

Bronchial Thermoplasty Demonstrates Efficacy

Experimental radiofrequency energy system reduced asthma attacks by 32%, ED visits by 84%.

BY DOUG BRUNK

SAN DIEGO — The Alair Bronchial Thermoplasty System produced significant improvements in quality of life in 79% of patients with severe asthma who underwent treatment, compared with 64% of sham controls, results from a randomized, multicenter pivotal trial demonstrated.

Moreover, patients in the treatment group had a 32% reduction in asthma attacks, an 84% reduction in emergency room visits for respiratory symptoms, and a 66% reduction in days lost from work, school, or other activities due to respiratory symptoms.

The findings exceeded the expectations of principal investigator Dr. Mario Castro, professor of medicine and pediatrics at Washington University, St. Louis. "These patients were getting maximal treatment with the standard of care," Dr. Castro said during an interview at an international conference of the American Thoracic Society, where the work was presented. "Beyond that we were able to get a marked improvement in quality of life, health care utilization, and days lost from school or work. Those are meaningful end points for our patients."

One of the patients Dr. Castro treated was a long-distance runner who had been sidelined because of the severity of his asthma. After undergoing bronchial thermoplasty he returned to running and went on to compete in a marathon.

"You can't get more of a testament than that," he said.

Developed by Asthmatx Inc. of Sunnyvale, Calif., the Alair Bronchial Thermoplasty system is an investigational device that delivers radiofrequency energy

to the airway walls during a bronchoscopic procedure in an effort to reduce the amount of airway smooth muscle.

The procedure, which takes 30-45 minutes to perform, is not designed to replace standard of care therapy, Dr. Castro said, but rather as "an add-on treatment we can do once patients are not achieving good control with the standard of therapy. It's nice to have something else to look forward to with these patients, because they come to your office and they're really desperate for something new in treatment."

After their first treatment patients return for two additional bronchoscopic treatments spaced 2-3 weeks apart. "It's definitely a time commitment in terms of getting the treatment, recovering, and getting the two additional treatments," noted Dr. Castro, who also directs Washington University's Asthma and Airway Translational Research Unit. "But you compare that to having to take a drug every day for the rest of your life, it's a small investment."

The Alair System has received a CE mark for use in the European Union. In the United States a premarket approval application has been submitted to the Food and Drug Administration, which is expected to review the application this summer.

The purpose of the Asthma Intervention Research 2 (AIR2) trial was to evaluate the safety and effectiveness of the Alair System in 297 patients with severe asthma at 30 centers in six countries who were symptomatic despite being treated with high doses of inhaled corticosteroids and long-acting bronchodilators.

The trial was randomized, double blind, and sham controlled, and the primary effectiveness end point was significant improvement from baseline in Asthma Quality of Life Questionnaire (AQLQ) score.



There was marked improvement in patients who were already 'getting maximal treatment with the standard of care.'

DR. CASTRO

Of the 297 patients 196 received bronchial thermoplasty while 101 received a sham bronchoscopy in which no radiofrequency energy was applied. The average age of patients was 41 years, and more than half were female.

Dr. Castro reported that 79% of patients in the treatment group had significant clinical improvements in their average AQLQ scores at 12 months, compared with 64% of patients in the sham group, a difference that was statistically significant.

Compared with patients in the sham group, patients in the treatment group had a 32% reduction in asthma attacks, an 84% reduction in emergency room visits for respiratory symptoms, a 36% reduction in patients reporting asthma (multiple symptoms) as an adverse event, and a 66% reduction in days lost from work, school, or other activities caused by respiratory symptoms.

If the Alair system is approved for use, Dr. Castro expects a significant impact on the pulmonology field. "This is a new treatment for a lung disease that is very common, so our field is going to have to get comfortable with this new device and new treatment," he commented.

"I think it's going to have a significant impact on how pulmonologists are trained on this new device. If this gets approved there will be a need for training workshops so that physicians are comfortable with its use. I think it's going to have a profound impact on our care of these patients with disabling asthma."

While the cost of the procedure will vary by practice setting, he expects it to be in the ballpark of a bronchoscopy.

Dr. Castro disclosed that he is a paid consultant for Asthmatx, which funded the study. ■

Low-Level Smoking More Damaging to Women Than Men

BY DOUG BRUNK

SAN DIEGO — Women are more susceptible to the lung-damaging effects of smoking, compared with men, results from a large case-control study demonstrated.

The gender effect seemed to be most pronounced when the level of smoking exposure was low and decreased in magnitude with an increasing number of pack-years, lead investigator Dr. Dawn L. DeMeo reported in a poster session at an international conference of the American Thoracic Society.

"This is crucial, especially from a public health standpoint, because many people feel that one, two, or five cigarettes per day is fine," Dr. DeMeo, assistant professor of medicine at Harvard Medical School and the Channing Laboratory, Boston, said in an interview. "What we want to promulgate from this study is that there is no safe exposure to cigarette smoke, especially for young women."

She and her associates evaluated data from a case-control study performed at Haukeland University Hospital in Bergen, Norway, between 2003 and 2005 that involved 583 men and 371 women with chronic obstructive pulmonary dis-



In smokers with similar COPD severity, women had less exposure to cigarettes.

ease (COPD). To be eligible for the trial, participants had to be white, at least 40 years of age, and current or ex-smokers with a history of 2.5 pack-years or more, and they had to have no severe alpha-1 antitrypsin deficiency.

The researchers observed no differ-

ences between men and women with respect to lung function and COPD severity, but the women were younger (a mean of 64 vs. 66 years) and had smoked significantly less than men (a mean of 24 vs. 32 pack-years).

Dr. DeMeo and her associates then restricted the analysis to two subgroups: an early-onset group of 316 patients who were younger than age 60 at the time of the study and a lower-exposure group of 241 patients with a smoking history of fewer than 20 pack-years. Analysis of these subgroups revealed that females had a later smoking onset and fewer pack-years compared with males.

Women in the study also had a more severe reduction of forced expiratory volume in 1 second for lower levels of smoking exposure, but after 25-30 pack-years the curves for males and females converged and showed a similar dose-response relationship.

"There seems to be a female predominance for the lung-damaging effects of cigarette smoke, but it seems to be most pronounced when the cigarette smoke exposure is on the lower end," said Dr. DeMeo, who is also with Brigham and Women's Hospital's lung transplantation program and the COPD center at the Center for Chest Diseases.

Reasons for the gender differences remain unclear, but could be related to the fact that women have smaller lungs than men. "That likely doesn't explain all of the potential impact here," she commented.

"There have been hormonal arguments cited and also social constructs associated with gender differences. Perhaps women are underreporting [their cigarette smoking]. One of the goals of our research group at the Channing Laboratory is to address what may be going on from genetic and epigenetic points of views. More research is needed," she said.

For now, Dr. DeMeo added, "the onus is on clinicians to think about COPD early, especially in women who report lower exposures to cigarette smoking."

She acknowledged certain limitations of the study, including its retrospective design and the fact that it was conducted only in Norwegian whites.

The study received funding from the Research Council of Norway, Glaxo-SmithKline, and the Foundation for Respiratory Research at Haukeland University Hospital. Dr. DeMeo was supported by a grant from the National Institutes of Health and an award from the Doris Duke Charitable Foundation. ■