Abstract. – This article describes the management of acute asthma exacerbation in the Emergency Department (ED). An asthma exacerbation can be defined as clinical worsening of disease or an asymptomatic decrease in peak flows. Acute exacerbations of asthma may represent reactions to airway irritants or failures of chronic treatment. Hospitalizations and ED visits account for a large proportion of the health-care cost burden of asthma. The assessment of an asthma exacerbation constitutes a process with two different dimensions: to determine the severity of attack, and to evaluate the response to treatment. The principal goals of managing an asthma acute exacerbation may be summarized as maintenance of adequate arterial oxygen saturation with supplemental oxygen, relief of airflow obstruction with repetitive administration of short acting beta-2 agonists (SABA), and treatment of airway inflammation with systemic corticosteroids (CS) to prevent future relapses. SABA, oxygen, and CS form the basis of management of acute asthma exacerbation but a role is emerging for anticholinergics.

Key Words: Asthma, Short acting β-2 agonists, Corticosteroids, Antileucotrienes, Theophylline.

Introduction

Asthma is an important healthcare problem worldwide. The overall prevalence of asthma in adults and children varies between countries, with estimates of 7% in France and Germany, 11% in the USA and 15-18% in the United Kingdom. Acute exacerbations occur as part of the natural history of the disease due to airways irritants and treatment failure. A substantial proportion of direct asthma costs results from the cost of treating acute asthma exacerbations. Acute asthma is also responsible for a significant amount of time off work, lost productivity and, in children, time off school. Acute asthma is one of the most frequent reasons for attendance at the Emergency Department (ED). Approximately 10% to 20% percent of patients who present to the ED will require admission to the hospital, and this rate varies depending on factors such as disease severity, the treatments received, and setting. The principal goals of managing an asthma acute exacerbation are the prompt recognition and the rapid reversal of the airflow obstruction to avert relapses and future episodes. Oxygen, short acting beta-2 agonists (SABA), and systemic corticosteroids (CS) form the basis of management of acute asthma exacerbation, but a role is emerging for anticholinergics and magnesium sulfate.

The management of such seriously ill patients requiring ventilatory support is beyond the scope of this article. Despite International Guidelines recommending appropriate therapy for acute asthma attacks, they are often poorly managed.

Acute Exacerbation of Asthma

There is no universally accepted definition of acute asthma exacerbation, and studies have applied inconsistent symptomatic and functional criteria. For practical purposes, an acute exacerbation can be generally defined as an acute or subacute episode of progressively worsening shortness of breath, cough, wheezing, and chest tightness or some combination of these symptoms. Exacerbations are characterized by decreases in expiratory airflow that can be documented and quantified by a simple measurement of lung function (forced expiratory volume in 1 second [FEV1] or peak expiratory flow rate [PEFR]). Lung function measures are more objective indicators of severity than the signs and the symptoms. The severity of asthma exacerbations ranges from mild to life-
threatening, as shown in Table I. Acute exacerbations may occur suddenly or progress over hours, days, or weeks. Slow-onset episodes are more likely to be triggered by a viral upper respiratory tract infection. They usually respond to treatment slowly and more likely to result in the hospital admission. Sudden-onset episodes typically are triggered by exposure to allergens, exercise, or psychosocial stress. These attacks often respond rapidly to the treatment and are less likely than slow-onset exacerbations to involve the hospital admission.

Clinical assessment

Acute exacerbation of asthma is a medical emergency that must be diagnosed and treated urgently. The assessment of an asthma exacerbation constitutes a process with two different dimensions: a static assessment to determine the severity of attack and a dynamic assessment to evaluate the response to the treatment. The history elicited should include duration of symptoms, possible triggers, progression of symptoms, nocturnal symptoms, regular medications and treatment already taken for the present exacerbation. Consideration must be given to adherence to the treatment regimen or poor control of the chronic asthma. Relevant points in the history are timing of last exacerbations or prednisone/prednisolone burst, recent ED visits or hospitalizations for asthma, seasonal pattern of exacerbations, and severity of previous exacerbations (e.g. intensive care unit [ICU] and intubation with mechanical ventilation). The physical examination should note overall degree of respiratory distress. The use of accessory muscles has received attention as an indicator of severe obstruction, and the presence of sternocleidomastoid retractions or suprasternal retraction correlated with impairment in lung function. Respiratory rate (RR) >30 breaths/min, tachycardia >120 beats/min or pulsus paradoxus (PP) >12 mmHg have been described as vital signs of acute severe asthma. Objective measures to confirm the presence and degree of airflow obstruction include PEFR and FEV₁ (Table I). Measurement of the change in PEFR or FEV₁ over time may be one of the best ways to assess the patients with an acute asthma and predict the need for the hospital admission. PEFR variation over baseline >50 L/min measured at 30 minutes after the beginning of treatment, are predictors of good outcome. Pulse oximetry to check arterial oxygen saturation is critical for optimal management. Patients showing fatigue, hypoxia, and PEFR or FEV₁ <50% predicted or personal best despite treatment should have an arterial blood gas (ABG) checked. Chest radiography plays only a small role in the assessment and management of patients with acute asthma. It is indicated in patients who present with signs or symptoms of pneumothorax, in patients with clinical findings suggestive of pneumonia, or in an asthmatic patient who after 6 to 12 h of intensive treatment does not respond to therapy.

