Alternative Approach May Help in Severe Asthma

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PHILADELPHIA — Some patients with severe or difficult-to-control asthma are still failing to achieve control, despite taking high doses of both inhaled corticosteroids and long-acting β-agonists as recommended by current practice guidelines.

"These findings highlight the unmet need in severe or difficult-to-treat asthma and the need for an alternative therapeutic approach," Dr. Larry Borish said at the annual meeting of the American College of Allergy, Asthma, and Immunology.

Dr. Borish, of the University of Virginia, Charlottesville, presented a subgroup analysis of the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study, the largest investigation to date of patients with severe or hard-to-control asthma.

Although there have been many clinical trials involving the salmeterol/fluticasone combination (SFC), most have been in patients with mild or moderate disease. TENOR is the first study in which researchers are examining the drugs' effects in patients with severe or hard-to-control disease, Dr. Borish said in an interview.

TENOR had patients with mild and moderate asthma (3% and 48%, respectively), but the disease was classified as difficult to treat in 98% of the group.

Dr. Borish's analysis described 24-month treatment outcomes in 1,253 adults: 205 on low-dose salmeterol/fluticasone (SFC with 100 mcg or 250 mcg fluticasone), 271 on high-dose SFC (500/50), and 777 on other medications and naive to SFC.

All of the patients were assessed at baseline and at 24 months with multiple measures, including the Asthma Therapy Assessment Questionnaire (ATAQ), the Asthma-Related Quality of Life (AQoL), and forced expiratory lung volume in 1 second (FEV_1). An important statistical point, Dr. Borish said, was that propensity scores were used to adjust for selection bias and confounding between the groups. "This is extremely robust and may approximate a randomized controlled experiment," he said in an interview.

Before adjustment, the low-dose SFC group had significantly higher quality of life scores, compared with the control group. However, although the difference persisted after adjusting for confounders, it was not clinically significant, Dr. Borish said. The high-dose SFC group had significantly lower quality of life scores, compared with the control group, a difference that was lost after adjustment.

The low-dose SFC group had higher quality of life scores, whereas the high-dose SFC group had lower quality of life scores, compared with controls.

ATAQ scores after adjustment were lower in the low-dose SFC group than in the control group, indicating better control. However, in the high-dose SFC group, the scores were not significantly different from those in the control group.

The high-dose SFC group had significantly higher FEV_1 after adjustment than did the control group, whereas FEV_1 values in the low-dose group were only marginally higher than they were in controls.

After 24 months of treatment, patients on low-dose SFC were significantly less likely than controls to be classified as having severe asthma, whereas patients on high-dose SFC were significantly more likely than controls to have severe asthma. However, asthma exacerbation rates were similar between controls and both treatment groups.

The results paint a picture of a group of asthma patients failing to respond well to therapy, despite receiving the high doses of SFC suggested by current guidelines, Dr. Borish said. "[Perhaps those] who were started on low-dose SFC and did well enough for their physicians to keep them on that low dose, by our outcome parameters, are doing better than the patients who were either started on or… moved to higher-dose SFC. Patients on the higher dose probably look worse because they are more likely to have a disease that is resistant to corticosteroids and either resistant to long-acting β-agonists or conceivably even exacerbated by them."

Many patients don't respond to the low-dose SFC but do well on the higher dose. Because their asthma is controlled, they were not included in the study, supported by a grant from Genentech Inc. ■

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