Critical Review Form
Therapy

PGY-2

Briones Claudett KH, Briones Claudett M, Chung Sang Wong M, et al. Noninvasive mechanical ventilation with average volume assured pressure support (AVAPS) in patients with chronic obstructive pulmonary disease and hypercapnic encephalopathy. BMC Pulm Med. 2013 Mar 12;13:12.

Objectives: **"to assess the use of BiPAP S/T [spontaneous/timed] with AVAPS [average volume assured pressure support] as a ventilatory strategy in patients with chronic obstructive pulmonary disease (COPD) and hypercapnic encephalopathy (GCS < 10) and to compare these results with those from patients treated with BiPAP S/T alone, upon immediate arrival in the emergency department/ICU." (p. 2)**

Methods: **This multicenter, prospective, case-control study was conducted at 3 hospitals in Guayaquil, Ecuador between February 2009 and September 2011. Eleven patients with "infectious exacerbations of COPD" with hypercapnic encephalopathy with a GCS < 10 were assigned to receive BiPAP wtih AVAPS. A control group of similar patients was selected from the emergency department, matched according to an APACHE II score within 4 points, age within 10 points, pH within 0.04, GCS within 2 points, and BMI within 2 points of patients in the AVAPS group. Exclusion criteria were facial deformity, obstruction in the upper airway from surgery or trauma, CNS alterations, cardiogenic pulmonary edema, pneumothorax, pulmonary embolism, hemoptysis, septic shock, need for emergency intubation, and systolic BP < 80 mmHg.**

Arterial blood gas (ABG) measurements were taken initially and at 1, 3, and 12 hours, then every 24 hours while on noninvasive ventilation. Weaning from noninvasive ventilation occurred when the respiratory rate was less than 24 breaths/min, heart rate was less than 90 BPM, awareness was improved, and "adequate SaO_2 in ambient air and a low percentage of inspired O_2 (3 liters)." Both groups received bronchodilators, IV corticosteroids, and antibiotic therapy consisting of beta-lactam (piperacillin/tazobactam) in combination with a new fluoroquinolone (Levofloxacin). The primary outcome was level of consciousness as measured by GCS; secondary outcomes were duration of mechanical ventilation, hospital length of stay, exhaled tidal volume, inspiratory pressure, and ABG changes.

A total of 22 patients were analyzed, with 11 in the control group and 11 in the AVAPS group. The mean age was 78.68 years, 13 (59.1%) were men, and the mean APACHE II score was 18.5.

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Guide	Comments
Are the results valid?	
Did experimental and control groups being the study with a similar prognosis?	
Were patients randomized?	No. This was a case control study at high risk of selection bias.
Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be "randomized" to a particular group?	N/A.
Were patients analyzed in the groups to which they were randomized?	N/A. This was a case control study in which group assignment was based on the mode of nonmechanical ventilation used, which was presumably at the discretion of the treating clinicians.
Were patients in the treatment and control groups similar with respect to known prognostic factors?	Uncertain. While there were no statistically significant differences between the two groups in terms of BMI, age, APACHE II score, or initial GCS score (the criteria used for control group matching), the authors provide no comparison of medical comorbidities, oxygen saturation, baseline $PaCO_2$, baseline respiratory rate, presence of sepsis, of presence of pneumonia.
Did experimental and control groups retain a similar prognosis after the study started?	
Were patients aware of group allocation?	Yes, although it seems unlikely that performance bias on the part of patients would have affected outcomes.
Were clinicians aware of group allocation?	Yes, and it is possible that performance bias on the part of clinicians could have affected outcomes.
Were outcome assessors aware of group allocation?	Presumably yes. The authors make no mention blinding of outcome assessors or how this would have been accomplished.
Was follow-up complete?	Yes. All outcomes were measured during the index hospitalization and hence would have been available from the records.
What are the results?	
How large was the treatment effect?	• GCS improved more in the AVAPS group than the S/T group at 3 hours, rising from a mean of 8.3 to 15 in the former and 8.3 to 13 in the latter ($p = 0.00001$). • While there was no significant difference in the change in pH at 3 hours, the pCO2 showed greater improvement in the AVAPS group (decrease in mean from 63 to 43.6) compared to the S/T group (decrease from 64.8 to 50.1, $p = 0.03$). • There was no statistically significant difference in hospital length of stay (mean 7.27 vs. 7.09 days, $p = 0.15$) or duration of noninvasive ventilation (mean 5.81 vs. 5.36 days, $p = 0.18$) between the S/T and AVAPS groups, respectively.
How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?)	This was a very small study with poor precision. The authors do not report effect sizes or confidence intervals, but instead report p values for differences in outcomes between groups.
How can I apply the results to patient care?	
Were the study patients similar to my patient?	No. This was a small study conducted at 3 hospitals in Ecuador and included patients with "infectious exacerbations of COPD," which is not well-defined. The authors provide no additional information regarding medical comorbidities for comparison with our patient population. Additionally, patients were treated with very broad-spectrum antibiotics which we would not use to treat COPD exacerbations or pneumonia, and

	the median duration of noninvasive ventilation was over 5 days in both groups, which would be very unusual for patients seen in our ED with COPD exacerbation (external validity).
Were all clinically important outcomes considered?	Mostly yes. The authors considered improvement in lab values and GCS, as well as hospital length of stay and duration of noninvasive ventilation. They did not report need for intubation or ED length of stay.
Are the likely treatment benefits worth the potential harm and costs?	Uncertain. This very small, case-control study found that patients treated with AVAPS compared to S/T BiPAP had significantly better improvements in mental status (measured by GCS) and pCO_2 at 3 hours with no significant difference in hospital length of stay or duration of noninvasive ventilation. The study included only patients with "infectious exacerbations of COPD," which was not defined, and was conducted in Ecuador. Further research on a larger patient population in disparate settings would help make these findings more robust.

Limitations:

1. **Several aspects of the STROBE guidelines for reporting in observational studies were missing from this article:**
    a. **No clear inclusion/exclusion criteria were reported, and the inclusion of "infectious exacerbations of COPD" was not defined.**
    b. **No sample size calculation was performed and the authors enrolled a very small cohort of patients.**
    c. **No details were provided for how control matched subjects were identified and selected.**
    d. **No information on medical comorbidities was provided.**
2. **This study was not randomized and hence at high risk for selection bias.**
3. **The authors used rather broad antibiotic coverage consisting of Zosyn and levofloxacin without clear indication, and patients in both groups were on noninvasive ventilation for a median of > 5 days, which would be very unusual in our institution (external validity).**

Bottom Line:

This very small, case-control study conducted at 3 hospitals in Ecuador found that among patients with "infectious exacerbations of COPD" requiring noninvasive ventilation, those treated with AVAPS had significantly better improvements in GCS and pCO2 at 3 hours compared to those managed with S/T BIPAP. These results are limited by a very small sample size, poor reporting, and apparent differences in management between study subjects and those in our institution.