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[EXCERPTS]

Major Recommendations

Component 4: Manage Asthma Exacerbations

Key Points

- Exacerbations of asthma (asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, or chest tightness, or some combination of these symptoms.
- Exacerbations are characterized by decreases in expiratory airflow that can be quantified and monitored by measurement of lung function (peak expiratory flow rate [PEF] or forced expiratory volume in one second [FEV_1]).
- The primary therapies for exacerbations include the repetitive administration of rapid-acting inhaled bronchodilators, the early introduction of systemic glucocorticosteroids, and oxygen supplementation.
- The aims of treatment are to relieve airflow obstruction and hypoxemia as quickly as possible, and to plan the prevention of future relapses.
- Severe exacerbations are potentially life threatening, and their treatment requires close supervision. Most patients with severe asthma exacerbations should be treated in an acute care facility. Patients at high risk of asthma-related death also require closer attention.
- Milder exacerbations, defined by a reduction in peak flow of less than 20%, nocturnal awakening, and increased use of short acting β2-agonists can usually be treated in a community setting.

Introduction

Exacerbations are characterized by decreases in expiratory airflow that can be quantified by measurement of lung function (PEF or FEV_1). The degree of symptoms may, however, be a more sensitive measure of the onset of an exacerbation because the increase in symptoms usually precedes the deterioration in peak flow rate.

Patients at high risk of asthma-related death require closer attention and should be encouraged to seek urgent care early in the course of their exacerbations. These patients include those:

- With a history of near-fatal asthma requiring intubation and mechanical ventilation
- Who have had a hospitalization or emergency care visit for asthma in the past year
- Who are currently using or have recently stopped using oral glucocorticosteroids
- Who are not currently using inhaled glucocorticosteroids
- Who are overdependent on rapid-acting inhaled β2-agonists, especially those who use more than one canister of salbutamol (or equivalent) monthly
- With a history of psychiatric disease or psychosocial problems, including the use of sedatives
- With a history of noncompliance with an asthma medication plan.

Management—Community Settings

Most patients with severe asthma exacerbations should be treated in an acute care facility (such as a hospital emergency department) where monitoring, including objective measurement of airflow obstruction, oxygen saturation, and cardiac function, is possible. Milder exacerbations, defined by a reduction in peak flow of less than 20%, nocturnal awakening, and increased use of short acting β2-agonists can usually be treated in a community setting.

Treatment

Bronchodilators

For mild to moderate exacerbations, repeated administration of rapid-acting inhaled β-agonists (2 to 4 puffs every 20 minutes for the first hour) is usually the best and most cost-effective method of achieving rapid reversal of airflow limitation. After the first hour, the dose of β-agonist required will depend on the severity of the exacerbation. Mild exacerbations respond to 2 to 4 puffs every 3 to 4 hours; moderate exacerbations will require 6 to 10 puffs every 1 or 2 hours. Treatment should also be titrated depending upon the individual patient's response, and if there is a lack of response or other concern about how the patient is responding, the patient should be referred to an acute care facility.

Bronchodilator therapy delivered via an MDI, ideally with a spacer, produces at least an equivalent improvement in lung function as the same dose delivered via nebulizer. No additional medication is necessary if the rapid-acting inhaled β-agonist produces a complete response (PEF returns to greater than 80% of predicted or personal best) and the response lasts for 3 to 4 hours.

Glucocorticosteroids

Oral glucocorticosteroids (0.5 to 1 mg of prednisolone/kg or equivalent during a 24-hour period) should be used to treat exacerbations, especially if they develop after instituting the other short-term treatment options recommended for loss of control (see "Stepping up treatment in response to loss of control" in Component 3 above and in the original guideline document).

If patients fail to respond to bronchodilator therapy, as indicated by persistent airflow obstruction, prompt transfer to an acute care setting is recommended, especially if they are in a high risk group.

Management—Acute Care Settings

Severe exacerbations of asthma are life-threatening medical emergencies, treatment of which is often most safely undertaken in an emergency department.

