

Asthma exacerbation - how important is it and how to treat it?



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Resumo

O termo “exacerbação da asma” refere-se a uma piora aguda dos sintomas da asma em relação aos sintomas basais, com consequente redução da função pulmonar, levando a morbidade e mortalidade significativas. Pode ocorrer em pacientes com diagnóstico prévio de asma ou, ocasionalmente, como a primeira manifestação da doença. A definição de exacerbação é a necessidade de corticosteroides por pelo menos três dias, hospitalização ou atendimento em pronto-socorro devido à asma. Uma avaliação rápida e objetiva é crucial para determinar a gravidade da exacerbação e orientar o tratamento. Os tratamentos devem ser administrados rapidamente e, frequentemente, simultaneamente para alcançar melhores resultados. Oxigênio suplementar e medicamentos inalatórios são cruciais em muitos pacientes com exacerbações de asma. Corticosteroides sistêmicos, sulfato de magnésio intravenoso e outras terapias adicionais devem ser utilizados em pacientes refratários. A alta hospitalar é um momento muito importante para organizar e orientar sobre a importância do acompanhamento ambulatorial.

Palavras chave: Exacerbação de asma; Ataque de asma; Asma grave

Abstract

The term “Asthma exacerbation” refers to an acute deterioration of asthma symptoms from baseline symptoms with associated reduction in lung function, leading to significant morbidity and mortality. It can occur in patients with a prior diagnosis of asthma or, occasionally, as the first manifestation of the disease. The definition of exacerbation is the need for corticosteroids for at least three days, hospitalization, or an emergency room visit due to asthma. A rapid and objective assessment is crucial to determine the severity of the exacerbation and guide treatment. Treatments should be administered quickly and, often, simultaneously to achieve better outcomes. Supplemental oxygen, inhaled medications are crucial in many patients with asthma exacerbations. Systemic corticosteroid, intravenous magnesium sulfate and others additional therapies should be used in refractory patients. Discharge is a very important moment to organize and advise about importance of the outpatient follow-up.

Keywords: Asthma exacerbation; Asthma attack; Severe Asthma



Introduction

The term “Asthma exacerbation” refers to an acute deterioration of asthma symptoms from baseline symptoms with associated reduction in lung function, leading to significant morbidity and mortality. It can occur in patients with a prior diagnosis of asthma or, occasionally, as the first manifestation of the disease. An exacerbation may be triggered by external factors such as allergens, pollution, or infection. Other terms like flare up or asthma attack are often used in clinical practice to refer to an exacerbation.¹

The definition of exacerbation is the need for corticosteroids for at least three days, hospitalization, or an emergency room visit due to asthma. Moderate exacerbations are defined as events that require a change in treatment to prevent progression to severe forms but are not intense enough to justify the use of oral corticosteroids.

Some parameters may help clinicians to identify risk of exacerbation in an outpatient setting. These risk factors increase the risk of exacerbations even if the patient has few asthma symptoms. The most important risk factors are : 1- Exacerbation history (ever intubated and/or been in the intensive care unit because of asthma, or one severe exacerbation in last year); 2 - high blood eosinophils; high FeNO or both, 3 – major psychological or socioeconomic problems; 4- Low FEV1 (< 60% predicted) or high bronchodilator response; 5 – Exposures to: cigarette smoking, e-cigarettes , viral infection, allergen exposure and air pollution, 6- Conditions like obesity, chronic rhinosinusitis and pregnancy; 7- Poor adherence or incorrectly inhaler technique; 8- High SABA overuse.¹

Other important point is to teach the patients to identify the worse of the symptoms that will require an emergency care. A written asthma action plan is suggested to help the patient showing how increase inhaled medication and when contact medical care.¹

The term mild asthma should be avoided because it could minimize the asthma both for the patient and the physician. Up to 30% of asthma exacerbations and deaths occur in people with infrequent symptoms.



Severe asthma exacerbations are potentially fatal medical emergencies that require immediate and effective management in acute care settings such as the emergency department. It is essential to evaluate if the exacerbation is related to an infection that triggered the worse of the symptoms.

The primary objectives in treating severe acute asthma are the rapid reversal of airflow limitation and the correction of hypoxemia or hypercapnia, if necessary. Airflow limitation is usually quickly relieved through a combination of repeated administration of inhaled bronchodilators and early initiation of systemic corticosteroids.

