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Deciding when to use BiPAP for patients with acute exacerbations of COPD

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ABSTRACT A clinical decision report appraising Carrera M, Marín JM, Antón A, et al. A controlled trial of noninvasive ventilation for chronic obstructive pulmonary disease exacerbations. *J Crit Care.* 2009;24(3).

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Clinical Context

Shanice Daniels [pseudonym] is a 62-year-old African American female with a history of chronic obstructive pulmonary disease (COPD) on three liters of home oxygen by nasal cannula and hypertension who presented to the emergency department (ED) with difficulty in breathing for two days. She has been out of her maintenance inhalers for over a month and has been unable to see her primary care physician due to lack of time from working extended hours and new obligations taking care of her father. Her stress has been increased because of these new factors and this has led her to start smoking again after being abstinent for three months.

In the ED, she was tachypneic and distressed on five liters oxygen by nasal cannula. Her treatment options were presented to her and she was given the option for a trial of nebulizer treatment or to go straight to trying noninvasive positive pressure ventilation (NIPPV) or bi-level positive airway pressure (Bi-Pap) with concurrent nebulizer treatment. Mrs. Daniels was uncomfortable with the thought of using a ventilator since she never used it before and worried she would not be able to come off the ventilator, leading to a prolongation of her stay and thus preventing her from returning to her familial and work obligations. She failed to have any symptomatic relief from medical therapy and her options were discussed amongst the medical team.

Clinical Question

Does non-invasive positive pressure ventilation improve clinical outcomes and reduce hospital stays in patients with an acute COPD exacerbation?

Research Article

Carrera M, Marín JM, Antón A, et al. A controlled trial of noninvasive ventilation for chronic obstructive pulmonary disease exacerbations. *J Crit Care.* 2009;24(3). <https://doi.org/10.1016/j.jcrc.2008.08.007>.

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Related Literature

A search of PubMed was done using following fields:

(noninvasive ventilation OR non-invasive ventilation) AND exacerbations AND chronic obstructive pulmonary disease NOT asthma NOT nasal cannula NOT stable

This yielded 360 results in which only randomized control studies and clinical trials were chosen yielding 35 articles. Of these, 9 studies were selected that addressed length of hospital stay of COPD patients using positive pressure ventilation in the treatment of an acute exacerbation.

Lindenauer et al. performed a cross sectional analysis in 2015 of 77,576 patients across 386 US hospitals looking at the outcomes of non-invasive ventilation (NIV) use in COPD exacerbations.¹ The size of this study is far greater than any other study looked. This study did find that length of stay was decreased by 1.3 days in hospitals that had high rates of NIV use in COPD patients. This study was excluded due to its focus on the outcomes of NIV in relation to the rates of NIV use in hospitals and this is not relevant in the clinical context of this case.

The Plant study in 2000 was a prospective multicenter randomized control study with 236 participants that compared conventional treatment to the use of NIV with participants split into two even treatment groups.² The study found improvement in physiological markers, mortality, and rates of intubations, but no significant change in length of stay. Though this was a strong study that was randomized with a large sample size, it was ultimately excluded due to a lack of placebo, age of the study, and poor adherence to NIPPV in comparison to the Carrera study.³

Five of the other studies selected were all prospective randomized control studies with similar treatment groups, which included an intervention group receiving NIPPV with medical management and a non-intervention group receiving standard medical management which entailed bronchodilator and steroid therapy in all the studies.⁴⁻⁸ They all had metrics focused on clinical outcome including an assessment of length of hospital stay. The Brochard study in 1995 was one of the first papers to look at the effect of NIPPV on hospital outcomes of 85 COPD patients over a 15-month period.⁴ They found a decrease in intubation, mortality, complications, and hospital stay in the intervention group. The Bardi and the Keenan study looking at 30 and 52 patients respectively found a non-significant decrease in hospital stay in the intervention group.^{5,6} The Castillo and Hilbert studies were relatively small studies with sample sizes of 41 and 84 respectively that had showed a significant reduction in length of stay.^{7,8} The Castillo, Bardi, and Keenan studies were excluded due to a low power due to a small sample size.^{5,6,7} Although the Brochard and Hilbert study had similar study sizes and metrics to the Carrera study, due to being earlier studies, a lack of a placebo and no blinding, the overall validity was less in comparison to the study by Carrera.^{3,4,8}

Thys et. al. conducted the only other placebo trial in 2002 for an assessment of the effectiveness of NIPPV in the care of acute COPD exacerbations.⁹ This study had a very low power with only 10 patients in each of the treatment arms and the study was only single blinded, decreasing validity of the study.

The Carrera et al. study from 2009 was ultimately selected as being the most ideal choice for appraisal in the context of Mrs. Daniels.³ This was the only prospective, double-blinded, placebo-controlled study done. The study split the groups into a placebo group with a sham BiPAP and a BiPAP group. This study also measured outcomes pertinent to the patient including length of hospital stay. For these reasons the strength of evidence from this article was the strongest and most pertinent to our patient.

The Carrera, et al study was located in Google Scholar and the "Related articles" function was used. Although this search identified other randomized trials, it did confirm that the chosen study is the only study that used a placebo group with a sham BiPAP and a BiPAP group, confirming that it was the most appropriate study to critically appraise.

