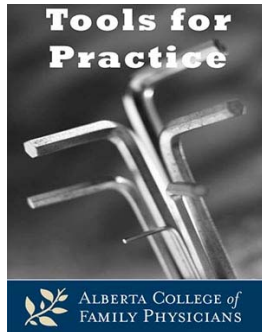


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Long-Acting Beta-Agonist Inhalers in Asthma: Breathing Evidence into the Debate?

Clinical Question:

Are the serious adverse events associated with Long-Acting Beta-Agonists (LABA) in asthma important enough to limit their use?

Evidence

The FDA reviewed¹ this data, and two publications^{2,3} report on their findings.

- Data from 110 trials (60,954 pts) including 11% adolescents and 6% children with a median follow-up of 24 weeks.
- For the primary end-point of asthma-related death, intubation, and hospitalization
 - Statistically significant increase of 2.8 extra events per 1000 asthmatic patients treated with LABA inhalers.^{2,3}
 - Number needed to harm (NNH) was 358.^{2,3}
- Examining asthma-related death, intubation, and hospitalization among asthmatics using LABA with or without inhaled steroids,
 - LABA alone, without inhaled steroid, led to a statistically significant increase of 3.63 extra events per 1000 asthmatics (NNH 276).^{2,3}
 - LABA, when used in combination with inhaled steroids, resulted in no statistically significant difference in these endpoints.^{2,3}

The risk increases with decreasing age (2/1000 in adults age 18-65 and 15/1000 in children age 4-11)²

Context

- These findings are supported by 4 Cochrane reviews of LABA safety in asthma.
 - Formoterol vs Placebo⁴: Formoterol alone led to a statistically significant increase in non-fatal serious events with a NNH = 149 over 16 weeks.
 - Salmeterol vs Placebo⁵: Salmeterol alone led to a statistically significant increase in non-fatal serious events with a NNH = 188 over 28 weeks.
 - Formoterol/steroid⁶ or Salmeterol/steroid⁷ vs steroid: No statistical increase in serious adverse events.
- Serious adverse events with LABA are NOT increased in COPD (Chronic Obstructive

Pulmonary Disease). COPD patients using LABA alone have no increase in mortality and a statistically significant reduction in the risk of exacerbations (number needed to treat (NNT) 24)⁸ and hospitalizations (NNT 32)⁹.

Bottom-line:

In asthmatic patients, Long-Acting Beta-Agonist (LABA) should not be used without inhaled steroids because alone, LABA inhalers cause an increase in serious adverse events. LABA does not increase adverse events in COPD patients or in asthma patients who use LABA in conjunction with an inhaled steroid.

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1. Drug Safety and Risk Management Advisory Committee and Pediatric Advisory Committee, December 10-11, 2008. Available at: <http://www.fda.gov/ohrms/dockets/ac/cder08.html#PulmonaryAllergy> Accessed Nov 8, 2009
2. [N Engl J Med. 2009; 360: 1592-95.](#)
3. [Chest 2009; 136: 604-607;](#)
4. [Cochrane 2008; 4: CD006923 \(formoterol alone\)](#)
5. [Cochrane 2008; 3: CD006363 \(salmeterol alone\)](#)
6. [Cochrane 2009; 2: CD006924 \(formoterol/steroid\)](#)
7. [Cochrane 2009; 3: CD006922. \(salmeterol/steroid\)](#)
8. [Ann Intern Med. 2007; 147: 639-653.](#)
9. [N Engl J Med. 2007; 356: 775-89](#)

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians. Archived articles are available on the Towards Optimized Practice and ACFP websites.

This communication reflects the opinion of the author and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.