While respiratory discomfort persists, patients must undergo strict monitoring, including serial vital sign assessments, pulse oximetry (SpO₂), and pulmonary function tests (e.g., Peak Expiratory Flow [PEF]) to evaluate the treatment response.

Initial Objective Assessment

A rapid and objective assessment is crucial to determine the severity of the exacerbation and guide treatment. A history taking considering trigger exposures and duration of the symptoms is important. A series of clinical findings and objective tests can help clinicians confirm the diagnosis of an asthma exacerbation, assess the severity of the asthma attack, and rule out complicating factors such as pneumonia, atelectasis, pneumothorax, and pneumomediastinum.

A focused history and physical examination should be obtained simultaneously with the initiation of therapy to confirm the diagnosis and assess severity.

Some clinical findings can help identify patients experiencing severe asthma attacks. Tachypnea (>30 breaths per minute), tachycardia (>120 beats per minute), use of accessory inspiratory muscles (e.g., sternocleidomastoid muscles), sweating, inability to speak in full sentences or phrases, inability to lie in the supine position due to shortness of breath, and paradoxical pulse (a drop of more than 12 mmHg in systolic blood pressure during inspiration) are all indicative of severe airflow obstruction.²

Unfortunately, these findings are not sensitive indicators of severe attacks. Up to 50% of patients with severe airflow obstruction may not exhibit any of these abnormalities.³



- **Oxygen Saturation (SpO₂):**

- Continuous monitoring is recommended, preferably via pulse oximetry. It is important to note that SpO₂ can be overestimated when the actual saturation is between 80–90%, particularly in individuals with dark skin.^{1 7}
- If SpO₂ < 90%: oxygen supplementation is indicated, starting with devices like a nasal cannula and titrating according to patient response.¹
- Saturation target: there is no established consensus yet. Generally, the target for adults is >92%, and for pregnant women, >95%.¹ Patients at high risk for chronic hypercapnia (e.g., those with COPD) should aim for 90–94%.

- **Pulmonary Function:**

- Measure Peak Expiratory Flow (PEF) or Forced Expiratory Volume in the first second (FEV₁) before treatment if possible, without delaying therapy.¹
- Monitor treatment response with subsequent measurements.
- Normal values vary by sex, height, and age. However, a peak flow rate below 200 L/min indicates severe obstruction for most adults, except for those who are very short or over 65 years old.⁴
- In terms of predicted percentage or personal best, an exacerbation is considered severe when PEF is ≤50% of predicted; moderate when PEF is >50% but <70% of predicted.

- **Arterial Blood Gas:**

- Not routinely necessary.⁸
- Consider sampling if PEF/FEV₁ <50% of predicted, inadequate response to initial therapy, or clinical deterioration.⁹
- Objective data suggesting respiratory failure: PaO₂ <60 mmHg or normal/elevated PaCO₂ (especially if PaCO₂ >45 mmHg).
- Marked hypoxemia (PaO₂ <60 mmHg or SpO₂ <90%) is uncommon during uncomplicated asthma attacks; its presence suggests life-threatening asthma or potential complications like pneumonia or atelectasis due to mucus plugging. Severe hypoxemia increases the risk of serious cardiovascular or neurological complications and death.⁴



○ In the absence of respiratory depressants like narcotics or sedatives, hypercapnia is rarely present when PEF is $\geq 25\%$ of normal or ≥ 150 L/min.⁵

- **Venous Blood Gas:**

- Measuring peripheral venous carbon dioxide tension (PvCO₂) is becoming more common in emergency departments.

- A normal or low PvCO₂ (<45 mmHg) reliably predicts a normal or low PaCO₂, and can be used to exclude hypercapnia.

- The overall correlation between PvCO₂ and PaCO₂ is low.⁶

- **Chest X-ray:¹⁰**

- Not routinely recommended.

- Indications: suspicion of complications (e.g., pneumothorax, pneumonia) or to assess alternative diagnoses.

Emergency Treatment

Treatments should be administered quickly and, often, simultaneously to achieve better outcomes.

- **Supplemental Oxygen:**

- Administer via nasal cannula or mask to maintain target SpO₂:¹

- Adults and adolescents: 93–95%

- Children aged 6–11 years: 94–98%

- Once the patient is stabilized, oxygen should be titrated and weaning should be attempted.

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- **Inhaled Short-Acting Beta2-Agonists (SABA):**

- Inhaled salbutamol (or albuterol) is the cornerstone of bronchodilator treatment.

