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Management of Acute Asthma in Adults in 2020

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Asthma is a chronic airway disease that typically presents with episodes of severe respiratory distress known as *exacerbations*. Asthma exacerbations result in 1.8 million hospitalizations per year, with an estimated mortality rate of 13.3 deaths per million per year in US adults.[1] This article summarizes evidence regarding management for acute asthma including (1) inhaled corticosteroids (ICSs), (2) azithromycin and magnesium, (3) nebulized bronchodilators vs metered-dose inhalers, and (4) innovative therapies undergoing investigation for treatment of adults with acute asthma exacerbations. Randomized clinical trials of acute asthma management published in major medical journals in the past 7 years were reviewed.

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Exacerbations of Asthma

An asthma exacerbation is an acute or subacute episode of increased dyspnea, cough, chest tightness, or wheezing associated with decreased lung function (decreased forced expiratory volume or peak expiratory flow rate compared with baseline parameters).[2] In general, the goals of treatment for adults with an acute asthma exacerbation include prompt identification of the exacerbation, determination of severity, initiation of appropriate therapy, and referral to an acute care facility if necessary (**Table**).[2,4,5]

Role of ICSs

A 2018 randomized trial[6] examined whether a temporary 4-fold increase in dose of ICSs (ie, from 80 µg of budesonide to 320 µg per day) improved outcomes in patients with an acute asthma exacerbation. A total of 1922 outpatients with asthma receiving chronic ICSs were randomized to an intervention group, in which patients were instructed to temporarily increase their ICS dose by 4-fold for up to 14 days at the time of deterioration in lung function, or a control group (n = 965), in which no changes in ICS dose were made. Participants in the intervention group previously receiving maintenance therapy with a combined long-acting β_2-agonist and ICS were prescribed an additional ICS inhaler to reach the quadrupled dose, whereas those receiving an ICS alone either increased the number of inhalations or were prescribed an additional metered-dose inhaler (MDI) with a higher steroid concentration. There was a higher frequency of oral candidiasis (19 events) in the intervention group vs the control group (7 events), with no increase in pneumonia frequency.[6] The intervention group reported fewer severe asthma exacerbations (45% vs 52%) and decreased oral corticosteroids use (33% vs 40%) than the control group.[6] Thus, self-management action plans that incorporate a temporary quadrupling of ICS are effective approaches to reduce severe asthma exacerbations and systemic steroids.

Role of Macrolides

The addition of azithromycin to standard care to manage an acute asthma exacerbation was evaluated in a double-blind, placebo-controlled trial.[7] Patients presenting within the first 24 hours of acute asthma exacerbations were randomized to receive standard care plus 500 mg of azithromycin (n = 97) or placebo (n = 102) for 3 days.[7] Azithromycin did not improve symptoms compared with placebo.[7]

Table. Management of Acute Asthma Exacerbations in Adults and Appropriate Care Venues

Exacerbation Severity	Appropriate Care Venues	Potential Treatment Options
Mild (PEFR >75%) to moderate (PEFR of 50%-75%)	Outpatient management	Increased frequency of SABA or SAMA use Temporarily quadrupling ICS Systemic corticosteroids if no response to initial therapy[a]
Severe (PEFR of 33%-50%)	Acute care facility (eg, emergency department, urgent care) Inpatient hospital admission if no improvement with initial therapies or 1 or more of the following: pregnancy, respiratory rate >25/min, heart rate >110/min, inability to speak in full sentences in 1 breath, concerns about adherence, or psychosocial issues or physical or mental disabilities	Increased frequency of SABA or SAMA use Systemic corticosteroids[a] Consider a single dose of intravenous magnesium sulfate[b]
Life threatening (PEFR <33%)	Intensive care unit for patients with 1 or more of the following: persistent or worsening hypoxia, hypercapnia, altered level of consciousness, respiratory arrest or respiratory acidosis, hypotension, or cyanosis	Increased frequency of SABA or SAMA use Systemic corticosteroids[a] Noninvasive ventilation
Near fatal	Intensive care unit Patients requiring intubation and mechanical ventilation with or without hypercapnia require high-level intensive care unit care	Increased frequency of SABA or SAMA use Systemic corticosteroids[a] Noninvasive ventilation or intubation and mechanical ventilation if no response to noninvasive ventilation

Abbreviations: ICS, inhaled corticosteroids; PEFR, peak expiratory flow rate; SABA, short-acting β_2-agonist; SAMA, short-acting muscarinic antagonists.

