Understanding the Risks and Benefits of Stepping Down Asthma Medications

4813 Workshop: Stepping Down Asthma Medications: Benefits and Risks

Monday March 3, 2014 4:45 pm to 6:00 pm
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Learning Objectives:

• Identify asthma patients who may be good candidates for stepping down their asthma medication

• Stepping Down Asthma Medications: Benefits and Risks
  • Risks / Benefits of Step Down Therapy
  • LABA/ICS to ICS without LABA
  • Discontinue ICS
  • Reduce ICS
  • ICS to LT inhibitor

• Compare and contrast different types of step down strategies
### Understanding the Risks and Benefits of Stepping Down Asthma Medication

<table>
<thead>
<tr>
<th>Potential Risks of Step Down</th>
<th>Potential Benefits of Step Down</th>
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</thead>
<tbody>
<tr>
<td>Loss of Asthma Control (increased symptoms)</td>
<td>Reduction in theoretical medication adverse effects</td>
</tr>
<tr>
<td>Asthma Exacerbation (Mild - Severe)</td>
<td>-steroid risks e.g. osteoporosis, height loss, pneumonia?, adrenal insufficiency etc.</td>
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<td>Risks associated with severe asthma exacerbation</td>
<td>-LABA “black box warning”</td>
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<tr>
<td>-ER / hospitalization</td>
<td>-Time / Cost to take medications</td>
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<tr>
<td>-Death</td>
<td>Patient preference to use less medications</td>
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<td>-Probable need for systemic steroids</td>
<td>Occasionally enable opportunity to exclude asthma as the diagnosis</td>
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<tr>
<td>Patient / family lack of trust in physician’s desire or ability to control asthma</td>
<td>Avoiding the current patient practice of “Self- Step Down or Self-Discontinuation”</td>
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</tbody>
</table>
**Figure 4-5. Stepwise Approach for Managing Asthma in Youths ≥12 Years of Age and Adults**

**Step 1**
- **Preferred:** Low-dose ICS
  - Cromolyn, LTRA, Nedocromil, or Theophylline
- **Alternative:** Medium-dose ICS
  - Low-dose ICS + LTRA

**Step 2**
- **Preferred:** Low-dose ICS + LABA
  - OR
  - Medium-dose ICS + LABA
- **Alternative:** Medium-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 3**
- **Preferred:** High-dose ICS + LABA
- **Alternative:** Consider Omalizumab for patients who have allergies

**Step 4**
- **Preferred:** High-dose ICS + LABA
  - AND
  - Consider Omalizumab for patients who have allergies

**Step 5**
- **Preferred:** High-dose ICS + LABA + oral corticosteroid
  - AND

**Step 6**
- **Preferred:** High-dose ICS + LABA + oral corticosteroid
  - AND

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Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

**Quick-Relief Medication for All Patients**
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA ≥2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
Asthma Case 1

- 54 year male well controlled on moderate dose ICS/LABA
- Albuterol use 2 puffs every 2 weeks average
- No ER visits, No Hospitalizations x 1 year
- Asthma Control Test Score 23
- FEV-1 92%
- Patient estimated adherence to ICS/LABA 85% of administrations taken.
- Step Down from ICS and substitute moderate dose ICS without LABA?
Long-Acting Beta 2 Agonist Step-off in Patients With Controlled Asthma
Arch Intern Med Vol 172 (No.18), Oct 8, 2012

• Type of Article: Meta-analysis
• Number of Studies: 5
• Comparison: Step Off LABA vs Continue LABA
• Number of Patients: 660 Step Off / 692 Continued LABA
• Primary End point: assess evidence supporting the discontinuation of LABA therapy once asthma control has been achieved with combination ICS and LABA
Long-Acting Beta 2 Agonist Step-off in Patients With Controlled Asthma
Arch Intern Med Vol 172 (No.18), Oct 8, 2012

- **Data:**
  - Reduced Asthma QOL questionnaire score mean difference 0.32 (95% CI, 0.14-0.51) points lower
  - Reduced asthma control mean difference in Asthma Control Questionnaire 0.24 (95%CI, 0.13-0.35) points higher
  - Increased symptom frequency (proportion of symptom-free days) mean difference, 9.15% (95% CI, 1.62%-16.69%) fewer symptoms
  - Increased risk of study withdrawal because of lack of efficacy or loss of asthma control (RR 3.27 (95% CI, 2.16-4.96)
  - Increased rescue inhaler 0.71 (95% CI, 0.29-1.14) more puffs / day
Data (continued):
- Trend increase but no statistically significant change in need for oral corticosteroid.
- No hospitalizations, No mechanical ventilations, no ICU admissions, no death

Limitations: Numerous limitations cited including “lack of information on treatment adherence”

Conclusion: Discontinuing LABA therapy in adults and older children with asthma controlled by a combination of ICS/LABA results in increased asthma-associated impairment

Take Home point: Increased symptoms but no increased oral steroids, hospitalizations, mechanical ventilation or death with d/c LABA
Asthma Case 2

- 28 year female well controlled on low dose ICS
- Albuterol use 2 puffs every 2 weeks average
- No ER visits, No Hospitalizations x 1 year
- Asthma Control Test Score 24
- FEV-1 94%
- Patient estimated adherence to ICS/LABA 80% of administrations taken.
- Step Down and discontinue low dose ICS?
The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials
JACI 2013; 131: 724-9

