



## Palliation of Refractory Dyspnea in a Patient with End Stage COPD (Chronic Obstructive Pulmonary Disease)

Sidra Anwar<sup>1</sup> and Amy Case<sup>2\*</sup>

<sup>1</sup>Department of Medicine, State University of New York at Buffalo, USA

<sup>2</sup>Division of Geriatrics and Palliative Medicine, University at Buffalo, USA

\*Corresponding author: Amy A. Case, MD, FAAHPM, Palliative Medicine Fellowship Program Director, Associate Professor of Medicine, Division of Geriatrics and Palliative Medicine, VA Western New York Healthcare System and University at Buffalo, USA, Tel: 716-862-3282, Fax: 716-862-8655, E-mail: [amy.case@roswellpark.org](mailto:amy.case@roswellpark.org)

### Abstract

This review article highlights the immense morbidity experienced by COPD patients, emphasizes the need for palliative care in this population, and focuses on treatment of refractory dyspnea with opioids as highlighted in our case.

### Keywords

Palliative care, COPD, Dyspnea, Shortness of breath, Opioids, Quality of life

### The Case

Mr. M was a 74-year-old male Korean War veteran who presented to the hospital with an acute exacerbation of his Chronic Obstructive Pulmonary Disease (COPD). The patient had a 50 pack-year history of smoking and continued to smoke one-and-a-half packs of cigarettes per day. He was frail with barrel chest and pursed lip breathing, tachypnea, and dyspneic at rest. He was on Albuterol, Ipratropium bromide, and Fluticasone propionate, in addition to home oxygen 3 liters, 24 hours per day. Recent pulmonary function test revealed a FEV1 of 26%, air trapping and markedly diminished diffusion capacity.

His condition was complicated with diabetes mellitus, hypertension, coronary artery disease, pulmonary hypertension, depression, and post-traumatic stress disorder. He was a widower who lived at home with his cat, and had a supportive niece who checked on him four times a week. She helped him with cooking and housekeeping. However, she was a single mother and worked full time.

This was his third exacerbation of COPD over the last year. His functional status was progressively worsening at home. Physical therapy prescribed him a walker for ambulation, which was limited to short distances around his apartment due to his breathlessness on mild exertion and sometimes at rest. His weight had been dwindling secondary to his abating appetite.

In the emergency department he was found to be tachypneic, hypoxic and hypercapneic and was admitted to the Intensive Care Unit with Bi level positive airway pressure (BiPaP), nebulized bronchodilators around the clock and empiric antibiotics. After a few

hours he tried to remove his mask in the effort to drink, however, he quickly desaturated and became cyanotic. He adamantly refused intubation and was reluctantly put back on BiPaP. Over the course of the next week, several attempts were made to remove his BiPaP but each time the patient would become cyanotic and dyspneic and was placed back on. At this point the palliative care team was consulted to help with advance directives and symptom management.

The palliative care team called in his niece for a family meeting. After a long discussion focusing on goals of care, Mr. M opted to have a “do not resuscitate” and “do not intubate” (DNR/DNI) on his file with only comfort measures to be employed. The palliative care team started him on a low dose opioid, morphine 5 mg orally every four hours around the clock, for refractory dyspnea along with sennakot twice daily. He later was transferred to the hospice inpatient unit where he was terminally weaned off the BiPaP as he no longer wished to struggle with the mask. We were prepared for him to have dyspnea and concerned he may tire out and die within hours after BiPaP removal.

He remained off BiPaP and despite looking cyanotic, did not have any dyspnea or tachypnea. He remained alert and awake and stated that he felt well. He used the opiates around the clock and his morphine dose was increased to 10 mg orally every 4 hours around the clock and 5 mg orally every 2 hours for breakthrough dyspnea, which he would take before he had to move around. He was able to visit with his family and friends while on the palliative care unit. The patient did have dyspnea on exertion, but was able to get into a chair during frequent visits from his niece and even his cat, who was allowed to visit him on the palliative care inpatient unit. The social worker and chaplain members of the palliative care team visited him, listening and encouraging him to talk about his life. He subjectively reported that these visits helped elevate his mood and improve his sleep. Mr. M lived for another 2 weeks before peacefully passing away, free from incapacitating breathlessness. Palliative care helped Mr. M live longer than expected with end stage COPD, in a dignified way with improved quality of life.

### Introduction

COPD (chronic obstructive pulmonary disease) is a chronic, inflammatory lung disease with impaired lung repair responses to noxious stimuli. Inhibition of repair may lead to tissue destruction

that characterizes emphysema, whereas abnormal repair can lead to the peribronchiolar fibrosis that causes airflow limitation in small airways [1]. However this does not mean that the effects of COPD in an individual are limited to the lungs. Indeed, left untreated and unmanaged this disease has significant detrimental effects not only on physical, but also social and psychological health [2].

