

Asthma Self-management

It's Not One Size Fits All



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KEYWORDS

- Asthma • Asthma exacerbation • Asthma self-management
- Asthma home management

KEY POINTS

- Asthma exacerbations are a significant cause of health care use.
- Home self-management of asthma exacerbations is possible and there are many treatment options available.
- An asthma home self-management therapy plan should be personalized for each patient.
- Continued research into best practices for home asthma management is needed.

INTRODUCTION

Asthma is one of the most common chronic health conditions, with an estimated 339 million people affected worldwide according to the Global Asthma Network.¹ In 2016 in the United States, 8.3% of both children and adults were affected. Asthma was in the top 20 leading primary diagnoses for emergency department visits with a total of 1.7 million visits reported in 2015.²

Asthma accounted for 3518 deaths in 2016 in the United States alone.³ According to the Centers for Disease Control and Prevention (CDC), 46.9% of people with asthma have reported 1 or more asthma exacerbations in the last year.³ Definitions for asthma exacerbations can vary but typically are characterized by an increase in asthma symptoms, increase in use of reliever medications, or a decrease in measured expiratory airflow.^{4–6} Exacerbations can result in acute care visits but some can be successfully managed at home. Self-management interventions have been associated with decreased health care use and improved quality-of-life outcomes.⁷ A written asthma action plan is essential for asthma self-management in exacerbations.^{5,7} This article focuses on multiple medication options available for self-management of asthma exacerbations in the home setting (**Fig. 1**).

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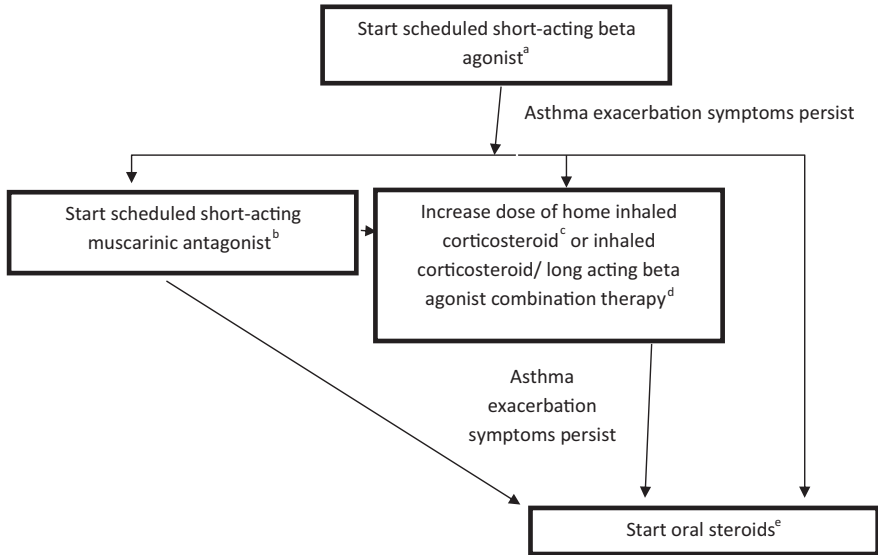


Fig. 1. Home management of asthma exacerbations. ^a Dosing varies by age. Consider 2 to 8 puffs with metered dose inhaler (MDI) with spacer or nebulizer treatment every 3 to 4 hours. ^b Dosing varies with age. Consider 2 puffs with MDI with spacer or nebulizer treatment every 6 hours. ^c Increase daily dose by 2 to 4 times. ^d Maximum dose suggested of 72 µg of formoterol in a day. ^e Dosing varies by age. In adults consider 1 mg/kg/d with maximum of 50 to 60 mg/d for 5 to 7 days. In children consider 1 to 2 mg/kg/d with maximum dosage of 40 to 60 mg/d for 3 to 5 days. There is no defined role for azithromycin, long-acting muscarinic antagonist, or leukotrienes in acute asthma exacerbations.

