PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #427
COPD: EMERGING THERAPIES WHICH CAN ALSO PALLIATE SYMPTOMS
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Background Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the world (1) and is associated with a symptom burden comparable to cancer (2). This *Fast Fact* focuses on noninvasive COPD-specific advances that have emerged in recent years that impact quality of life. For additional information on COPD see *Fast Facts* #199, #200, #158, #230, and #231. *Fast Fact* #376 comprehensively reviews dyspnea therapies.

Pathophysiology COPD is an inflammatory obstructive lung disease characterized by airflow limitation (4). The pathophysiological mechanism of dyspnea in COPD is dynamic lung hyperinflation, leading to hypoxemia, hypercapnia, and neuromechanical disassociation (4). Additionally, evidence from functional imaging studies shows that there is a significant *affective* component to breathlessness, leading to the emerging framework of "total dyspnea" which emphasizes the behavioral and mood aspects of dyspnea alongside physiologic inputs (5).

Interrupting the dyspnea-anxiety cycle There is increasing recognition that COPD requires a palliative care model composed of the integration of non-pharmacological and pharmacological interventions (3). One example is "The Breathing, Thinking, Functioning" model used by the Cambridge Breathlessness Intervention Service (CBIS). This cognitive behavioral model addresses three aspects of the cycle of breathlessness: inefficient breathing, anxiety, and muscle deconditioning (3). It provides targeted cognitive behavioral and self-management techniques for each aspect and has been shown to reduce anxiety, depression, emergency room visits, and hospitalizations (3). Examples of such techniques include passive fixation of the shoulder girdle by placing the hands on the hips and having the patient lean forward when sitting to dome the diaphragm and improve inspiratory force generation.

Inhaler improvements Patients with severe COPD often suffer from dynamic hyperinflation that prevents generation of sufficient inspiratory flow to effectively use traditional metered-dose-inhalers or dry powder inhalers. Newer inhaler devices utilize a prolonged aerosol mist delivery system. Delivering the drug through a prolonged aerosol mist facilitates ease of use and improves drug delivery even in the situation of reduced inspiratory flow (7). Combined aerosol mist inhalers that include long-acting beta agonists and long-acting muscarinic antagonists are a useful way to maintain guideline suggested therapies even in the setting of reduced inspiratory flow. Currently these devices are marketed with "inhalation spray" and "Respimat" in the drug names (e.g., tiotropium bromide inhalation spray, which is marketed as "Spiriva Respimat").

Oscillating Positive Expiratory Pressure (OPEP) There is increasing evidence for the use of OPEP devices (sometimes called a 'flutter valve') to reduce dyspnea, respiratory secretions, and exacerbations (8). OPEP devices, which look like a handheld inhaler device, provide rapidly oscillating positive pressure to patients' airways when they exhale through it. These high frequency oscillations aid in secretion clearance and have been shown to reduce dyspnea and rates of exacerbations (8). OPEP devices can be used even in the setting of reduced inspiratory flow as they rely only on expiratory flow and are not affected by dynamic hyperinflation. The use of bronchodilators prior to using OPEP devices may also help prevent coughing and further aid in secretion clearance.

Azithromycin reduces respiratory secretions through an anti-inflammatory mechanism as well as by reducing bacterial load (9). The addition of chronic azithromycin (patients are typically prescribed it for many months to years) reduces exacerbations in patients who continue to experience exacerbations despite recommended therapy (10). Since chronic antibiotics can impact bacterial gastrointestinal flora and lead to antibiotic resistance, referral to a pulmonologist prior to starting chronic azithromycin may be wise if prognosis and length of use is anticipated to be prolonged

Roflumilast is an oral phosphodiesterase-4 inhibitor that acts as an anti-inflammatory through inactivation of cyclic adenosine monophosphate and cyclic guanosine monophosphate (11).

Its main indication is to reduce the number of exacerbations in patients experiencing 2 or more exacerbations a year from severe COPD. Post-marketing data also indicate it can reduce cough, respiratory secretions, and breathlessness through anti-inflammatory effects on mucus production (12). Its major side effects are anorexia/weight loss and diarrhea; rarely it causes anxiety and mood changes (12). Although roflumilast is currently indicated to reduce exacerbations, it may be useful as an adjunct to reduce respiratory secretions. In 2021 its non-discounted monthly cost is approximately $400 USD.

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