Symbicort's Dual Effect Controls, Relieves Asthma

BY TIMOTHY F. KIRN
Sacramento Bureau

VAIL, COLO. — The new asthma drug Symbicort can be used by patients as both their controller medication and their relief medication, Dr. Carolyn M. Kercsmar said at a meeting sponsored by the American Academy of Pediatrics.

This is because one of the two components of the drug—formoterol—is a long-acting β_2-agonist with a rapid onset, said Dr. Kercsmar, director of the children's asthma center at Rainbow Babies & Children's Hospital, Cleveland.

The new product—a combination of the corticosteroid budesonide and formoterol (in formulations of 80/4.5 mcg and 160/4.5 mcg per inhalation)—was approved for use in the United States in July.

A growing number of trials have shown that when asthma patients have used the combination, exacerbations dropped greatly—and by as much as 79% versus fixed-dose regimens in a recent pediatric study.

That study randomized 341 children (aged 4-11 years) with asthma into three treatment groups: maintenance treatment with Symbicort, plus as-needed use; treatment with a fixed formulation of budesonide/formoterol at the same dose, plus terbutaline as rescue medicine; or treatment with a fourfold higher maintenance dose of budesonide, plus terbutaline as rescue medicine (Chest 2006;130:1733-43).

The reduction in exacerbations is thought to result from the fact that, when patients feel an asthma attack coming on and use Symbicort as a β_2-agonist reliever medication, they also get some additional corticosteroid.

Formoterol has an onset of action of fewer than 15 minutes. The other combination product available in the United States—Advair—contains the long-acting β_2-agonist salmeterol, which does not act so rapidly, she said.

Formoterol "starts working just as fast as albuterol," said Dr. Kercsmar, who has no financial links to Symbicort or its maker, AstraZeneca Pharmaceuticals LP.

"You're not going to reach for your albuterol; you're going to reach for this and take a puff instead," she added.

The Symbicort studies have shown that even with this type of use, patients do not get exposed to excessive doses of corticosteroid. Probably, they are achieving greater asthma control over the long term, and not using reliever medication as much.

In the pediatric study, only 6 of 118 (5%) patients using Symbicort for control and rescue ever used it seven or more times a day at one time, compared with 23% on the fixed-dose regimen and 15% on the fixed-dose budesonide; the average rescue use with Symbicort was 0.58 times per day, compared with 0.76 and 0.74 in the other two groups, respectively. The study reported that the yearly growth of the patients on the Symbicort was better than that of patients assigned to only budesonide.

"This decreases exacerbations in a very, very safe fashion," she said.

Dr. Kercsmar said she intends to advise patients to use Symbicort as a reliever the same way she would advise them to use albuterol. They should use it when they begin to feel an asthma attack, and wait 4 hours before using it again, and should contact a health care provider if they need to use it three times within 12 hours, she said. However, the initial Food and Drug Administration–approved labeling will reflect daily scheduled use as a controlled medication only. ■

Expert: Cough-Variant Asthma Is Overdiagnosed

BY TIMOTHY F. KIRN
Sacramento Bureau

VAIL, COLO. — Cough-variant asthma is "markedly overdiagnosed" in children, Dr. Carolyn M. Kercsmar said at a meeting sponsored by the American Academy of Pediatrics.

These children sometimes end up being treated with a number of different asthma drugs they do not need because nothing works, said Dr. Kercsmar, director of the children's asthma center at Rainbow Babies and Children's Hospital, Cleveland.

Anywhere from 6% to 15% of children will have asthma at some time, but only about 5%-10% of children with asthma will have cough primarily.

Some of the overdiagnosis results from the fact that children presumed to have cough-variant asthma are not evaluated for evidence of airway obstruction. And, while some children with cough-variant asthma do not have wheezing obstruction, if a physician cannot demonstrate airway obstruction with abnormal spirometry testing results, or if the child does not respond to a bronchodilator, then the physician should not diagnose cough-variant asthma, she said.

Physicians can institute a trial of an inhaled corticosteroid, but it should only be given 2 weeks. "If that cough is not gone in 1-2 weeks, it is not asthma," she said.

Most children with asthma will have a strong family history of either asthma or allergy in a first-degree relative, and that also can be an important piece of information to use for diagnosis.