- Delivery via pressurized metered-dose inhaler (pMDI) with spacer is preferred over nebulization, being more cost-effective and efficient.^{11, 12}

- Dose: 2–6 puffs, up to 10 puffs in severe cases, repeated every 20 minutes during the first hour, as needed.
- Nebulizers can be considered for patients unable to use the pMDI with spacer but increase the risk of aerosol transmission.¹³
- **Combination of ICS-formoterol as an Alternative to High-Dose SABA:**
 - Studies show comparable safety and efficacy of high doses of budesonide-formoterol compared to high doses of SABA.¹⁴
- **Muscarinic Antagonists:**
 - Adding an inhaled Short-Acting Muscarinic Antagonist (SAMA), such as ipratropium bromide, to inhaled SABA is recommended for patients presenting to the emergency department with moderate to severe asthma exacerbations, especially during the first hour of treatment.^{1, 15}
 - A meta-analysis indicates that combined SAMA + SABA therapy can reduce hospitalization rates (especially in adults) during severe exacerbations and improve respiratory function.^{16, 17, 18}
 - **Dose:**
 - Nebulization: 500 mcg per dose
 - pMDI with spacer: 4 to 8 puffs per dose
 - Generally administered with SABA every 20 minutes during the first hour or as clinically indicated.¹⁵
- **Inhaled Corticosteroids (ICS):**
 - High doses of ICS within the first hour may reduce the need for hospitalization in patients not already on systemic corticosteroids.¹⁹
 - The evidence on the benefit of adding ICS to systemic corticosteroids is conflicting in adults but may reduce hospitalization risk in children.²⁰
- **Systemic Corticosteroids:**
 - They tend to accelerate resolution of exacerbations and reduce the likelihood of relapse.^{21, 22}

- Should be administered early (ideally within the first hour),²¹ especially if:
 - The initial SABA response is inadequate
 - The patient is already on oral corticosteroids (OC)
 - There is a history of previous severe exacerbations requiring OC
- The oral route is as effective as intravenous, generally preferred for being faster, less invasive, and cheaper.^{23, 24}
- Intravenous administration should only be considered if the patient cannot use the gastrointestinal route (e.g., invasive ventilation, vomiting).
- **Recommended dosage and duration:**
 - **Adults:**
 - 50 mg of prednisolone once daily in the morning
 - or 200 mg of hydrocortisone in divided doses²⁵
 - Duration: 5 to 7 days^{26, 27}
 - **Children (6–11 years):**
 - 1–2 mg/kg, maximum of 40 mg/day²⁵
 - Duration: 3 to 5 days²⁸
- Tapering the dose is generally not necessary.
- **Intravenous Magnesium Sulfate:**
 - Not recommended for routine use.
 - Consider a single 2-gram IV dose infused over 20 minutes in adults with severe exacerbations or those who do not respond adequately to intensive initial therapy, while maintaining hypoxemia. It may reduce the need for hospitalization in adults.^{29, 30, 31}

Additional Therapies for Refractory Patients

When a patient with severe asthma exacerbation does not respond adequately to aggressive initial measures (inhaled bronchodilation, systemic corticosteroids, oxygen supplementation, and intravenous magnesium), they are considered refractory. In such cases, advanced respiratory support therapies may be necessary.



- **Non-Invasive Ventilation (NIV):**

- NIV aims to reduce respiratory effort, improve gas exchange, prevent respiratory muscle fatigue, and potentially avoid endotracheal intubation. It may be considered for patients with severe and progressive respiratory distress who remain alert, cooperative, capable of protecting their airway, and hemodynamically stable despite maximal pharmacological therapy.

- NIV is also useful in cases of moderate hypercapnia. However, scientific evidence is still controversial and less robust compared to COPD exacerbation or acute pulmonary edema. Thus, NIV is not considered standard treatment for asthma exacerbations. It should be carried out in an intensive care unit where immediate invasive mechanical ventilation is available and there is suitable expertise.

- Contraindications are similar to those in other conditions, such as imminent respiratory arrest, severe hemodynamic instability, reduced level of consciousness, or vomiting.

- **Invasive Mechanical Ventilation (IMV):**

- IMV is reserved for patients with imminent or established respiratory failure. The objectives are to ensure adequate oxygenation and ventilation, reduce respiratory effort, and allow time for bronchodilator and anti-inflammatory therapies to take effect.

