Triple Therapy Benefits Patients with Severe COPD

A large trial showed that adding a third drug to a two-drug COPD regimen produces superior bronchodilation and reduces exacerbations.

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February 23, 2017 - The TRILOGY study for chronic obstructive pulmonary disease (COPD) showed that, compared with standard two-drug therapy, treatment with two long-acting bronchodilators and one inhaled corticosteroid produced significantly greater improvements in bronchodilation and a 23% lower rate of COPD exacerbations in patients with severe or very severe COPD.

Dave Singh, MD, with the University of Manchester, UK, and colleagues published their findings from the study in the September 3rd, 2016 issue of *The Lancet*.

COPD is typically treated with either a long-acting muscarinic antagonist or with an inhaled corticosteroid combined with a long-acting B_2 agonist. When these treatments are inadequate to prevent a patient's COPD exacerbations, patients are commonly placed on triple therapy, which consists of treatment with a long-acting B_2 agonist, a long-acting muscarinic antagonist, and an inhaled corticosteroid. However, the efficacy of triple therapy for preventing exacerbations is unclear, though previous studies have shown that triple therapy provides greater bronchodilation than the two-drug treatment.

The TRILOGY study was a randomized, double-blind trial conducted at sites in 14 countries. The trial was designed to compare improvements in bronchodilation, dyspnea, quality of life, and the rate of exacerbations, in participants treated either with BDP/FF (the inhaled corticosteroid beclometasone dipropionate plus the long-acting B_2 agonist formoterol fumarate), or with BDP/FF/GB triple therapy (BDP, FF, and the long-acting muscarinic antagonist glycopyrronium bromide).

A total of 1368 patients with COPD were included in the trial; all met the study criteria for disease severity, including post-bronchodilator forced expiratory volume in 1 second (FEV_1) of less than 50%, and were currently being treated with an accepted COPD regimen other than triple therapy. Participants were placed in an open-label run-in period for two weeks in which they received BDP/FF twice daily. Participants were then randomized at a 1:1 ratio to receive twice-daily doses of either BDP/FF or triple therapy (BDP/FF/GB) delivered using a single inhaler.

Dosing continued for 52 weeks, and three co-primary endpoints were measured at week 26. Results showed that patients on triple therapy had significantly greater improvement than those on BPD/FF for the first and second endpoints, change from baseline in pre-dose FEV_1 (0.081 L greater improvement; 95% CI 0.052-0.109; $p<0.001$) and change from baseline in 2-hour post-dose FEV_1 (0.117 L greater improvement; 95% CI 0.086-0.147; $p<0.001$). For the third primary endpoint, transition dyspnea index (TDI) focal score (a self-reported measure of breathlessness),

results suggest a greater benefit with triple therapy, but the difference was not statistically significant.

Compared with BDP/FF, patients on triple therapy also experienced 23% fewer moderate or severe COPD exacerbations (rate ratio 0.77; 95% CI 0.65-0.92; p=0.005), less frequent use of rescue inhalers, and significantly greater improvements in COPD-related quality of life.

No significant differences in adverse events were observed between the two treatment groups.

The authors stated that this trial provides evidence that triple therapy is beneficial for patients with severe COPD and that the trial "allows clinicians to better understand the consequences of escalation of maintenance therapy in patients with COPD already treated with inhaled corticosteroid/long-acting β2-agonist therapy."

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