracoabdominal movement
Wheezing	Present	Present	Auscultatory silence
Consciousness	Normal	Normal	Impaired
Paradoxical pulse	Absent	> 10-25 mmHg	Absence (muscular fatigue)
FEV ₁ or PEF (reference values)	> 70%	< 70%	
SaO ₂ (%)	> 95%	90-95%	< 90%
PaO ₂ mmHg	Normal	80-60	< 60
PaCO ₂ mmHg	< 40	> 40	> 40

Abbreviations: FEV₁: forced expiratory volume during the first second; PEF: peak expiratory flow; x': per minute; SaO₂: oxyhaemoglobin saturation; PaO₂: arterial oxygen pressure; PaCO₂: arterial carbon dioxide pressure.



Abbreviations: FEV₁: forced expiratory volume during the first second; PEF: peak expiratory flow; SaO₂: oxyhaemoglobin saturation; PI: pressurised inhaler; NEB: nebulized; er: endovenous route; ICS: inhaled glucocorticoids; NIMV: non-invasive mechanized ventilation; min: minute; mg: milligram; µg: microgram; e/: every.

Figure 4.1. Diagnostic and therapeutic management of adult asthma exacerbations. (from the ALERTA 2008 Guide) [199].

D when the presence of symptoms including fever, pain or intense dyspnea, suggest the possibility of complications, such as pneumothorax or an infection of the lower respiratory tract, or when the therapeutic response as measured by means of objective parameters, is inappropriate [203].

4.2 Treatment

The immediate aim of attacks treatment is to preserve the life of the patient by reversing airflow obstruction and hypoxemia, if it is present, as fast as possible and then to instate or revise the therapeutic plan to prevent new attacks. Figure 4.1 and Table 4.3 show the pharmacological treatment that must be employed, depending on severity, and the normally recommended doses.

4.2.1 Mild Exacerbation

D In addition to the hospital ED, milder crises can be treated at home by the patient and at Primary Care Centers, as long as a proper clinical assessment of PEF is made and there is a response to treatment in the first two hours.

C Patients with written action plans for treating mild attacks, who record their PEF at home, are using the best strategy for managing mild exacerbations since they can apply it early in an attack [204]. They need to be trained to recognize

C early indicators of an exacerbation and to act immediately in accordance with the action plan designed for them and that must include the measures that need to be taken depending on the response to treatment.

The treatment regimen to be followed does not depend on the place where the patient receives treatment. Basically, it must include the administration of fast-acting β_2 adrenergic agonist bronchodilators (salbutamol or terbutaline), oral glucocorticoids and oxygen (if necessary). Inhaled short-acting β_2 adrenergic agonists are the fastest and more effective bronchodilator drugs for the treatment of asthma exacerbations. Salbutamol (or terbutaline) is employed at 200 to 400 μg doses and is administered using an inhalation chamber (2 to 4 inhalations) every 20 minutes during the first hour [205,206]. A lack of response, in cases of outpatient management, means that patients must be transferred to a hospital ED. When the response is good, salbutamol at a dose of two inhalations every 3-4 hours must be continued until the attacks remits.

A If the patient progresses favorably in the first two hours of treatment (disappearance of symptoms, PEF higher than 80% of its theoretical value or best personal value) and this improvement is maintained for 3-4 hours, no further treatment is necessary.

A The use of systemic glucocorticoids accelerates the resolution of exacerbations. Except in very mild attacks, they should always be administered [207], especially if: a) a reversal of airway obstruction is not achieved with inhaled

Table 4.3. Drugs and doses for the treatment of asthma exacerbations

Therapeutic Groups	Drugs	Dose
Inhaled β_2 adrenergic agonists	Salbutamol or terbutaline	– 4-8 puffs (100 μg /puffs) e/10-15 min (PI + spacing chamber) – 2.5-5.0 mg e/20 min (intermittent NEB) – 10-15 mg/h (continuous NEB)
	Formoterol	– 24-36 μg (Turbuhaler)
Systemic β_2 adrenergic agonists	Salbutamol	– 200 μg iv in 20 min followed by por 0.1-0.2 $\mu\text{g}/\text{kg}/\text{min}$.
Anticholinergics	Ipratropium bromate	– 4-8 puffs (18 μg /puff) e/10-15 min (PI + spacing chamber) – 0.5 mg e/20 min (intermittent NEB)
Systemic Glucocorticoids	Prednisone	– 20-40 mg e/12 h (or)
	Hydrocortisone	– 100-200 mg e/6 h (er)
Inhaled Glucocorticoids	Fluticasone Budesonide	– 2 puffs (250 μg /puff) e/ 10-15 min. (PI + spacing chamber) – 800 μg every 20 min (NEB)
Systemic magnesium sulphate		– 2 g to be taken in 20 min. (IV)
Inhaled magnesium sulphate		– 145-384 mg in isotonic solution (NEB)
Aminophylline		– 6 mg/kg to be taken in 30 min followed by 0.5-0.9 mg/kg/h

Abbreviations: PI: pressurised inhaler; NEB: nebulised; or: oral route; er: endovenous route; ICS: inhaled glucocorticoids; kg: kilogram; min: minute; mg: milligram; μg : microgram; e/: every; h: hour.

