

DRUG & THERAPEUTICS LETTER



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Steroids For Asthma

The indications for inhaled corticosteroids and the choice of dose are two of the most important questions in asthma management today.

One reason why there is uncertainty regarding optimal treatment is that the natural history of mild asthma in adults is not well documented. The Global Initiative for Asthma (GINA) guidelines define patients with mild asthma as those who experience symptoms at least once a week but less than once a day over a three-month period, including exacerbations which may affect sleep and activity.

Several recent, shorter studies shed light on the consequences of untreated asthma and the relative merits of treatment. These suggest that some untreated patients with

mild asthma have a frequency of severe exacerbations approaching that for moderate to severe asthma. Their symptoms will improve with low-dose inhaled corticosteroids, but if left untreated some patients will have significantly poorer lung function over time.

Inhaled corticosteroids vs short-acting bronchodilators

In an early study of patients with newly diagnosed asthma, an inhaled corticosteroid (budesonide 1200 microgram daily) was compared to a short-acting beta2 agonist (terbutaline 500 microgram twice a day). After two years, patients given budesonide had better lung function, symptom control and airway responsiveness. In addition, improvement was maintained in only 33% of the patients who ceased budesonide after two years. This shows that in some patients the improvements achieved by taking a low daily dose of budesonide for two years may be temporary. However, improvement in airway responsiveness was maintained suggesting that inhaled corticosteroids may have a disease-modifying effect at least in some patients.

The evidence suggests that inhaled corticosteroids confer important benefits in mild persistent asthma. Although in children this may be at the price of some initial growth slowing, studies show that children taking inhaled corticosteroids over longer periods attain their predicted adult height. However, a recent multicentre study appears to challenge the role of regular inhaled corticosteroids.

All guidelines agree that inhaled corticosteroids are the first choice preventer for adults with asthma and that the starting dose should be appropriate to the severity of the disease. For mild persistent asthma, they advise starting with low doses of inhaled corticosteroids upto 250 microgram daily of beclomethasone or fluticasone, or 400 microgram daily of budesonide .

The question of whether to start with a low dose or a higher dose has been partly answered by a recent systematic review of 13 clinical trials of inhaled corticosteroids. The trials compared different starting doses in adults who had not previously taken inhaled corticosteroids for asthma of varying severity. Meta-analysis showed that there was no significant difference between high or moderate doses of inhaled corticosteroids for day and night symptom scores, and reliever use.

It is important to note that several studies show smokers with mild

persistent asthma have a poor response to low-dose inhaled corticosteroids, but may respond to higher doses.

In all these studies, it is clear that a minority of patients do respond to higher doses. Importantly, the relationship between dose and adverse effects shows a much stronger dose-response effect. High doses are associated with a steep rise in the risk of adverse effects, both local and systemic.

All guidelines emphasise the importance of ensuring good device use and checking compliance, inhaler technique and reviewing trigger factors before considering further increases in treatment if patients have not achieved good asthma control. Reduce the dose of any inhaled corticosteroid when the patient's asthma is stable to the lowest clinically effective dose that maintains good control. If good asthma control is not achieved by low-dose inhaled corticosteroids, a long-acting bronchodilator should be added.

When an appropriate dose is chosen, the available inhaled corticosteroids are of similar efficacy so the choice of steroid may depend on delivery device.

A recent meta-analysis undertaken for the National Asthma Campaign in preparation for the revised Asthma Management Handbook showed that combination therapy with an inhaled corticosteroid and a long-acting beta

agonist achieved statistically greater improvements in lung function tests than inhaled corticosteroids alone in patients aged 4-80 years who had previously not received corticosteroids.

Conclusion: Mild persistent asthma in adults and children has better outcomes if it is treated with low-dose inhaled corticosteroids. These doses have an extremely low risk of adverse effects in adults. They may slow growth in children, but do not affect the attainment of final predicted height. Low-dose inhaled corticosteroids alone achieve excellent outcomes in mild asthma, but adding a long-acting bronchodilator is indicated if optimal control is not achieved.

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Brief Information

Managing Bell's Palsy

Bell's palsy results from inflammation of facial nerve in the internal auditory canal. The cause of inflammation is unknown. However, herpes simplex was first suggested as a likely etiological agent more than 30 years ago. One hypothesis is that Bell's palsy results from reactivation of herpes simplex virus.

Bell's palsy can develop at any age but seems to be most common in those people aged between 15 and 60 years. Men and women appear equally likely to be affected but a higher incidence has been reported in pregnant women. Bells palsy is characterized by unilateral facial weakness, which in most patients resolves spontaneously without treatment. However, about 13% are left with slight facial weakness and 16% with moderate to severe weakness.

Patients with Bell's palsy commonly have reduced tearing and difficulty in closing eye on the affected side. So, in these patients, appropriate eye care is crucial to avoid permanent damage to the cornea. Patients presenting with Bell's palsy should routinely be given advice regarding eye care, and same day referral to an ophthalmologist is necessary if the cornea is left exposed on attempting to close the eye lid of the affected eye.

Over the last 50 years, corticosteroids

have been the principal drug treatment for Bell's palsy, the rationale being that they might reduce the associated inflammation. Corticosteroids are not contraindicated in pregnancy but should only be used if the benefits outweighs the risks.

The reviewers have concluded that " more randomized controlled trial with greater numbers of patients are needed to determine reliably whether there is real benefit (or harm) from the use of corticosteroids therapy in patients with Bell's palsy" .

Non-randomised prospective studies of outcomes after surgical decompression compared with those after prednisolone therapy do not provide convincing evidence to justify routine use of such operations in patients with Bell's palsy.

On current evidence, it is unclear what place, if any, acupuncture and physiotherapy have in the management of patients with Bell's palsy. Patients with Bell's palsy should be informed of the lack of evidence on the efficacy of the various treatment options.

Gatifloxacin withdrawn from market

The Associated Press on May 1, 2006 reported that Gatifloxacin, a newer fluoroquinolone, plagued by serious blood sugar complications is coming off the market.

Gatifloxacin was prescribed for chronic bronchitis, sinusitis, pneumonia, urinary tract and other infections.

Bristol-Myers Squibb Co. confirmed that it plans to stop making and selling Gatifloxacin.

Approved for sale in 1999, Gatifloxacin has faced questions about its effects on blood sugar, being associated with both high and low blood sugar in some patients.

A public interest group in US, meanwhile, petitioned the FDA (Food and Drug Administration) for a ban on this antibiotic. In its petition, Public Citizen said there have been 388 patients with blood sugar irregularities associated with the drug including 20 deaths and 159 hospitalizations since Jan 1, 2000.

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