

Asthma Medications: Pills, Dry Powders, MDIs, or Biologics?

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Disclosures

- I have no conflicts of interest.



Learning Objectives

- Describe key consideration for choosing the proper medication/s when treating children with asthma.
- Discuss reasons for black box warnings on some asthma medications.
- Discuss criteria for starting children with asthma on biologics.



Basic Physiology

- Hyper-responsiveness of the airways
- Bronchoconstriction
- Inflammation
 - Increased mucous production
- This is key to your teaching, and patient understanding of the need for bronchodilators and anti-inflammatories



Guidelines for the Diagnosis and Management of Asthma

- 1991-EPR1. Asthma is an inflammatory disease
- 1997-EPR2. Early recognition and treatment
 - 2002-EPR2 update on selected topics
- July 2007-EPR3. Full Report, 450 pages
 - Oct 2007-EPR3. Summary Report, 75 pages



Major Changes in EPR3

- Focus on monitoring asthma control as the goal.
- Severity (intermittent, mild, moderate, severe persistent)
- Control (well controlled, not well controlled, very poorly controlled)



Major Changes in EPR3

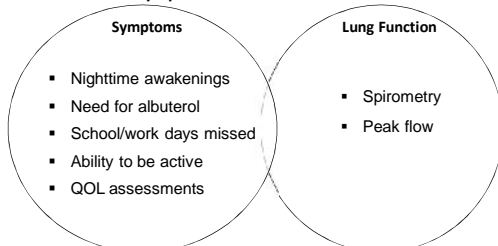
- Assess severity and control by evaluating two domains: impairment and risk.
- Impairment: frequency and intensity of symptoms.
- Risk: the likelihood of a future exacerbation.

Major Changes in EPR3

- Modification of the stepwise approach
 - 3 age groups
 - 0-4 y
 - 5-11 y
 - >12 y
 - 6 step now, rather than 4.

Assessing Asthma Severity: Impairment

Impairment = Frequency and Intensity of
Symptoms and Functional Limitations



National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3 2007). U.S. Department of Health and Human Services. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgin.pdf>. Accessed August 29, 2007.

How to reduce risk of Asthma Exacerbations

- Prevent recurrent exacerbations of asthma and minimize the need for ED visits or hospitalizations.
- Prevent loss of lung function; for children, prevent reduced lung growth.
- Provide optimal pharmacotherapy with minimal or no adverse effects of therapy.

Classifying Asthma Severity and Assessing Asthma Control

In patients not on long-term controller
medications

- Severity based upon domains of impairment and risk
- Level of severity based upon most severe category in which any feature appears

National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3 2007). U.S. Department of Health and Human Services. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgin.pdf>. Accessed August 29, 2007.

Classifying Asthma Severity and Assessing Asthma Control

- In patients on long-term controller medications
 - Severity based upon lowest step required to maintain clinical control
 - Control of asthma based upon domains of impairment and risk
 - Level of control based upon most severe impairment or risk category
 - Asthma Control Tests (ACT) are helpful

National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3 2007). U.S. Department of Health and Human Services. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgin.pdf>. Accessed August 29, 2007.

Website for 2007 NHLBI guidelines

www.nhlbi.nih.gov/guidelines/asthma

Asthma Control Tests

Childhood Asthma Control test for children 6 to 11 years old.

Know the score.

Read all questions and be sure you have read each question carefully. Think for a while before choosing an answer. If you are not sure, choose the answer that you think is most likely to be correct. There are no right or wrong answers. The test is only a guide to help you and your doctor.

How many times in the last 4 weeks has your child had an asthma attack?

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18. How many times in the last 4 weeks has your child had an asthma attack?

19. How many times in the last 4 weeks has your child had an asthma attack?

20. How many times in the last 4 weeks has your child had an asthma attack?

Asthma Control Test[®] for teens 12 years and older. Know the score.

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Asthma Severity

Intermittent Asthma

- Quick acting bronchodilator as needed
- Can use quick-acting bronchodilator preventatively:
 - Such as 5-10 minutes prior to exercise
 - Should not be needed >2 times per week

Mild Persistent Asthma

- Preferred: Low-dose inhaled corticosteroid
- Alternative:
 - Leukotriene modifier
- Use quick acting bronchodilator as needed

Moderate Persistent Asthma

- Preferred: Low dose inhaled corticosteroids *plus* long-acting inhaled bronchodilator
- Alternatives:
 - Medium-dose inhaled corticosteroids
 - Low-to-medium dose inhaled corticosteroid *plus* leukotriene modifier
- Use quick-acting bronchodilator as needed

Severe Persistent Asthma

- Preferred: High dose inhaled corticosteroid *plus* long-acting inhaled bronchodilator
- Corticosteroid tablets or syrup daily or every other day, if needed
- Use quick acting bronchodilator as needed.
- Biologics??

