Asthma Is Underdiagnosed in Children Under 4

BY BRUCE JANCIN

KEYSTONE, Colo. — Failure to appreciate the key differences between childhood asthma and the adult version of the disease has led to widespread underdiagnosis of young asthmatics.

“Many of the current treatments and guidelines are only a whole list of synonyms—reactive airway disease, wheezing bronchitis—that we used without saying a child has asthma... which leads to underdiagnosis and undertreatment,” the authors stated.

The Centers for Disease Control and Prevention statistics are revealing. During 2003-2005, the prevalence of asthma among children up to 4 years of age was 6.2%, well below the 9.3% figure for 5- to 10-year-olds and the 10.0% rate in 11- to 17-year-olds. Yet the rate of emergency department visits for asthma in 2003-2004 was 164/10,000 people among the under-5 set, markedly greater than the 83/10,000 for children aged 5-10 years and the 69/10,000 for those aged 11-17 years.

Moreover, the hospital admission rate for asthma was 61/10,000 in children through age 4 years, compared to just 24/10,000 in 5- to 10-year olds and 12/10,000 in 11- to 17-year-olds.

The rate of ambulatory visits for asthma was more than 50% higher in children younger than age 5 years than in older pediatric cohorts, added Dr. Gelfand, chairman of the department of pediatrics at National Jewish Health and professor of pediatrics and immunology at the University of Colorado.

Childhood asthma is more likely to be episodic, especially in younger children. Also, children tend to have greater involvement of the peripheral, airways, so larger particle size inhaled medications may never reach the hyperresponsive portion of their airways.

Also, many children with asthma have normal-range forced expiratory volume in 1 second (FEV1) values when stable because they can hyperinflated lungs. Thus, children do not have good pulmonary function and inflammation in children, the forced expiratory flow over the middle half of forced vital capacity, or FEF25%-75%, is a more sensitive indicator of airflow obstruction than is FEV1, he said.

The Childhood Asthma Management Program Research Group (CAMP) study (N. Engl. J. Med. 2000;343:1054-63) provided the first signal of the limitations—or as Dr. Gelfand put it, the failings—of long-term corticosteroid therapy in children with asthma. While aggressive therapy with oral and high-dose inhaled corticosteroids often improve symptoms as long as the child is using them, they are not disease modifying and don’t prevent severe airway remodeling.

The Achilles heel of corticosteroid therapy is that it doesn’t inhibit reticular basement membrane thickness.

The new AstraZeneca-supported meta-analysis (Ann. Intern. Med. 2009;360:1671-2) involving all of the other current-generation leukotriene receptor antagonists target leukotriene C4 and D4, but not B4, which recent studies from Children’s Hospital of Boston suggest is another important pathway in asthma. And then there is leukotriene B4, which increasingly looks to be a major player in asthma pathogenesis but is also not addressed by the leukotriene modifiers reaching the market.

New Meta-Analysis Shows Safety of LABA Combinations

BY BRUCE JANCIN

KEYSTONE, Colo. — A new meta-analysis of more than 23,000 asthma patients randomized either to formoterol-containing combination regimens or to treatment without a long-acting beta-adrenergic agent showed no asthma-related deaths.

The analysis looked at all 42 AstraZeneca-sponsored randomized, blinded, prospective clinical trials and found no evidence of increased risks of all-cause mortality, asthma-related deaths, or intubations in patients receiving combination therapy with the long-acting beta-agonist (LABA) formoterol. The majority of patients were between the ages of 18 and 64.

The findings support those of an earlier meta-analysis (Ann. Intern. Med. 2008;149:33-42) that involved 16,000 patients in 57 studies involving the other current-generation leukotriene receptor antagonists target leukotriene C4 and D4, but not B4, which recent studies from Children’s Hospital of Boston suggest is another important pathway in asthma. And then there is leukotriene B4, which increasingly looks to be a major player in asthma pathogenesis but is also not addressed by the leukotriene modifiers reaching the market.

Another priority is developing alternatives to spirometry for monitoring lung function and inflammation in young children. The Asthma Predictive Index hinges on the finding of one major criterion—either a parent with asthma, early sensitization to an allergen, or concurrent atopic dermatitis—or two minor criteria in the form of wheezing apart from colds, food sensitization, or eosinophilia.

Outcomes, Formoterol vs. Non-LABA Therapies

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Formoterol combinations</th>
<th>Non-LABA therapies</th>
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</thead>
<tbody>
<tr>
<td>Patient-years of exposure</td>
<td>6,500</td>
<td>5,000</td>
</tr>
<tr>
<td>All-cause mortality (per 1,000 patient-years of exposure)</td>
<td>0.53</td>
<td>0.82</td>
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<tr>
<td>Asthma-related deaths</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asthma-related hospitalizations (per 1,000 patient-years of exposure)</td>
<td>12.05</td>
<td>16.4</td>
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<tr>
<td>Study discontinuation rate</td>
<td>12.7%</td>
<td>15.4%</td>
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Source: Dr. Nelson