Alternatives for asthma

Ironically, a class of drugs used to prevent wheezing and shortness of breath in asthma sufferers can increase the risk of serious asthma attacks, new research suggests

According to a major pooled analysis by the US Food and Drug Administration (FDA) published last month, the use of long-acting beta-agonists, or LABAs, is associated with a significantly increased incidence of serious asthma-related adverse events, including hospitalizations and death (Pediatrics, 2011; 128: e1147–54).

The FDA studied the data from more than 100 studies involving around 60,000 people with asthma across all age ranges. They found that, compared with patients who didn't take LABAs, those who did were 27-per-cent more likely to be hospitalized, require intubation or die because of an asthma attack.

More alarming, the risk was greatest among children. Those aged four to 11 taking a LABA were 67-per-cent more likely to end up in hospital than those not taking LABAs. This equates to an extra three periods of hospitalization for every 100 children taking LABAs over a one-year period.

However, the researchers also noted that patients who took an inhaled corticosteroid, another type of anti-asthma drug, along with a LABA showed no extra risks of hospitalization.

In fact, this combination of treatments is already being recommended by the FDA, and drug manufacturers are now required to have it stated on LABA labels that the drug should not be taken without a long-term asthma medication such as an inhaled corticosteroid. Indeed, some asthma medications, such as GlaxoSmithKline's Advair and AstraZeneca's Symbicort, contain both a LABA and corticosteroid in one product.

Nevertheless, lead author of the study Dr Ann McMahon said there are still not enough data to show that taking an inhaled corticosteroid along with a LABA would entirely eliminate the risks.

"Although we were able to be somewhat reassured . . . it was a small enough sample that we didn't feel entirely confident, and we need to have further analysis," McMahon said.

Worryingly, previous research carried out in the US has suggested that the concomitant use of inhaled corticosteroids does not adequately protect against the risks associated with LABAs.

In an analysis of 19 trials involving nearly 34,000 asthma patients, researchers from the Santa Clara Valley Medical Center in San Jose, CA, and Cornell University in Ithaca, NY, revealed that LABAs increased the risk of severe asthma exacerbations and asthma-related deaths by two- to fourfold. They also reported that, after separately evaluating trials in which more than 75 per cent of the participants were taking inhaled corticosteroids in combination with LABAs, "concomitant inhaled corticosteroids do not adequately protect against the adverse effects".

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The patients still had a two-fold increased risk for asthma-related hospitalizations.

The reason why LABAs may actually worsen asthma control, the researchers said, is because, although these medications may relieve asthma symptoms, their regular use can also promote bronchial inflammation and sensitivity without warning.

Inhaled corticosteroids have been shown to partially protect against the adverse effects seen with regular LABA use, reducing bronchial inflammation and asthma exacerbations, but it also appears that they become less effective over time.

This means that even those patients who are taking LABAs and inhaled corticosteroids at the same time have a significantly increased risk of serious, perhaps even life-threatening, asthma attacks. The study concluded that LABAs such as salmeterol and formoterol "could be associated with a clinically significant number of unnecessary hospitalizations, intensive care unit admissions, and deaths each year".

Indeed, the report's authors estimated that around 4000 of

Fact**file:** Other treatments

- **Acupuncture**. A recent meta-analysis (using pooled results) of 22 trials, involving more than 3000 cases of asthma, reported that the total effective rate of acupuncture was significantly superior to the use of a control technique (Zhongguo Zhen Jiu, 2010; 30: 787–92).
- **Yoga**. A trial of bronchial asthma patients found that yoga breathing exercises in conjunction with standard drug treatment significantly improved lung function compared with a control treatment (Indian J Physiol Pharmacol, 2009; 53: 169–74).
- **Vitamins and minerals**:
  - **Vitamin C**. A double-blind trial found that supplementing ascorbic acid (1 g/day for 14 weeks) reduced the severity and frequency of attacks among Nigerian adults with asthma (Trop Geogr Med, 1980; 32: 132–7). More recently, US researchers reported that 1500 mg/day may be of benefit to people with exercise-induced asthma (Respir Med, 2007; 101: 1770–8).
  - **Magnesium**. Low intakes of this mineral have been linked to asthma. In a recent trial of men and women with mild-to-moderate asthma, supplementing with 170 mg twice a day for six months led to reduced bronchial reactivity as well as improvements in asthma control and quality of life (J Asthma, 2010; 47: 83–92).
  - **Selenium**. Asthma involves free-radical damage that selenium, a potent antioxidant, may be able to protect against. One small double-blind study found that 100 mcg/day of sodium selenite for 14 weeks resulted in clinical improvement in six out of 11 patients compared with only one out of the 10 taking a placebo (Allergy, 1993; 48: 30–6).
- **Fish oil** may be of benefit to asthmatic patients. In one trial, children who received 300 mg/day of fish oil (providing 84 mg of EPA and 36 mg of DHA) showed significant improvements in their asthma symptoms. However, these benefits were observed in hospital, where exposure to food and environmental allergens was being kept strictly under control (Eur Respir J, 2000; 16: 861–5).