NONPHARMACOLOGIC INTERVENTIONS

Common sense and current Expert Panel Report 3 (EPR-3) guidelines suggest that removal of allergens and irritants should help in preventing asthma exacerbations.⁴ This advice includes controlling common indoor allergens such as dust mites and indoor animal dander exposure, mold removal, and decreasing secondhand smoke exposure. Suggestions for allergen control include air purification, carpet removal, vacuuming using a high-efficiency particulate air-filtered machine, and use of dust mite repellent mattress covers or even acaricides to kill dust mites. In addition, removal of stuffed animals and house pets from the bedroom may help prevent allergen-related exacerbations.⁴ However, a recent review of these interventions showed that although quality of life improved with a single intervention, it did not alter asthma-related health care use or lung function testing.⁸ It is yet to be studied whether specific intervention combinations have more of an effect than others. Aside from the aforementioned exposures, β-blocker therapy and nonsteroidal antiinflammatory drug (NSAID) use should also be assessed to evaluate for nontraditional triggers and drug-drug interactions.⁴

It is well known that secondhand smoke exposure can lead to asthma exacerbations in both children and adults.⁹ There are strong recommendations to avoid secondhand smoke exposure in the home and in the car, and to avoid personal use of cigarettes.⁴ Not much is known about long-term exposure to electronic nicotine delivery systems (vaping). Early research suggests this environmental irritant may also be a trigger to asthma exacerbations and should be avoided, similar to conventional cigarette smoke.¹⁰

CLASSIC PHARMACOLOGIC INTERVENTIONS FOR ASTHMA EXACERBATION

Short-Acting Beta Agonist

Short-acting beta agonists (SABAs) (albuterol, salbutamol, and levalbuterol) work by binding to the beta-2 adrenergic receptors on small airway smooth muscle, leading to muscle relaxation and bronchodilation. Guidelines recommend early initiation of this therapy in asthma exacerbations.^{4,5}

SABAs can be administered through oral inhalation in multiple ways, including through metered-dose inhaler (MDI) with spacer, dry powder inhaler, and a nebulizer. In an MDI format, albuterol is 90 µg per puff or 2.5 mg/3 mL nebulizer ampoule. Smaller-dose nebulizer dosing is available at 1.25 mg/3 mL.⁴ Salbutamol is 100 µg per puff and similarly 2.5 mg/3 mL nebulizer ampoule. Levalbuterol is 45 µg per puff and 1.25 µg/3 mL ampoule generally.⁴ Dosing in an exacerbation is distributed by age. Global Initiative for Asthma (GINA) guideline recommendations for patients 5 years of age and younger are to use 2 puffs of SABA with a spacer up to every 3 to 4 hours. For patients 6 years of age and older, this can be increased to 4 to 8 puffs.⁵ EPR-3 guidelines recommend up to 2 treatments spaced 20 minutes apart of 2 to 6 puffs of SABA through an MDI or nebulized treatment. The SABA treatment is then recommended every 3 to 4 hours for 24 to 48 hours.⁴ This increase in SABA use is also generally accompanied by other increases in therapy described further in this article.

There are multiple side effects to consider with SABAs but the benefits far outweigh the potential side effects because of their effectiveness with bronchodilation. The most common side effects include tachycardia and tremors. Other possible side effects include headache, hypokalemia, and hyperglycemia. These side effects are more common when albuterol is dosed more frequently than every 4 hours, such as in the emergency room or during hospitalizations.⁴

A major drug interaction to consider for SABAs is β -blockers, which may decrease the efficacy of SABAs. Loop and thiazide diuretics may enhance the hypokalemic effect of beta agonists. Sympathomimetic drugs enhance tachycardia and tremors.¹¹

Short-Acting Muscarinic Antagonist

Short-acting muscarinic antagonists (SAMAs) reverse cholinergically mediated bronchospasm.⁴ SAMAs have been shown to have additive benefit to SABA when used in the emergency department.^{4,12} If initiated at home in combination with SABA therapy, patients may benefit from the earlier initiation of the additive benefit. This treatment may prevent the need for further escalation of care.