Assessment

The history should include severity and duration of symptoms, including exercise limitation and sleep disturbance; all current medications, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy; time of onset and cause of the present exacerbation; and risk factors for asthma-related death.

The physical examination should assess exacerbation severity by evaluating the patient's ability to complete a sentence, pulse rate, respiratory rate, use of accessory muscles, and other signs detailed in **Figure 4.4-2** in the original guideline document.

Functional assessments such as PEF or FEV_1 and arterial oxygen saturation measurements are strongly recommended as physical examination alone may not fully indicate the severity of the exacerbation, particularly the degree of hypoxemia.

Oxygen saturation should be closely monitored, preferably by pulse oximetry. Oxygen saturation in children should normally be greater than 95%, and oxygen saturation less than 92% is a good predictor of the need for hospitalization (**Evidence C**).

In adults a chest x-ray is not routinely required, but should be carried out if a complicating cardiopulmonary process is suspected, in patients requiring hospitalization, and in those not responding to treatment where a pneumothorax may be difficult to diagnose clinically. Similarly, in children routine chest x-rays are not recommended unless there are physical signs suggestive of parenchymal disease.

Although arterial blood gas measurements are not routinely required, they should be completed in patients with a PEF of 30% to 50% predicted, those who do not respond to initial treatment, or when there is concern regarding deterioration. The patient should continue on supplemental oxygen while the measurement is made. A partial pressure of oxygen in arterial blood (PaO_2) <60 mm Hg (8 kPa) and a normal or increased partial pressure of carbon dioxide in the arterial blood ($PaCO_2$) (especially >45 mm Hg, 6 kPa) indicates the presence of respiratory failure.

Treatment

<u>Oxygen</u>

To achieve arterial oxygen saturation of 90% (95% in children), oxygen should be administered by nasal cannulae, by mask, or rarely by head box in some infants.

Rapid-Acting Inhaled β2-Agonists

Rapid-acting inhaled β2-agonists should be administered at regular intervals (**Evidence A**). The most cost effective and efficient delivery is by meter dose inhaler and a spacer device.

A modestly greater bronchodilator effect has been shown with levalbuterol compared to racemic albuterol in both adults and children with an asthma exacerbation. In a large study of acute asthma in children, and in adults not previously treated with glucocorticosteroids, levalbuterol treatment resulted in lower hospitalization rates compared to racemic albuterol treatment, but in children the length of hospital stay was no different.

A reasonable approach to inhaled therapy in exacerbations would be the initial use of continuous therapy, followed by intermittent on-demand therapy for hospitalized patients.

Additional Bronchodilators

Ipratropium Bromide

A combination of nebulized β2-agonist with an anticholinergic (ipratropium bromide) may produce better bronchodilation than either drug alone (**Evidence B**) and should be administered before methylxanthines are considered. Combination β2-agonist/anticholinergic therapy is associated with lower hospitalization rates (**Evidence A**) and greater improvement in PEF and FEV_1 (**Evidence B**). Similar data have been reported in the pediatric literature (**Evidence A**). However, once children with asthma are hospitalized following intensive emergency department treatment, the addition of nebulized ipratropium bromide to nebulized β2-agonist and systemic glucocorticosteroids appears to confer no extra benefit.

Theophylline

In view of the effectiveness and relative safety of rapid-acting β2-agonists, theophylline has a minimal role in the management of acute asthma. Its use is associated with severe and potentially fatal side effects, particularly in those on long-term therapy with sustained-release theophylline, and their bronchodilator effect is less than that of β2-agonists.

Systemic Glucocorticosteroids

Systemic glucocorticosteroids speed resolution of exacerbations and should be utilized in the all but the mildest exacerbations (**Evidence A**), especially if:

- The initial rapid-acting inhaled β2-agonist therapy fails to achieve lasting improvement
- The exacerbation develops even though the patient was already taking oral glucocorticosteroids
- Previous exacerbations required oral glucocorticosteroids.

Oral glucocorticosteroids are usually as effective as those administered intravenously and are preferred because this route of delivery is less invasive and less expensive.