- The respiratory drive almost invariably increases in acute asthma, leading to hyperventilation and a correspondingly decreased PaCO_2 . Thus, a normal PaCO_2 (eucapnia) during an asthma exacerbation indicates that airway narrowing and dynamic hyperinflation are so severe that tidal volume and alveolar ventilation are beginning to decrease despite an intense and persistent central respiratory drive. Hypercapnia and respiratory failure can then rapidly develop with any further airway obstruction or respiratory muscle fatigue. Progressive hypercapnia during an asthma exacerbation is generally an indication for mechanical ventilation.

- Ventilatory strategies in asthma are challenging due to severe airflow obstruction. It is essential to recognize, measure, and control hyperinflation and intrinsic



positive end-expiratory pressure (auto-PEEP) to achieve good outcomes in intubated asthmatic patients. Strategies to reduce hyperinflation and auto-PEEP include:

- **Reducing Respiratory Rate (RR):** the most effective strategy to increase expiratory time and decrease air trapping.^{32, 33}
- **Reducing Tidal Volume (Vt):** also helps limit hyperinflation, but its use is constrained by increased dead space.^{32, 33}
- **Shortening Inspiratory Time (Ti):** achieved by increasing inspiratory flow (e.g., using a square wave pattern), allowing more time for expiration in each cycle.^{32, 33}

○ Additionally, reducing respiratory rate may lead to hypercapnia. Hypercapnia is often well tolerated in this patient profile, even with arterial PaCO₂ levels up to 90 mmHg. In selected cases, it may be safer to accept hypercapnia rather than hyperventilate to normalize PaCO₂, due to the risk of critical hyperinflation. However, permissive hypercapnia is contraindicated in cases of anoxic brain injury or severe myocardial dysfunction.³⁴

○ In clinical practice, safety targets established by consensus, such as plateau pressure (Pplat) < 30 cmH₂O and auto-PEEP < 15 cmH₂O,³⁵ are useful for guiding treatment, although they are not validated predictors of complications.³⁵

○ According to Mayo and Radeos (in Brenner, B. Emergency asthma, 1999; pp. 469–487),³³ controlled mechanical ventilation is recommended, adjusting respiratory rate to a low value (10 breaths per minute), tidal volume (Vt) to 7–8 mL/kg of ideal body weight, peak inspiratory flow to 60 L/min (with constant flow pattern) or 80–90 L/min (with descending flow), and inspired oxygen fraction (FiO₂) set to 1.0.

○ Sedation and analgesia are generally necessary for patient comfort and ventilator synchrony. Neuromuscular blockade may be considered in difficult cases.

- **Extracorporeal Membrane Oxygenation (ECMO):**

This strategy is reserved for patients with asthma and hypoxemia and/or hypercapnia refractory to optimized mechanical ventilation. It is considered a last-resort rescue therapy in specialized centers. ECMO provides extracorporeal life support by oxygenating the blood and removing carbon dioxide outside the body. In respiratory failure, the veno-venous configuration (VV-ECMO) is typically used.³⁶



Treatments NOT routinely recommended in the emergency department

- Epinephrine (Adrenaline): indicated only if the asthma exacerbation is associated with signs of anaphylaxis and/or angioedema.
- Intravenous Aminophylline/Theophylline: increase adverse effects without significant additional benefit.³⁷
- Antibiotics: use only if there is strong evidence of bacterial infection (e.g., concomitant pneumonia).³⁸
- Intravenous SABA: reserved for specific situations in the Intensive Care Unit (ICU), not recommended in the general emergency setting.
- Sedatives/Anxiolytics: should be avoided due to the risk of respiratory depression and potential precipitation of hypercapnic respiratory failure.
- Leukotriene Receptor Antagonists (LTRAs): few well-designed studies; initially, no benefit demonstrated in the acute setting.
- Helium-Oxygen Mixture (Heliox): limited evidence; may be considered in severe and refractory cases, but it is not a standard treatment.³⁹

Future Perspectives

The use of biologics has become increasingly common in clinical practice and is still under investigation for exacerbation cases.

The ABRA study, a randomized, double-blind, placebo-controlled clinical trial, evaluated the efficacy of benralizumab, a monoclonal antibody targeting the interleukin-5 receptor, in the treatment of acute eosinophilic exacerbations of asthma and COPD.

Three groups were compared: benralizumab alone, benralizumab combined with prednisolone, and prednisolone alone (standard treatment).

The results showed that benralizumab, with or without prednisolone, significantly reduced therapeutic failures over 90 days, improved symptoms within 28 days, and demonstrated a favorable safety profile compared to systemic corticosteroids alone. The initial treatment response rate was the same as OCS and thus Benralizumab should not be considered as a treatment to resolve the initial symptoms, but can be used in place of OCS in those with an eosinophilic phenotype at exacerbation.



