COPD Hospitalization Rate Low for Tiotropium

BY BRUCE JANCIN

SAN DIEGO — Patients whose chronic obstructive pulmonary disease was treated with tiotropium monotherapy had significantly fewer disease-related hospitalizations during a 12-month window than those on other long-acting bronchodilator regimens, a large national study shows.

The retrospective study looked at COPD-related inpatient admissions in Thomson MarketScan, a large U.S. administrative claims database.

The analysis involved 52,274 commercially insured patients with COPD who had one or more prescription claims for a long-acting bronchodilator (LABD) from 2004 to 2006, Emily D. Durden, Ph.D., reported at the annual meeting of the American College of Chest Physicians.

The COPD patients were categorized into five LABD regimens.

Those who were on monotherapy with tiotropium (Spiriva) had significantly lower rates of disease-related hospital admissions during 12 months of follow-up than those using salmeterol (Serevent), formoterol fumarate (Foradil), salmeterol/fluticasone propionate (Advair), or combination therapy with two or more LABDs, said Dr. Durden of Thomson Reuters in Austin, Tex. (See chart.)

The association between LABD regimen and COPD-related hospital admissions was evaluated in a multivariate logistic regression analysis that adjusted for potential confounders including age, gender, urban versus rural location, comorbid conditions, insurance type, emergency department use, and respiratory hospitalizations during the 6 months immediately prior to the 12-month study period.

Patients in the tiotropium monotherapy group had significantly more comorbidities than those in the other study arms. They also were more likely to have been vaccinated against influenza. Mean health care costs in the 6-month pre-period were lowest in the salmeterol group at $12,885 and highest in patients on combination LABD therapy, at nearly $17,100.

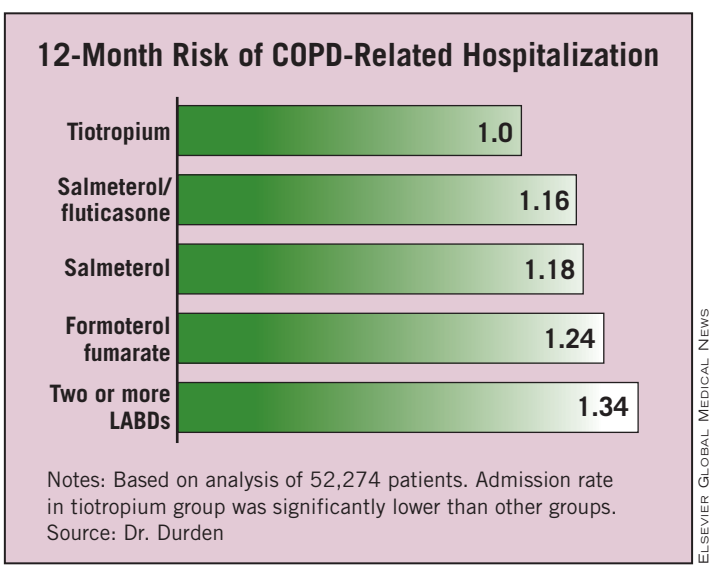
Dr. Durden noted that the retrospective, nonrandomized nature of her study means that it cannot provide proof that tiotropium was the actual cause of the significantly lower hospitalization rate.

However, Dr. Donald P. Tashkin described a new meta-analysis that he and his coworkers recently conducted, which incorporated data from 30 placebo-controlled clinical studies of tiotropium in COPD patients, including the massive 4-year Understanding Potential Long-Term Impacts on Function With Tiotropium (UPLIFT) trial (Chest 2010;137:20-30).

The results of this meta-analysis indicate that tiotropium provided a 12% reduction in the risk of all-cause mortality relative to placebo and a 17% reduction in the risk of composite cardiovascular events, including stroke as well as MI, said Dr. Tashkin, professor emeritus of medicine at the University of California, Los Angeles.

The relative risks of acute MI and of heart failure were reduced by 23% and 17%, respectively, in this analysis, which was based upon more than 13,000 patient-years of exposure to the LABD. ■

Disclosures: *Dr. Tashkin's meta-analysis and Dr. Durden's study were both funded by Boehringer Ingelheim and Pfizer, which comarket tiotropium. Dr. Tashkin is a consultant to both companies. Dr. Durden reported having no financial conflicts.*



ELSEVIER GLOBAL MEDICAL NEWS

Prevention Getting Closer for Pulmonary Hypertension

BY SALLY KOCH KUBETIN

SANTA MONICA, CALIF. — Management of pulmonary hypertension in systemic sclerosis is inching its way toward a new age of prevention.

