Drugs 2000; 59 Suppl. 1: 43-45
0012-6667/99/0001-0043/$25.00/0

Questions and Answers

Question: Why is asthma now more common in children?

Dr Valacer: While theories abound, hard data are lacking. Reasons may include the following: changes in housing that promote increased exposure and sensitisation to environmental allergens (dust mites, cockroaches) or irritants (environmental tobacco smoke, exhaust gases); changes in atmospheric air quality; changes in diet; changes in the frequency and types of childhood infections; and a heightened awareness of asthma with resulting increased identification of milder cases. Of course, none of these theories are mutually exclusive and varying theories may be true for different populations at different times.

Question: How important is food allergy in asthmatic children?

Dr Valacer: The true prevalence of food allergy in asthmatic children is difficult to determine because double-blind food challenges, the gold standard of diagnosis, are impossible to perform in large epidemiological studies. Published reports suggest an overall prevalence of disease-relevant food allergy of 2% in asthmatic adults and between 5 and 10% in asthmatic children. Prevalence appears to be highest in the youngest patients with asthma. The mechanism by which ingested food can result in pulmonary symptoms is unknown, but most often appears to involve IgE-mediated sensitivity. The degree to which food allergy affects chronic asthma has not been studied, although Sicherer and Sampson have reported anecdotal evidence of improvement in severe, corticosteroid-dependent asthma in adults after removal of foods to which they showed a positive response after double-blind, placebo-controlled food challenge.[1]

Question: Will leukotriene modifiers be useful for controlling asthma in children?

Dr Valacer: Present evidence suggests that leukotrienes are active inflammatory mediators in airway inflammation in children as well as adults. Placebo-controlled clinical trials with montelukast in children aged 6 to 14 years have produced clear evidence that this leukotriene receptor antagonist has a significant effect in preventing exercise-induced bronchoconstriction and improving lung function, as well as quality of life and symptom parameters, while reducing rescue β_2-agonist use and circulating eosinophils. Leukotriene modifiers have been shown to positively affect parameters of airway inflammation, including eosinophilia and nitric oxide exhalation. It has been shown that montelukast is well accepted by parents and paediatric patients, with long term open label efficacy comparable to that with low dose inhaled beclomethasone dipropionate, and that it is associated with better adherence to long term treatment than inhaled sodium cromoglycate. The safety profile of montelukast for children and adolescents with asthma is excellent, with no known drug interactions or serious drug-related adverse effects.

Question: Dr Witzmann and Dr Fink, with respect to the systemic adverse effects of inhaled corticosteroids in children, are there dosage thresholds below which these effects are insignificant?

Dr Kimberley Witzmann and Dr Robert Fink: This is an important question, but currently data do not exist to answer it adequately. Differences exist between inhaled corticosteroids; those exhibiting decreased systemic absorption and rapid hepatic inactivation will demonstrate fewer systemic effects. A 'safe threshold' is difficult to establish, because both short and long term adverse systemic effects of inhaled corticosteroids have been documented. Therefore, inhaled corticosteroids in children should be titrated to the lowest dose that achieves effective clinical control of symptoms.

Question: Does uncontrolled asthma suppress growth in children?

Dr Witzmann and Dr Fink: Historically, some children with severe asthma have exhibited significant growth failure. It is difficult to ascertain whether this was due to poorly controlled inflammation, or to frequent systemic exposure to corticosteroids. With the advent of improved controller agents (including inhaled corticosteroids), clinically significant growth failure has been less frequently observed. Nonetheless, it is imperative that all children with asthma have their heights plotted on a standardised growth chart, to identify those individuals with growth suppression, so that appropriate changes in medical management are instituted.

Question: Professor Helms, the US and British guidelines recommend inhaled cromones as an alternative to inhaled corticosteroids in schoolchildren with mild persistent asthma (step 2). How do leukotriene modifying agents compare with inhaled cromones in this group?

Professor Peter J. Helms: Although prospective clinical trial data in children have not yet been reported in this clinical setting, a recent report on user acceptability has clearly shown that children prefer the leukotriene modifying agent, montelukast (Singulair™) over the regular inhaled sodium cromoglycate.

Question: In children with moderate to severe asthma, is there a case to be made for using combination therapy to reduce the required dosage of inhaled corticosteroids?

Prof. Helms: Any effective corticosteroid-sparing strategies are to be welcomed, and what evidence there is in both children and adults supports the introduction of leukotriene modifying agents. Experience in clinical practice in paediatrics, which is corroborated by a recently reported placebo-controlled adult study, indicates a role for leukotriene modifying agents in reducing the dosages of inhaled corticosteroids while maintaining satisfactory symptom control.

