First-Line Inhaled Steroids for Pediatric Asthma Gain Support

BY BRUCE JANCIN
Denver Bureau

KEYSTONE, Colo. — Clinically meaningful indicators of asthma control in children with mild to moderate persistent asthma improved significantly more with an inhaled corticosteroid than with a leukotriene inhibitor in a randomized, double-blind crossover study, Dr. Joseph D. Spanh reported at a meeting sponsored by the National Jewish Medical and Research Center.

The number of days per week in which asthma was under control was significantly greater and the need for supplemental albuterol less, by 1 year after their surgery, than in children using a leukotriene inhibitor before surgery, as previously reported (J. Allergy Clin. Immunol. 2005;117:233-42).

The study has come under considerable criticism—legitimately, in Dr. Spanh’s view—and he was a study coauthor—for this choice of a primary end point. Because the mean baseline FEV1 was already 96% of predicted, a child had to exceed an on-treatment FEV1 in excess of 100% to be classified as significantly improved.

That’s setting the bar very high, he said.

In all, 25% of the children met the primary end point while on fluticasone only; 5% on montelukast only, and 17% on both drugs.

The more recent analysis by Dr. Spanh and his colleagues looked at a broader range of clinical, pulmonary, and inflammatory responses to therapy (see box). Fluticasone consistently came out ahead, providing the first solid evidence-based support for current national and international guidelines that relied on expert opinion in recommending inhaled corticosteroids as the preferred first-line therapy for mild to moderate persistent asthma in children.

Predictors of a greater therapeutic response to fluticasone than to montelukast in terms of asthma control days per week included greater baseline albuterol use, more positive skin test responses, and higher levels of exhaled nitric oxide, a marker of airway inflammation (J. Allergy Clin. Immunol. 2006;117:45-52).

Responses to Fluticasone and Montelukast

<table>
<thead>
<tr>
<th>End Point</th>
<th>Baseline Mean</th>
<th>Adjusted Mean on Fluticasone</th>
<th>Adjusted Mean on Montelukast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. no. of asthma control days/week</td>
<td>2.2</td>
<td>5.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Albuterol puffs per week</td>
<td>7.5</td>
<td>3.1</td>
<td>4.4</td>
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<tr>
<td>Asthma control questionnaire score</td>
<td>0.96</td>
<td>0.59</td>
<td>0.76</td>
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<tr>
<td>Morning peak expiratory flow (L/min)</td>
<td>307.6</td>
<td>334.2</td>
<td>324.8</td>
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<tr>
<td>FEV1/forced vital capacity (%)</td>
<td>80.1</td>
<td>82.2</td>
<td>79.0</td>
</tr>
<tr>
<td>Exhaled nitric oxide (ppb)</td>
<td>39.5</td>
<td>20.6</td>
<td>30.9</td>
</tr>
</tbody>
</table>

Source: Journal of Allergy and Clinical Immunology

Omalizumab Controls Severe Allergic Asthma

BY PATRICE WENDLING
Chicago Bureau

MIAMI — Omalizumab maintained control of severe allergic asthma and reduced the need for inhaled corticosteroids during 3 years of treatment in an analysis of data from the open-label extension of the study that showed it can improve asthma control and reduce the need for inhaled corticosteroids and rescue medications while improving symptom scores and quality of life, compared with placebo.

A first extension to this trial showed that these favorable efficacy and safety findings were sustained for a further 96 weeks of treatment.

In a second extension of the trial, researchers enrolled 178 patients, of whom 149 (84%) completed the study. Patients underwent a washout period of 12 weeks or more before receiving omalizumab subcutaneously at a dose of 0.016 mg/kg or more per IU/mL of IgE every 2 weeks or 4 weeks for up to 52 weeks. Mean forced expiratory volume in 1 second (FEV1) showed no decline between the start of the first extension (baseline) and week 52 of the second extension (2.24 L vs. 2.26 L). Good or excellent asthma control, based on the physician’s overall assessment, was sustained from baseline to week 52 in 121 of the 149 (81%) patients.

During the same period, inhaled corticosteroid doses decreased about 20% among 96% of patients who received the same inhaled corticosteroid throughout the first and second extensions and were not taking oral corticosteroids, reported Dr. Hébert, director of the Centre de Recherche Appliquée en Allergie, Quebec City. He has no financial interest in either of the study’s sponsors.

Of the 178 patients who enrolled in the second extension, 134 (75%) had at least one adverse event, generally of mild or moderate severity.

Asthma Medication Use Drops Following Tonsillectomy

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

MIAMI BEACH — Adenotonsillectomy in children with asthma is associated with a significant improvement in their symptoms, Dr. David E. Karas reported in a poster presented at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

All of the children in Dr. Karas’ prospective study received their surgery for usual indications, including chronic tonsillitis and obstructive sleep apnea. Nevertheless, by 1 year after their surgery, Dr. Karas said in an interview, many experienced significant decreases both in medication use and asthma severity, while their parents reported missing many fewer days of work to care for children during asthma exacerbations.

“We’re not saying get a tonsillectomy if you have asthma,” said Dr. Karas, a pediatric otolaryngologist at Yale University, New Haven, Conn. “But it’s clear that the surgery improves upper respiratory congestion and chronic sinusitis. When the upper airway is not doing well, that eventually takes a toll on the lower airway, and when we treat the upper airway, the lower airway can improve.”

He enrolled 31 patients aged 2-12 years who underwent adenoidectomy and/or tonsillectomy and had a diagnosis of asthma. Before the surgery, each caregiver filled out a questionnaire about medication use, asthma severity, and school and work days missed because of asthma exacerbation. Caregivers were contacted a mean of 1 year later and asked the same questions.

Medication use dropped significantly after surgery. The number of patients using inhaled steroids decreased from 23 to 14, albuterol from 30 to 18, and leukotriene receptor antagonists from 16 to 11. The single patient who was taking a long-acting β2 agonist before surgery was no longer taking it afterward.

The use of systemic steroids decreased as well. Before surgery, 22 patients used the drug at least once a year; 8 required one course, 5 required two courses, 3 required three courses, and 6 required four courses. After surgery, only eight patients were using systemic steroids; all required one or two courses.

Caregivers also reported an average decrease from 2.0 to 0.81 in asthma severity symptom scores. All classes of asthma severity decreased: The number of children with severe persistent asthma declined from 4 to 0; with moderate persistent from 6 to 2, with mild persistent from 7 to 3, and with mild intermittent from 14 to 13. At the 1-year follow-up, 11 caregivers reported that their child had no asthma symptoms at all.

Of those children who attended school, the average number of missed school days per year decreased from 12.5 to 6. Caregivers’ missed work days decreased as well, from 13 to 2 per year.

The relationship between upper airway infection and lower airway dysfunction may explain why some children with asthma experience exacerbations during winter and fall, when upper respiratory infections are more common, and why their symptoms improve with both oral corticosteroids and antibiotics, Dr. Karas said. “There’s nothing that shrinks the tonsils like steroids—it’s like you’re giving a temporary medical tonsillectomy. And antibiotics treat the infective component by preventing those infections that might be micro-aspirated and start up a reactive airway process.”

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