[Indian J Chest Dis Allied Sci 2014;56:213-215]

Editorial

Non-Invasive Ventilation: Challenges in Usage and Applications

Non-invasive ventilation (NIV) is an assisted form of ventilatory support without the invasion of the airways. It is now being used frequently in critical care settings and emergency departments in the context of acute respiratory failure (ARF). Common indications include conditions with hypercapnic respiratory failure (acute exacerbation of chronic obstructive pulmonary disease (COPD), facilitation of extubation), and hypoxaemic respiratory failure (cardiogenic pulmonary oedema, immunosupressed patients). Emerging applications but without definite evidence include acute asthma, prevention of post-surgical respiratory failure, orders of do not intubate, symptom palliation and acute respiratory distress syndrome (ARDS).[1] Recently, small trials have been carried out to evaluate its role in pre-oxygenation before intubation, improvement in oxygenation status during fiberoptic bronchoscopy, and reduction of risk of broncho-pulmonary dysplasia in pre-term infants. It has also been used in patients with chronic respiratory failure due to COPD, obstructive sleep apnoea, neuromuscular diseases and kyphoscoliosis. Thus, the scope of use of NIV is expanding every day and has emerged as a substitute to mechanical ventilation in different clinical settings.

One should be aware of indications, contraindications and pitfalls of application of NIV. Its predicted benefits along with probability of failure in an individual patient should be assessed before initiation. The patient selection criteria, technical aspects of the machine and its settings, use of an appropriate interface and close monitoring are keys to success. Optimal synchronisation between the patient's respiratory effort and the ventilators output is a major challenge to the success of NIV. Explaining the procedure of application of NIV to the patients and encouraging them to voluntarily synchronise the respiration with ventilator is important. Attention to trigger sensitivity, leaks, use of optimum expiratory positive airway pressure (EPAP) and the inspiratory positive airway pressure (IPAP) are essential to the success of NIV.

Prompt recognition of the causes of early and late failure is another challenge in patients with COPD. Early predictors of failure in COPD, such as copious secretions, Glasgow coma scale $\geq$11, lack of compliance, a pH <7.25, a respiratory rate >35/min and air leaks should be recorgnised. Late failure is estimated to be responsible for around 15% of NIV failures. It is associated with functional limitation before admission, a lower pH at admission, occurrence of infectious complication, multiple organ failure and delirium.[2]

In patients with acute lung injury, NIV may improve oxygenation, reduce work of breathing and unload respiratory muscles. Few studies on the application of NIV in patients with ARDS but without multi-organ failure have shown reduced cumulative time on ventilation, length of intensive care unit (ICU) stay, greater improvement of oxygenation as compared to patients on invasive ventilation. Analysis of severity of ARDS and identification of signs of deterioration on NIV is important while mild and early ARDS may respond to NIV. SAPS-II >34, high level of inspiratory support requirement, lack of improvement in partial pressure of arterial oxygen (PaO_2) after one hour of NIV support, concomitant shock and metabolic acidosis are the factors indicating the need to stop it and intubate.[3] Application of NIV in ARF caused by SARS and other similar infectious diseases is controversial. Use of NIV was discouraged initially due to a risk of spread of virus to clinician during intubation. However, later studies showed no viral spread if adequate precautions were taken. Success rate in ARF due to H1N1 varies from 23% to 76% in various studies.[1]

Although the use of NIV in cardiogenic pulmonary oedema, especially in the setting of acute coronary syndrome has been debated, a large trial[4] has shown its efficacy especially in hypercapnic respiratory failure. However, in spite of its established efficacy and safety, its use in this condition is sub-optimal.

Use of nebulisations during asthma exacerbations through NIV has shown to improve airflow and inspiratory capacity as compared to nebulisation alone with greater reduction of breathing rate and minute ventilation. However, no difference in radio-aerosol deposition or pulmonary clearance was noted.[5] Non-invasive ventilation may be used in acute severe asthma when muscle fatigue and hyperventilation as indicated by normocapnia develops. Correct prescription of long-term oxygen therapy along with NIV is another challenge as the fraction of inspired oxygen (FiO_2) levels vary with domiciliary low flow systems depending on patient tidal volume and respiratory rate. Non-invasive ventilators equipped with air oxygen blenders are ideal to ensure precise FiO_2 levels. Hospital NIVs usually have oxygen blenders providing fixed oxygen flows. Non-invasive ventilators without blenders as in domiciliary NIVs, higher FiO_2 levels are usually associated with lower inspiratory and expiratory pressures and use of single arch valves. Oxygen injection sites have the greatest impact on the FiO_2 with the site closest to patient delivering the highest.[6]

Non-invasive ventilators now has an established role in assisting weaning in patients with COPD and other airway diseases but may lead to higher mortality if there is a delay in intubation.[7] A recent meta-analysis on the efficacy of NIV as compared to invasive methods on difficult to wean-off critically-ill patients, mostly having COPD, showed that non-invasive weaning was

significantly associated with reduced mortality ventilator-associated pneumonia, length of stay in the ICU and hospital, total duration of ventilation, and duration of invasive ventilation.[8] We also found it to be as effective or probably better in patients with COPD.[9]