The study reinforces the potential of benralizumab as a more effective and safer approach to treat acute exacerbations in patients with eosinophilic inflammation, promoting a personalized treatment model based on inflammatory endotypes.

However, further studies are needed to incorporate biologics into the emergency treatment of acute asthma and COPD exacerbations.⁴⁰

Criteria for Hospital Admission vs. Medical Discharge

The decision to admit a patient or discharge from the emergency department depends on the response to initial treatment and the assessment of future deterioration risk.^{41,42}

● Post-Treatment Pulmonary Function:

Peak Expiratory Flow (PEF) or Forced Expiratory Volume in 1 second (FEV₁) measured 1 hour after treatment is a crucial factor:¹

- If PEF/FEV₁ remains < 40% of predicted or the patient's personal best value: admission indicated;
- If PEF/FEV₁ is > 60–70% of predicted or personal best: consider medical discharge for patients with sustained clinical improvement, maintaining clinical and hemodynamic stability, and adequate support network;
- If PEF/FEV₁ is between 40–60%: individualized decision weighing risk factors.

● Risk factors that increase the chance of admission:^{31, 43}

- Female sex, advanced age, and non-white race;
- High use of SABA (>8 puffs) in the previous 24 hours;
- Severity of initial presentation (e.g., significant hypoxemia, use of accessory muscles);
- History of previous severe exacerbations, especially requiring intubation;
- Unscheduled emergency visits or urgent consultations for asthma.



Discharge Planning and Outpatient Follow-up

Careful discharge planning is essential for all patients treated in the emergency department for asthma exacerbations—even those discharged directly from the emergency service—to reduce the risk of recurrence.

● Maintenance Therapy:

- Ensure the patient has a prescription for continuous maintenance therapy containing an inhaled corticosteroid (ICS). This may mean starting treatment or temporarily increasing the dose for 2–4 weeks after the exacerbation.⁴⁴
- The Maintenance and Reliever Therapy (MART) strategy, using a combination of ICS-formoterol, is preferred in post-exacerbation follow-up as it helps control inflammation and provides rapid relief.⁴⁵

● **Action Plan:** Provide or review a written asthma action plan. This plan should guide the patient on how to monitor symptoms and peak expiratory flow (PEF, if applicable), adjust medication, and know when to seek medical help.

● Inhaler Technique:

Check and correct inhaler technique as necessary. Incorrect use is a common cause of poor asthma control.

● Follow-up After Discharge:¹

Arrange outpatient follow-up with the attending physician or specialist within a short period—ideally 1 to 7 days for adults and 1 to 2 days for children.

● Optimization of Long-term Treatment:

The goal of follow-up is to review and optimize maintenance treatment to prevent future exacerbations and minimize the need for oral corticosteroids (OCS). It is crucial to recognize the cumulative risks associated with OCS use, even in short and intermittent courses.





Conclusion

Identify risk factors in outpatient setting is important to prevent exacerbation and have to be part of all of the patient care.

Effective management of asthma exacerbation in the emergency department is a fundamental step in patient care but represents only the beginning of a continuous process. Initial intervention must be rapid and focused, prioritizing the use of inhaled bronchodilators and early systemic corticosteroids to reverse bronchial obstruction and correct hypoxemia. In refractory cases, other therapeutic strategies should be considered depending on the severity of the condition.

Careful and frequent reassessment of clinical and functional response—especially through monitoring SpO₂ and pulmonary function (PEF/FEV₁) after the first hour of treatment—is essential to determine the patient's trajectory and guide decisions regarding hospital admission or safe discharge. The decision to admit or discharge should consider not only objective parameters but also the patient's clinical history, risk factors, and sustainability of improvement.

Crucially, discharge from the emergency department does not conclude the care episode. A robust discharge plan is mandatory for all patients. This plan includes initiating (or optimizing) maintenance therapy with inhaled corticosteroids, verifying inhaler technique, and scheduling early outpatient follow-up (ideally within 1–7 days).

In summary, asthma management in the emergency setting begins with acute stabilization and extends to effective care transition planning and outpatient follow-up. The ultimate goal is not only to resolve the current crisis but also to optimize long-term disease control, empower patient self-management, prevent future exacerbations, and minimize risks associated with repeated systemic corticosteroid use. Integration between emergency care and outpatient follow-up is key to improving outcomes in patients with asthma.

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