SAMA dosing may vary by age.⁴ According to the GINA guidelines, ipratropium bromide may be given at 2 puffs of 80 µg or 250 mg nebulized every 20 minutes for the first hour.⁵ This dose is typically given in the emergency department. For ages 12 years and older, EPR-3 guidelines suggest 2 to 3 puffs of the 17 or 18 µg per puff MDI or 0.25 to 0.5 mg of a nebulized solution of ipratropium bromide every 6 hours with no specific recommendations made for those less than 12 years old.⁴

Common potential side effects to consider for SAMAs include drying of oral and respiratory secretions and blurred vision if sprayed in the eye. Bronchospasm is a rare side effect experienced by some individuals.⁴ It is important to consider that SAMAs may enhance the effect of anticholinergic drugs and may decrease the effects of cholinergic drugs.¹³

SYSTEMIC ORAL CORTICOSTEROID

Oral steroids decrease airway inflammation in patients with asthma. Guidelines suggest consideration of oral steroids if the patient has an incomplete or poor response

to SABA.⁴ Steroids do not provide immediate benefit but may start to provide benefit within 3 hours of administration.¹⁴ This point is important because patients with longer duration of symptoms are more likely to require hospital admission.¹⁵ New pediatric evidence suggests that incorporation of a home supply of oral steroids into the home management of patients with moderate to severe asthma was associated with a significant decline in emergency department visits without any increase in hospitalizations or pediatric intensive care unit stays.¹⁶

Recommended dosage for oral corticosteroids in adults is 1 mg/kg/d, with a maximum dose of 50 to 60 mg for 5 to 7 days. Some patients require a longer course.^{5,17} For children less than 12 years of age, the recommended dosage is 1 to 2 mg/kg/d for 3 to 5 days, with a maximum dose of 40 mg to 60 mg.^{4,5,17} Pediatric patients may also require a longer course.⁴

Common side effects can include sleep disturbance, mood changes, psychosis, hypertension, and increased appetite.^{5,17} When used for an extended period of time or very frequently, side effects may also include decreased bone mineral density, immunosuppression, adrenal suppression, delayed wound healing, cushingoid changes, and increase in psychiatric symptoms.^{4,18} Despite an extensive list of potential side effects, the benefits of oral steroids outweigh the risks when treatment is required for the inflammation contributing to moderate to severe asthma exacerbations. Lack of appropriate treatment could result in severe morbidity and possible death.

Many drug-to-drug interactions exist with systemic corticosteroids. An all-inclusive list is beyond the scope of this article but common interactions include enhanced anti-coagulation with warfarin, hypokalemia with loop diuretics, and enhanced adverse effects of NSAIDs. Systemic steroids diminish the effects of vaccinations. Of note, when given with cytochrome P3A4 (CYP3A4) inhibitors, the effects of corticosteroids are likely to increase as the serum concentration is increased.¹⁹

ADDITIONAL PHARMACOLOGIC INTERVENTIONS

In an attempt to decrease oral corticosteroid use and the associated extensive list of side effects, other options can be considered in the home management of an asthma exacerbation.

INHALED CORTICOSTEROID

Inhaled corticosteroids (ICSs) are a mainstay of long-term asthma controller therapy.⁴ They work to decrease inflammation by inhibiting inflammatory cell migration and activation, which decreases airway hyperresponsiveness.⁴ Intermittent use or increased doses of the controller therapy ICS can be used in the treatment of asthma exacerbations.⁵ New evidence suggests that, in children less than 5 years of age with history of wheezing during respiratory infections, intermittent ICS use in conjunction with SABAs decreases risk of exacerbations requiring oral steroids compared with SABA use alone.^{20–23} There was no difference in risk of exacerbation requiring oral steroids in a similar group when intermittent ICS dosing compared with ICS use as a controller.²⁴ In the limited number of studies done in patients aged 12 years and older, there was no significant difference in risk of exacerbation requiring oral steroids when comparing intermittent ICS with ICS controller versus ICS controller alone and intermittent ICS versus ICS controller.^{25–28} A recent study in the United Kingdom showed that, in patients aged 16 years and older with asthma, quadrupling the dose of their ICS controllers resulted in fewer severe asthma exacerbations (based on use of systemic steroids or unscheduled health care visits) compared with the group that did not increase their

