Data Mixed on Anticholinergic Use for COPD

BY MITCHEL L. ZOLER
Philadelphia Bureau

PHILADELPHIA — Despite recent hints of danger, inhaled anticholinergic drugs remain a mainstay of treatment for many patients with chronic obstructive pulmonary disease.

Inhaled anticholinergic drugs such as ipratropium and tiotropium should not be used in patients with chronic obstructive pulmonary disease (COPD) who are also at high risk for cardiovascular disease complications. This high-risk group includes patients with a significant cardiac arrhythmia, a recent cardiovascular disease event, ischemic heart disease, or heart failure, Dr. R. Graham Barr said at the annual meeting of the American College of Chest Physicians. An inhaled anticholinergic drug should also be avoided in patients with glaucoma.

But treatment with an inhaled anticholinergic agent is still a good option for COPD patients who do not have a history of cardiovascular disease or another condition that potentially could be worsened by these drugs, said Dr. Barr, an internal medicine physician and epidemiologist at Columbia University in New York.

He supported the continued use of an anticholinergic drug in selected patients with COPD despite results from two studies reported last September that called into question the safety of this drug class in patients with COPD.

Those findings, as well as results from a report in October from a randomized, controlled trial with nearly 6,000 patients with COPD showing that tiotropium was safe, were the focus of a meeting session.

In the first case-control study that examined the risk of for dealth among more than 350,000 newly diagnosed COPD patients, those patients on an inhaled corticosteroid had a significantly reduced risk for cardiovascular death or all-cause death, and patients treated with a long-acting β-agonist had a significantly reduced risk for all cause death (Ann. Intern. Med. 2008;149:380-90).

In contrast, patients treated with ipratropium (the only inhaled anticholinergic examined in the analysis) had a significantly increased risk for both cardiovascular death and all-cause death. In addition, patients treated with theophylline had a significantly increased risk of respiratory death.

The second set of results that revealed possible adverse effects from inhaled anticholinergics came from a meta-analysis of 17 previously reported studies that involved a total of 14,783 patients with COPD. Nine of the studies involved a placebo control, and eight used an active arm with an alternative drug regimen as the control group. Twelve of the studies used tiotropium, and five used ipratropium (JAMA 2008;300:1439-50).

The results showed that the relative risk for cardiovascular death, myocardial infarction, or stroke was 58% higher in the patients treated with an inhaled anticholinergic drug, compared with the control patients, a significant difference. This increased risk in the combined end point was not part of the published report, but was reported at the meeting by Dr. Curt D. Furberg, professor of public health sciences at Wake Forest University, Winston-Salem, N.C., and a coauthor of the meta-analysis.

Another new analysis reported at the meeting showed that a significant increase in cardiovascular risk occurred primarily in the five studies that involved treatment that extended beyond 6 months, with an increased risk of 73%. In the 12 studies in which treatment duration ranged from 6 weeks to 6 months, the increased cardiovascular risk with anticholinergic treatment was 16%, a difference that was not statistically significant, Dr. Furberg said.

A separate randomized study compared 4 years of tiotropium therapy with placebo in 5,993 patients with COPD. The Understanding Potential Long-Term Impacts on Function with Tiotropium (UPLIFT) study failed to find a significant difference between tiotropium and placebo for the study's primary end point, the rate of decline in lung function (N. Engl. J. Med. 2008;359:1543-54). The results did show significant improvements with tiotropium treatment, compared with placebo, for some secondary efficacy end points, including health-related quality of life and a delay in time to first exacerbation.

The safety analysis showed that treatment with tiotropium was linked with a significant, 16% relative reduction in death from any cause, compared with placebo. Dr. Barr said that he had no financial conflicts of interest relevant to his analysis. ■