Daily doses of systemic glucocorticosteroids equivalent to 60-80 mg methylprednisolone as a single dose, or 300-400 mg hydrocortisone in divided doses, are adequate for hospitalized patients, and 40 mg methylprednisolone or 200 mg hydrocortisone is probably adequate in most cases (**Evidence B**). A 7-day course in adults has been found to be as effective as a 14-day course, and a 3- to 5-day course in children is usually considered appropriate (**Evidence B**). Current evidence suggests that there is no benefit to tapering the dose of oral glucocorticosteroids, either in the short-term or over several weeks (**Evidence B**).

Inhaled Glucocorticosteroids

Inhaled glucocorticosteroids are effective as part of therapy for asthma exacerbations. In one study, the combination of high-dose inhaled glucocorticosteroids and salbutamol in acute asthma provided greater bronchodilation than salbutamol alone (**Evidence B**), and conferred greater benefit than the addition of systemic glucocorticosteroids across all parameters, including hospitalizations, especially for patients with more severe attacks.

Patients discharged from the emergency department on prednisone and inhaled budesonide have a lower rate of relapse than those on prednisone alone (**Evidence B**). A high dose of inhaled glucocorticosteroid (2.4 mg budesonide daily in four divided doses) achieves a relapse rate similar to 40 mg oral prednisone daily (**Evidence A**).

Magnesium

Intravenous magnesium sulphate (usually given as a single 2 g infusion over 20 minutes) is not recommended for routine use in asthma exacerbations, but can help reduce hospital admission rates in certain patients, including adults with FEV_1 25%-30% predicted at presentation, adults and children who fail to respond to initial treatment, and children whose FEV_1 fails to improve above 60% predicted after 1 hour of care (**Evidence A**). Nebulized salbutamol administered in isotonic magnesium sulphate provides greater benefit than if it is delivered in normal saline (**Evidence A**).

Leukotriene Modifiers

There are little data to suggest a role for leukotriene modifiers in acute asthma.

Sedatives

Sedation should be strictly avoided during exacerbations of asthma because of the respiratory depressant effect of anxiolytic and hypnotic drugs. An association between the use of these drugs and avoidable asthma deaths has been demonstrated.

Criteria for Discharge from the Emergency Department vs. Hospitalization

Patients with a pre-treatment FEV_1 or PEF <25% predicted or personal best, or those with a post-treatment FEV_1 or PEF <40% predicted or personal best, usually require hospitalization. Patients with post-treatment lung function of 40%-60% predicted may be discharged, provided that adequate follow-up is available in the community and compliance is assured. Patients with post-treatment lung function ≥60% predicted can be discharged.

For patients discharged from the emergency department:

- At a minimum, a 7-day course of oral glucocorticosteroids for adults and a shorter course (3 to 5 days) for children should be prescribed, along with continuation of bronchodilator therapy.
- The bronchodilator can be used on an as-needed basis, based on both symptomatic and objective improvement, until the patient returns to his or her pre-exacerbation use of rapid-acting inhaled β2-agonists.
- Ipratropium bromide is unlikely to provide additional benefit beyond the acute phase and may be quickly discontinued.
- Patients should initiate or continue inhaled glucocorticosteroids.
- The patient's inhaler technique and use of peak flow meter to monitor therapy at home should be reviewed. Patients discharged from the emergency department with a peak flow meter and action plan have a better response than patients discharged without these resources.
- The factors that precipitated the exacerbation should be identified and strategies for their future avoidance implemented.
- The patient's response to the exacerbation should be evaluated. The action plan should be reviewed and written guidance provided.
- Use of controller therapy during the exacerbation should be reviewed: whether this therapy was increased promptly, by how much, and, if appropriate, why oral glucocorticosteroids were not added. Consider providing a short course of oral glucocorticosteroids to be on hand for subsequent exacerbations.
- The patient or family should be instructed to contact the primary health care professional or asthma specialist within 24 hours of discharge. Prospective data indicate that patients discharged from the emergency department for follow-up with specialist care do better than patients returned to routine care.

Referral to an asthma specialist should be considered for hospitalized patients.

Definitions: Description of Levels of Evidence [available online]

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