

Ventilator-associated pneumonia in advanced lung disease: A wakeup call

In the intensive care units across the globe numerous patients are placed on invasive mechanical ventilation for various life-threatening conditions. Mechanical ventilation while lifesaving may at times result in complications, which may place the very life at peril that needs to be saved. Mechanical ventilation may result in ventilator induced lung injury, or predispose patients to acquire ventilator-associated pneumonia (VAP).^[1] Pneumonia may result from aspiration of secretions contaminated with pathogens secondary to inoculation of upper airways or reflux of gastric contents.^[2] Ventilator-associated pneumonia is the most common nosocomial infection acquired in the critical care units and may occur in 9-20% of the ventilated patients.^[3-6] Among the factors that make it difficult to ascertain the exact morbidity and mortality related to VAP, the important most is the difficulty in establishing a clinical diagnosis of VAP. Presence of pulmonary infiltrates suggestive of pneumonia on chest radiograph, which is one of the main criteria for diagnosing VAP, may also be caused by other conditions like pulmonary edema, atelectasis or pulmonary haemorrhage. Conflicting reports exist over the mortality due to VAP,^[3-6] and a poor correlation exists between the clinical and histopathological features leading to ambiguity and variability in clinical diagnosis of VAP.^[7] A recent study estimated the attributable mortality due to VAP to be 13% which was high among surgical patients but low in medical patients, patients with trauma and in those with very low or very high-severity scores.^[8] Regardless of the debate about its mortality, VAP is an unwanted hospital acquired condition that is associated with increased morbidity and cost, a calamity which no patient should have to endure.^[3-6,8]

In this issue of the Journal, Hadda *et al.*, present a study of 153 patients with chronic obstructive pulmonary disease (COPD) who required invasive mechanical ventilation. Of these 35 patients (22.8%) developed VAP; 9 were early and 26 late. The study reported an in-hospital mortality of 51% among patients diagnosed

with VAP and 53% among those without VAP. While the risk of mortality was not affected by presence of VAP, the duration of mechanical ventilation, as well as, hospital stay was prolonged among patients with VAP, on average by more than twice as compared to those without VAP. *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were the two main pathogens isolated from the respiratory cultures.^[9]

The main strengths of this study are that, it included a large group of potentially homogenous patients with COPD exacerbation requiring invasive mechanical ventilation and it was conducted in a well-known center in India over a relatively short period of time. The definition of a VAP was based on published criteria for VAP. The authors did not include details about any existing protocols for diagnoses, treatment and prevention of VAP present in the medical center at the time of study. Also the manuscript does not address whether this study was powered enough to detect a measurable difference in mortality.

Notwithstanding some shortcomings, this study brings to light several important issues which need very serious consideration. First and foremost, this study shows that even in absence of risk of increased mortality there is a significant increase in the duration of mechanical ventilation and length of stay; thus increased suffering and cost associated with VAP. Although, details of treatment with antibiotics were not included in the study, the development of VAP means institution of antibiotics; extra burden in terms of cost and potential for increased bacterial resistance. Isolation of *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, aggressive organisms from the respiratory secretions from majority of these patients speaks for itself. Isolation of resistant organisms from patients with VAP is associated with increased risk of death and prolonged length of stay.^[10] This is particularly troubling since there have been reports of isolation of high risk multidrug resistance pathogens in this part of the world.^[11]

The best way to treat VAP is to prevent it. This can be achieved by avoiding intubation and invasive mechanical ventilation with the use of non-invasive ventilation in patients without contraindications. Non-invasive positive pressure ventilation should be offered to hemodynamically stable patients with respiratory failure who are cooperative, have a reserve, are not facing impending respiratory arrest and do not have contraindications like excessive secretions, facial injury or claustrophobia. In absence of dedicated

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non-invasive ventilators, regular ventilators (which are apparently available) can be used to provide non-invasive ventilation with appropriate facial interface. These patients need to be monitored closely and placed on invasive mechanical ventilation on the earliest signs of worsening as delay in intubation is associated with increased mortality.^[12] For those patients who end up on invasive mechanical ventilation other measures that may prevent VAP need to be initiated soon after intubation; thus reduce further morbidity and cost. Daily interruption of sedation and early liberations from mechanical ventilation through use of protocols has been shown to decrease mortality. Use of protocol based “awakening and breathing controlled trial” reduced duration of mechanical ventilation, length of stay as well as mortality; for every seven patients treated with the intervention, one life was saved (number needed to treat was 7.4, 95% CI 4.2 to 35.5).^[13] Other measures that have been used to prevent VAP include elevation of head of the bed and appropriate oral care etc.^[14]

Once VAP is diagnosed antibiotics should be initiated without delay. Appropriate material for cultures should be obtained prior to initiation of antibiotics. Generally broad-spectrum antibiotics are started based on the clinical presentations and institutional patterns of bacterial sensitivity and resistance. Sepsis remains one of the major causes of mortality in VAP and any delay in initiating appropriate antibiotics results in increased mortality. After culture results are available and patients are stabilized, antibiotic therapy needs to be de-escalated and tailored to the clinical scenario.^[15-17] In the USA, partly due to lack of gold standard and objective criteria for diagnosis of VAP, there is now an attempt to move beyond the VAP and initiate surveillance for what is called as ventilator-associated condition (VAC). In a patient who has been on ventilator and stable, any change for worse needs to be scrutinized for potential complication related to ventilation.^[18]

The study by Hadda *et al.* also highlights a very troubling scene which seems to be emerging.^[9] India has a very large burden of patients with COPD as recently highlighted in this Journal. Almost one in 5 COPD related deaths in the world are expected from India.^[19] A large proportion of aging population with COPD will require hospitalized care and a substantial number may require mechanical ventilation. This will cause a great constrain on the already limited health care expenditure. It is surprising as well as tragic to note that more than 80% of patient who presented to this medical centre with exacerbation of COPD ended up on invasive mechanical ventilation with a very high mortality. Almost two decades after the publication of the first successful study on non-invasive ventilation, this was not routinely available to the subjects of this study. The benefits of Non-invasive ventilation.(NIV) are well documented in patients with COPD with hypercapnic respiratory failure.^[12,20]

It would be interesting to follow these types of patients prospectively for any long-term effects of VAP, assess post-hospitalization survival, readmission and quality

of life. Considering the prolonged hospitalization and a toss-of-a-coin chance of survival, physicians need to have a candid discussion with their patients who require invasive ventilation. Patients with advanced COPD may choose to live the remaining days of their lives receiving care only aimed to keep them comfortable with better quality of life preferably in company of their loved ones, rather than tied to a ventilator in an intensive care unit. Even among those patients who choose not to be intubated, non-invasive ventilation can be used as active therapy to prolong life or for palliation in selected conscious and co-operative patients to relieve distress.

The physician community taking care of these patients needs to do everything in their power to advocate for the availability of these resources to their patients. The policy makers in healthcare need to keep this in mind that in many institutions around the world it would be considered less than optimal care if non-invasive ventilation is not offered as an alternative to mechanical ventilation in patients with respiratory failure due to COPD exacerbation, in absence of contraindications.

This study is testimony to the continued suffering of patients with COPD resulting in prolonged mechanical ventilation and hospitalization, more so for those who develop VAP; thus a wake-up call for the physicians as well as administrators and policy planners for implementing appropriate prevention and management strategies for routine care of such patients.

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