Medication Categories

Long-Term Control

- Taken daily, over a long period of time
- Used to reduce inflammation, relax airway muscles, and improve symptoms and pulmonary function
- Inhaled corticosteroids
- Long-acting beta2-agonists
- Leukotriene modifiers
- Biologics

Long Term Control: Inhaled Corticosteroids

- Fluticasone (Flovent)
- Budesonide (Pulmicort) Only nebulized option
- Ciclesonide (Alvesco)
- Mometasone (Asmanex)- dry powder or HFA
- Beclomethasone (QVAR) – Now as dry powder
- Flunisolide (Aerospan) New in 2014
- Fluticasone furoate (Arnuity Ellipta) New in 2015
- Fluticasone propionate (ArmonAir RespiClick) New in 2018

Benefits of Inhaled Steroids

- Improved lung function
- Decreased hyper-responsiveness
- Fewer asthmatic symptoms
- Reduce use of quick relief medications
- Improved health related quality of life
- Decreased risk of death or near death from asthma

Adverse Effects of Corticosteroids

- Oral candidiasis (thrush)
- Hoarse voice (dysphonia)
- Medium to high dose inhaled steroids associated with small effect on linear growth (1cm per year) during first year

Combination Inhaled Corticosteroids and Long Acting Beta Agonists

Advair

- Fluticasone/Salmeterol
- MDI or Discus
- Approved for 6 years and older

Symbicort

- Budesonide/Formoterol
- MDI –requires a spacer
- Approved for 12 y.o

Combination Inhaled Corticosteroids and Long Acting Beta Agonists

Dulera

- Mometasone/Formoterol
- Approved for 12 olds

Breo Ellipta

- Fluticasone furoate/vilanterol
- Approved for 18 year olds

Combination Inhaled Corticosteroids and Long Acting Beta Agonists

- AirDuo RespiClick
 - Fluticasone propionate and Salmeterol
 - Approved for ages 12 years
 - Dry Powder
 - Also available as a generic
 - Only combination med not requiring a prior authorization on Mass Health

Two Other Inhalers

- Combivent
- Albuterol and Atrovent combined
- Used in ED and ICU commonly
- May be prescribed by specialists
- Spiriva – tiotropium bromide
- Approved for 12 year old
- QD dosing for difficult to control asthma



Long Acting Beta Agonists

- Salmeterol (Serevent)
- Formoterol (Foradil)
- Vilanterol (In Breo Ellipta)
- Not recommended:
 - Oral beta-agonists (Volmax, Vospire ER)

Long-acting Betaz Agonists

- Relax bronchial smooth muscle
- Available as DPI
- 12 or 24 hour duration of action
- Most effective when in combination with inhaled steroids (not mono therapy)
- Effective control for nocturnal symptoms

Long Acting β_2 Agonists (LABA): Are they safe?

- Black box warning. What is it?
 - Serious adverse reactions may occur with LABA--Advair, Symbicort, Serévent, Foradil.

WARNING

Long-acting beta₂-adrenergic agonists (LABA), such as salmeterol, may increase the risk of asthma-related death. Therefore, when treating patients with asthma, physicians should only prescribe LABAs for patients not adequately controlled on other asthma-controller medications or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies.

- No other country has this black box warning.

Leukotriene Modifiers

- Montelukast (Singulair) – Once daily tablet, chewable, & sprinkles
 - Approved for ages \geq 1 year
 - 4 mg, 5 mg, 10 mg
- Zafirlukast (Accolate) – Twice daily tablet
 - Ages \geq 5 year
 - Requires routine monitoring of Liver function
- Zileuton (Zyflo) – BID or QID
 - \geq 12 years
 - Requires routine monitoring of Liver function

When to use Leukotriene Blocking Drugs

- Patients with severe asthma on high-dose inhaled steroids
- Steroid dependent asthma
- Mild to moderate asthma in persons fearful or intolerant of inhaled steroids

How to make the selection?

- Nebulized medications
 - No blow by treatments!
- Metered Dose inhalers
 - Must use a valved holding chamber (spacer)
- Dry power inhalers
 - Can child hold his/her breath and swim under water?

Biologics

- For patients with severe persistent asthma who do not respond well to other treatments
- Only ~60 of our 10,000 patients receive this medicine.

Omalizumab (anti-IgE)

- Binds free IgE & inhibits its binding to mast cell
- Reduces early & late allergic responses
- Reduces exacerbations 50% (moderate and severe asthma)
- Expensive (\$10-30k/year)
- Requires bimonthly or monthly visits
- May have delayed anaphylactic response, so must have epi-pen on hand

Who qualifies for Xolair

- 6 years or older
- Moderate or Severe Persistent Asthma
- Daily asthma symptoms
- 2 or more asthma attacks/week
- Positive skin test or blood test for allergies
- Symptoms even on inhaled steroids
- IgE levels are 30-1300 IU/ml
- Body weight 40-330 lbs.

Mepolizumab (Nucala)

- Add-on maintenance treatment
- 12 years old, with severe Eosinophilic asthma
- Reduces blood eosinophils, which may contribute to asthma
- Reduces steroid use

Reslizumab (Cinqair)

- Add-on maintenance treatment
- 18 years old, with severe asthma
- Reduces blood eosinophils, which may contribute to asthma
- IV infusion, 3 mg/kg, every 4 weeks, over 25-50 minutes

Benralizumab (Fasenra)

- Add on treatment
- Approved for patients age 12 years
- For severe eosinophilic asthma
- Maintenance dosing every 8 weeks
- 6 other biologics are also in the pipeline