- Type of Article: Meta-analysis
- Number of Studies: 7
- Comparison: Stop ICS vs Continue ICS
- Number of Patients: 532 Stop / 508 Continue
- Primary End point: to evaluate the risk of asthma exacerbation after stopping low-dose ICSs compared with continuing low-dose ICSs in randomized controlled trials in patients with stable asthma, as measured in randomized controlled trials
The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials
JACI 2013; 131: 724-9

• Data:
  • relative risk for an asthma exacerbation in patients who stopped ICSs compared with those who continued use was 2.35 (95% CI, 1.88-2.92; P < .001; I² 0%), as determined by using data pooled from trials with a mean follow-up of 27 weeks.
  • decreased FEV₁ of 130 mL (95% CI, 40-210 mL; P 5 .003; I² 53%)
  • decreased mean morning peak expiratory flow of 18 L/min (95% CI, 6-29 L/min; P 5 .004; I² 5 82%),
  • increased mean standardized asthma symptom score of 0.43 SDs (95% CI, 0.28-0.58 SDs; P < .001; I² 5 0%).
The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials
JACI 2013; 131: 724-9

• Limitations:
  • Patients stable x 4 weeks (not 3 months as per guidelines)
  • Variability on definition of asthma exacerbation
  • Inconsistency for the outcomes of FEV1, PEF, and asthma specific QOL
  • Age of study participants 6-65 reflecting previous studies

• Conclusion: Patients with well controlled asthma who stop low dose ICS have an increased risk of asthma exacerbation

• Take Home point:
  • “For every 4 patients with stable asthma who stop low-dose ICSs, 1 will have an exacerbation in the next 6 months that is attributable to stopping the ICS.”
Asthma Case 3

• 28 year female well controlled on low dose ICS (Twin sister of previous patient)

• Albuterol use 2 puffs every 2 weeks average

• No ER visits, No Hospitalizations x 1 year

• Asthma Control Test Score 24

• FEV-1 94%

• Patient estimated adherence to ICS/LABA 80% of administrations taken.

• Step Down and reduce low dose ICS?
The risk of asthma exacerbation after reducing inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials

Abstract ACAAI 2013

- Type of Article: Meta-analysis
- Number of Studies: 6
- Comparison: Reduce ICS vs Continue ICS
- Number of Patients: 448 Stop / 444 Continue
- Primary End point: to evaluate the risk of asthma exacerbation after reducing ICS compared to maintaining a stable dose of ICS in individuals with stable asthma as measured in randomized controlled trials (RCTs).
The risk of asthma exacerbation after reducing inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials
Abstract ACAAI 2013

• Data:
  • Asthma exacerbations were statistically no more likely among individuals who reduced ICS compared to those who maintained their ICS dose 1.25 (95% CI 0.96,1.62; p=0.10; I²=0%)
  • The pooled absolute risk difference for an asthma exacerbation was 0.02 (95% CI, -0.02,0.07; P=0.30; I²=0%), with an event rate of 0.17 for individuals continuing ICS and 0.21 for those who discontinued ICS based on an average study length of 22 weeks
  • mean decreased FEV1 % predicted of 0.87% (95% CI -1.58%,3.33%; p=0.49, I²=58%)
  • mean decreased morning PEF of 9.57 L/min (95% CI 1.25,17.90; p=0.02; I²=74%)
The risk of asthma exacerbation after reducing inhaled corticosteroids: A systematic review and meta-analysis of randomized controlled trials

Abstract ACAAI 2013

• Limitations:
  - Two studies used on-demand ICS
  - Patients stable for 4 weeks, not 3 months
  - Different asthma exacerbation definitions in each study
  - Applicability possibly limited to specific patient groups

• Conclusion:
  - Reducing ICS may have lower risk for subsequent asthma exacerbations than previously studied step down.

• Take Home point: These findings support the current guidelines that suggest a 25-50% ICS dose reduction be considered after 3 months of asthma stability.
Asthma Case 4

• 10 year male aspiring 4 foot 2 inch aspiring basketball player well controlled on low dose ICS
• Albuterol use 2 puffs every week on average
• One ER visit, No Hospitalizations x 1 year
• Asthma Control Test Score 20
• FEV-1 88%
• Patient estimated adherence to ICS/LABA 95% of administrations taken.
• Step Down from low dose ICS to montelukast?
Peters SP et al 2007, Randomized Comparison of Strategies for Reducing Treatment in Mild Persistent Asthma

- Type of Article: Randomized Controlled Trial
- Number of Studies: 1
- Comparison: to determine whether asthma control can be maintained after reducing treatment from fluticasone (100 µg twice daily) to montelukast (5 or 10 mg each night)
- Number of Patients: 169 continue ICS vs 166 step down to montelukast: ages > 6yo
- Primary End point: time to treatment failure.
Peters SP et al 2007, Randomized Comparison of Strategies for Reducing Treatment in Mild Persistent Asthma

• Data over 16 week period:

• Approximately 20% of patients assigned to receive continued fluticasone had treatment failure

• Versus 30.3% of subjects switched to montelukast experienced treatment failure

• “Patients taking montelukast remained free of symptoms on 78.7% of treatment days.”
Peters SP et al 2007, Randomized Comparison of Strategies for Reducing Treatment in Mild Persistent Asthma

• Limitations:
  • Limited to 16 weeks observation
  • Unexplained reduction of viral respiratory infections in the montelukast group (7.3% of montelukast vs 15.5% in ICS group)

• Conclusion:
  • Asthma control was maintained in a majority of patients stepped-down from ICS to montelukast

• Take Home point: Many patients on low dose ICS remain stable for 16 weeks after discontinuing ICS and initiating montelukast