Accepted Manuscript

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Authors: Robert B. Banzett, Richard M. Schwartzstein, Robert

W. Lansing, Carl R. O'Donnell

PII: S1569-9048(17)30154-4

DOI: http://dx.doi.org/10.1016/j.resp.2017.08.010

Reference: RESPNB 2849

To appear in: Respiratory Physiology & Neurobiology

Received date: 14-5-2017 Revised date: 14-8-2017 Accepted date: 15-8-2017

Please cite this article as: Banzett, Robert B., Schwartzstein, Richard M., Lansing, Robert W., O'Donnell, Carl R., AEROSOL FUROSEMIDE FOR DYSPNEA: HIGH-DOSE CONTROLLED DELIVERY DOES NOT IMPROVE EFFECTIVENESS.Respiratory Physiology and Neurobiology http://dx.doi.org/10.1016/j.resp.2017.08.010

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ACCEPTED MANUSCRIPT

AEROSOL FUROSEMIDE FOR DYSPNEA: HIGH-DOSE CONTROLLED DELIVERY DOES NOT IMPROVE EFFECTIVENESS

Robert B Banzett^{1,2}, Richard M Schwartzstein^{1,2}, Robert W Lansing¹, Carl R O'Donnell^{1,2}

¹ Division of Pulmonary, Critical Care, and Sleep Medicine Beth Israel Deaconess Medical Center Boston, MA, 02215.

²Department of Medicine Harvard Medical School Boston, MA, 02115 USA

HIGHLIGHTS

- We tested hypotheses that might explain failure of aerosol furosemide to alleviate experimental dyspnea.
- Control of aerosol delivery did not increase the proportion of subjects who responded.
- Doubling furosemide dose did not increase the proportion of subjects who responded..
- Response variation was partially explained by variation of response to large breaths.

Supported by NIH-NR12009

ABSTRACT

Published studies have shown great variability in response when aerosolized furosemide has been tested as a palliative treatment for dyspnea. We hypothesized that a higher furosemide dose with controlled aerosol administration would produce consistent dyspnea relief. We optimized deposition by controlling inspiratory flow (300-500 ml/s) and tidal volume (15% predicted vital capacity) while delivering 3.4 micron aerosol from either saline or 80 mg of furosemide. We induced dyspnea in healthy subjects by varying inspired P_{CO2} while restricting minute ventilation. Subjects rated "Breathing Discomfort" on a Visual Analog Scale (BDVAS, 100% Full Scale \equiv intolerable). At the PETCO2 producing 60% BDVAS pre-treatment, furosemide produced a clinically meaningful reduction of BDVAS (i.e., > 20%FS) in 5/11 subjects; saline reduced dyspnea in 3/11 subjects; neither treatment worsened dyspnea in any subject. Furosemide and saline treatment effects were not statistically different. There were no significant adverse events. Higher furosemide dose and controlled delivery did not improve consistency of treatment effect compared with prior studies.

Keywords: Dyspnea, Furosemide, Palliative care, Symptom management

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