A methacholine challenge test "can be useful, but not entirely diagnostic" because 10% of normal, nonasthmatic individuals react to a challenge, she said.

A study conducted by investigators at the University of Leicester (England) suggested how uncommon cough-variant asthma may be among children with a chronic cough, Dr. Kercsmar noted.

The study followed 125 preschool children with a reported recurrent cough for between 2 and 4 years. Over the follow-up period, 56% of the children lost their cough and 37% had continued chronic cough. But, only 7% went on to develop asthmalike wheezing, and that percentage was no different from those in a comparison control group (Pediatr. Pulmonol. 1998;26:256-61).

Estimates of asthma suggest that anywhere from 6% to 15% of children will have asthma at some time, but only about 5%-10% of children with asthma will have cough primarily, Dr. Kercsmar said. ■

Automatic Airway Pressure Devices Can Treat Simple Apnea

BY JANE SALODOF MACNEIL
Southwest Bureau

SCOTTSDALE, ARIZ. — Automatic devices that adjust continuous positive airway pressure in response to changes in airway resistance or flow are as effective as conventional machines for the treatment of uncomplicated obstructive sleep apnea, Dr. Neil S. Freedman said at a meeting on sleep medicine sponsored by the American College of Chest Physicians.

AutoCPAP (APAP) will never be superior to fixed continuous positive airway pressure (CPAP) as a treatment, but it offers two advantages: faster treatment of apnea, and the potential for lower costs, according to Dr. Freedman, who is with a group practice that specializes in sleep disorders in Bannockburn, Ill., and the sleep center at Lake Forest (Ill.) Hospital.

Citing long waits for sleep studies, he said that he will put a patient on APAP pending a sleep study if the person weighs 300 pounds, snores, has had observed apnea, and is drowsy during the day. In such cases, he said, the sleep study must still be done within 30 days to secure reimbursement and to determine pressures.

Although attended APAP in a sleep laboratory is currently accepted as useful for titrating fixed CPAP pressures in uncomplicated patients, Dr. Freedman said that unattended APAP has not been established as useful for that purpose. Unattended APAP also is not established as a treatment for patients who have never used CPAP, but Dr. Freedman said this may no longer be valid.

AutoCPAP will never be superior to fixed CPAP, but it's faster and less expensive.

DR. FREEDMAN

He cited a randomized controlled trial in which 360 patients were randomized to standard CPAP, APAP titrated at home, or titration at home by a predicted formula (Am. J. Respir. Crit. Care Med. 2004;170:1218-24). Successful home titration of APAP went from 83% on the first try to 96% on the second try. All groups had equivalent improvements in quality of life, and nearly all patients wanted to continue the treatments to which they had been assigned.

Dr. Freedman listed various monikers for the new technology—automated, auto-titrating, auto-adjusting, and self-titrating—but settled on APAP as a common term. The devices vary considerably in efficacy, he advised, and their role in treating obstructive sleep apnea is not well defined.

"All APAPs are not the same," he said, warning against generalizing conclusions from clinical studies of any one APAP technology to APAP devices as a class.

He emphasized that the devices use different detection methods, employ different algorithms, and have different response times. Notably, whereas some monitor inspiratory flow, others measure resistance.

"They all respond in different ways," he said. "Nobody knows what the best algorithm is."

Among the studies he cited was a benchmark testing of five APAP machines (Eur. Respir. J. 2004;24:649-58). All five suppressed obstructive apnea, but none suppressed flow limitation. The investigators reported considerable variation in residual hypopnea, control of snoring, and response to mask leaks. Four of the machines inappropriately increased pressure in response to central apnea.

Dr. Freedman suggested APAP machines that use a forced oscillation technique (FOT) may be better suited than flow-based APAP for evaluation of central apnea.

"You don't want a machine to make central apnea worse," he said.

APAP should not be used to treat patients who hyperventilate, have heart failure or COPD/chronic lung disease, or do not snore, according to Dr. Freedman. All these conditions have been excluded from the studies performed so far.

He said the lack of data also makes APAP's efficacy unclear for obstructive sleep apneas that are related to rapid eye movement, are position dependent, involve high pressures, or occur in patients who are intolerant of CPAP. ■