Given the above literature, this body of evidence would be a Grade B strength of recommendation based on the SORT criteria.¹⁰

Critical Appraisal

The study by Carrera et al. was a prospective multicenter randomized double blinded and placebo controlled study that looked at 75 patients with COPD and a diagnosis of an acute exacerbation of COPD (AECOPD) with symptoms of cough, sputum production, or dyspnea.³ This study was intended to expand the strength of evidence by being the first study to use a double blinded placebo trial in the assessment of the efficacy of NIPPV in the treatment of AECOPD over a four-day period. The 75 patients were recruited from seven hospitals in Spain and randomly assigned to two groups, BiPAP and sham. The patients mean age was 72±10 in the BiPap group and 69±7 in the sham group. Both groups received medical therapy that consisted of oxygen therapy targeting a saturation of 90%, bronchodilators, and oral steroids. The inclusion criteria and mean ages of participants of both groups are similar to the medical and demographic profile of our patient. Though this study did not comment on the ethnic demographics of their study population, they used spirometric reference values for a Mediterranean population suggesting that their study population was Mediterranean. This could raise concerns of clinical correlation due to our patient being African American.

This study would be classified as a level 2 evidence per the Strength of Recommendation Taxonomy criteria.¹⁰ The study was double blinded by blinding the physicians administering treatment and the patients. The physicians were blinded by using two separate clinical teams. Respiratory therapist administered the ventilator treatment in evenings (3PM-8AM) without the physician present. The physician would see the patient's in the morning and afternoon (8AM-3PM) while the subject was not on a ventilator and decide treatment and discharge plans. This ensured the physicians were blinded. This came at the cost of only being able to administer BiPAP during a specific segment of the day, where in real-life BiPAP could be administered day and night as tolerated. Patients were blinded by excluding patients that have used NIPPV in the past to ensure patients would not know if the treatment they were receiving was a sham or not. The sham device itself was tested using a randomized crossover study and it was found provide the same FiO2 as a venture mask used in the standard treatment of AECOPD. The sham was found to not affect respiratory rate, rebreathing, or blood gases when compared to the venture mask, ensuring the validity of results in the placebo group.

The 75 patients were split relatively evenly with, the 37 patients receiving BiPAP and 38 patients receiving a sham BiPAP with 5 patients in the treatment arm meeting intubation criteria versus 13 patients meeting intubation criteria in the placebo group. There was an absolute risk reduction of 20.5% for intubation in patients using BiPAP with the number needed to harm being 4.83.

This study's primary outcome was looking at rates of patients meeting a fixed criterion for intubation between treatment groups and secondary outcomes of length of hospital stay and arterial blood gases. Intubation criteria were defined as a pH <7.2, two pH readings between 7.2-7.25, cardiorespiratory arrest, or a Glasgow coma scale <8. If these criteria were met, the study was ended for that patient and care was handled by a physician not involved in the study. This provides room for misleading results due to not all patients being intubated despite meeting intubation criteria. In the sham group, of the 13 patients meeting criteria for intubation, only 4 individuals were intubated while the remaining received NIPPV or medical treatment. In comparison, the treatment group had 5 individuals meet intubation criteria of which 4 were intubated. This could be interpreted as both groups having the same rates of intubation. This study used the same criteria as the Plant and Brochard study, which helps correlate results but can also lead to misleading results if the limits at which the pH was set are not clinically significant for intubation.^{2,4}

There was significant improvement in pH and PaCO₂ in the treatment group compared to the placebo group. This study found a non-significant decrease in length of stay for patients using BiPAP, with a median of 8.5 days versus 10.5 days (P=.65) in the placebo arm. This finding could be attributed to limited time intervals for treatment or a small sample size requiring a greater difference for significance. Due to this study being focused in the ICU, outcomes in the ED may not be comparable.

Clinical Application

When discussing that she would have to begin BiPAP after not responding to medicine, Ms. Daniels stated she could not afford to stay in the hospital longer than she had to and was concerned about getting back to work to support herself and her father. Though the Carrera et. al. paper studied patients similar to Ms. Daniels in regard to age and symptomology. The study showed a non-significant decrease in hospital stay, Ms. Daniels' primary concern.

A discussion was had with Ms. Daniels about her concerns with returning home and how she might benefit from BiPAP. Although she was initially apprehensive, we explained how a BiPAP machine works, informed her about



delivery options she could use to obtain her prescriptions, and helped her find a new PCP that was closer to her house making follow up easier. This helped ease her stress and made her more amenable to using the BiPAP in the emergency department.

New Knowledge Related to Clinical Decision Science

Prolonged hospital stays for any patient can be a major burden on finances, social relationships, and the patient's own health. This is true for Mrs. Daniels, who wanted treatment for her AECOPD but did not want to stay in the hospital for a long period of time because of her responsibilities to her family and her work. She also was concerned about BiPAP, worrying that she would have to remain ventilated for a long period of time. This situation stresses the importance of discussing all treatment options with the patient, providing adequate education (the harms and benefits) about the treatment. In this case, adequate education for the patient was dependent on adequate education for the treating physicians.

As in most of the clinical research literature, the authors' conclusions have a bias toward the treatment being more "effective". But, the patient's primary concern is not the outcome variable measured in the research. Additionally, by the clinician using the filter of "incidence of intubation" in each group rather than meeting an arbitrary "indication for intubation" as the outcome, the evidence changes from a positive study into a negative study. The further question that needs to be answered within the domain of Clinical Decision Science is an analysis of patient's expressed outcome of interest versus protocol outcome and how that affects the bedside decision. How is "the standard of care" constructed within the social interactions of medical practice? Whose voice contributes to that discussion?

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