Review Article

The role of noninvasive ventilation in cancer patients with acute respiratory failure

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Abstract

The poor prognosis of ventilated patients with cancers, especially hematological malignancies, has been a major incentive in the use non-invasive ventilation in such patients. With experience of more than a decade, a few recommendations can be made. While experience in non invasive ventilation is of prime importance, it is the early use especially in conditions requiring supplemental oxygen and a drop in SaO_2 of > 10% that the most benefit is expected. Use of the helmet to provide noninvasive ventilation (NIV) may improve patient compliance. With appropriate use during diagnostic bronchoscopy, NIV may prevent endotracheal intubation. NIV has also been shown to provide relief from dyspnoea to a select group of do-not-intubate patients. While outcome in this group of patients is poor, appropriate use of NIV has been shown to reduce mortality. The coming years and more experience will improve our understanding and refine the use of this modality in this critical condition.

Key words: Non-invasive ventilation, NIV, NIPPV, cancer, hematological cancers, acute respiratory failure

The last decade has seen an increasing confidence in the use of noninvasive ventilation in the management of respiratory failure, especially hypercapnic respiratory failure. The low incidence of nosocomial respiratory infections with the use of this modality is its most attractive feature.

Acute respiratory failure is the commonest indication for admission to ICU in patients with cancer and mortality in this group remains at least three times higher than admission from any other cause.[1] Mortality varies depending on the underlying malignancy; patients with bone marrow transplants requiring ventilatory support have ICU mortality rates ranging from 80-95% and patients with hematological malignancies needing mechanical ventilation have mortality rates of 70-80%. Even patients with solid organ tumors requiring mechanical ventilation, unrelated to surgery, have a poor hospital outcome with a 70-90% mortality.

While this appears very disappointing, the last decade has seen a three-fold improvement in prognosis in this group of sick patients.[2,3]

This has been ascribed to improvements in oncohematology, intensive care and advances in mechanical ventilation. The impact of the use of noninvasive ventilation (NIV) in cancer has been demonstrated by Azoulay.[2] In his retrospective analysis of matched cohorts in two time periods, only two variables showed an association with mortality: the severity of the patients' condition on admission to the ICU and the need for mechanical ventilation. Patients ventilated

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noninvasively had a better outcome compared to those needing invasive ventilation. In reviewing the mortality in mechanically ventilated patients, Azoulay and Schlemmer found that invasive mechanical ventilation was associated with a 75% mortality, as compared to 50% with NIV.[4]

Both, classical prognostic factors e.g. presence of neutropenia, type of malignancy and physiological scores are not helpful in triaging patients to ICU.[2,3,5] However, the nature and number of organ failures at admission and the rapidity with which multiorgan failure ensues is directly correlated with risk of death.[6,7]

The differential diagnosis of ARF in cancer[4] includes:

Progression or spread of underlying cancer
ARDS
Infection
Chemotherapy or radiation induced lung injury
Pulmonary thromboembolism
Tumour emboli
Diffuse alveolar hemorrhage
Pulmonary leukostasis
Lymphangitic carcinomatosis
Transfusion related lung injury
Airway obstruction
Paraneoplastic syndromes

The above are associated with a primarily hypoxemic lung injury pattern. With such pathophysiology, prognosis can be worse than in patients who have a hypercapnic respiratory failure, which is independent of the underlying disease state or a cardiogenic pulmonary edema.

It is imperative to understand thoroughly how to put our newfound confidence in this technique to best use in this group of patients.

NIV in Cancer

That invasion of the respiratory tract by the endotracheal tube contributes to increased rates of nosocomial infections is well established.[8] This uncompromising fact led clinicians to use NIV on immunocompromised patients as early as 1990, when case controlled studies showed that NIV was an effective supportive therapy.

Tognet *et al* reported the first improvement in outcome with the use in patients with hematological malignancies.[9] Though pilot studies done through the 90's showed a benefit, it was the publication by Hilbert *et al* in 2001, which gave an impetus to the modality in this clinical scenario.

In this prospective randomized trial[10] intermittent NIV was compared to standard treatment with supplemental oxygen and no ventilatory support, in fifty two immunosuppressed patients with pulmonary infiltrates, fever and an early stage of hypoxemic acute respiratory failure (PaO_2/FiO_2 ratio <200). The large majority of the patients had a hematologic malignancy and neutropenia or drug-induced immunosuppression. Periods of NIV delivered through a facemask were alternated every three hours with periods of spontaneous breathing with supplemental oxygen. The decision to intubate was made according to standard, predetermined criteria. The main results of the study were that fewer patients in the NIV group than in the standard-treatment group required endotracheal intubation (12 vs 20; $P = 0.03$), had serious complications (13 vs 21; $P = 0.02$), died in the ICU (10 vs 18; $P = 0.03$) or died in the hospital (13 vs 21; $P = 0.02$). Overall, this study clearly showed that early implementation of NIV was associated with significant reduction in the rate of intubation, serious complications and death, both in the ICU and in the hospital.