  In addition, a combination of omega-3 fatty acids, vitamin C and zinc was recently found to improve lung function and asthma control in children with moderately persistent asthma. In this study, although each supplement had beneficial effects on its own, all three taken together in combination had the greatest impact (Acta Paediatr, 2009; 98: 737–42).
- **Herbs,** such as Amrita Bindu, an Ayurvedic salt–spice herbal preparation, have proved effective against asthma in one study. When children with severe asthma were given 250–500 mg (depending on their age) of Amrita Bindu twice daily after meals, after three months, most of the children were able to stop their asthma medications and were no longer suffering from asthma attacks (J Ethnopharmacol, 2004; 90: 105–14). However, as there was no control group for comparison, we don't know to what extent these results might have been due to a placebo effect.

  Other herbal formulas that may also help against asthma include ivy-leaf extract, powdered picrorhiza root and *Ginkgo* leaf tincture. For best results, consult a qualified medical practitioner.

the 5000 asthma deaths that occur in the US each year are actually due to these drugs, and they now question whether these agents should still be on the market (Ann Intern Med, 2006; 144: 904–12).

Currently, black-box warnings on the labelling for LABAs clearly outline the increased risk for asthma-related deaths associated with their use. Nevertheless, these warnings do not appear to have led to any changes in doctors' prescribing habits.

Other drugs

Sadly, LABAs are not the only asthma drugs linked to serious side-effects. The injected antibody drug omalizumab (Xolair) has been found to increase the risk of anaphylaxis—a severe life-threatening allergic reaction—and the drug has been slapped with a black-box warning saying so. There are also concerns that the drug may cause cancer, adrenal insufficiency and Churg–Strauss syndrome, a serious condition affecting the blood vessels as well as the lungs, nerves and skin—and which, ironically, can also lead to severe asthma (see *WDDTY* vol 18 no 6, page 16).

Even inhaled corticosteroids, the mainstay of asthma treatment, are not as safe as the drug companies would have us believe. Evidence suggests that patients taking these drugs have a significantly greater risk of pneumonia and death from pneumonia—a risk that disappears once steroid use is stopped.

Other side-effects associated with these drugs include lower bone density, thinning of the skin, stunted growth and altered fat metabolism (see *WDDTY* vol 18 no 7, page 16).

Better breathing

Given all these risks with asthma medications, it's not surprising that more and more patients are looking to complementary and alternative medicine, and the evidence suggests that a variety of natural methods can help (see box, left).

One of the most popular and interesting methods is the Buteyko breathing technique, developed by Russian doctor Konstantin Buteyko in the 1950s after having observed the breathing patterns of hundreds of hospitalized patients.

The technique is based on his theory that certain disorders, including asthma, are caused by overbreathing, or hyperventilation, which reduces the body's carbon dioxide levels and, as a consequence, starves the tissues of oxygen.

The breathing technique developed by Buteyko was designed to retrain the body's breathing patterns to correct this hyperventilation and therefore cure the body of disease.

At the heart of the method is a series of reduced-breathing exercises that focus on nasal breathing, breath-holding and relaxation—all of which can especially benefit asthma patients, advocates say. Buteyko

practitioner Christopher Drake claims that around a third of his asthma patients are completely cured of their symptoms, while another third enjoys a vast improvement.

Although there are few published scientific studies on the method outside of Buteyko's own trials, what data have been collected—mostly in asthma patients—are promising.

In one study carried out in New Zealand, the Buteyko breathing technique was tested against a placebo in 38 asthma patients. Those in the Buteyko group halved their use of steroids and reduced their use of beta-2-agonists by 85 per cent. In the control (placebo) group, steroid use remained the same, while beta-2-agonist drug use was reduced by only 37 per cent (N Z Med J, 2003; 116: U710).

In a UK study of 90 asthma patients, the Buteyko method was tested against a yoga breathing technique and a 'dummy' breathing device. After six months, symptoms were unchanged in the yoga-breathing and dummy-device groups, but were reduced in the Buteyko group, which was also able to reduce the use of a bronchodilator by two puffs a day (Thorax, 2003; 58: 674–9).

Yet another study involved 39 asthma patients with substantial medication use who were randomized to practise the Buteyko breathing technique or attend asthma-control classes (controls).

After four months, the Buteyko group showed reductions in both hyperventilation and their use of beta-2-agonist drugs. The researchers also noted a continuing trend towards a reduced use of inhaled steroids and a better quality of life (Med J Aust, 1998; 169: 575–8).

More recently, the Buteyko technique was tested against general breathing and relaxation techniques taught by a physiotherapist. Although both groups showed similar improvement in asthma control, only the Buteyko group showed a significant reduction in inhaled steroid use (Respir Med, 2008; 102: 726–32).

Despite these positive findings, there's a lack of evidence to support the concepts behind Buteyko's theory, and some argue that any benefits are merely due to a placebo effect. Others point out that the method so far hasn't produced changes in objective measures of asthma such as the forced expiratory volume in one second (FEV1), a measure typically used to assess asthma severity (Med J Aust, 1998; 169: 573–4).

Still, at the very least, Buteyko breathing appears to be helping asthma patients reduce their dependency on dangerous medications and control their condition more effectively—and that can only be a good thing.

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For more information on the Buteyko breathing technique, go to www.learnbuteyko.co.uk.