ICS dosing.²⁹ There was insufficient evidence to draw any conclusions for ages 5 to 11 years.²⁰

GINA guidelines recommend increasing ICS dosing during an acute exacerbation to at least double the usual dosage, and possibly quadruple the normal dosage (a maximum of 2000 µg/d).⁵ This dosage can be administered via MDI with spacer, dry powder inhaler, or nebulized solution.⁴ ERP-3 specifically states that doubling the dose has not shown improved outcomes; however, this was associated with a study with delayed initiation of increased dosing.⁵ These guidelines are being reevaluated in the context of the new evidence available regarding intermittent ICS use.²⁰

Acute side effects of inhaled steroids include development of oral thrush, particularly if not using with a spacer and not rinsing the mouth after use. Other complaints include cough and dysphonia. Long term, there is a known effect on linear growth, although this seems to be dose dependent. At high doses there is the potential for adrenal suppression and development of Cushing syndrome along with the other aforementioned side effects of systemic corticosteroids.⁴

Several drug-drug interactions should be considered with ICS use. Fluticasone, budesonide, and mometasone specifically are metabolized by the CYP3A4 isoenzyme leading to interactions with drugs also metabolized by this system. Specifically, antifungal azole medications and ritonavir may increase concentrations of inhaled steroids.⁴

COMBINATION INHALED CORTICOSTEROID AND LONG-ACTING BETA AGONIST THERAPY

The long-acting beta agonist (LABA) formoterol has a fast onset of action similar to short-acting bronchodilators.^{4,6} Studies in patients more than ages 12 years on maintenance combination therapy with ICS and formoterol have suggested that this combination can be used for symptom relief in acute exacerbations.³⁰ This treatment is often referred to as single maintenance and relief therapy (SMART) or adjustable maintenance dosing (AMD).^{6,30}

There has been concern about the safety of SMART or AMD therapy in the United States because it is not approved by the US Food and Drug Administration (FDA).^{6,31,32} It has been more readily adopted in Canada and European countries.^{5,31} A systemic review and meta-analysis published in 2018 evaluated 16 trials of SMART. Fifteen of these trials evaluated budesonide and formoterol combination therapy. This meta-analysis showed decreased risk of asthma exacerbations requiring systemic oral steroids, hospitalization, or emergency department visit.³⁰ Supporters think that increasing the ICS dosing in combination with the long-acting beta agonist formoterol provides benefit from both therapies and allows ease of use with only 1 inhaler needed for both prevention and rescue treatment. Limited evidence exists for use in children between the ages of 4 and 11 years.^{5,30,33,34} No evidence exists to support use in children less than 4 years of age.³⁰

Various dosing of ICSs/LABAs were used in the studies reviewed. GINA guidelines suggest a maximum of 72 µg of formoterol in a day.⁵ This dose can be administered via MDI with spacer or dry powder inhaler. However, this dose does exceed the FDA-approved dosing in the United States at this current time.³²

Formoterol should only be used in combination with an ICS to avoid increased risk of asthma-related deaths.⁴ Side effects and drug interactions of the ICS component were discussed earlier. Common potential side effects associated with formoterol include rhinitis, hypertension, tremors, and pharyngitis. Less common side effects include insomnia, hyperglycemia, hypokalemia, and tachycardia.³⁵ The likelihood of

the less common side effects may increase with the higher dosing used in SMART. Potential side effects may be increased by drug-drug interactions. For example, formoterol may enhance tachycardia caused by short-acting bronchodilators and hypokalemia with loop diuretics. Caffeine may enhance the side effects and β -blockers may diminish the effect of formoterol.³⁵