With the aging population, prevalence of COPD is increasing worldwide [3]. COPD is associated with significant morbidity. The National Heart, Lung, and Blood Institute estimated the total (direct plus indirect) annual cost of COPD to the U.S. \$38.8 billion in 2005 dollars [4]. COPD is responsible for more than 120000 deaths per year in USA alone [5].

## Health Related Quality of Life (HRQoL) in COPD

COPD patients experience dyspnea, poor appetite, limitations of physical activity, emotional distress, and overall poor health-related quality of life (HRQoL) [6-8], which can be reduced even in mild stages of the disease [9]. HRQoL is defined as the degree to which a patient's health status affects his or her self-determined evaluation of satisfaction or quality of life [10]. Organizations such as Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) have identified HRQoL as a crucial measure to be monitored for people across all life stages [11].

Studies have shown that HRQoL is a predictor of mortality in COPD [12,13]. Compared to patients with lung cancer, patients with chronic lung disease have similar [14] or worse symptom burden and HRQoL, impacting their physical functioning, social functioning, mental health, general health perceptions, and ordinary daily activities [15]. Patients with chronic lung disease also are more likely to be institutionalized in a long-term care setting and to receive long-term home care [16].

The factors determining the HRQoL in COPD include sex, FEV1, use of oxygen therapy, comorbid conditions of anxiety and depression, number of visits to emergency rooms, hospital admissions for exacerbations, and the severity of dyspnea [9,17-20].

## The Burden of dyspnea in COPD and the need for Palliation

Dyspnea is defined as "a subjective sensation of difficulty in breathing" [21]. Numerous sensory afferent sources contribute to the multiple sensations of dyspnea, such as work or effort, tightness, and air hunger. Activation of cortico-limbic structures also is involved in the complex pathophysiology of breathlessness [22].

Dyspnea is the cardinal symptom in COPD. It typically starts with exercise, and as the disease progresses, it carries on during rest. At the end stages of the disease, dyspnea can be debilitating [23]. Patients cite dyspnea as one of the major symptoms that impact their quality of life [24]. Hajiro et al. found, in fact, that the HRQoL of COPD patients is more clearly separated by the level of dyspnea than by the American Thoracic Society disease staging [25]. Dyspnea is a predictor of hospitalization [26] and mortality in patients with COPD [27].

Palliative care focused on symptom management and maintenance of a reasonable quality of life, including management of dyspnea, is necessary for this chronic, debilitating illness and should be an integral part of management [28]. Palliative care focuses on open and effective communication, assisting informed decision making, and assisting a patient in coping with symptoms [29]. As defined by the WHO, "Palliative care means patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Throughout the continuum of illness palliative medicine involves addressing physical, intellectual, emotional, social and spiritual needs and to facilitate patient autonomy, access to information and choice" [30]. Often Palliative care is provided through a multi-disciplinary team that includes a physician, palliative care nurse, pharmacist, psychologist, bereavement counselor, social worker and chaplain or other clergy.

To date, there are many barriers to palliative care. These barriers can be broadly classified into physician and patient-related factors. Physicians struggle with identification of suitable patients for palliative care [31,32], inadequate information about the likely course of COPD at diagnosis [33], lack of time, limited resources, [34] and insufficient research data on the benefits of palliative care to COPD patients. Indeed, the research shows that palliative care for COPD patients reduces healthcare utilization and improves their quality of life [35].

For patients and caregivers, barriers to life-improving palliative care include limited awareness of palliative care [36] (including a lack of knowledge about associated services), uncertainty about care preferences [37], and poor communication with physicians [38].

Nevertheless, the importance of palliative medicine is underscored by available data suggesting that palliative care potentially improves quality of life by avoiding aggressive yet unsuccessful end of life interventions and cuts down on the costs [39].

Palliative care in COPD patients must target the disease's detrimental physical, emotional, and psychosocial effects. Caregivers should give special focus on treating the incapacitating symptom of dyspnea. Treatment should be aimed at the patient's expression and sensation of dyspnea and *not* objective findings of tachypnea or oxygen levels [40]. Although mainly treated with oxygen, inhaled bronchodilators, corticosteroids, and methylxanthines, there are many patients whose dyspnea cannot be alleviated through further treatment of their COPD and are diagnosed with refractory dyspnea [41].

## Management of Refractory Dyspnea

### Opioids

Opioids are the mainstay of palliative management of dyspnea. The mechanisms of action of opioids to reduce dyspnea include a reduction in the central perception of dyspnea and a decreased sensitivity to hypercapnia. The frequency of breathing is lowered, allowing for longer expiration times and decreasing hyperventilation and oxygen consumption. This also breaks the cycle of escalating anxiety associated with the dyspnea [42-44].

In 1981 dihydrocodeine was used in COPD patients and resulted in improved breathlessness and increased exercise tolerance. The concomitant use of supplemental oxygen augmented these effects [45]. Building on this initial study, in 1989 morphine was shown to decrease dyspnea related to exertion and, therefore, increase exercise capacity in COPD patients [46].

