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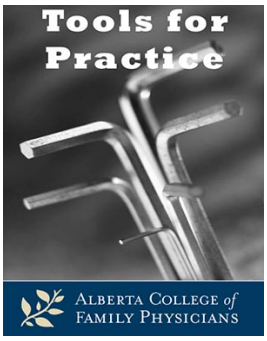


# Tempered Enthusiasm for Tiotropium in Asthma

## Clinical Question: Is tiotropium useful as add-on therapy in asthmatic patients who are poorly controlled on an Inhaled Corticosteroid (ICS) or ICS + Long-Acting Beta Agonist (LABA)?

**Bottom-line: In moderate-severe asthma, uncontrolled on ICS or ICS+LABA, the addition of Tiotropium prevents exacerbations for one in 18-36 patients over 4-52 weeks. Much of the research is at high risk of bias and changes in other surrogate outcomes (like $FEV_1$) are of uncertain clinical importance.**

**Evidence:**

- Systematic review, 13 RCTs (4,966 patients >12 years), asthma, 4-52 weeks duration, 11/13 trials used Respimat® inhaler:[1]
  - Tiotropium + ICS versus ICS (moderate asthma):
    - Improved PEF (22-24 L/min) and $FEV_1$ (140-150 mL).
    - Reduced number of patients with ≥1 exacerbation [10.5% versus 13.3%, Number Needed to Treat (NNT)=36].
  - Tiotropium + ICS + LABA versus ICS + LABA (severe asthma):
    - Improved PEF (16-20 L/min) and $FEV_1$ (80-120 mL).
    - Reduced number of patients with ≥1 exacerbation (18.2% versus 24.0%, NNT=18).
  - No difference in adverse events.
  - Minimum clinically important difference (MCID) for $FEV_1$ is 230 mL.[2]
  - Limitations: 6/13 trials were unpublished manufacturer trials.
- Two of the above unpublished trials were subsequently published together.[3]
  - 2,103 asthma patients on ICS, randomized to once-daily tiotropium (Respimat® inhaler), twice-daily salmeterol or placebo, 24 weeks:
    - Both tiotropium and salmeterol had similar statistically significant improvement in $FEV_1$ although neither reached MCID.[2]
    - Asthma exacerbations (requiring oral steroids) not well reported, conflicting results.
    - Limitations: Industry-sponsored, multiple outcomes with selective reporting, no mention of rescue medications or hospitalizations.
- Smaller systematic reviews (5-6 RCTs) report that tiotropium added to ICS ± LABA increases PEF and FEV1.[4,5]

**Context:**

- 2015 Global Initiative for Asthma guidelines state tiotropium is an option in patients on medium- to high-dose ICS + LABA in patients ≥18 years.[6]
- Tiotropium is available in two types of inhalers: HandiHaler® (dry powder capsule inhaler) and Respimat® (aqueous solution soft mist inhaler).[7]
- There is controversy regarding the possibility of increased mortality with tiotropium delivered via the Respimat® inhaler in COPD, particularly in those with cardiovascular disease and arrhythmias, but the data is inconsistent.[8-10]

**Authors:**
Arden Barry PharmD ACPR, Christina Korownyk MD CCFP

**Disclosure:**
Authors do not have any conflicts to disclose.

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