The change is coming from the appreciation that the finding of exercise-induced pulmonary hypertension (PH) likely represents abnormal hemodynamic manifestation in patients with systemic sclerosis (SSc) who have normal resting mean pulmonary artery pressure. And that this finding may flag those patients who are most likely to benefit from early, aggressive treatment.

Currently, by the time most cases of resting PH in SSc are diagnosed, the underlying hemodynamic disease process has become irreversible. "We are able to treat it. However, we are not able to cure it," said Dr. Rajeev Saggar. As a result, the prognosis is grim.

Until the concept of screening for exercise-induced PH in systemic sclerosis catches on, 'before you ever treat a patient with PH, you have to get a right heart catheterization.'

PH-SSc tends to have a poorer prognosis, compared with other WHO Group I diagnoses. Recently, isolated PH-SSc survival, while receiving pulmonary vasodilator therapy, was reported at 78% at 1 year and 47% at 3 years. Furthermore, survival in PH-SSc associated with interstitial lung disease is even worse, said Dr. Saggar, a pulmonologist in the lung transplant and pulmonary hypertension division of the University of California, Los Angeles.

In an investigational program at his institution, treatment is being started in patients who have exercise-induced PH.

The exercise stress regimen involves patients, with a right heart catheter in place, riding a stationary supine bicycle for 3-9 minutes.

Those with an exercise mean pulmonary artery pressure greater than or equal to 30 mm Hg and a pulmonary wedge pressure less than or equal to 18 mm Hg receive treatment with an endothelin antagonist. All of these patients have normal resting mean pulmonary artery pressures.

Recent data from a U.K. study of 42 SSc patients with exercise-induced PH showed that 8 progressed to resting PH within 2-3 years, and 4 died from complications of pulmonary vascular disease within 3 years. "By waiting to diagnose this disease until it is present in the resting state, we are losing our opportunity to treat it," he said.

These findings support the observation that "patients with SSc should be evaluated for exercise-induced PH. It's abnormal and should be treated in the context of a clinical study," said Dr. Saggar said at a meeting sponsored by RHEUMATOLOGY NEWS and Skin Disease Education Foundation.

For now, until the concept of screening for exercise-induced PH catches on, "before you ever treat a patient with PH, you have to get a right heart catheterization. Right heart catheterization is not that invasive in the right hands. The risk of associated mortality is less than 0.05%," he said. Prognosis can be based on the findings from this test, he added.

Not all physicians are comfortable going straight to right heart catheterization. For them, yearly echocardiography and spirometry can be used to screen for PH. Certain clinical findings in scleroderma patients can identify which patients are likely to have PH. Early screening with noninvasive studies such as an echocardiogram and pulmonary function tests may detect these patients earlier.

Typical symptoms of any patient with scleroderma who has unexplained shortness of breath should also raise the physician's concern. Likewise PH should be on the short list of the differential diagnosis in any young scleroderma patient who has syncope. "These patients tell their physicians: 'I coughed and passed out.' Or 'I stood up and passed out,' " Dr. Saggar said at the meeting.

However, once a patient develops unexplained breathlessness, it is necessary to do right heart catheterization, he said. Breathlessness in any patients with PH associated with SSc is a sign that the disease is progressing. Aggressive management is the best hope for survival in SSc patients with PH.

The available treatments for PH remain of "arguable" efficacy, especially when they are initiated late in the course of the disease, when it has become incurable, according to Dr. Saggar.

In this progressive disease, increased pulmonary pressure is only part of the pathology. The benefit of serial right heart catheterization is that it enables the physician to assess the degree of right ventricular impairment. "What you are really worried about is the right ventricle. Failure of the right heart drives death," he said.

As long as vascular resistance continues to increase, the patient remains in jeopardy. The right ventricle begins to fail in response to the increased vascular resistance.

PH is very rare. It is estimated to occur in 2.3-10 cases per 1 million population. Patients with SSc make up about 20% of all newly diagnosed PH patients. A recent French study that screened for PH in SSc using echocardiography and right heart catheterization showed a prevalence of 7.9%. However, findings from an autopsy study show that 60% of patients with SSc have findings typical of PH.

"This disease goes undiagnosed a lot of the time," said Dr. Saggar. ■

Disclosures: *Dr. Saggar reported no financial relationships that are relevant to this presentation. This newspaper and Skin Disease Education Foundation are owned by Elsevier.*