Treatment

When managing an acute exacerbation, the goals are to maintain an adequate arterial oxygenation, relieve the airflow obstruction, reduce the airway inflammation, and prevent the future relapse. Primary therapies include oxygen administration, SABA, and intravenous (IV) or oral corticosteroids. Treatment to be tailored to the severity of the exacerbations (Table I). In summary, symptoms and signs guide the treatment decisions, but the repeated measurement of PEFR or FEV₁ compared to baseline joined with continuous monitoring of O₂ saturation is critical to evaluate the severity of airflow obstruction, the adequacy of gas exchange and the response to the treatment.

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>Initial PEFR (or FEV₁)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Dyspnea only with activity</td>
</tr>
<tr>
<td>Moderate</td>
<td>Dyspnea interferes with or limits usual activity</td>
</tr>
<tr>
<td>Severe</td>
<td>Dyspnea at rest, interferes with conversation</td>
</tr>
<tr>
<td>Subset: life threatening</td>
<td>Too dyspneic to speak; perspiring</td>
</tr>
</tbody>
</table>
**Treatment for acute asthma in the Emergency Department: practical aspects**

**Table II. Treatment acute exacerbations of asthma**

<table>
<thead>
<tr>
<th>FEV₁ or PEFR &gt; 40% (mild to moderate)</th>
<th>FEV₁ or PEFR &lt; 40% (severe)</th>
<th>Impending or Actual Respiratory Arrest</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Inhaled short-acting β-2 agonists (SABA) by metered-dose inhaler (MDI) plus valved or nebulizer, up to three doses in first hour</td>
<td></td>
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</tr>
<tr>
<td>- Oxygen to achieve O₂ saturation &gt; 90%</td>
<td></td>
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<tr>
<td>- Oral systemic corticosteroids if no immediate response</td>
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<tr>
<td>- Inhaled short-acting β-2 agonists (SABA) and ipratropium bromide (IB) by metered-dose inhaler (MDI) plus valved or nebulizer every 20 minutes or continuously for 1 hour</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Oxygen to achieve O₂ saturation &gt; 90%</td>
<td></td>
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<tr>
<td>- Oral systemic corticosteroids</td>
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<td></td>
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<tr>
<td>- Intravenous corticosteroids</td>
<td></td>
<td></td>
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<tr>
<td>- Consider adjunct therapies</td>
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</table>

**Oxygen**

Oxygen is recommended in patients with hypoxia to maintain O₂ saturation >90% (>95% in pregnant women or in patients who have coexistent heart disease)⁶. Some patients who have normal pulse oximetry on first presentation develop hypoxemia after bronchodilator therapy because of ventilation-perfusion mismatch⁶. Usually, mild hypoxemia can be corrected by 2-4 L/min of oxygen via a nasal cannula or mask. There is evidence that hyperoxia may be harmful for some patients. Recently studies showed that patients received 100% oxygen had an increase in PaCO₂, particularly those patients with PaCO₂ before oxygen treatment ≥40 mmHg⁹.¹⁰. These data emphasize that efforts should be made to confirm the presence of hypoxia by pulse oximetry before administering oxygen.

**Short-acting β-2 agonists (SABA)**

Short-acting, inhaled, selective β-2 agonists are the drugs of choice to treat acute asthma. Their main action is to mediate airway smooth muscle relaxation by binding the β-2 adrenergic receptors, thus relieving bronchospasm. The most commonly used agent in this class of drugs is salbutamol. Other used drugs are terbutaline and fenoterol. The usual onset of action for SABA is within 5 minutes, and the duration of action in 4-6 hours. The inhaled route has a fast onset, fewer adverse effects, and is more effective than systemic route. More rapid onset and profound bronchodilation with fewer side effects and less time in the ED can be achieved when sufficient doses of β-agonists are administered using MDI plus valved than when conventional doses are administered with a jet nebulizer¹¹. Only 6-8 puffs (540-720 µg) of salbutamol from the MDI may be needed to achieve an effect equivalent to 2.5 mg of nebulized salbutamol⁶. Available evidence does not support the use of IV β-2 agonists in the treatment of patients with severe acute asthma¹².

**Anticholinergics**

The quaternary ammonium derivative of atropine, ipratropium bromide (IB), is a nonspecific muscarinic receptor-blocking agent that has been used to treat bronchospasm in acute asthma. It has a marginal effectiveness in acute asthma when used by itself⁶.¹³. A meta-analysis of 10 adult studies that used single doses of IB added to SABA showed that IB significantly improved FEV₁ and PEFR above those seen for patients who received SABA with placebo¹⁴. As a result, the addition of multiple doses of IB to SABA seems indicates a first line therapy in adult patients with severe exacerbations of asthma. Doses of four puffs (80 µg) every 10 minutes delivered by MDI and large volume spacer, or 500 µg per dose every 20 minutes in nebulized form are quite effective².