A fast-acting β_2 adrenergic agonists; b) the patient was already taking oral glucocorticoids; c) the patient has already treated his previous loss of control with other therapeutic options without success; d) there is a history of previous exacerbations requiring oral glucocorticoids. The daily dose is 0.5 to 1 mg of prednisone/kg (or the equivalent amount of other steroids) of the patient's ideal weight, maintaining the same dose for 5 to 10 days (without requiring progressive dose reduction) in order to achieve faster improvement and to avoid early relapses [208-210].

D When the response to the first doses of inhaled bronchodilator treatment is satisfactory, hospital referral is not necessary. The patient needs to be instructed about how to follow subsequent treatment properly and about changes in his therapeutic maintenance plan, or his asthma educational program must be reviewed [211].

4.2.2 Moderate-severe Exacerbation

C The first line of action consists of administering oxygen in order to maintain a SaO_2 level higher than 90%, avoiding the administration of high concentrations that can lead to hypercapnic respiratory failure [212], especially in patients with more severe obstruction.

A After that, it is advisable to administer a short-acting β_2 adrenergic agonist. Repeated administration at regular intervals and evaluating the treatment response, has been shown to be effective in eliciting a bronchodilator response in asthma attacks [213]. Depending on the system used, up to three consecutive nebulizations of salbutamol (2.5 mg) can be administered every 30 minutes or 12 puffs (4 every 10 minutes) if they are delivered with a pressurized inhaler and an inhalation chamber. In serious cases continuous nebulization can also be used at a rate of 10 mg/h [214].

C Salbutamol must only be administered intravenously or subcutaneously in patients who are ventilated or who fail to respond to inhaled treatment, as there is no difference in its efficacy and it has more side effects [215].

B Formoterol (a long-acting and rapid-onset β_2 adrenergic agonist), administered using a powder system, is equivalent to salbutamol in patients with moderate or severe attacks [216].

A The use of nebulized ipratropium bromate (0.5 mg) during the initial phase of asthma crises in patients with severe asthma or with a poor initial response to β_2 adrenergic agonists provides a significant increase in bronchodilation [217].

A Systemic glucocorticoids must be administered at an early stage (during the first hour of treatment in ED) in all patients who have moderate or severe exacerbations or who fail to respond to initial treatment. A systematic review demonstrated that prompt administration of steroids lowers the rate of readmissions and hospitalizations in patients with asthma exacerbations [218]. The recommended dose of steroids is 100-200 mg of hydrocortisone or 40-60 mg of methylprednisolone when initiating treatment. The studies available do not show differences between high and low doses or between intravenous and oral administration [207].

A The repeated administration of inhaled glucocorticoids in conjunction with bronchodilators, at intervals no longer than 30 minutes and during the first 90 minutes of treatment, elicits

a significant improvement in lung function and a reduction in the number of hospitalizations [219].

The nebulization of salbutamol in an isotonic magnesium sulphate solution produces no additional benefits, except in a subgroup of patients with a FEV_1 value lower than 30% [220]. In the case of patients with very severe attacks and a poor response to treatment, intravenous magnesium sulphate can be used as a single 1-2 g dose administered over a period of 20 minutes [221].

With respect to other drugs, such as aminophylline [222], heliox, [223] antibiotics and leukotriene receptor antagonists, there is no data to support their use in the treatment of moderate-severe asthma exacerbations.

4.2.3 Failure to Respond to Treatment

Should refractory respiratory failure or symptoms or signs of severe exacerbation persist despite treatment, there is still the possibility of using non-invasive mechanical ventilation (NIMV) or transferring the patient to the ICU for orotracheal intubation and mechanical ventilation. Few studies using NIMV have been carried out to date. The decision to perform intubation is a matter of clinical judgement, when there is progressive deterioration or failure of the respiratory muscles. Permissive hypercapnic ventilation has demonstrated better results than the usual ventilation methods [224].

4.3 Hospitalisation Criteria

Various studies have shown that, once the peak bronchodilator response plateau has been reached, further administration of medication is not synonymous with greater clinical improvement [213,225]. This explains why it is usually recommended that decisions about hospital admissions should be made three hours after initiating treatment. Patients who have received adequate treatment during that time and continue to show symptoms, who require oxygenotherapy to maintain a SaO_2 level higher than 90% and demonstrate a persistent reduction in pulmonary function (FEV_1 or PEF below 40%) must be hospitalized [226].

In all cases in which the criteria for hospitalization are not met, it is recommended that the patient be kept under observation for 60 minutes to confirm his clinical and functional stability before discharge.

4.4 Hospital Discharge Criteria

Patients who have been admitted to the hospital for an asthma exacerbation, can be discharged if they comply with the following criteria: disappearance or significant improvement in asthma symptoms; PEF higher than 70% of the patient's best personal value in a stable situation; daily PEF variability less than 20%; short-acting β_2 adrenergic agonists need to be used as needed less than three times a day, absence of significant dyspnoea on walking and the patient has already started to receive inhaled glucocorticoids [227,228].

RECOMMENDATIONS

- The evaluation of any asthma exacerbation must include the identification of signs and any history of life-threatening risk and the use of objective measurements (PEF or spirometry) to quantify the degree of airflow obstruction (**static assessment**). **R2**
- In patients with an asthma attacks we recommend considering the initial therapeutic response to airflow obstruction in order to decide how to proceed (**dynamic assessment**). **R2**
- In asthma attacks, treatment with **inhaled β_2 adrenergic agonists** is recommended. **R1**
- In **moderate-severe exacerbation** prompt administration of systemic glucocorticoids and oxygen at the minimum concentration that will permit a $\text{SaO}_2 > 90\%$ is recommended. **R1**