Hilbert used intermittent NIV, very early in his series of hypoxemic patients.

NIV improves hypoxemic ARF by physiologic mechanisms related to PEEP, such as recruitment of underventilated alveoli, redistribution of extravascular lung water, prevention of atelectasis and high FiO_2-induced lung toxicity, as well as to those related to the inspiratory assist by pressure support involving the reduction in the work of breathing and an increase in tidal volume with adequate alveolar ventilation.

In immunocomprомized patients with ARF caused by pneumonia and ARDS, interruption of NPPV can rapidly worsen gas exchange, sometimes leading to NPPV failure and endotracheal intubation. If NIV is attempted via a facial mask for a longer time frame, compliance may be an issue. Improved compliance and tolerability of NIV with the helmet as the interface avoids the need for NPPV discontinuation. The helmet allows the patients to freely communicate, drink and expectorate, improving collaboration with caregivers and clearance of the airways.

Rocco in a case-controlled study[11] has demonstrated the use of the helmet as a valid alternative to a facemask in immunocompromized patients with lung infiltrates and hypoxemic ARF. They were able to increase the number of hours of continuous NPPV without interruptions and decrease the rate of complications directly related to the administration of NPPV. It is necessary to remember that CO_2 washout is suboptimal with the helmet.[12]

All patients with cancer and pneumonia do not necessarily need ventilatory support. The time after onset of pneumonia and transfer to ICU can be up to seven days and delay in initiating supportive therapy can worsen outcomes.[10] Therefore, Gruson *et al.* attempted to define variables which would predict the need of transfer to ICU. In their series of fifty three patients,[13] the factors associated with ICU admission were: numbers of involved quadrants: 2.3 vs 1, (P =0.001) and oxygenation parameters (initial level of oxygen supplementation: 3.5 vs 0.9 l/min, P<0.05), the presence of hepatic failure (58% vs 10%, P<0.01), Gram negative bacilli isolated in blood culture (7 vs 1, P=0.01). In the multivariate analysis, a decrease of 10% in the SaO_2 and the requirement of nasal supplementary O_2 at the onset of acute respiratory failure increased the risk of admission to MICU.

At present, the ability to predict success with the use of NIV is best for hypercapnic respiratory failure. No indices are uniformly suitable for the multiple pathophysiological processes leading to hypoxic respiratory failure.[14] Therefore, when NIV is used in acute hypoxemic respiratory failure it is mandatory to set definite end points and criteria for invasive ventilation. Patients who have delayed intubation have a poor prognosis.[15] Azoulay and his colleagues found that patients who required only NIV had a 15% mortality, while those that had late failure of NIV (requiring intubation after 48h of NIV) had a 93% mortality and those who had a noncardiac cause of respiratory failure and required intubation after three days of NIV had a 100% mortality.[16]

It must be noted at this point, that NIV in hypoxemic respiratory failure, even in a non cancer setting, is not an alternative ventilatory mode and is useful only in the very early or initial setting of the pathology.

Certain factors are predictive of the need for invasive mechanical ventilation and a poor outcome. They are radiological and oxygenation parameters, the presence of hepatic failure, Gram-negative bacilli isolated in blood culture, poor performance status, cancer status, older age and the number of organ failures at admission to ICU.[17] The appropriate use of such easily available clinical characteristics will help in deciding about the use of NIV.

Yet another use of NIV is to avoid intubation during and after diagnostic flexible fibreoptic bronchoscopy in patients with early or borderline respiratory failure undergoing diagnostic bronchoscopy and broncho-alveolar lavage. Either CPAP or pressure support ventilation may be used and may be delivered either via full-face mask or helmet.[18-20]

The dilemma of how to provide relief to a terminally ill cancer patient with ARF, especially one with specific DNR or a do-not-intubate order is faced by most of us. NIV can provide relief of dyspnoea and sometimes reverse the acute deterioration. Levy[21] has shown that despite a high overall mortality rate, when such patients are treated with NPPV, those with diagnoses such as congestive heart failure or chronic obstructive pulmonary disease, who have a strong cough or who are awake have a better prognoses.

It can be argued that this may merely prolong the process of dying but such studies add to our ability to counsel families and patients with conviction.

Conclusion

While the outcome of critically ill cancer patients is still disappointing, it has been demonstrated that avoidance of invasive ventilation is associated with a better outcome. NIV is a feasible alternative to intubation in specific groups of patients. The two keys to successful use being experience and training of the staff involved in care and the timing i.e., the early use of the technique. We encounter many challenges in the successful treatment of this group of patients and the coming years with well-designed trials may improve our ability to improve outcomes.

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