**Corticosteroids**

Systemic corticosteroids have an integral role in the treatment of acute exacerbations. US National Institutes of Health (NIH) guidelines recommend these agents for every level of asthma exacerbations (Table II). In moderate to severe exacerbations, they should be initiated immediately after recognition of an acute attack and assessment of lung function⁵. These agents are not bronchodilators but are extremely effective in reducing airway inflammation present in virtually all asthmatics. Early use of systemic steroids is associated with lower hospital admission rates¹⁵.
According to a 12-study meta-analysis of the management of acute exacerbations in both adults and children, use of intravenous (IV), intramuscular (IM), or oral corticosteroids within 1 hour of arrival at the ED reduced admission rates by 60%. No clear evidence supports any one route of systemic corticosteroid administration over another. Therefore, the mode of delivery depends primarily on episode severity and patient-specific factors. Oral corticosteroids are recommended as initial therapy in patients with mild airflow obstruction (FEV₁ or PEFR >50%) in patients who do not respond immediately and completely to inhaled SABA and oxygen, or if the patients recently took an oral corticosteroid. IV corticosteroids are recommended as initial therapy in impending or actual respiratory arrest, on intensive care unit (ICU) admission, and as an alternative to oral steroids on hospital admission. The IV route may also be preferred in severely dyspeptic patients. However, in those who are vomiting, unable to swallow, or otherwise unable to consume oral medication the IV route is clearly the only possible one. The dosing of systemic corticosteroids is somewhat controversial. Some physician may prefer to initiate treatment with higher dosages in severe asthma to gain better control over the inflammatory process. The high end of the dosage range used effectively in clinical practice for acute asthma appears to be 125 mg IV methylprednisolone every 6 hours. Inhaled corticosteroids (ICS) are best used for long-term control of asthma but few studies have compared the efficacy of ICS to systemic CS. One randomized, double blind study that treated severe asthmatics experiencing an acute exacerbation with oral CS or ICS found oral CS to be superior to ICS in reducing hospital admissions. ICS compared with placebo reduced hospital admission rates in patients with acute asthma. Corticosteroids are associated with a number of serious adverse effects, particularly when used in high doses for prolonged periods. These effects include the hypothalamic-pituitary-adrenal axis suppression, osteoporosis, cataract formation, dermal thinning, myopathy, hypertension, diabetes mellitus/hyperglycemia, infection, acute psychosis, inappropriate euphoria, and growth suppression in children.

**Magnesium Sulfate**

Magnesium sulfate causes bronchodilation believed to be mediated via inhibition of the calcium channels in the airway smooth muscle cells. A large multicenter study demonstrated that IV magnesium sulfate only improves pulmonary function when administered as an adjunct to standard therapy in a very select subgroup of patients (FEV₁ < 20% of predicted). In general, this drugs is safe and inexpensive in the usual clinical dose of 1.2 to 2 g IV over 20 minutes.

**Heliox**

Heliox is a mixture of helium and oxygen (60:40, 70:30 or 80:20), which is lighter and less dense than oxygen. Studies have found varying results with regard to its utility in acute asthma, with a systematic review concluding that heliox treatment does not have a role in the initial treatment of patients with severe or moderate asthma. Additionally, research using heliox mixtures has demonstrated a greater percentage of lung particle retention and a large delivery of salbutamol from both MDI and jet-nebulizers. This suggests that one of the beneficial effects of heliox use may include improved deposition of aerosolized bronchodilators.

**Antileukotrienes**

The antileukotrienes or leukotriene receptor antagonists (LTRAs) are a relatively new class of drugs for the treatment of asthma. There is a substantial body of evidence for their benefit in the management of chronic asthma in both adults and children, and particularly in specific types of asthma such as exercise-induced and aspirin-sensitive asthma. Few studies are evaluating the effect of an LTRA in acute asthma and they are limited by the lack of clinically relevant outcomes such as hospitalization and relapse rates.
Conclusion

Early treatment of asthma exacerbations is the best strategy for management. Initial assessment should include a brief history, brief physical examination, and, for most patients, objective measures of lung function. FEV₁ or PEFR to provide important information about the level of airflow obstruction both initially (Table I) and in response to treatment (Table III). The principal goals for treating asthma exacerbations are: (1) Correction of significant hypoxemia, in moderate or severe exacerbations, by administering supplemental oxygen; (2) Rapid reversal of airflow obstruction by repetitive or continuous administration of a SABA and, early in the course of treatment, administration of CS to patients who have moderate or severe exacerbations or to patients who fail to respond promptly and completely to SABA treatment; (3) Reduction of the likelihood of relapse of the exacerbation or future recurrence of severe airflow obstruction by intensifying therapy. The response to initial treatment in the ED is a better predictor of the need for hospitalization (Table III) than is the severity of an exacerbation on presentation.

References


16) Rowe BH, Spooner CH, Ducharme FM, Bretzaff JA, Bota GW. Early emergency department


