

Edited by

Darrell A. Owens, PhD, ARNP, ACHPN



## *Nebulized Furosemide for the Treatment of Dyspnea*

Dyspnea is a bothersome symptom experienced by patients with a variety of terminal illnesses, including cancer, chronic obstructive pulmonary disease (COPD), congestive heart failure, and some neurological disorders.<sup>1</sup> Dyspnea is experienced by 33% to 47% of all patients with cancer and between 50% and 70% of those with end-stage disease.<sup>1,2</sup> In those with advanced disease, management of dyspnea may be difficult, even when the underlying cause is identified. The inability to catch one's breath is a complicated phenomenon that is often described using the terms *dyspnea* and *breathlessness*. Dyspnea, which refers to excessive exertion with breathing, differs from breathlessness, which is the unpleasant urge to breathe associated with the sensation of suffocating.<sup>1</sup> Dyspnea generates not only an unpleasant sensation but also the subjective response that accompanies it, referred to as *symptom distress*. Because the sensation is subjective, it is highly individualized and not always associated with objective measures of lung function.<sup>1</sup>

Treatments historically used in hospice and palliative care include opioids, anxiolytics, diuretics, and oxygen, all with varying degrees of efficacy. A recent review of the evidence related to the treatment of dyspnea found data, albeit limited, on the use of nebulized furosemide for the treatment of dyspnea. The studies examining this topic are primarily case reports, although there are several randomized controlled trials, each with a small number of participants.<sup>3,4</sup>

The use of nebulized furosemide for the treatment of dyspnea was first reported in a patient with advanced Kaposi sarcoma.<sup>1</sup> More recent studies reported that patients with dyspnea refractory to traditional treatment, including parental morphine, responded well to nebulized furosemide. Twenty milligram of furosemide delivered via handheld nebulizer reduced dyspnea and respiratory rate within 20 to 30 breaths/min, providing relief for approximately 4 hours. For several patients, use of accessory muscles and respiratory rate also decreased.<sup>2</sup> Diuresis could not explain the improvement in symptoms, as urine output did not increase during the study period. In

a study conducted by Kohara and colleagues,<sup>5</sup> dyspnea was reduced in 12 of 15 patients who received 20 mg of nebulized furosemide. One study of seven patients with advanced lung cancer actually found that dyspnea worsened after nebulized furosemide, although not significantly.<sup>6</sup>

Nebulized furosemide prevents bronchospasm and may alleviate dyspnea because of bronchodilatory effects.<sup>1</sup> Theoretical, nebulized furosemide reduces dyspnea by suppressing pulmonary C fibers in bronchial epithelium. It also inhibits cough and bronchospasm when the lungs are exposed to aerolized dosing. Furosemide also stimulates pulmonary stretch receptors and may relieve dyspnea by duplicating the effects of large tidal volumes.<sup>1</sup>

The evidence supporting the use of nebulized furosemide in dyspnea for COPD and advanced cancer is lower-level clinical evidence, but promising. These limited studies suggest that benefits may outweigh burdens, but further studies are needed.

### ❖ SUMMARY OF THE EVIDENCE

- A small number of case studies and randomized clinical controlled trials have found that nebulized furosemide relieves dyspnea in patients with COPD and advanced cancer.
- The average dose is 20 mg in 3 mL of normal saline, which provides relief within 20 to 30 minutes, lasting up to 4 hours.
- At least one small study found that dyspnea worsened in seven patients after receiving nebulized furosemide.

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**Darrell A. Owens, PhD, ARNP, ACHPN**, is Clinical Assistant Professor and Director, Palliative Care Consult Service, University of Washington Harborview Medical Center, Seattle, WA. He is also an Associate Editor for the *Journal of Hospice and Palliative Nursing* and coordinates "Evidence for Practice."



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