

Cochrane for Clinicians

Putting Evidence into Practice

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Safety of Long-Acting Beta Agonists in Adults with Asthma

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Clinical Question

Are long-acting beta agonists (LABAs), with or without inhaled corticosteroids, safe in the treatment of adult asthma?

Evidence-Based Answer

LABAs appear to be safe when used with inhaled corticosteroids. LABA monotherapy is associated with an increase in asthma-related mortality and nonfatal serious adverse events, but not in all-cause mortality.¹ (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Asthma affects 8.2% of the U.S. population, and disproportionately affects those who are poor and black. Despite effective therapies, 3,404 U.S. deaths were attributed to asthma in 2010.¹ Two types of inhaled pharmacologic agents are used for asthma control: inhaled corticosteroids and LABAs. Concerns about the safety of LABAs have risen with reports of increased hospital admissions and deaths.

This Cochrane review focused on LABA safety in adults with asthma. The authors included six previous reviews and five new randomized trials totaling 70,444 persons 12 years and older. There was no significant increase in all-cause mortality with LABA monotherapy compared with placebo (odds ratio [OR] = 1.37; 95% confidence interval [CI], 0.88 to 2.13; n = 33,952). However, asthma-related deaths were higher in those taking LABA monotherapy (OR = 3.54; 95% CI, 1.36 to 9.19; n = 33,313), and LABA monotherapy was associated with a small increase in nonfatal serious adverse events (i.e., events that are life-threatening, require hospitaliza-

tion, or result in significant disability; OR = 1.14; 95% CI, 1.02 to 1.29; n = 35,954).

All-cause mortality did not increase among patients using LABA/inhaled corticosteroid combination therapy compared with those using inhaled corticosteroid monotherapy (OR = 1.42; 95% CI, 0.60 to 3.38; n = 24,718). Only one asthma-related death occurred among these patients. There was no significant increase in nonfatal serious adverse events in the LABA/inhaled corticosteroid group vs. the inhaled corticosteroid monotherapy group (OR = 1.07; 95% CI, 0.90 to 1.27; n = 24,718). Because of differing study methodologies, the authors were unable to compare deaths among patients on LABA monotherapy and those on LABA/inhaled corticosteroid combination therapy.

Multiple organizations have issued guidelines on the use of LABAs. The Department of Veterans Affairs/Department of Defense guidelines state that LABAs are contraindicated as monotherapy for maintenance treatment of asthma, but they do allow adding LABAs to an inhaled corticosteroid for persistent asthma.² Similarly, the Institute for Clinical Systems Improvement states that after a patient starts a medium-dose inhaled corticosteroid, a LABA may be added to enhance control. It also recommends against the use of LABA monotherapy.³ The British Thoracic Society states that LABAs should be used only in patients already taking an inhaled corticosteroid.⁴ A prudent approach would be to use an inhaled corticosteroid as first-line treatment for patients with persistent asthma; LABAs are best reserved as adjunct treatment for those already taking an inhaled corticosteroid.

SOURCE: Cates CJ, et al. Safety of regular formoterol or salmeterol in adults with asthma: an overview of Cochrane reviews. *Cochrane Database Syst Rev*. 2014;(2):CD010314.

The practice recommendations in this activity are available at <http://summaries.cochrane.org/CD010314>.

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Psychological Therapies for Chronic Posttraumatic Stress Disorder

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Clinical Question

Which psychological therapies are most effective for chronic posttraumatic stress disorder (PTSD) in adults?

Evidence-Based Answer

Trauma-focused cognitive behavior therapy (CBT) and eye movement desensitization and reprocessing (EMDR) are more effective than other therapies in reducing PTSD symptom severity up to four months after treatment, but more robust studies are needed to evaluate the long-term effectiveness. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

PTSD can develop after a major traumatic event and is characterized by at least one month of recurrent nightmares or distressing thoughts about the event; mood and thought alterations; and hyperarousal symptoms, including sleep disturbance, irritability, and hypervigilance. PTSD can be considered chronic after three months of symptoms. Overall, 7.8% of American adults have PTSD at some point, but the prevalence varies by type of stressor. Women who have been physically assaulted have a lifetime prevalence of PTSD of 29%, whereas combat experience in men leads to a lifetime prevalence of 39%.¹

Different therapies have been used to treat PTSD in adults. Previous Cochrane reviews in 2005 and 2007 reported that trauma-focused therapies were more effective than other types. Trauma-focused CBT is a variant of CBT that incorporates exposure to memories of the event to change thought processes and behavioral response. EMDR is a psychological therapy that uses guided eye movements while the patient recalls distressing images, beliefs, and sensations. This Cochrane review updates the evidence for the treatment of chronic PTSD in adults.

The researchers identified 70 randomized controlled trials (RCTs) of psychological therapies for chronic PTSD with 4,761 participants. About one-half of the trials were conducted in North America (37 trials), with the remainder from Europe (20 trials), Australia (seven trials), Asia (four trials), and Africa (two trials). The majority of the trials involved trauma-focused CBT or EMDR. The authors compared individual trauma-focused CBT and EMDR with each other, and with usual care (wait-listed participants who may have been receiving medications and/or other supports), non-trauma-focused CBT, group trauma-focused CBT, and other therapies. Fewer studies compared group trauma-focused CBT, non-trauma-focused CBT, and other therapies with usual care and with each other. The primary outcomes were clinician-rated PTSD symptoms and drop-out rates. Secondary outcomes included self-reported PTSD symptoms, depression, anxiety, PTSD diagnosis after treatment, and adverse effects.

Individual trauma-focused CBT and EMDR appear to be similarly effective when compared directly. They are also the most effective compared with wait-list/usual care, non-trauma-focused CBT, group trauma-focused CBT, and other therapies in reducing clinician-rated PTSD symptoms and associated depression and anxiety. Some evidence shows the benefits of trauma-focused CBT and EMDR extending one to four months after treatment compared with other therapies. Drop-out rates were much higher in trauma-based therapies compared with others, perhaps because of reexposure to traumatic thoughts.

The authors caution that many factors limit the strength of these findings. Significant heterogeneity in most of the comparisons, small sample sizes, and unclear risk of bias contribute to an overall low quality of evidence assessment. None of the studies reported on adverse effects of treatment.

The National Institute for Health and Care Excellence guidelines recommend trauma-focused CBT and EMDR as treatments of choice.² Although this Cochrane review reinforces these recommendations, additional large, well-designed trials that compare psychological therapies and better assess drop-out rates and adverse effects are needed.

SOURCE: Bisson JJ, et al. Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane Database Syst Rev*. 2013;(12):CD003388.

The practice recommendations in this activity are available at <http://summaries.cochrane.org/CD003388>.

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