Question: Dr Kemp, would physicians do better to comply with existing asthma guidelines, rather than treat according to anticipated future changes?

Dr James P. Kemp: First of all, we must remember that asthma treatment guidelines are just that – guidelines – and not dogma. Not only can they not account for the great heterogeneity of asthma and the diversity of patients who have this syndrome, but they are also often outdated the day they are published. Each patient with asthma should be treated as an individual. Any programme of management should be certain that 'the emphasis must be placed on developing a partnership among the healthcare professional(s), the patient and the patient's family'.[2]

To have a successful partnership, healthcare professionals must change their traditional role of teacher to that of listener. Educate, but then give choices when they are available. In this way, no one should feel locked into a specific treatment or be concerned about the role of new therapies.

Question: Does use of asthma treatment algorithms preclude individualisation of asthma treatment?

Dr Kemp: Definitely not. Algorithms can never take into account the many and varied aspects of this disease and the socioeconomic factors that influence a patient's willingness and ability to adhere to a treatment plan. I am not a fan of algorithms in medicine. They are great for computers and for those who don't want to think. Biological systems will always challenge such regimented approaches. Why select the brightest students to become doctors if it can all be diagrammed on paper? Information can be placed thus, wisdom cannot.

Question: What new recommendations regarding leukotriene modifiers are likely to be included in the next set of asthma guidelines?

Dr Kemp: Since the revisions of the guidelines will be data based, we would expect the antileukotrienes to have a more established place in the guidelines in future. In addition, consideration must be given to the mistaken concept that all but a very few patients respond to inhaled corticosteroids. In the zeal to treat the inflammatory compo-

nent of asthma with a very potent and effective medication (inhaled corticosteroids), the limitations of this treatment have been minimised. For many patients a single agent is adequate. Polypharmacotherapy is necessary in many patients with moderate asthma and for all patients with severe asthma.

Question: Professor Becker, with the introduction of leukotriene receptor antagonists, there are now several classes of agents (i.e. leukotriene antagonists, theophylline, inhaled cromones and inhaled long-acting β_2-agonists) that may be used as adjuncts to inhaled corticosteroids. How would you rank these drug classes in terms of their usefulness in children with asthma?

Professor Allan Becker: Leukotriene receptor antagonists, long acting β_2-agonists and/or theophylline may be considered as alternatives to increasing from moderate or higher doses of inhaled corticosteroids to achieve control of persistent asthma symptoms in children or adults. There are data in adults supporting the value of all three adjunctive therapies. However, in children, only the leukotriene receptor antagonists have been shown to provide additional benefit when used as adjunctive therapy. These issues are dealt with in some detail in the Canadian Asthma Consensus Report 1999.[3]

Question: Dr Price, when choosing treatment for a child with newly diagnosed asthma, what factors would you consider in selecting a preventive therapy?

Dr David Price: Firstly, severity of asthma. In patients with severe asthma an inhaled corticosteroid would be my first-line treatment of choice. In mild-to-moderate disease the debate is more open in terms of treatment choice. Secondly, patient and parent choice. No treatment that the parent or child is not prepared to take has any worth. One that is slightly less efficacious but that is complied with is generally a better choice. Thirdly, pattern of disease. If there are features in the asthma history of significant exercise- or activity-induced symptoms, I would then consider an antileukotriene agent a good choice.

Question: Are there any features that can be used to differentiate between available antileukotriene agents?

Dr Price: The main consideration at present is that licences differ according to the age of the user, with montelukast generally licensed for those aged from 6 years and zafirlukast for those aged from 12 years.**1** Also, in some countries the two products have differing asthma indications. It is also worth considering whether a once-daily regimen for montelukast or a twice-daily one for zafirlukast is preferred by the parent or child.

References

1. Sicherer SH, Sampson HA. The role of food allergy in childhood asthma. Immunol Allergy Clin N America 1998; 18 (1):49-60
2. Global initiative for asthma - March 1993, National Institutes of Health - NHLBI, publication number 95-3659, January 1995, p. 71
3. Boulet L-P, Becker A, Bérubé D, et al., on behalf of the Canadian Asthma Consensus Group. Canadian asthma consensus report, 1999. Can Med Assoc J 1999; 161 (11 Suppl.): S1-62

1. Zafirlukast has recently been approved in the US for use in children aged 7 years or older.