[a] 1 mg/kg of prednisolone per day or equivalent (maximum of 50 mg per day) for 5 to 7 days; oral is preferred over intravenous.[1]

[b] 2 g intravenously over 15 to 30 minutes.[3]

Therefore, there is no benefit of adding azithromycin during an acute asthma exacerbation.

However, azithromycin may be useful for preventing an acute asthma exacerbation. In a trial by Gibson et al,[3] 420 patients with symptomatic asthma were randomized to receive standard care plus azithromycin (500 mg 3 times per week) or placebo for 48 weeks. Participants randomized to receive azithromycin had 1.07 asthma exacerbations per person per year vs 1.86 exacerbations per person per year in the control group ($P < .001$).[3] Although antibiotics should typically be reserved for management of acute asthma exacerbations with strong evidence of bacterial infections, these results suggest some benefit, although the mechanism of this benefit is incompletely understood.

Emergency Care Management of Severe Asthma Exacerbations

Patients experiencing an acute severe or life-threatening asthma exacerbation should be referred to the emergency department.[2] Guideline-based emergency evaluation and management of severe asthma exacerbations in adults consists of supplemental oxygen to maintain pulse oximetry at measured oxygen saturation levels of 93% to 95%,[2] short-acting β_2-agonists (SABAs) and short-acting muscarinic antagonists (SAMAs), and systemic corticosteroids. The method of SABA delivery does not appear to affect outcomes. A Cochrane review reported that among patients presenting with a severe exacerbation, there was no association of treatment with SABA via a nebulizer vs treatment via MDI and a spacer for the outcome of hospitalization rates after the emergency department.[4] However, the combination of SABA and SAMA bronchodilators was associated with a lower hospitalization rate in adults presenting with a severe asthma exacerbation compared with SABA alone.[4] Chest imaging should be reserved for patients in whom pulmonary consolidation or pneumothorax is suspected.

The role of magnesium sulfate (intravenous or inhaled) as an adjunctive treatment to manage asthma exacerbations has been controversial. Goodacre et al[8] conducted the largest clinical trial to date on the effect of magnesium sulfate on hospitalization rates in individuals with severe asthma exacerbations. This multicenter double-blind trial randomized 1109 patients to receive nebulized magnesium sulfate ($MgSO_4$), intravenous $MgSO_4$, or placebo in addition to standard care. Compared with placebo, intravenous $MgSO_4$ was associated with a nonsignificant decrease of hospital admissions (odds ratio, 0.73 [95% CI, 0.51-1.04]). A subsequent Cochrane meta-analysis[5] that included the Goodacre et al[8] trial and 10 others estimated that intravenous $MgSO_4$ was associated with reduced hospital admissions, with an odds ratio of 0.75 (95% CI, 0.60-0.92), supporting the use of this treatment in the management of severe acute exacerbations in the emergency care setting. Another Cochrane meta-analysis[9] that also incorporated the Goodacre et al[8] trial assessed inhaled $MgSO_4$ in individuals with acute asthma and concluded that, while current evidence precludes certainty, inhaled $MgSO_4$ is unlikely to be associated with benefit beyond current standard treatments.

Potential Future Therapies: Biologic Agents

Within the past decade, biologic therapies, composed of highly specific antibodies directed against critical molecules in asthma pathogenesis, have been increasingly used to manage chronic asthma, but are currently not used to manage acute exacerbations. A multicenter, randomized, double-blind, placebo-controlled trial examined outcomes after administration of benralizumab during an asthma exacerbation in the emergency department.[10] A total of 110 patients presenting with an acute asthma exacerbation were randomized to receive 0.3 mg/kg of benralizumab, 0.5 mg/kg of benralizumab, or placebo. All groups received a course of oral prednisone and an ICS. Compared with placebo, a single dose of benralizumab at either dosage was associated with reduced rates of asthma exacerbations (1.82 vs 3.59) and hospitalizations (0.65 vs 1.62) over the following 12 weeks.[10] Although these results are promising, future studies are required to confirm these results before routine implementation of biologic agent therapy can be recommended for acute asthma exacerbations.

Conclusions

Appropriate management of asthma exacerbations consists of acutely restoring lung function and preventing disease progression. Essential strategies include prompt aerosol administration of β_2-agonists, muscarinic antagonists, systemic corticosteroids, and oxygen as necessary.

ARTICLE INFORMATION

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