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Disturbing asthma statistics reflect suboptimal management

A patient who regularly needs a beta agonist has enough inflammation to warrant anti-inflammatory therapy

Clinical practice in asthma care lags behind current scientific knowledge, as many physicians continue to take a suboptimal approach to its diagnosis and treatment. Underdiagnosis, ineffective treatment (with inadequate use of inhaled steroids and overreliance on beta agonists), and failure to use objective measurements of asthma severity may all be contributing to the continuing high mortality rate in this disease. A few disturbing trends:

- Of the estimated $3.6 billion per year spent on asthma care, 43% goes for emergency and hospital care, reflecting failure of outpatient treatment.[1]
- Over the last two decades, asthma prevalence has increased from 30.2 per 100 000 to 36.8 per 100 000.
- The overall mortality rate in asthma is not decreasing, and is in fact increasing in African Americans.

Both physicians and patients need better training on treating asthma, according to an expert panel convened by the National Institutes of Health (NIH).[2]

This article will briefly summarize key points in the management of asthma and discuss several new developments, including the newly approved leukotriene receptor antagonist zafirlukast (Accolate) and recent findings on the efficacy of allergy shots for treating asthma.

HOW TO TREAT ASTHMA

The NIH panel suggests using objective monitoring and suppressive therapy to treat asthma better.

Measure the forced expiratory volume (FEV_1) in the office; have the patient use a peak-flow meter at home

Physicians do not treat hypertension on the basis of how many headaches the patient has, nor diabetes by how thirsty the patient feels. Yet, many physicians do something very similar in treating asthma, relying on auscultation and symptoms to guide treatment.

The problem with this subjective approach is that patients[3] and physicians[4] often underestimate the severity of asthma (although patients may do better than physicians, according to one report[5]). In another study,[6] patients with fatal or near-fatal asthma had a lower perception of dyspnea than did normal subjects or asthma patients without near-fatal episodes.

The FEV_1 is the best measure of asthma severity. For longitudinal home monitoring, the peak expiratory flow rate can be used. Unlike the FEV_1, peak expiratory flow is effort-dependent, and different meters give different readings. Yet, trends in the peak flow rate (in the same patient, using the same meter) can give the physician an idea of how well the patient is doing.

Give inhaled corticosteroids as maintenance therapy; save beta agonists for attacks

Asthma therapy must go beyond controlling symptoms, to suppressing the chronic inflammation that underlies asthma. Medications that block inflammation should be front-line therapy.

In a 2-year study, patients with mild asthma treated with an inhaled corticosteroid (budesonide) tolerated a histamine-challenge test better, had higher peak expiratory flow rates and fewer symptoms, and used "as needed" beta agonists less than did patients who received a beta agonist (terbutaline) alone.[7] In two thirds of the patients, these benefits disappeared after they stopped taking the corticosteroid.[8]

Increasing beta-agonist use is a warning sign. Retrospective studies have shown a dose-response relationship between the number of beta-agonist canisters used per month and the risk of death,[9–11] increasing dramatically at 1.4 canisters per month.[10]

Zafirlukast is indicated for preventing and treating chronic asthma

Steady use of beta agonists is associated with low risk for asthma mortality and morbity. However, increasing use (eg doubling) of beta agonists is a serious warning sign.

Beta agonists are indicated to relieve symptoms during acute attacks and to prevent exercise-induced asthma. However, if a patient needs a beta agonist on a regular, long-term basis, he or she has enough inflammation to warrant corticosteroid therapy.

ROLE OF NEW LEUKOTRIENE RECEPTOR ANTAGONISTS

Leukotrienes contribute to inflammation and bronchoconstriction in asthma. Inhibiting their synthesis or blocking their receptors can block the obstructive response in inhalational challenge.[12,13]

One of the inflammatory mediators indentified to play a role in asthma is leukotriene LTD_4. In one study, patients with moderate asthma (FEV_1 40% to 77% of predicted) who took a leukotriene LTD_4-receptor antagonist experienced a modest increase in peak flow, from 12 to 26 L/minute above baseline.[14] The change in FEV_1 was dose-dependent. In a study in exercise-induced asthma,[13] the FEV_1 decreased less in patients taking a leukotriene LTD_4 receptor antagonist than in patients taking placebo.

Using zafirlukast

Zafirlukast (Accolate), an LTD_4-receptor antagonist, was recently approved by the Food and Drug Administration.

Indications. Classified as a controller and reverser of asthma, zafirlukast is indicated for the prevention and therapy of chronic asthma.

Advantages over corticosteroids. Zafirlukast begins to work sooner than do inhaled steroids, which may require up to 8 weeks to produce a noticeable effect. Available in pill form, it is more convenient for some patients to take and eliminates the problem of variable delivery sometimes seen when patients do not know how to take inhaled medications correctly.

The efficacy of zafirlukast has not been compared with inhaled corticosteroids. More study is needed to determine whether the anti-inflammatory activity of zafirlukcast can replace or is additive to inhaled corticosteroids.

Adverse effects. In clinical trials headache was the most common side effect reported (13% vs 12% placebo). Zifirlukast potentiates warfarin and may be antagonized by erythromycin and theophylline.

Dosage—one 20-mg pill twice a day.

Cost—$60 per month.

ROLE OF ALLERGEN IMMUNOTHERAPY

Allergen immunotherapy is widely accepted and used in allergic rhinitis. However, its use in allergic asthma remains controversial.[15] In one double-blind study,[16] 53 patients with asthma exacerbated by ragweed pollen underwent allergen immunotherapy or placebo treatment for 2 years. In the first year, patients who received active therapy had a significantly higher peak expiratory flow rate than did

those who received placebo (489 vs 453 L/minute) and used less concomitant medications. However, in the second year, these differences were not significant. There was no difference in symptom scores between the groups in either year. The authors concluded that the clinical effects were limited and many were not sustained for 2 years.

The NIH guidelines recommend consideration of allergen immunotherapy only for select patients in whom asthma cannot be controlled by other means. ■

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New treatment options for epilepsy

Most patients with epilepsy face a lifetime of drug therapy. Approximately 70% of patients with epilepsy have satisfactory seizure control with standard anticonvulsants. Of the remaining patients, 15% may be helped by epilepsy surgery, but treatment options for patients with uncontrolled seizures and who are not surgical candidates have been limited. Four new anticonvulsant drugs have gained approval by the Food and Drug Administration in the past 3 years, and more are on the horizon.

A "perfect" drug for treating epilepsy has not yet been found, but with the approval of these new drugs and with others in development, we are drawing closer. Some patients resistant to other anticonvulsants will experience greater seizure control with these new compounds. Further, these newer drugs (particularly gabapentin and lamotrigine) have side-effect and drug-interaction profiles that compare favorably with those of older drugs.

Despite these advantages, clinicians must take into account the higher cost of the newer treatments and bear in mind that little is known about possible adverse effects of long-term use.

NEW ANTICONVULSANTS

The four newest approved anticonvulsant drugs—gabapentin (Neurontin), lamotrigine