LONG-ACTING MUSCARINIC ANTAGONIST

Long-acting muscarinic antagonists (LAMAs) have become an important component in asthma care.^{4,5} Tiotropium is the most common LAMA used in practice and in trials.³⁶ A recent systemic review and meta-analysis evaluated 15 trials that examined the effect of the addition of LAMA in asthma care. Only 2 trials evaluated children, including those aged 12 to 17 years. Compared with a placebo as add-on therapy to ICS, the LAMA therapy regimen showed an improvement in lung function in individual studies.^{37–39} A meta-analysis of these studies showed a lower risk of asthma exacerbations requiring oral steroids.^{36–39} There was no identified difference between the addition of a LAMA versus LABA. Combination of both LAMA and LABA with ICS did not show any additional decrease in asthma exacerbations but may improve spirometry and asthma symptom control scores.^{20,36} The lack of rapid onset of the LAMA currently limits the potential for use for SMART and AMD.^{20,40}

LAMA dosing may be adjusted by age and asthma severity.⁴⁰ Tiotropium 5 μ g daily or 2.5 μ g daily was used in trials for maintenance therapy.³⁶ This dose can be administered via a dry powder inhaler and a soft mist inhaler. Spacer use is not required with these forms.

Most common side effects to consider with LAMA therapy are pharyngitis, sinusitis, headache, and bronchitis.⁴⁰ Other adverse effects to consider include glaucoma, constipation, and dry mouth. Worsened bronchospasm is a rare side effect.⁴⁰ These side effects may be more prominent when LAMA is used in combination with other anticholinergic medications because of the potential for an additive effect.⁴⁰

MACROLIDE THERAPY

There is limited evidence to support the use of macrolide therapy in acute asthma exacerbations, and routine use is not recommended in current asthma guidelines.^{4–6,41} A study done in children aged 12 to 71 months with a history of recurrent severe wheezing suggested that azithromycin given at onset of viral symptoms prevented severe exacerbation of their respiratory symptoms.^{42,43} A study focusing on children aged 1 to 3 years noted a decrease in symptom duration with exacerbation of respiratory symptoms after azithromycin administration.⁴⁴ This effect could not be duplicated in preschool-aged children prescribed azithromycin for wheezing after presentation to the emergency department.⁴⁵ In adults, azithromycin use in asthma exacerbations failed to show any benefit compared with placebo.⁴⁶ More research is needed on the topic of macrolides in asthma in all age ranges.

There is no standard dosing for oral/enteral azithromycin described in guidelines. Pediatric studies used 10 to 12 mg/kg/d.^{4,5,41,42} A study done in the emergency department prescribed 10 mg/kg/d on the day of presentation followed by 5 mg/kg/d for 4 additional days.⁴⁵ In adults, the study described 500 mg daily for 3 days during an exacerbation.⁴⁶

Side effects to consider with azithromycin therapy include hypersensitivity reactions, arrhythmias, vomiting, and diarrhea.⁴⁷ More data are required to evaluate the emergence of macrolide-resistant bacteria and alteration of the lung microbiome on macrolide therapy.⁴¹

Many potential drug interactions exist with azithromycin. It is important to recognize that macrolides may enhance the effects of QT interval–prolonging agents and the myopathic effects of some statin drugs. Macrolide therapy may also increase serum concentration of tacrolimus if used concurrently.⁴⁷

LEUKOTRIENE RECEPTOR ANTAGONIST

Guidelines do not support routine use of intermittent leukotriene receptor antagonist (LTRA) therapy to treat asthma exacerbations. Studies on this treatment have had mixed results. One study did find modest benefit in reduction of symptoms and health care use when LTRA was used at the start of asthma symptoms in children aged 2 to 14 years with intermittent asthma.⁴⁸ A 2015 Cochrane Review found no evidence of benefit though when it was compared with a placebo in children aged 1 to 6 years who had history of episodic viral wheezing.⁴⁹ Studies in adults were also unable to show statistically significant benefit.^{50,51} Further research is needed before a recommendation on intermittent LTRA use for asthma exacerbations can be made.

FUTURE CONSIDERATIONS/SUMMARY

Asthma is a common chronic disease in both adult and pediatric populations. Asthma exacerbations are common and proper management is essential to prevent mortality and decrease health care use. Many options exist to customize an asthma exacerbation management plan for patients at home. It is important to understand that it is not one size fits all with asthma management.

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