A 2002 systematic review supported the continued use of oral and parenteral opioids to treat dyspnea in patients with advanced disease [47]. The side effects reported were typical and treatable, and there was no evidence that opioids had a deleterious effect on arterial blood gases or oxygen saturation in the patient population studied. A subsequent review of nebulized opioids in COPD, however, failed to demonstrate a statistically significant beneficial effect on dyspnea in COPD [48].

In 2003, Abernathy *et al.* published results from a randomized, double-blind, placebo-controlled crossover study showing that sustained release oral morphine 20 mg provided significant symptomatic improvement in refractory dyspnea [41]. This was the first adequately powered randomized controlled trial that supported the use of an opioid for the symptomatic relief of dyspnea. Secondary analysis of the data did not show any relationship between the baseline severity of dyspnea and response to opioids [49].

Currently, there is no consensus regarding dosing of opioids for dyspnea. In addition to the studies mentioned, one trial showed a morphine dose of 5 milligrams every 4 hours delivered subcutaneously for opioid-naïve patients was useful and safe for controlling dyspnea [50]. More recently, oral morphine sustained-release 10 mg once daily, in opioid-naïve individuals, was found to be safe and effective,

significantly reducing patient ranking of breathlessness with no reported occurrences of respiratory depression, decreased level of consciousness, or delirium [51]. Furthermore, there was no opioid withdrawal reported in patients who chose to cease treatment.

Even today, however, many physicians are reluctant to prescribe opioids because they may lack necessary related knowledge and experience, and they may fear potential adverse effects from the drugs and/or possible legal action [52]. In a cross-sectional observational study, Janssen *et al.* found that only 1.9% of patients with advanced COPD were treated with opioids such as morphine and 57.1% reported severe dyspnea [53]. Patients and families suffer from this gap in care.

This is unfortunate because the evidence shows that opioids relieve dyspnea without a decrease in respiratory rate or oxygen saturation [41,54]. In the setting of terminal extubation, opioids have not been shown to hasten death. To the contrary [55], opioids have been linked to delayed time to death after withdrawal of life support [56,57].

Fears and misconceptions, often result in treating physicians opting for a “start low, go slow” approach when initiating opioids for dyspnea in COPD [58]. Rocker *et al.* propose avoiding a “forced pace” regimen so as not to risk losing patients’ confidence with opioids, and titrating treatment according to each individual. The goal is to minimize non-compliance due to side effects from the medication. Counselling regarding occasional delayed therapeutic responses should be performed. Patients and caregivers could benefit from written literature that discusses the common myths, fears, and side effects of opioids. Physicians also should provide their contact information once these medications are initiated, in order to provide reassurance to families.

### Advance care planning

Palliative management of refractory dyspnea in COPD patients must also include advance care planning, with a particular focus on BiPaP, intubation, and mechanical ventilation. Amongst a cohort of 105 subjects with chronic lung conditions, 98.9% of the patients wanted patient-physician advance directives discussions. The study found that only 19.0% had such discussions, 15.2% had discussed life-support, and only 14.3% thought that their physicians understood their end-of-life wishes [59]. Since physicians often feel incapable of accurately prognosticating COPD, they tend to avoid advance care discussions [34,38,60]. The natural course of COPD over the long term remains largely unknown, particularly as it relates to its duration, the impact of successive exacerbations, and the effect on mortality [61].

The repercussions of this oversight are immense. Patients and their families frequently do not understand that severe COPD can be a progressive and terminal illness [62]. When nearing end-of-life, COPD patients receive fewer symptom-alleviating treatments as compared to lung cancer patients [63]. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments showed that COPD patient were more likely than patients with lung cancer to receive invasive mechanical ventilation, cardiopulmonary resuscitation, or tube feeding before dying, even though both groups were equally likely to prefer care that was focused on comfort rather than extending life [64].

Patients who are under the care of a palliative care team have the opportunities to communicate and find out information about their disease that leads to their better understanding and preparation about what to expect. These patients experience greater symptom relief and are less likely to undergo aggressive care in the ICU, resulting in lower inpatient costs and improved quality-of-life [34].

Appropriate and timely referrals to Hospice will also greatly benefit individuals with COPD. Medicare guidelines for eligibility to enter hospice services for COPD are dyspnea at rest, hypoxia on room air, and signs of progression of disease including hospitalization [65].

## Conclusions

COPD is a relentless disease with increasing prevalence across the globe. This patient population has numerous unmet needs and suffers from refractory dyspnea that can be addressed with effective palliative care. The goal of palliative interventions in end-stage COPD is to decrease symptoms, clarify goals of care, and improve functional status and overall quality of life for patients [66]. As illustrated by Mr. M’s case, opioids are an effective tool to help COPD patients experience relief from their debilitating dyspnea and allow them maximal comfort prior to death. Without this intervention, Mr. M likely would have continued to struggle with BiPaP, refractory breathlessness, and anxiety until his efforts exhausted him and lead to his demise. This would have been a disservice to him and every other individual struggling with end-stage COPD. Physicians have an obligation to treat and aim for not only a better life, but a better death for all our patients.

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