

# Popular COPD treatment increases risk for cardiac events, cardiac death

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New research out of Wake Forest University School of Medicine shows that use of the most commonly prescribed once-a-day treatment for chronic obstructive pulmonary disease (COPD) for longer than one month increases the risk of cardiovascular death, heart attack or stroke by more than 50 percent.

Researchers Sonal Singh, M.D., M.P.H., and Curt Furberg, M.D., Ph.D., of Wake Forest, along with Yoon K. Loke, at the University of East Anglia, UK, conducted a meta-analysis of 17 double-blind, randomized trials involving a total of 14,783 patients with COPD. Participants received treatment with inhaled anticholinergics, another form of active therapy or a placebo inhaler.

An analysis of the data showed that use of inhaled anticholinergics for more than one month significantly increased the risk of cardiovascular death, heart attacks, or strokes in COPD patients by 58 percent.

The results appear in the Sept. 24 issue of *The Journal of the American Medical Association*.

Inhaled anticholinergics are a class of drugs that relax the airways and prevent them from getting narrower, making it easier to breathe. They also protect the airways from spasms that can suddenly cause the airway to become narrower (bronchospasm).

The two most commonly used inhalers from the anticholinergic class are

tiotropium bromide, marketed by Pfizer as Spiriva™, and ipratropium bromide, made and marketed by Boehringer Ingelheim as Atrovent™.

"Patients with COPD who use these inhalers are at a high risk of excess serious cardiovascular events due to their use," said Singh, an assistant professor of internal medicine. "In absolute terms, if these inhalers are used for one year, nearly one in 40 patients using these inhalers may develop cardiac death related to the drug, and nearly one in 174 patients may develop a heart attack associated with these inhalers."

COPD is the fourth-leading cause of chronic morbidity and mortality in the United States, and is projected to rank fifth in 2020 in burden of disease worldwide. Cardiac death is leading cause of death among patients with COPD. Inhaled tiotropium is indicated for the long-term, once-daily maintenance treatment of symptoms associated with COPD and is the most widely used drug in COPD treatment. More than 8 million patients worldwide have used inhaled tiotropium since its approval.

The increased risk of cardiovascular events and cardiovascular death was particularly manifest in the five long-term trials (longer than 6 months) studied. In the 12 short-term trials, the direction of the drug effect was similar to that of the long-term trials.

"A regulatory reassessment of the cardiovascular safety concerns with this class of inhalers in patients with COPD is urgently needed," Singh said.

"These findings, especially the magnitude of the risk, and the consistency of the risk for heart attack, stroke and cardiac death, urge caution in the widespread use of these agents," he added. "Patients and doctors should decide whether these serious long-term cardiovascular risks outweigh their symptomatic benefits."

Source: Wake Forest University Baptist Medical Center

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