

EDITORIAL



Choosing Asthma Step-up Care

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Asthma is both easy and hard to treat. It is easy to treat because the vast majority of patients with asthma require little medication for a lot of benefit. In a patient with asthma previously untreated with a controller (i.e., a medication whose primary mechanism of action is not acute bronchodilation), initiating therapy with a controller often results in an improvement in asthma symptoms and lung function and a reduced number of asthma exacerbations. In the language of current asthma thinking, this approach addresses both the impairment and risk domains of asthma treatment. Asthma becomes hard to treat when asthma control is not obtained with the health care provider's first choice of a controller; this usually means that treatment needs to be stepped up and leads to the question, "My patient needs more treatment, but what will offer the greatest likelihood of improvement?"

In this issue of the *Journal*, the Childhood Asthma Research and Education (CARE) Network, which is sponsored by the National Institutes of Health, provides an answer to this question for children 6 to 17 years of age.¹ In their study, Lemanske et al. enrolled children who despite receiving treatment with 100 μ g of inhaled fluticasone twice daily had mild-to-moderate asthma that did not meet a clear definition of control during a run-in period of 2 to 8 weeks. The investigators then assigned the children to receive one of three therapies in random order for 16 weeks each: 2.5 times the dose of inhaled fluticasone, the original inhaled fluticasone dose plus inhaled salmeterol, or the original dose of fluticasone plus oral montelukast. Each child received all three therapies, and treatment success was determined on an individual basis. The

medication assignments were masked with the appropriate use of dummy inhalers or placebo pills. The investigators measured many clinical and physiological aspects of the children in the hope that they would be able to predict which child would have a response to a given step-up therapy.

During each treatment period, the investigators kept a close eye on each child's asthma. They recorded asthma exacerbations requiring oral prednisone, the number of days each child's asthma was under control, and the child's lung function. At the completion of the treatment sequence, the investigators ranked the step-up therapies in each child on the basis of these outcomes and categorized the child as either having a differential response to step-up treatment (and if so, which therapy provided the best response) or not having a differential response. The case definitions that were used to determine a differential response were reasonable.

A total of 182 children underwent randomization, and 157 of them completed the study; 165 children received at least two treatments and thus could be evaluated for a differential response. Treatment adherence, as assessed by pill counts and inhaler-puff counters, exceeded 80%. Some 98% of the children had a differential response to step-up therapy. The probability that a given step-up therapy would provide the best response was about 45% for adding inhaled salmeterol and just under 30% for either adding montelukast or doubling the dose of inhaled fluticasone. Despite a valiant effort, the investigators found no strongly compelling way of predicting which step-up therapy would work best in a given patient. Furthermore, because of the de-

sign of the study, no new insights can be derived about the relative long-term safety of any of these treatments.

Do these data inform clinical practice? We think so. We have taken some license with the findings to present here a view about what to do for a child, or perhaps even a young adult, whose asthma is not controlled with a single puff of an inhaled corticosteroid twice daily, although we have not distinguished between a lack of control stemming from repeated asthma exacerbations and that stemming from daily asthma symptoms or abnormal lung function. Since any of the three step-up therapies may work in an individual patient, we would base our first choice for a given patient on three things: surety of safety, price, and convenience, in that order. Since we still have lingering concern about the safety of long-acting beta-agonists in the treatment of asthma,^{2,3} in that they may promote severe exacerbations or fatal asthmatic events, even with concomitant inhaled corticosteroid treatment, our first choice would be either increasing the dose of an inhaled corticosteroid or adding a leukotriene modifier to the therapeutic regimen. Regardless of which step-up therapy is chosen, the onus lies with the treating practitioner to follow

patients closely and to be sure that they improve as a result of the therapeutic step-up. If there is no improvement, the patient should be switched to an alternative medication and again closely monitored.

The study by Lemanske et al. shows that the practitioner must stay closely tuned to the patient's condition. For the patient whose asthma is hard to control, there is simply no substitute for attentive individual follow-up. The words of Francis Weld Peabody remain true today, that "the secret of the care of the patient is in caring for the patient."⁴

Disclosure forms provided by Dr. von Mutius are available with the full text of this article at NEJM.org.

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