Use of long-term NIV in patients with COPD and chronic respiratory failure seems to reduce the use of health-care resources by reducing the number of severe exacerbations and hospital visits. The rationale underlying domiciliary NIV in chronic hypercapnic COPD is an improved alveolar ventilation with reduced inspiratory effort. Increased central responsiveness to CO_2, improved ventilation-perfusion matching, recruitment of under-ventilated alveoli and reduction in pulmonary artery pressures are the likely mechanisms for its beneficial effects. Selection of adequate NIV pressures is a challenge and a key to its success. Starting with an EPAP that is comfortable for the patient, with an aim of offsetting the intrinsic positive end-expiratory pressure (PEEP) to reduce the work of breathing and increasing the IPAP-EPAP difference to resolve hypoventilation is the appropriate approach. The spontaneous mode appears to be as effective as spontaneous / timed mode with respect to gas exchange in patients who can adequately trigger the machine.

Some studies have shown a reduction in hypercapnia and hypoxaemia, a better quality of life and neuro-psychological function, and a higher survival rate with the use of NIV in COPD.[10] However, a meta-analysis[11] in patients with stable COPD showed that pulmonary function, gas exchange, or sleep efficiency did not improve with the NIV support after three months, though some patients did have an improvement in their walking distance. Use of a low IPAP (10-12 cm H_2O) has not shown to improve lung functions and gas exchange in patients with COPD. Recent randomised, controlled trials using high inspiratory pressures (16-22 cm H_2O) have shown that these may be more effective. Use of high intensity NIV (HI-NIV) with high inspiratory pressures ($\approx$30 cm H_2O) and high respiratory rates (20 breaths / min) lead to a maximum fall in partial pressure of arterial carbon dioxide ($PaCO_2$).[10] Titration of pressures based on clinical experience and judgment may lead to patient ventilator mis-match and disturbed sleep as compared to physiologic titration. It is believed that NIV more likely benefits those patients with COPD who have marked day-time hypercapnia with additional nocturnal hypoventilation.

Controlled trials of NIV in neuro-muscular disorders are lacking. A randomised trial[12] carried out on patients with neuro-muscular disease has shown that the use of nocturnal NIV before the occurrence of day-time hypercapnia may be beneficial. Establishment of consistent triggering of device during sleep is essential. Use of spontaneous timed mode is advocated in patients with significant diaphragmatic weakness. The EPAP should be titrated to prevent upper airway obstruction.

Traditionally, pressure support mode of ventilation is used in patients with COPD. Newer dual control modes of ventilation have been developed to improve the patient's ventilation demand and ventilatory support. These are targeted for a better adaptation to altered respiratory mechanics in assisted ventilation and for control of airway pressure while achieving desired minute ventilation. Volume-assured pressure support (VAPS) is an assist, pressure controlled and flow cycled mode. It modulates pressure support to reach a preset tidal volume while maintaining minute ventilation on breath to breath basis. In patients with reduced tidal volumes or increased airway resistance, it truly increases assistance. In contrast, when the patient's respiratory effort increases leading to an increase in tidal volume, the ventilator reduces the assistance. It is used mainly in patients with chronic hypoventilation, such as those with obesity hypoventilation syndrome, neuro-muscular diseases, and COPD. The advantage is that it guarantees a certain tidal volume despite variability in patient effort, airway resistance, and lung or chest wall compliance.[13] A particular potential advantage is that it may adapt to disease progression, as may occur in patients with progressive neuro-muscular diseases. A randomised, cross-over trial of AVAPS (Average Volume-Assured Pressure Support) *versus* standard pressure support in patients with obesity hypoventilation led to a small improvement in nocturnal PCO_2, but no improvement in long-term quality of life.[14] Published studies are still limited to clearly define the status of dual modes.

Another challenge is to define the sites where NIV can be used. Apart from traditionally being used in the intensive care and high dependency units, use of NIV has expanded to wards, emergency departments, in pre-emergency services as well as at home. In resource-limited countries, like India, NIV is used often in small nursing homes and hospitals without adequate training. A recent Indian questionnaire-based study carried out to analyse the practice of NIV revealed that around 72% of physicians (intensivists, anaesthesists, respiratory physicians) used NIV in their practice. Lack of experience was the most common reason for not using NIV. The most common indication was COPD with no clear favourable indication in hypoxemic respiratory failure. Surprisingly around 62% of physicians do not use conventional mode of NIV support.[15]

In our experience, conventional ICU ventilators seem to be equal or more effective than the portable ventilators. Proper application of masks and minimising air leaks is one of the most vital factor in improve patient compliance and ensuring improved ventilation. Adequate training of residents as well as nursing staff is mandatory. In the intensive care setting, knowledge and awareness of indication,

contraindication, monitoring and when to discontinue in favour of intubation are required to ensure improved outcomes. A protocol-based use of NIV need to be adopted. Domicilliary use of NIV in patients with chronic hypercapnic COPD and patients with obstructive sleep apnoea can lead to mark improvement in their quality of life with long-term cost benefits. Non-invasive ventilation is clearly a major tool in armamentarium of pulmonologist and intensivists.

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